MICROBIOLOGY TODAY

QUARTERLY MAGAZINE OF THE SOCIETY FOR GENERAL MICROBIOLOGY VOLUME 30 MAY 2003

Contents

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Above: A woodcut of a man and a woman being treated for syphilis in ca 1497–1498, shortly after the first European syphilis epidemics of 1494. At the upper right a physician is examining a urine sample as part of a diagnosis. At the lower centre another physician applies an ointment to the pustules. *National Library of Medicine/Science Photo Library*

Vol. 30, Part 2, May 2003

In this issue we consider some interactions between micro-organisms and sex.

In humans the incidence of sexually transmitted infections (STIs) is rising rapidly, bringing misery and many social problems in its wake. Epidemiologist Kevin Fenton gives an overview of recent UK trends on p. 55, whilst Cathy Ison and Iona Martin focus on bacterial STIs (pp. 56–57). On pp. 63–65 Philip Mortimer and Barry Evans discuss the serious implications of the changing face of HIV infection. *Chlamydia* can affect fertility in men as well as women, as Adrian Eley describes on pp. 61–62 and on pp. 58–60 Heather Cubie explores the link between human papilloma virus and cervical cancer.

Not all sexual activity is restricted to people. Bacteria can also be said to have a sex life and Chris Thomas explains the benefits of the different ways that they exchange genetic material on pp. 66–67. Alternatively, microbes can affect the sex of invertebrates as Mike Majerus describes (pp. 68–70).

In Comment, virologist Wendy Barclay ponders on the possibility of a new pandemic of influenza, in the light of recent scares about avian 'flu that have hit the headlines (p. 100).

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

Articles

Regular Features

Other Items

Microbiology Today goes bananas

Our esteemed magazine has received yet another accolade. We came second out of nearly 100 entries in the APE 'Golden Banana' competition. Not as silly as it sounds, the annual Advice to Publishers and Editors (hence APE) event has been organized by the Hardy Group, one of whose associated companies has printed *Microbiology Today*, for many years. It is aimed at publishers and editors of magazines, journals and newspapers run by small editorial teams and consists of an exhibition and a range of useful seminars.

The judges were Marcus Lynch of Adobe, Sara Haggerty, an international magazine designer, and Ken Stanger of Hardy Printing. Their verdict on *Microbiology Today*:

'By far the best cover design from all the entries and a good example of 'academic journal' meets 'consumer magazine'. Inside Microbiology Today has potentially difficult and often wordy subject matter, but this is no obstacle for the team to create very readable, well executed layouts. The magazine flows and different areas are very well sectioned off. It also uses white space masterfully combined with a strong consistent typographic house style. Overall, the magazine has an authoritative design which assists in making the subject matter of great interest to the reader and is easy to navigate.'

As readers will know by now, the in-house editorial team consists of **Janet Hurst** (Managing Editor), **Janice Meekings** (Assistant Editor) and **Ian Atherton** (Production Editor). Ian can take all the credit for the layout as he sets it, although not always without critical input from the other two! Unfortunately none of them were able to attend the award ceremony; Janice and Janet were on leave and Ian had an important SGM journals meeting to attend. Luckily **Dariel Burdass** of the External Relations Office was in London on that day and was able to accept the certificate on their behalf, as shown in the photograph below.

Whilst the Marlborough House team is pleased to have external approval for their work, credit is also due to **Ruth Gregory** who came up with the original design concept that Ian has modified and developed considerably since 1999 and our printers, the **Warwick Printing Company Ltd**, who turn that disc into a high quality magazine every quarter so professionally. Thanks to Paul and his colleagues at Warwick – we appreciate their high standards of service.

Journal production milestones passed

In September 2002, the decision was taken to transfer the contract for production of three of the SGM journals from Cambridge University Press to The Charlesworth Group. The January 2003 and subsequent issues of *Microbiology*, *Journal of General Virology* and *International Journal of Systematic and Evolutionary Microbiology*, paper and online, have all been produced under the new arrangements. In general, the transfer has gone very smoothly, with only a few delays and technical glitches. It has been a complex and laborious task, and I'm grateful to the editorial staff at Marlborough House for the expertise and dedication they have brought to it. SGM also took over control of manufacturing of *Journal of Medical Microbiology* from the January 2003 issue, and the new, harmonized design for all four journals was introduced at this point, so there has been a lot going on. It is a mark of the global nature of the printing industry that the three Charlesworth journals are typeset in Beijing, printed in Huddersfield and bound in Wakefield, while JMM is typeset in Dorset by Keytec and printed and bound in Aberystwyth by Cambrian Printers. All four are produced online at HighWire Press in California.

One major benefit of transferring the typesetting to Charlesworth is that IJSEM Online, like the other three journals, now appears in full-text HTML format as well as the PDF version. This had previously been delayed by technical problems. The HTML offers full-text searching, including tables, and all the enhanced functions such as reference linking. This now includes CrossRef, which allows linking to and from a range of journals outside the HighWire system using the unique DOI (Digital Object Identifier) code at the top of each article. Also from January, the four journal home pages and the umbrella SGM journals home page (http://sgmjournals.org) have been redesigned and new features have been added. These include listings of the most-read articles in the past month, most-cited articles, CiteTrack alerts, and enlarged versions of the cover images.

● ***Ron Fraser, Executive Secretary***

Recent trends in sexually transmitted infections in Britain

Kevin Fenton

Sexually transmitted infections (STIs) cause considerable reproductive morbidity and poor health outcomes, including pelvic inflammatory disease (PID), infertility, ectopic pregnancy, cervical cancer, neonatal disorders and death. They are often associated with significant social stigma and are a source of psychological stress, with adverse impacts on individuals and their relationships. Early diagnosis and treatment of STIs, as well as targeted prevention efforts, can significantly reduce the likelihood of these complications occurring.

Between 1991 and 2001, new episodes seen at GUM clinics in England, Wales & Northern Ireland rose from 669,291 to 1,332,910. Clinic workload increased by 155 %; diagnoses increased by 61 %; uncomplicated gonorrhoea increased by 35 %; genital chlamydial infection increased by 122 % and infectious syphilis (primary, secondary and early latent) increased by 207 %. Between 2000 and 2001, new episodes seen in these clinics rose from 1,195,641 to 1,332,910. Genital chlamydial infection (uncomplicated) rose by 9 % in males and 10 % in females; uncomplicated gonorrhoea increased by 8 % in males and 6 % in females; infectious syphilis increased by 143 % in males and 36 % in females; genital herpes simplex infection increased by 5 % in males and 6 % in females and genital warts increased by 2 % in males and 3 % in females.

The burden of STIs continues to fall unequally in the population: young heterosexuals, men who have sex with men (MSM) and minority ethnic groups are at increased risk. 42 % of females with gonorrhoea and 36 % of females with genital chlamydial infection are under 20 years old. In 2001 22 % of diagnoses of gonorrhoea were in MSM, 53 % of which were in London. As Cathy Ison and Iona Martin discuss in more detail on pp. 56–57, the rapid increase in bacterial STIs probably reflects a general deterioration in sexual health amongst young people and MSM, although increased testing for genital chlamydial infection and improved test sensitivity have also contributed.

Recent trends in HIV are also of concern as Philip Mortimer and Barry Evans describe on pp. 63–65. The current best estimate of the total number of adults living with HIV, undiagnosed or diagnosed, in the UK at the end of 2001 is 41,200. Approximately 15,100 MSM were living with diagnosed HIV at the end of 2001 and an estimated 4,200 remained undiagnosed. Of HIV infected MSM, 57 % live in London. MSM remain the group at greatest risk of acquiring infection in this country. While numbers of prevalent diagnosed HIV infections increase, the proportion of individuals infected through sex between men has fallen from 52 % in 2000 to 50 % in 2001. In contrast the proportion of individuals infected through heterosexual sex has risen, from 31 % in 2000 to 36 % in 2001.

Population patterns of sexual behaviour are major determinants of STI and HIV transmission. The most recent data on sexual behaviour in Britain are derived from the MRC-funded second National Survey of Sexual Attitudes and Lifestyles (Natsal 2000). This study confirmed that there have been many changes in both social norms, reflected in more tolerance towards sexual diversity, and in sexual behaviour in the UK in the past decade. These include numbers of heterosexual partners, age at first sexual intercourse, homosexual partnership, concurrent partnership, heterosexual anal sex and payment for sex. For both men and women the numbers of lifetime heterosexual partners have increased substantially since 1990, and these increases have been highest in young people. Natsal 2000 found that while reported condom use has increased in the UK, the increase in numbers of sexual partners may have discounted some of the public health advantages of this increase. Age at first intercourse has declined from 21 for women and 17 for men in 1990 to 16 for men and women born in the early to mid 1980s. Young people do not always have the negotiation skills to ensure the use of condoms consistently and effectively, and yet are a group with both higher rates of partner change and more concurrent partners.

Apart from patterns of high-risk sexual behaviour, other factors may influence STI transmission, including: high levels of asymptomatic infection; ineffective partner notification measures; and poor access to GUM clinic services. Consequently, the development of prevention measures should always consider not only the behavioural context, but the provision and utilization of sexual health services as well.

The surveillance and research data confirm that STIs are becoming more common and that changes in the patterns and distribution of high-risk sexual behaviour are contributing to these increases. Increasing STI diagnoses reflect increasing GUM clinic throughput as well as rising disease prevalence in the community. As many clinics are now operating at maximum capacity, the effectiveness of their prevention measures, such as partner notification and behavioural counselling, are at risk as they fail to cope with demand. The National Strategy for Sexual Health & HIV Action Plan set a national standard for England for the offering and acceptance of HIV testing in GUM clinic attendees, and the reduction of new acquisitions of HIV and gonorrhoea. By increasing the profile of sexual health, adopting a multi-disciplinary approach to tackling inequalities, and committing additional investment it is hoped that true gains will be made in improving Britain's sexual health.

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Behaviour and bacteria?

Catherine Ison & Iona Martin

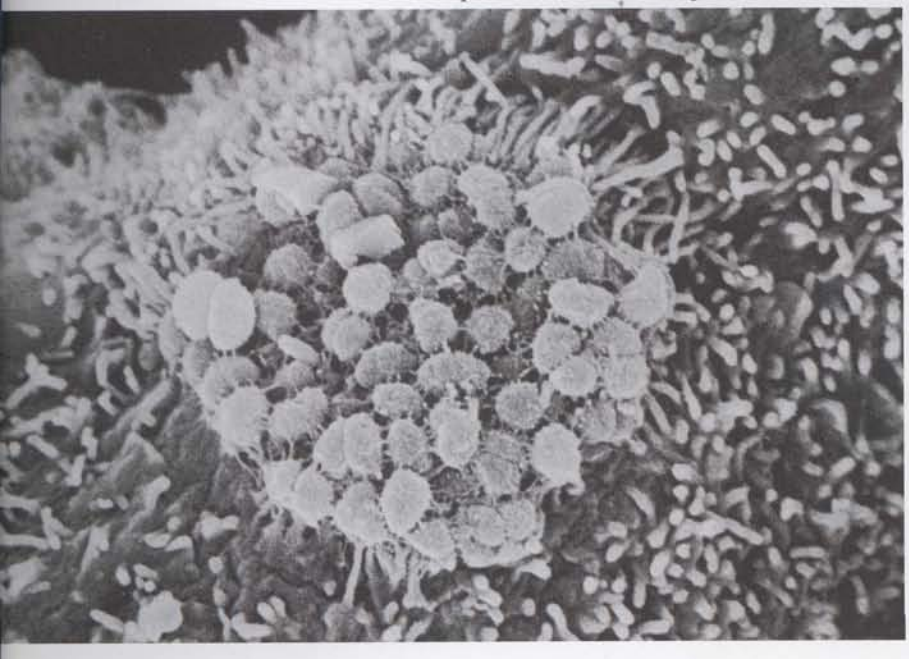
The incidence of bacterial sexually transmitted infections has rocketed in recent years. Cathy Ison and Iona Martin review current treatments and prevention strategies in the light of changing patterns of behaviour in both humans and bacteria.

Sexually transmitted pathogens, such as *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Treponema pallidum*, are obligate human pathogens with no other natural host. They are highly adapted pathogens which either evade the host's immune response, causing repeated episodes of infection in the same host, such as *N. gonorrhoeae*, or can remain undetected for many years during latent infection, such as *T. pallidum*. Bacterial sexually transmitted infections (STIs) are associated with increased acquisition of HIV infection and intervention with effective therapy has reduced the acquisition of HIV in some studies. Of all the bacterial STIs gonorrhoea has been used as a marker for sexual activity of populations because it is unequivocally sexually transmitted and there is generally a short duration before symptoms are evident. The causative agent, *N. gonorrhoeae*, is antigenically and genetically diverse, which is believed to result from its extraordinary ability for horizontal gene exchange and genetic recombination. *In vivo* this probably takes place during mixed infections, which are most likely to occur in sexually active populations with high rates of partner exchange. Such groups of individuals have been considered 'core groups' and are believed to be responsible for the persistence of STIs in most populations.

Changing epidemiology of bacterial STIs

In England and Wales the number of new episodes of STIs reached more than 1 million in the year 2000. Bacterial STIs have doubled since 1990, chlamydial infection has increased by 108 % since 1996, gonorrhoea by 87 % and syphilis by 486 %. These dramatic increases follow a period of decline subsequent to the advent of HIV infection, the first fatal sexually transmitted infection. Health promotion campaigns regarding safe sex and fear of AIDS produced a change in sexual behaviour, believed to be the primary cause of the reduction in cases. Good diagnostic tests, effective first-line therapy and tracing of contacts also made a significant contribution. For example, prior to the appearance of AIDS, approximately 50,000 cases of gonorrhoea were reported annually, followed by a steady decline between 1984 and 1994, resulting in a reported 10,216 infections in 1994. The decrease occurred in all groups but was particularly marked among men who have sex with men. Since 1994 the pattern of gonococcal infection has changed. Initially small increases in the number of cases were reported, followed by sustained increases between 1997 and 2002.

Syphilis also decreased dramatically, but has re-emerged in outbreaks, first in Bristol and now in London, Manchester and Brighton. Chlamydial infection has increased but much of this has resulted from the use of nucleic acid amplification tests (NAATS), which has revolutionized the diagnosis of this infection, particularly for use with non-invasive specimens, such as urine, and has allowed the screening of asymptomatic populations, such as women under the age of 25 years.



Treatment and antimicrobial resistance

Chlamydial infection and syphilis, once correctly diagnosed, are essentially treatable. *N. gonorrhoeae* was also inherently susceptible to most antimicrobial agents, but as successive therapeutic agents have been introduced, resistant mutants have emerged under selective pressure of continual usage or plasmids acquired from other bacteria. Today antibiotic-resistant *N. gonorrhoeae* presents a major therapeutic challenge.

Ciprofloxacin, a fluoroquinolone, is the treatment of choice for gonorrhoea in the UK and was used by 74 % of genitourinary medicine clinics in 2001. *N. gonorrhoeae* was exquisitely sensitive to ciprofloxacin when it was first used to treat gonorrhoea, but in the intervening years high-level resistance has emerged due to misuse and over-use of several generations of quinolones in other parts of the world. Resistance is now spreading to the UK, and has been highlighted by the national surveillance programme (GRASP). In the UK ciprofloxacin-resistant *N. gonorrhoeae* has shown marked variation according to geographical location, with high levels in the North West (8·6 %) and the lowest level in London (1·8 %) in 2001. A worrying increase has occurred during the surveillance period of 2002 with levels rising to 7·1 % in London and to 12·4 % out of London. These levels are now above 5 %, the point at which it is recommended that an alternative should be used for first line treatment. Ciprofloxacin-resistant gonococci were previously associated with infection acquired through sexual contact abroad in areas where

there is a high incidence of resistance, such as the Far East and Indian subcontinent. However, with increasing levels of resistance there is an apparent change to infections transmitted from sexual contacts within the UK. Amoxycillin is the second most commonly used agent (17 % of clinics in 2001), but resistance to penicillin, which can both be chromosomally or plasmid-mediated and has remained relatively unchanged over the last 5 years, is now also above the 5 % level. The identification of risk factors associated with individuals being infected with a resistant strain is necessary to prolong the useful life of the current antimicrobial agents as there is little evidence of new antibiotics on the horizon.

Burden of infection and prevention

The greatest burden of bacterial STIs is in young people. For instance, in the UK the highest incidence of gonorrhoea is seen in men aged 20–24 years and women aged 16–19 years. In 2001, 42 % of women with gonorrhoea were under 20 years old. Gonorrhoea is concentrated disproportionately in men and women of black ethnic groups and there has been an increase in men who have sex with men.

In attempts to control and promote sexual health, the recently published UK Government's Sexual Health Strategy has set what might appear to be an ambitious target of reducing infections of gonorrhoea by 25 % by 2007. STI surveillance initiatives have been developed, and various safer sex health promotion campaigns have been launched, targeting different age groups and sexual orientations. There have been specific intensive campaigns for the syphilis outbreaks that have occurred over the past few years, but unfortunately the outbreaks in Manchester and London still persist, despite increased efforts in the tracing of sexual contacts, screening programmes and campaigns increasing awareness of the infection.

Behaviour or bacteria?

Sexually transmitted infections are a major international problem. The most recent estimates from the World Health Organization put the worldwide annual incidence of gonorrhoea at 62·35 million cases in 1999. The highest prevalence is in sub-Saharan Africa, the Western Pacific region and other parts of the developing world where resources for good diagnosis and treatment are often not available. However, STIs continue to increase in areas such as the UK where there is a unique network of specialized clinics for sexual health, good diagnostic tests and where effective therapy is available to individuals presenting with symptoms. So what is happening between the host and the bacteria? As mentioned above there is evidence for behavioural changes, but it may also be that these versatile pathogens are adapting to a changing host environment. There is some evidence that there are greater levels of asymptomatic infection, caused by particular phenotypic variants of *N. gonorrhoeae*, although the true level of asymptomatic untreated infection is unknown. It could be that during the large decrease in incidence during the mid-1980s to 1990s that the bacteria evolved mechanisms to evade detection, thus ensuring their survival. We propose that the increase in the incidence of gonorrhoea in the UK is likely to be a balance of human behaviour and the adaptation of the bacteria. Either way increasing incidence and antimicrobial resistance pose a serious challenge to improving sexual health.

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THIS PAGE:
An image from an STI prevention campaign.
COURTESY WELSH ASSEMBLY GOVERNMENT

OPPOSITE PAGE:
Adherence of *Neisseria gonorrhoeae* to cultured HEC-1-B cells.
PHOTO NUSI DEKKER, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, USA

Further reading

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When is an STD not an STD? – HPV and cervical cancer

Heather A. Cubie

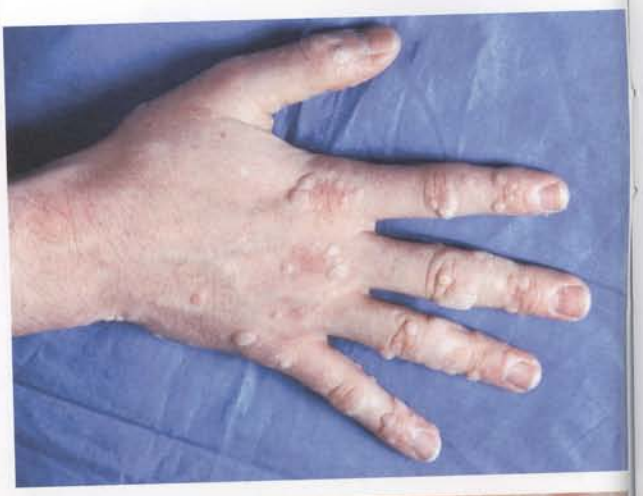
The link between human papillomavirus (HPV) and cervical cancer is well established, yet cervical cancer is not a sexually transmitted disease in the traditional sense. Heather Cubie argues that HPV testing may be more effective than cytological screening programmes in identifying the disease.

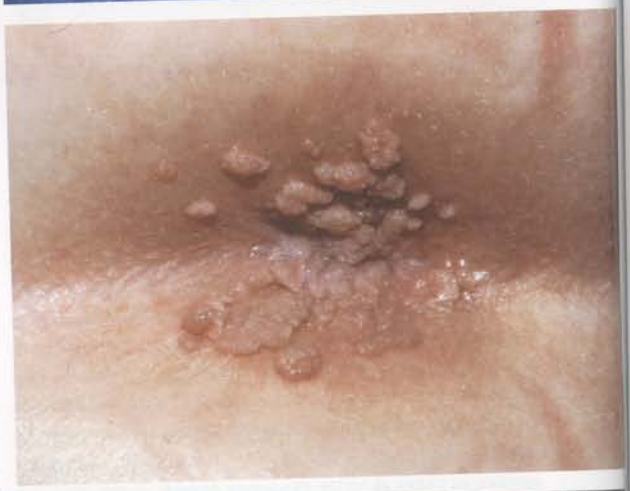
Papillomaviruses (PVs) are ancient viruses – stable, ubiquitous and evolutionarily well adapted to their hosts. They belong to the family *Papillomaviridae* with members in every vertebrate species. PVs have fascinated virologists for over a century, from early transmission experiments which showed that sterile cell-free filtrates could transmit skin and genital warts, to the recognition in the 1930s that transfer of cottontail rabbit papillomavirus to domestic rabbits resulted in malignant tumours.

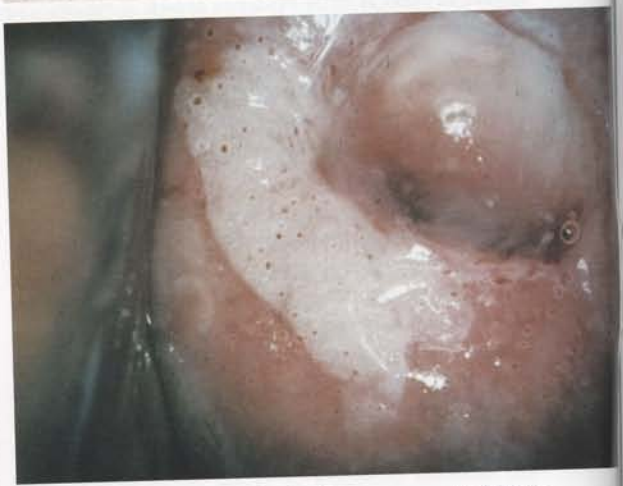
Mid 20th century, human papillomaviruses (HPVs) were of interest clinically only to dermatologists and 'venereal disease' physicians where hand warts, plantar verrucae and genital warts contributed hugely to outpatient clinics (Fig. 1). The incidence of genital warts, as for other STDs, increased dramatically between the 1950s and the 1970s, as a consequence of greater sexual freedom. About 20 years ago, an association between HPV and malignant transformation was shown in cervical cancer and, inevitably since then, interest in HPVs has escalated exponentially. While the first international PV meeting in Lyon in 1975 had around 30 participants, the 20th International Papillomavirus Conference in Paris in October 2002 attracted over 600 worldwide PV researchers.

PVs are small icosahedral viruses (Fig. 2). with a supercoiled DNA genome approximately 8 kb in length and organized into two 'late' and six or more 'early' genes. Over 100 potential types have been identified and new types are being proposed every year. HPVs infect both squamous and mucosal epithelium, with around 30 types known to infect anogenital epithelium. Different clinical pictures are mirrored by the clustering of HPV types by molecular phylogenetic analysis. They can be segregated into non-oncogenic, cutaneous types; low risk types (LR-HPV) associated with external genital warts and mild cytological abnormalities; and high risk types (HR-HPV) with the potential to progress to severe abnormalities and cancers. The most common cutaneous types are HPV1–4, genital warts are most often associated with HPV6 and 11 and the five most common HR-HPV types in cervical cancers are HPV16, 18, 31, 33 and 45.

Most people will experience HPV infection at some stage in their lives, generally in childhood for cutaneous types (hand and plantar warts) and in early adulthood for mucosal types by sexual transmission. The chance of developing an HPV infection during life has been estimated at 80–85 %, with a large proportion of women having been infected by age 30. However, active HPV16 infection has also been shown in the buccal mucosa of primary school children. Furthermore, in a study we carried out on schoolgirls aged 11–12 in Edinburgh, at least 7 % had antibodies to HPV16. Surely such children are not all sexually active! Several studies have shown a few cases of cervical HPV infection in virginal women.







RIGHT
Fig. 1. Examples of hand warts associated with HPV2 (top), genital warts (middle) and flat cervical warts (bottom).
PHOTOGRAPHS KINDLY PROVIDED BY DR CLAIRE BENTON (TOP AND MIDDLE) AND DR MARY BUNNEY (BOTTOM), DEPARTMENT OF DERMATOLOGY, UNIVERSITY OF EDINBURGH

Thus, while there is no doubt that most genital HPV infection is transmitted sexually, transmission from other sites is also possible.

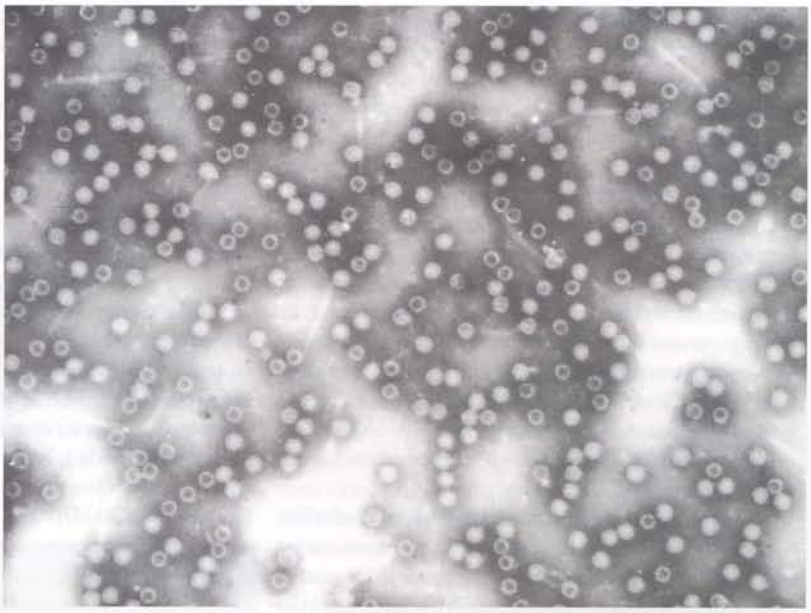
Like many other virus infections in healthy individuals, most (around 80 %) of HPV infections clear spontaneously, sometimes with the development of specific neutralizing antibodies which protect against

reinfection. In the remaining 20%, HPV infection persists, but regression of milder premalignant lesions is common and is associated with clearance of virus. Further infections with different types is of course possible, particularly for women with continued exposure through higher numbers of sexual partners. Only a very small number of persistent infections progress to cervical cancer.

Cervical cancer (Fig. 3) is the second most common malignancy in women worldwide. It can take many years to develop, but the pre-cancerous stages [called cervical intraepithelial neoplasia (CIN)] are detectable by cytological changes and are readily treated. A causal role for HR-HPV has been clearly shown from both epidemiological and experimental information. Not only are HR-HPV types found in 99% of cervical cancers worldwide, but viral DNA is integrated into the host genome in at least two out of three cancers. The transforming genes E6 and E7 of HR types are transcriptionally active, interact with cellular tumour suppressor genes p53 and pRB and disrupt cell cycle control. In contrast, E6 and E7 of LR-HPV types do not show these oncogenic properties.

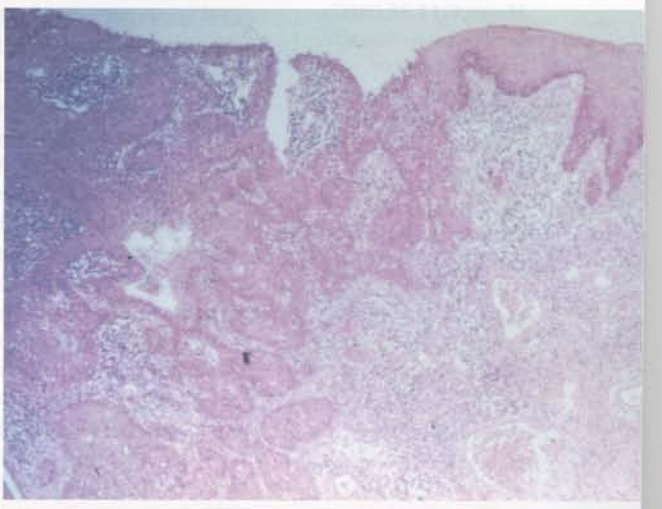
Inevitably, the traditional factors associated with STDs, such as age at first intercourse, multiple sexual partners, increased parity and presence of other STDs have been extensively investigated as co-factors in cervical cancer. In addition, behaviours such as smoking and oral contraceptive use and genetic and other factors such as socio-economic status have been studied. Although many may appear to increase risk, the only independent variable, other than HR-HPV, directly associated with cervical cancer is smoking.

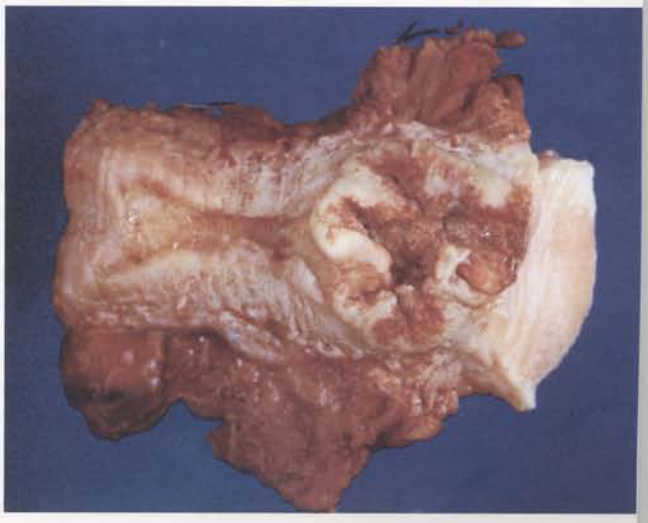
It is not HPV *acquisition*, however, which is associated with cervical cancer, but HPV *persistence* and this occurs in only a tiny minority of infections. In this sense, HPV does not act as a typical STD, where infection is linked to a socially unacceptable level of sexual activity. Detecting persistence of HR-HPV infection will help identify women at greatest risk of developing cervical cancer, yet we do not understand what causes persistence in these few. It is not simply their sexual behaviour, but more probably a genetic predisposition with inadequate immune responses and uncontrolled cellular activity. We must not stigmatize women with cervical cancer because we consider they have had an STD when we cannot determine what else makes this minority different from most healthy women. The development of cervical cancer must be seen as a rare complication of a common infection acquired many years previously.



LEFT:
Fig. 2. Electron micrograph of HPV particles from skin scrapings.
PHOTOGRAPH KINDLY PROVIDED BY HEATHER CUBIE

BELOW:
Fig. 3. Histological picture of invasive cervical cancer (top) and gross pathology of cancer of the cervix (bottom).
PHOTOGRAPHS KINDLY PROVIDED BY DR MARK ARENDS (TOP) AND DR ALISTAIR WILLIAMS (BOTTOM), DEPARTMENT OF PATHOLOGY, UNIVERSITY OF EDINBURGH





Cervical screening

Most people are aware of the media attention which has been given to 'missed' cases of cervical cancer, despite the existence in the UK of a population-based National Cervical Screening Programme using cytology. The public does not understand the limitations of 'screening' programmes and in cancer screening the issues are much more emotive. Cervical screening aims to detect cervical epithelial cell changes that precede the development of cancer in, and is based on, the premise that early

detection and treatment of pre-malignant changes will prevent progression to invasive disease. The problem is that conventional screening uses 50-year old technology which on its own has probably outlived its usefulness. It has a sensitivity of only 50–70 % and in a recent audit in Scotland, 50 % of women with cervical cancer had actually had a negative smear within 5 years. There is therefore an urgent need for better identification of women at high risk.

There are two further major problems with current screening methods. First, up to 10 % of smears can be inadequate and must be repeated. The introduction of new automated methods of cytological preparation (liquid based cytology; LBC) will address this issue. In our Edinburgh studies we showed that LBC reduced the inadequate smear rate to less than 1 % and was at least as sensitive as conventional smears.

Second, 5 % of smears are reported as borderline (inconclusive) and referred for colposcopic examination if persistent. This is wasteful of resources since around 60 % will be within normal limits. The addition of HR-HPV testing would identify women most at risk and ensure treatment is targeted towards those who need it most. HPV cannot grow in cell culture, so we are dependent on molecular tests, using nucleic acid hybridization with or without amplification. These include a commercially available screening test (Hybrid Capture Assay, hc2, produced by Digene Corporation) used in a number of large-scale trials both for primary screening and triage of borderline and mild abnormalities, and several, as yet in-house, genotyping assays based on PCR followed by hybridization with type-specific probes. This allows detection of multiple types and distinguishes persistence from reinfection.

But herein lies the dilemma. There are no other cancer screening programmes which use a test which detects an apparent STD. How then can we introduce HPV testing to a cervical screening programme? Perhaps we will need to find surrogate biomarkers or look first for genetic polymorphisms which appear to be associated with greater host susceptibility to disease. I believe it would be better to educate the public about the nature of HPV infection and remove the stigma of HPV as an STD. HR-HPV tests can be easily linked into LBC screening protocols for selected groups of women, such as those with borderline abnormalities. For countries without organized cytology screening, HPV testing would be a more efficient starting point with a higher sensitivity for detecting high grade disease. This is already being trialled within Central and South American countries.

In the USA where individual healthcare needs are considered, cervical cytology with local excision of any suspicious lesions is carried out annually by gynaecologists. Lack of understanding of the nature of virus infections and their frequent resolution has led to significant over-treatment, scarring and has even affected sexual function. The high negative predictive value of a negative HPV test could avoid such unfortunate outcomes and greatly reduce the cost of cervical surveillance. Is this not far more important than concern about how and by whom the original infection was transmitted?

Conclusions

There is an urgent need to increase public understanding of the way in which cervical cancer develops and to get rid of the perception that cervical cancer is a sexually transmitted disease. There is also an urgent need to educate women themselves in the ubiquity and natural history of HPV infection. Education leaflets are woefully inadequate, often written by academics or professionals with great knowledge, but set at a reading level beyond that of many of the women they address. A recent study of more than 20 HPV leaflets showed that all required above average ability to comprehend them. Finally, medical practitioners themselves and healthcare teams need to be more informed and dissociate themselves from the old view of HPV as an STD.

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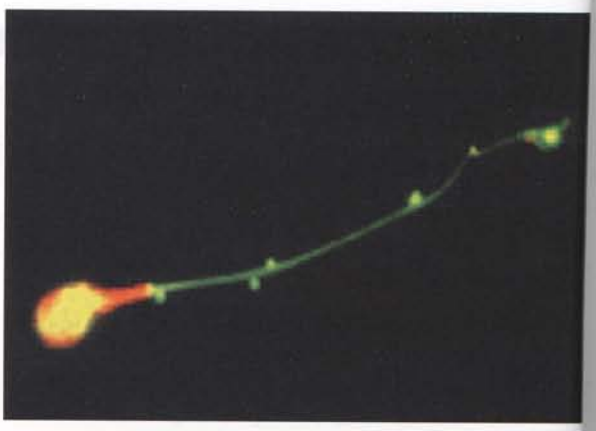


RIGHT:
Attachment of green fluorescent *Chlamydia trachomatis* elementary bodies to human sperm.
COURTESY S HOSSEINZADEH

BELOW:
Number of genital chlamydial infections in England, Wales and Northern Ireland between 1996 and 2001 (●, females; ■, males).
COURTESY PHLS AND IAN GEARY

Interaction of *C. trachomatis* with sperm

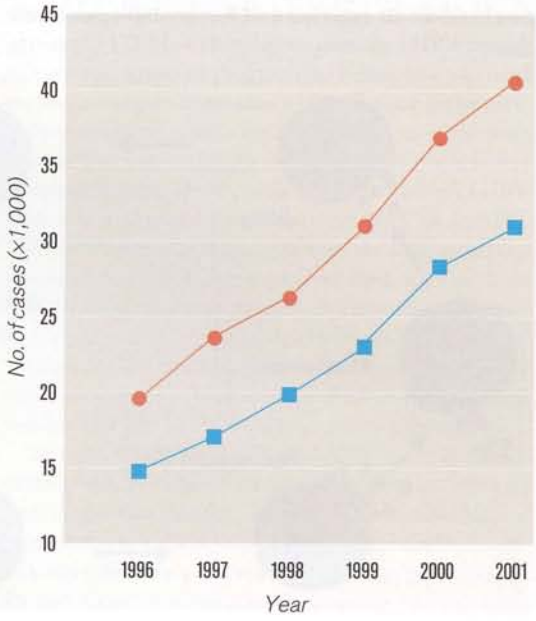
Genital infections in the male often begin with a urethritis which can sometimes progress to the upper genital tract and lead to epididymitis and prostatitis. Although the role of *C. trachomatis* in prostatitis is less clear, in young males chlamydial infection can lead to inflammatory blockage of the epididymis and a much reduced number of sperm. It is also known that *C. trachomatis* can attach to sperm (a process sometimes known as hitchhiking), and this has been thought to be a means of spreading infection from males to females. Few studies, however, have considered whether direct exposure to *C. trachomatis* itself may compromise sperm function and thereby lead to subfertility by a route which is independent of any damage to the reproductive epithelium.

The results of previous work on whether *C. trachomatis* infection has a significant effect on human sperm function have been confusing. Some work has suggested that chlamydial infection is associated with reduced semen quality whilst other studies suggest not. However, these investigations are open to criticism because:

- no study takes into account the significant inter- and intra-individual variation that is known to exist in semen quality;
- unreliable semi-quantitative manual methods to assess semen quality have been used that are known to be subject to large measurement errors;
- poor methods have been used to diagnose chlamydial infection which are known to be problematic and produce inaccurate findings.

With improved methods now in use it has been clearly shown that when chlamydial EBs are added to sperm there is a dramatic decrease in motility and concomitant loss in viability after only a few hours co-incubation. Exactly how chlamydial EBs are able to cause sperm death is currently unknown, but we do know that lipopolysaccharide (LPS) is the principal virulence factor. Furthermore, in comparison with LPS extracted from enterobacteria including *Escherichia coli*, LPS from *C. trachomatis* has been shown to be 500 times more potent, which suggests that the presence of even relatively small quantities of chlamydial LPS in either the male or the female genital tract is likely to be spermicidal. Chlamydial infection in men could directly reduce semen quality by reducing sperm activity. Indirectly, sperm in the female genital tract in contact with chlamydia could be compromised. Therefore, if we apply *in vitro* findings of co-incubation to those which may occur *in vivo*, chlamydial infection of either or both partners could reduce fertility by effects on sperm function.

In the light of these findings, now is the time to reconsider the following issues. If *C. trachomatis* is spermicidal, then we need to make sure that in *In Vitro* Fertilization (IVF) treatment both partners are screened and treated if necessary to exclude chlamydial infection or the outcome may not be successful. Perhaps we should also be looking more closely at the long-term effects of chlamydial infection on semen quality and whether conventional antimicrobial therapy is sufficient to restore it. With improved laboratory diagnosis and screening this should be more of a possibility.



Conclusions

The idea that urogenital infections, including those caused by *C. trachomatis*, influence male fertility has long been controversial. What we now know from *in vitro* experiments using human sperm is that *C. trachomatis* is rapidly spermicidal. If shown to be true from *in vivo* studies, these findings would have major consequences for some types of infertility and their management. This would certainly further raise the profile of what is already a major genital pathogen. It is arguable that sperm quality has been on the decline in the Western World for some considerable time, and the finding that we have a potentially spermicidal and infectious causal agent in increasing numbers in society is unwelcome news.

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The changing face of HIV infection: the world's most important sexually transmitted infection

Philip Mortimer & Barry Evans

The global background

The HIV pandemic is now a global crisis. It was first recognized more or less simultaneously in North America, Western Europe and East Central Africa in the early 1980s. By the mid 1980s it was being widely reported in sub-Saharan Africa, and in South America, South and South East Asia and Australasia. By the 1990s other foci of HIV had sprung up in China and the Former Soviet Union. Now virtually every country has its epidemic, though varying in size, intensity and types and sub-types of HIV involved.

HIV type 1, in particular, causes in its human host a chronic depletion of B lymphocytes and thereby allows repeated super-infection either by *Mycobacterium tuberculosis*, or by less familiar bacterial, fungal or parasitic agents, or by viruses such as human herpes virus 8, the cause of Kaposi sarcoma. The prognosis of HIV 1 infection is somewhat improved by young age at infection, but without access to combined anti-retroviral drug treatment the median time of survival from infection is only 10 years. For most this treatment is not available and many millions worldwide have died or are suffering from AIDS, the end stage of HIV 1 infection. For many African countries HIV 1 has become a barely sustainable health and economic burden.

The title of this article is more than justified by the extent of the morbidity and mortality caused by HIV infection compared to any other sexually transmitted, or indeed other infection. HIV now ranks with tuberculosis and malaria as an outstandingly important infectious disease, and in sub-Saharan Africa it is threatening social cohesion by killing young economically productive adults in very large numbers. There is so far no evidence that its virulence has been mitigated by its interaction with its human host and one can only speculate how long it may take before HIV achieves a more stable and less aggressive parasitism.

In the UK, which has a very modest epidemic by international standards, the HIV indicators are beginning to reflect the global trend more clearly.

The UK scene

At a time when public awareness of HIV has waned and public anxiety been blunted by as yet unfulfilled warnings of rapid spread, that spread has begun to materialize. There have been steady increases in the numbers with diagnosed HIV infection in the UK over the last 5 years (Table 1) and this trend extrapolates to over 40,000 people living with an HIV diagnosis by the end of 2004, with perhaps a doubling of that number by the end of the decade.

Four elements are contributing to the rising numbers in the UK alive with diagnosed HIV. The first is the rate of new diagnoses. The second is the decrease in death rate due to HIV, mostly as a consequence of more people receiving treatment. The third is the rising prevalence that stems from successful treatment. The fourth is the rising incidence of recognized new infections. In addition to all this, account must be taken of undiagnosed HIV infection which in the UK is currently estimated to constitute roughly a third of the total living with HIV.

Data sources and data security

UK governments have invested heavily in HIV data collection through the Communicable Disease Surveillance Centre (CDSC) and the Institute of Child Health in London, and the Scottish Centre for infection and Environmental Health in Glasgow, so that the UK has what is internationally regarded as unusually good HIV data sets for such a populous country. This data collection and analysis makes continuous and heavy demands on clinical staff and public health clerical personnel, however. Particularly because of the stigma still attached to HIV infection, it has been essential to maintain clinical confidentiality and ensure secure data handling, and these patient-related data have been supplemented by the anonymized testing of very many samples collected for other purposes. The latter has helped to quantify sub-clinical and unrecognized HIV infection.

'The epidemic is taking 8,000 lives and causing 13,000 new infections a day.'

[Anon. (2003). 'Pro-life' policy threatens US HIV/AIDS initiative. *Lancet* 361, 887.]

Table 1. Probable routes of HIV infection: first UK diagnoses of HIV infection by year of diagnosis

Year of diagnosis	*n*	Sex between men (%)	Sex between men and women (%)	Injecting drug users (%)	Mother to infant (%)	Blood/tissue transfer or blood factor (%)	Other/ undetermined (%)
1990	2,543	67	21	8	1	1	2
1991	2,717	63	24	9	1	1	2
1992	2,740	60	28	7	2	1	2
1993	2,614	57	29	8	3	1	2
1994	2,574	58	31	6	2	1	2
1995	2,643	55	32	7	2	1	2
1996	2,687	57	31	6	2	1	2
1997	2,730	51	37	6	3	1	2
1998	2,806	48	41	5	3	0	2
1999	3,054	44	46	4	3	1	3
2000	3,819	39	51	3	3	1	3
2001	4,909	34	56	3	2	0	5

Numbers will rise, particularly for recent years, as further reports are received.

These sources have together proved an adequate basis for HIV surveillance, even though it may become difficult to maintain the collection of comprehensive and representative data as patients increasingly assert their right to limit data sharing between health professionals. In future, the exercise of patient autonomy may compromise the reliability of national HIV data.

The UK HIV data sources at present most relied upon are the reports made to CDSC by clinicians of first UK diagnoses of HIV infection, and those made by laboratories of confirmed positive HIV tests. For data recording a 'Soundex' code of the surname is generated either before the report is made or at data entry. Duplicate reports are recognized and removed by identifying matches on Soundex code, date of birth and sex. In addition, at various sites, anonymous testing unlinked from patients' names or other identifying elements has been used for more than a decade to plot annual anti-HIV prevalences in sexually transmitted disease, antenatal, pregnancy termination and drug dependency clinics. This research has been enhanced by employing tests that allow HIV incidence as well as prevalence to be estimated. Other tests that can be done on specimens collected as oral fluid or as urine have allowed access to 'hard to reach' groups such as injecting drug users. Together with the anonymized testing in clinics, this work has enabled the number of undiagnosed carriers of HIV in the country to be estimated (Table 2).

Towards the end of each year, on 1 December (World AIDS Day), CDSC updates the information shown in Tables 1 and 2, and in each recent year there have been several thousand new HIV diagnoses added. UK reports of new diagnoses for 2002 show a 26 % rise on reports made by the same stage for 2001. An ultimate total of more than 6,500 reports of new HIV diagnoses is expected for 2002.

ABOVE:
A scene from an AIDS vigil held in Trafalgar Square, London, UK, commemorating those who have died of AIDS.
JOHN COLE / SCIENCE PHOTO LIBRARY

The UK risk groups

The continuing HIV 1 epidemic among men who have sex with men (MSM)

This is an HIV 1 subtype B epidemic in which new diagnoses are being made at an increasing rate in both young and middle-aged men. At the same time the rising numbers of reports of gonorrhoea and syphilis in MSM suggest that concurrent unrecognized HIV infections are occurring, but unless laboratory tests are done these primary HIV infections are difficult to diagnose. Continued sexual risk taking in this generally well informed and 'street-wise' part of society is a depressing feature of the current stage of the UK HIV epidemic and seems to have negated the potential benefits of widespread combined anti-retroviral treatment in lowering transmission rates.

Continuing new HIV infection in the face of extra investment in treatment suggests that not only is risky sexual behaviour widespread, but that there is uneven compliance with what are admittedly complicated drug regimes, so that infectivity in some treated men is not being effectively suppressed.

Table 2. Estimates of diagnosed and undiagnosed UK residents living with HIV infection for 2001 (*n*=41,200)

	Diagnosed	Undiagnosed
Living with homosexually acquired HIV	15,100	4,200
Living with heterosexually acquired HIV	11,200	8,300
Living with HIV acquired through other routes	2,000	400
Total	28,300	12,900

Key point: 75 % of heterosexually acquired HIV infections newly diagnosed in the UK in 2001 were in people from Africa, or were associated with exposure there.

Low level of HIV incidence in injecting drug users (IDUs)

HIV indicators have remained low in IDUs (Table 1), even though injecting paraphernalia are still often shared and rates of HBV and HCV infection in IDUs are high. Such HIV 1 infections as have been diagnosed have mostly been subtype B and many of them have apparently been acquired abroad. The UK pattern is more favourable than has been seen in IDUs in southern and, more recently, eastern Europe, perhaps as a result of local needle exchange programmes.

Mother to infant HIV infection

The combination of perinatal antiviral treatment of the HIV-infected mother and her infant, delivery by caesarean section and the withholding of breast feeding has to a great extent protected children from 'vertical' HIV infection. However, this can only be achieved if maternal infection is recognized in time. Since 1998 every mother giving birth in the UK has, as far as possible, been offered an anti-HIV test, and acceptance rates have been encouragingly high (>80 %). Now, very few babies born in UK to mothers with diagnosed HIV infection become infected with HIV each year though there may of course be a small unrecognized incidence of neonatal HIV infection due to missed diagnoses in their mothers.

HIV transmission through blood and blood products

This route of HIV infection only needs to be mentioned for the sake of completeness. HIV is very effectively controlled by blood donor selection, donation testing and product inactivation measures, and HIV transmissions due to transfusions in the UK are very rare indeed.

Heterosexual transmission

Since 1999 heterosexually infected cases of HIV have formed the majority of new cases diagnosed in the UK each year. It is believed that about 10 % of these infections have been acquired in the UK, 10 % elsewhere in the world outside Africa and almost 80 % in sub-Saharan Africa. The proportion of the known infections in women is >60 %, and the infections are now recognized to be of several HIV 1 subtypes. Laboratory tests that recognize incident infection are being developed, but they have not yet been shown to be applicable to subtypes other than B and thus it is not yet possible to study heterosexual spread in the UK of the other subtypes. HIV infection in immigrants is contentious and bound up with politicized issues such as asylum seeking. Uncertainty in residency status is associated with risks to individuals of late diagnosis, and the consequences to public health of failure to diagnose and treat HIV infection in a timely fashion.

In common with several other countries of the European Union (e.g. France, Belgium, Portugal) the UK has former colonial ties with African countries where HIV has been hyperendemic for at least 10 years. In many sub-Saharan African countries HIV prevalence in young adults in urban areas exceeds 20 %, and the substantial migratory flows between these countries and in and out of Europe have meant that HIV infections acquired in Africa are frequently being diagnosed in clinics throughout Europe.

Future HIV control and prevention in UK

There is uncertainty as to where recent trends are leading in terms of the control of HIV in the UK. It had been assumed that better case finding and treatment that suppressed viral load would render more patients non-infectious, but it seems also to have encouraged less defensive sexual behaviours and so paradoxically may have promoted the spread of HIV.

Suggestions that are now being made to limit HIV transmission in UK are to:

- maximize case finding, allowing counselling and, where indicated, treatment;
- renew HIV awareness in the population through intensified publicity;
- seek HIV infection in social milieus such as clubs and pubs, using on-site offers of non-invasive testing;
- acknowledge more frankly both the risks taken by, and the medical and social needs of, the main social groups affected by HIV – effective treatment can diminish infectious risk to others and restore economic self-sufficiency in those infected;
- screen and treat immigrants into the UK for HIV and *M. tuberculosis* infection;
- outside the UK, especially in sub-Saharan Africa, encourage and support education, behaviour modification programmes and other HIV prevention and control initiatives.

Conclusion

HIV is now pandemic, and no country can remain unaffected. The UK and other former colonial powers with worldwide trading links are likely to be increasingly affected by this globalization of HIV infection. The logic of this is for these developed economies to invest in HIV prevention in developing countries where HIV infection is out of control for want of adequate public health resources. These interventions should also aim to restore economic activity and stem the population movements that exacerbate the spread of HIV, both within and from the affected countries. The case for a collective multinational effort, especially in sub-Saharan Africa, can and should be being made more persuasively.

Worldwide, HIV is a refractory public health problem with high treatment costs, no effective vaccines yet in sight and the possibility of significant drug resistance emerging. It has already caused life expectancy to fall in the worst affected countries, and is expected to check it up to 2050 at least, at a time when overall globally life expectancy will rise from 65 to 74 years. Even for the UK, HIV dwarfs all other infections, sexually transmitted or otherwise, in importance and so demands resources be spent on care and prevention on the same scale that other common and chronic life-shortening diseases such as coronary artery disease, cancers and diabetes receive as a matter of course. As the HIV epidemic in the UK is still at an immature stage, investment in its control now will avoid greater costs later on, and in developing this strategy a special emphasis should be put on HIV case finding, counselling and treatment. Resource fatigue should not be allowed to impede this rational and proportionate re-direction of effort.

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Acknowledgement

The databases referred to in this article are only maintained through the co-operation and trust of patients, the dedication of clinic and laboratory staff and the sustained funding provided by the UK Departments of Health.

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Sources of further information

Updates of UK HIV and AIDS data are published annually by the Communicable Disease Surveillance Centre. The most recent, for 2001, is available on request. Annual reports of the Unlinked Anonymous Testing programme for HIV and hepatitis are available from the Department of Health (England).

Disclaimer

The opinions offered in this article are personal ones and not necessarily those of the Health Protection Agency.

Bacterial sex

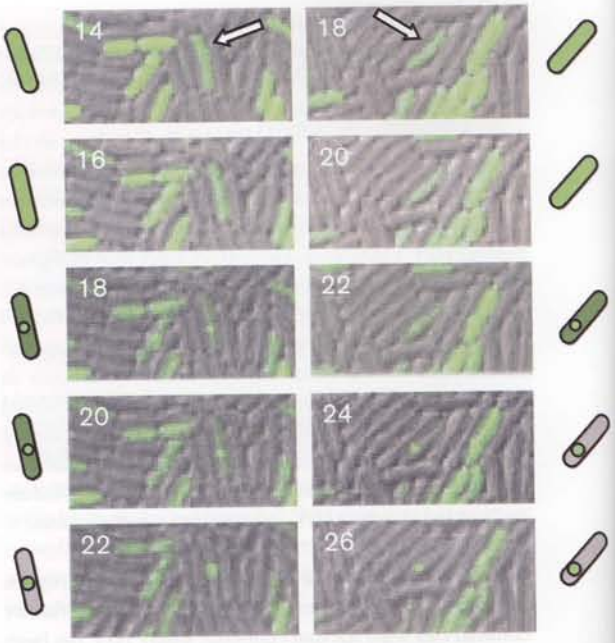
Christopher M. Thomas

Chris Thomas explains the ins and outs of genetic transfer between bacteria.

Sex as a genetic process provides a way of counteracting the accumulation of deleterious mutations as well as helping to increase the genetic variations that underpin adaptation and evolution. Although bacteria are haploid and do not have a sexual cycle, they do have a variety of mechanisms for genetic exchange that provide some of the advantages of sex. Transformation (uptake of naked DNA), transduction (bacteriophage-mediated DNA transfer) and conjugation (cell–cell contact-mediated transfer) can all result in DNA movement from one bacterium to another. However, conjugation is the only process that could transfer the whole of the chromosome. Conjugation is also the process that is most like sex in higher organisms – it appears to occur between pairs of bacteria, one of which is designated male on the basis of carrying the conjugative apparatus that is needed for mating-pair formation and subsequent DNA transfer.

F is no longer the only paradigm

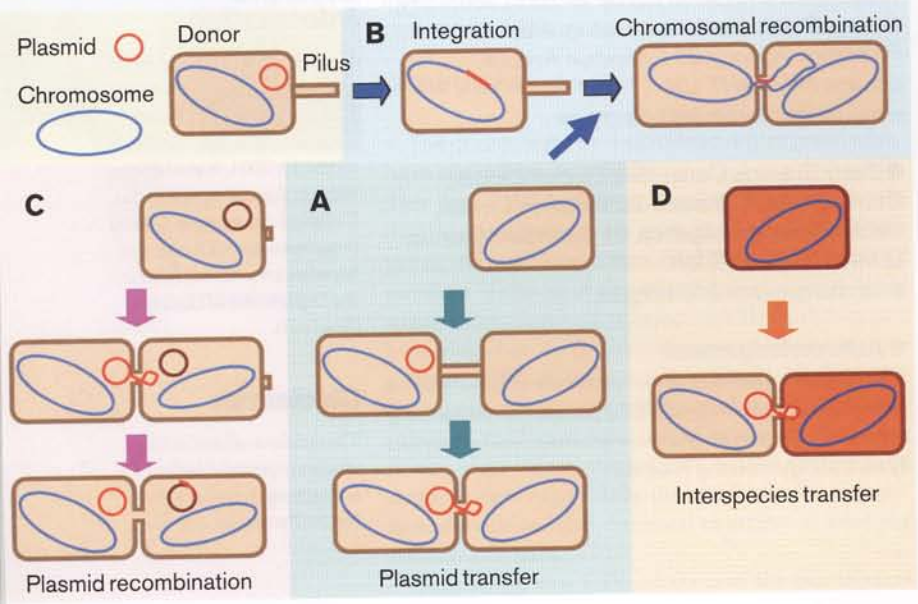
Bacterial sex, originally discovered by Joshua Lederberg, is mediated by a plasmid called F (for Fertility factor) (Fig. 1). Many other mobile genetic elements (plasmids and transposable elements) also encode conjugative transfer systems. The broad host range IncP-1 plasmids and the Ti plasmids from *Agrobacterium tumefaciens* are now the most intensively studied systems from Gram-negative bacteria. Ti plasmids carry two transfer systems – one for sex between bacteria and the other for sex between bacteria and plants. Remarkably, DNA sequencing has revealed that the basic apparatus for both Ti transfer processes and the IncP-1 transfer are fundamentally the same. There are also remarkable similarities between this DNA transfer process and toxin protein export to target eukaryotic cells in *Bordetella pertussis* as well as DNA uptake during transformation of *Helicobacter pylori*. Given this apparently all-purpose mechanism for macromolecular transfer, these systems have rightly become the centre of much attention.



Other types of transfer systems also exist, especially in Gram-positive bacteria. The pheromone-stimulated transfer among enterococci and the simple transfer systems of *Streptomyces*, which appear to depend on hyphal fusion rather than a sophisticated mating-pair formation apparatus, illustrate this diversity.

Why is bacterial sex encoded by mobile genetic elements?

Since sex is such an obvious benefit to the host bacteria why shouldn't this be a basic chromosomal function? Well, the transfer systems that we know would not have evolved so rapidly if they were a permanent part of the chromosome – in practice mating pairs undergoing conjugation normally break down before there is time to transfer the whole chromosome. Mutant transfer systems better able to transfer DNA would not be selected because the mutant transfer apparatus would not be inherited by the bacteria to which DNA transfer takes place. However, if the transfer apparatus is part of a smaller element then it will transfer completely and more efficient mutants will be selected. The fact that a conjugative element can integrate into the chromosome at many sites allows all chromosomal genes to benefit from the transfer process, rather than the limited set if there was always just one transfer origin at a fixed point. Thus conjugative mobile DNA can benefit both itself and its host while promoting genome evolution.



BELOW:
Fig. 1. Plasmid-positive donor bacteria produce a pilus that contacts recipient bacteria (A) and draws them together so that surface fusion takes place, creating a bridge through which DNA can be driven by rolling circle replication initiated by nicking at *oriT*, the transfer origin, in the donor bacterium. Integration into the chromosome (B) can mobilize chromosomal DNA. Transfer to plasmid-containing bacteria (C) can promote inter-plasmid recombination. Broad host range plasmids can allow transfer of genes to diverse species (D). COURTESY C.M.THOMAS

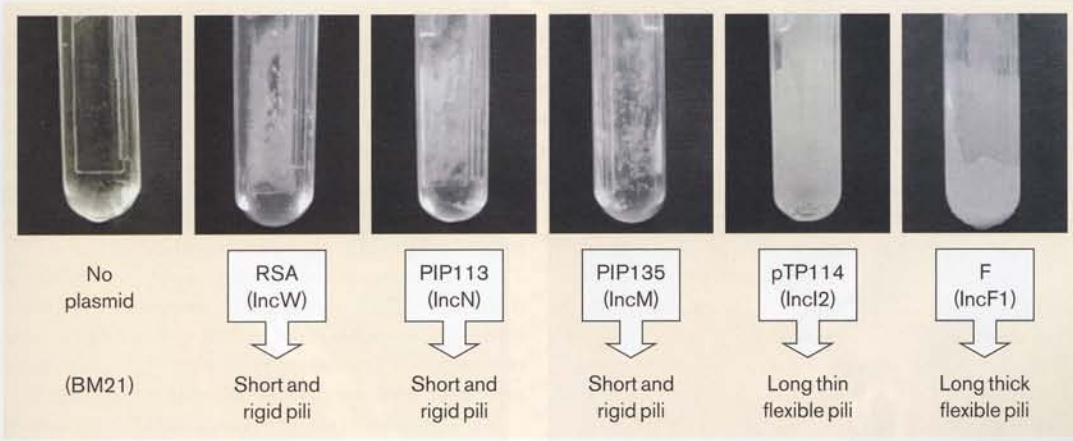


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Fig. 2. Time-lapse fluorescence microscopy of R751 plasmid DNA entering *Escherichia coli* recipient cells (arrows). Cartoons highlighting the cell of interest are adjacent to each time-lapse series. Non-fluorescent donor cells contain the plasmid R751::*lacO* that has been engineered to carry binding sites for the fluorescent hybrid protein LacI-GFP that is being made in the green recipient cells. As R751::*lacO* enters into the recipient during conjugative transfer, LacI-GFP rapidly aggregates to the plasmid molecule and allows visualization of plasmid establishment. The timing of images is indicated in minutes at the top-left hand corner of each image.
REPRODUCED FROM LAWLEY *ET AL.*, (*MOL MICROBIOL* 44, 947–956) WITH THE KIND PERMISSION OF TREVOR LAWLEY, BLACKWELL PUBLISHERS

ABOVE LEFT (THIS PAGE):
Fig. 3. The presence of a variety of plasmids can promote biofilm formation on a glass slide in standard growth medium as compared to the bacterial host without a plasmid that leaves the slide completely clean. This property is not confined to plasmids with just one type of pilus, although the effect is most marked with F-like plasmids.
COURTESY JEAN-MARC GHIGO, PASTEUR INSTITUTE FRANCE

Visualizing the transfer process

Søren Molin's group in Lyngby, Denmark, has pioneered the use of plasmids tagged with a reporter gene encoding green fluorescent protein to visualize transfer as it occurs. This reporter is repressed by a gene inserted into the chromosome of donor bacteria. When transfer takes place to a bacterium without this repressor, the reporter gene gets switched on and the cell becomes fluorescent. Transfer into recipients can therefore be enumerated *in situ*, for example in a biofilm, without the need to isolate the bacteria. An alternative way of visualizing the process is illustrated in Fig. 2. Such studies should help to reveal aspects of the transfer process at the single-cell level not previously accessible.

Conjugation is not an exclusively heterosexual process

F^+ bacteria are not good recipients in F-mediated transfer – a phenomenon called surface exclusion and found in most other conjugative systems. These functions help dissociate mating bacterial pairs when transfer has taken place. Surface exclusion should prevent one plasmid transferring into a cell that is already occupied by an identical or closely related plasmid. However, recent data shows that F-like plasmids undergo frequent recombination with each other – so they must frequently enter the same cell. Data with IncP-1 plasmids and small bacteriocin-producing plasmids suggest that recombination between related plasmids may be a widespread phenomenon.

Conjugative elements and biofilms

F and many other plasmids will promote biofilm-formation (Fig. 3) by helping adherence to a variety of surfaces and recruitment of other bacteria. The plasmid transfer apparatus appears to play a role in this effect, but surprisingly, this effect can be seen in a pure culture of F^+ bacteria – 'recipients' are not needed. The explanation may be that in many natural environments at low temperature, only a small proportion of the bacteria express surface exclusion so F can transfer into bacteria already carrying F. Thus recombination can take place between the incoming and resident plasmid. The result will be that genetic changes occurring within a population will rapidly be shuffled between bacteria and fitter plasmids will evolve quickly.

The horizontal gene pool

Bacterial sex allows rapid adaptation to changing circumstances. Traits useful in specialized niches but dispensable in others are retained by only a few bacteria, but these dominate in selective environments. Thus any one strain may only carry a fraction of the traits to which the species has access. Since mobile elements can establish themselves without homologous recombination, they can carry such extra genes to diverse species. This provides a pool of genes accessible to many, and exclusive to none. Conjugative mobile elements therefore play a vital role in the diversity and adaptability of bacteria and the study of this pool should form a vital component of any genomics programme.

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A new dimension to sex wars: microbes that benefit female hosts

Michael E. N. Majerus

Parasitic microbes live in the cells of many invertebrates, where their presence can markedly benefit the female host. Mike Majerus describes the impact of these hijackers on the lives of certain insects.

Most parasitic microbes care little whether the organism they attack is male, female or hermaphrodite. However, the interests of one group of micro-organisms are very much in favour of being in female rather than male hosts. These are the bacteria, viruses and protists that live in the cells of their hosts and are transmitted to the next host generation in the cytoplasm of sex cells. As sperm have little cytoplasm, while eggs have a lot, the inheritance of these symbionts is through female, not male hosts. Consequently, these parasites have evolved a variety of strategies – feminization, induction of asexual reproduction and assassination of males – to promote their own continued existence by favouring female hosts at the expense of males.

Strategies to favour female hosts

Two of these strategies, feminization and induction of secondary asexual reproduction, or parthenogenesis, directly cause a reduction in the production of males. Feminization, which is caused by α-proteobacteria of the genus *Wolbachia* and various protists, such as micro-sporidians, affect a number of crustaceans, for example brine shrimps (*Gammarus* spp.) and woodlice (*Armadillium* spp.), and some moths (*Ostrinia* spp.). Here, feminization is caused by inhibition of the androgenic gland, which produces the male development-inducing hormone, androgen. In the absence of androgen, individuals with male sex chromosomes develop as females. Due to these feminizers, all members of some crustacean populations have male sex chromosomes (crustaceans and moths are male homogametic, their sex chromosomes being ZZ). The females are all feminized males (ZZ + feminizing microbe). The transmission efficiency of these feminizing microbes is not perfect, so while about 90 % of progeny are female, the remaining 10 % that do not inherit the symbiont develop normally as ZZ males.

Microbe-induced parthenogenesis (MIP) is also caused by *Wolbachia*, and as yet has only been reported from haplo-diploids, such as hymenopterans. Here the *Wolbachia* cause unfertilized eggs to develop as females, rather than males as normally occurs in haplo-diploid systems. Species of asexually reproducing parasitoid wasps, from which males have not previously been recorded, produce males following treatment with antibiotics.

The third strategy of these inherited microbes, male-killing, is less sophisticated. Bacteria in male hosts are at an evolutionary dead-end as they can only be passed on by female hosts. Consequently, they kill male hosts, and by so doing increase the fitness of sibling female hosts that carry clonally identical copies of themselves. Male-killers of this type are known from a diverse array of insect hosts, with ladybirds, butterflies, moths and milkweed bugs being hot-spots for them. The range of male-killing micro-organisms is similarly diverse, with α- and γ-proteobacteria, mycoplasmas, flavobacteria and microsporidians having been identified.

The fitness advantages of male-killing bacteria to female hosts have been most fully studied in ladybirds.

ABOVE:
The ladybird *Cheilomenes 6-maculatus*, which hosts a male-killing γ-proteobacterium also has a nuclear gene that rescues males from the bacterium's pathogenicity.

RIGHT:
The benefits of male-killing in ladybirds: neonate female larvae of the ladybird *Harmonia axyridis* gain a nutritional benefit by eating the eggs containing their dead brothers.

Here males are killed early in embryogenesis. Ladybird eggs are laid in clutches, and neonate female larvae consume their dead brothers, gaining a rich extra meal. In addition, as cannibalism is rife amongst ladybirds, with early-hatching larvae eating late-developing siblings, then in batches where half the eggs die as a result of male-killer infection, the level of cannibalism of slow-developing female offspring is reduced. This is because there are fewer cannibalizers and more unhatched eggs to choose from.

Impact on the microbial hosts

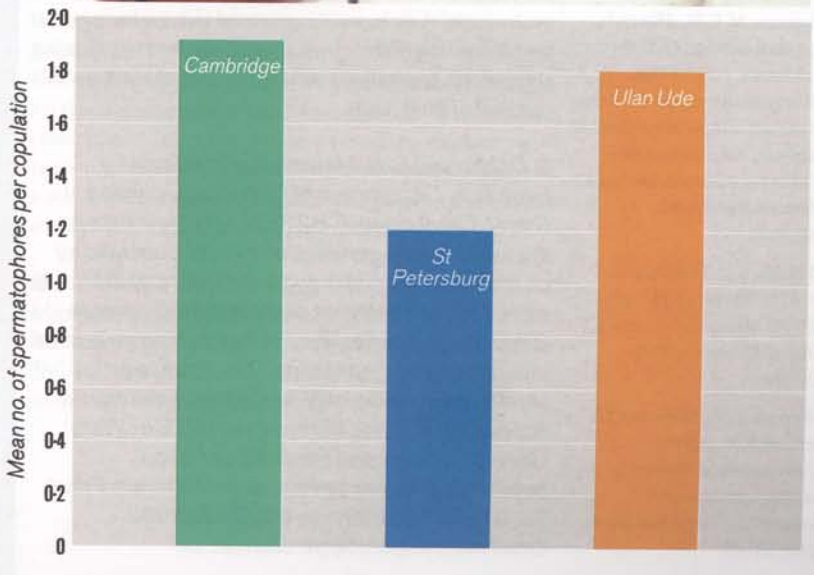
Microbes that employ these female-promoting behaviours may impact on the evolution of their hosts in various ways. First, because they are cytoplasmically inherited, they are in conflict with the nuclear genome of their host. In consequence, they will promote the evolution of nuclear suppresser host genes that ameliorate their detrimental effect on males. Indeed, in one ladybird, *Cheilomenes 6-maculatus*, a male rescue gene has been found. Second, as a 1 : 1 sex ratio is usually optimal due to negative frequency-dependent selection, if the sex ratio of a population is biased towards females, genes that promote the production of males may be selected for. Again we have some evidence for this, a masculinizing gene having been found in woodlice.

Distortion of population sex ratios can have quite profound affects on host reproductive strategies. Some populations of the 2-spot ladybird, *Adalia bipunctata*, host four different male-killing bacteria; a rickettsia, a spiroplasma, and two strains of *Wolbachia*. The sex ratio of 2-spot populations varies from equality to two females for every male. Males are capable of multiple ejaculation within a single copulation, passing one, two or three sperm packages. The number of sperm packages is inversely correlated to male frequency. Here then, male investment per mating is dependent on the availability of future mating opportunities. If females are easy to come by, males invest less in each mating than when females are in short supply.

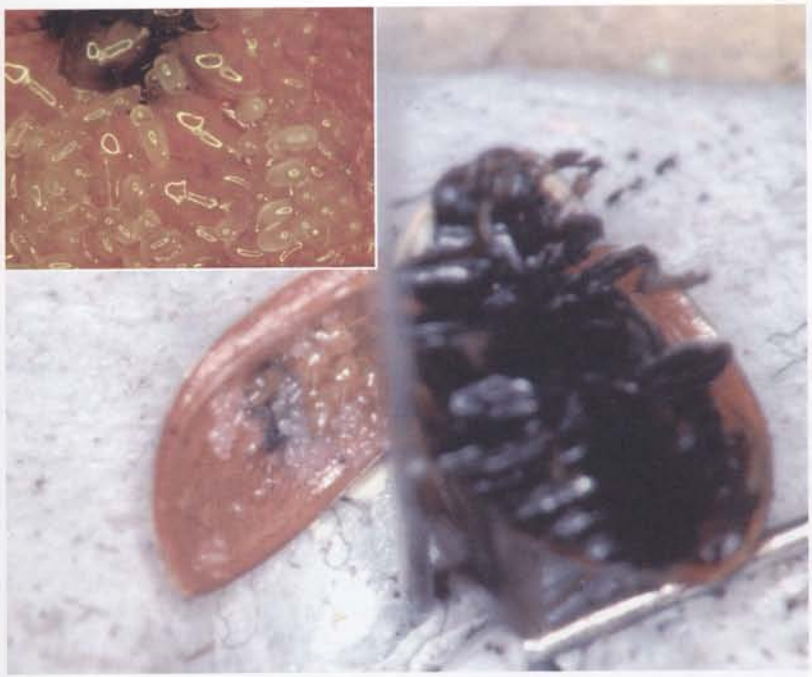
In some nymphalid butterflies, such as *Acraea encedon*, population sex ratios are even more skewed as a result of a high prevalence, low cost male-killing *Wolbachia*. Here, some colonies have over 90 % of females infected, and less than 5 % of the population is male. Males only live for about 2 weeks and can only mate once a day. The result is that a large proportion of females, over 80 % in some colonies, die virgin. This has led to complete sex role reversal, with females aggregating and competing with one another at lekking sites, and males visiting these sites to find mates.

LEFT:
Female lekking in the butterfly *Acraea encedon*
COURTESY DR F.M. JIGGINS

BELOW (TOP):
A 2-spot ladybird infected with a male-killing rickettsia takes her medicine: golden syrup laced with tetracycline.



BELOW (BOTTOM):
Sex ratio distorters can influence host reproductive strategies. Here male investment is shown for male 2-spot ladybirds from three populations with differing male-killer prevalences (Cambridge, 6–11 %; St Petersburg, 50 %; Ulan Ude, 3 %).



ABOVE:
Biased population sex ratios will cause changes in the epidemiology of STDs, such as the mite *Coccipolipus hippodamiae*, here shown sucking blood from the underside of a 2-spot ladybird wing case. The inset shows a section of the ventral surface with adult female mites and offspring.

Effects on the epidemiology of STDs of hosts

The population sex ratio distortion caused by male-killers and feminizers, may also impact on the epidemiology of sexually transmitted diseases (STDs) of hosts. Not only does the 2-spot ladybird host four male-killers, it also suffers from two sexually transmitted diseases; one a mite, *Coccipolipus hippodamiae*, the other a *Laboulbeniales* fungus. The mite, at least, is very costly, female ladybirds becoming sterile within 3 weeks of contracting this ectoparasitic blood-sucker. The 2-spot is highly promiscuous, both females and males mating with many different partners. In populations with female-biased sex ratios, the prevalence of STDs will increase more rapidly than in 1:1 sex ratio populations. This is because males, due to their rarity, will have more mating partners and so more chance to both contract and pass on the diseases.

The proportion of insect species that harbour ultra-selfish inherited bacteria of one genus, *Wolbachia*, has been estimated to be between 15 and 20%. If other groups of parasitic microbes are included, it may be that the majority of invertebrates host such symbionts. Given the impacts that these microbes can have on the evolution of their hosts, it is essential that we increase our understanding of their biology, and that we start viewing them as an integral and influential part of the heritable material of their hosts.

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Further reading

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Medical Society for the Study of Venereal Diseases

www.mssvd.org.uk

Sexually transmitted infections in the UK are primarily diagnosed at a unique network of 230 genitourinary medicine (GUM) or sexual health clinics. Physicians with expertise in sexual health belong to the Medical Society for the Study of Venereal Diseases (MSSVD). Initially for doctors with an option to propose membership for renowned scientists, since 1998 the society has opened its membership to a wide range of health care professionals, including microbiologists. This more open approach recognizes the necessity for doctors, nurses, health advisors and microbiologists to work in partnership to improve sexual health. The MSSVD is actively encouraging more basic science in the field of sexually transmitted infections. Non-medical members are invited to present their work at the annual spring meeting and prizes for the best presentation or poster are open to young investigators who are either clinically or non-clinically qualified.

Special interest groups were initiated in 1999 with the remit to encourage and improve the study and practice of the diagnosis and treatment of sexually transmitted infections. The eight groups include bacterial STIs, Human Immunodeficiency Virus, and Human Papilloma Virus. The Bacterial Special Interest Group (BSIG) aims to promote communication between microbiologists and clinicians involved in the diagnosis and treatment of STIs by offering courses in specialist areas, production of educational material, organization of symposia on new areas and arranging update sessions.

Microscopy for the diagnosis of bacterial STIs is an area where the BSIG has been active in the training of nurses and GUM clinicians. In many clinical laboratories microscopy is used for presumptive diagnosis of infection and is manned predominantly by nurses. A one-day course, which has a large practical element, is organized twice yearly and covers the use and care of the microscope and techniques for the diagnosis of STIs using microscopy. The need for training in microscopy has been highlighted in recent years by the increasing use of dark ground microscopy for the diagnosis of primary syphilis, a technique available in only a few specialist centres. The continuing outbreaks of syphilis require this expertise to be more widely disseminated and training in dark ground microscopy has been incorporated as a major element in the course. The BSIG also has a commitment to improve standards for microscopy and has produced a laboratory manual, for use in GUM clinics and laboratories. A pilot in quality assurance in microscopy for STIs is underway.

The society is also aware of the necessity to destigmatize sexually transmitted infections in the 21st century and to reach as wide a population as possible through health promotion. With this in mind the name of the society will be changed from the Medical Society for the Study of Venereal Diseases to the British Association for Sexual Health and HIV when it merges with its sister society in November 2003.

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Obituary – Hans Veldkamp

Honorary Member of SGM and former Member of Council

On 23 December 2002 **Professor Hans Veldkamp**, Emeritus Professor of Microbiology at the University of Groningen, The Netherlands, passed away during his eightieth year in his home town of Paterswolde.

Hans Veldkamp became fascinated by the diversity of bacteria during his studies on biology at the University of Leiden and Amsterdam during and after World War II. He subsequently transferred to the Technical University of Delft where he came under the influence of the 'Delft School of Microbiology', studying the oxidation of ethylene glycol with Professor Albert-Jan Kluyver and developing ideas that set the course for his life. From 1946 until 1950 he was assistant at the Department of Botany in Leiden where he taught general microbiology.

After his graduation in 1950 he was appointed to the Department of Microbiology of the University of Wageningen. His thesis on *A study of the aerobic decomposition of chitin by micro-organisms* was completed in 1955 and he was promoted to Reader in 1961. A sabbatical in the lab of Kees van Niel at the Hopkins Marine Station in Pacific Grove, California, established both a long-lasting friendship between the two men and consolidated his interest in microbial metabolism. His research became focused on free-living, anaerobic spirochaetes, and on applied microbiology, especially amino acid- and vitamin-producing bacteria.

In 1963 he was invited to become Professor of Microbiology at the University of Groningen and establish a new Department of Microbiology. The characteristic feature of its degree was an intensive four-week study of General Microbiology, influenced by van Niel's famous course integrating microbial physiology and ecology. The morning sessions were filled with lectures and from afternoon until late into the evening the students carried out experiments, especially with enrichment cultures. Committed students were attracted as the reputation of the course for excellent teaching, challenging discussion and hard work spread.

Around 1970 it was still possible for a professor in the Netherlands to appoint permanent scientific and technical staff. Hans built up a department during the seventies with three main research groups: Microbial ecology, Microbial physiology and Molecular microbiology. His hard working team of scientists included several who were later appointed to chairs themselves, including Wim Harder, who became leader of the Microbial physiology group and Wil Konings who led Molecular microbiology.

Hans led the Microbial ecology group himself, with Gijs Kuenen and Hans van Gemerden within the group. His specialization was the (aut)ecology and ecophysiology of bacteria, particularly competition of bacteria under growth-limiting conditions. However, projects ranged from psychrotrophs to phototrophs, from heterotrophs to chemolithotrophs and from butyric acid to lactic acid bacteria. He recognized the importance of continuous cultivation for a quantitative analysis of the ecology and ecophysiology of bacteria and performed pioneering research in this area. Among his many achievements that received national and international recognition, he was Chairman of the Federation of European Microbiological Societies from 1983 to 1986 during which period *FEMS Microbiology Ecology* commenced publication in 1985 with him as Chief Editor. He guided the new journal with great enthusiasm during its formative years.

One of the strong features of Hans Veldkamp was his realization of the limitations in his knowledge of microbiology. By 1980 the Department had grown to about 100 staff members and he relinquished day-to-day supervision of research to others. Its continuing success, together with his developing health problems, contributed to his decision to retire at the age of 63 to focus on his favourite hobby of bird watching. He went regularly to an inlet of the Waddensea, the Lauwersmeer, to observe migrating birds, an activity that offered him great joy. His health problems gradually increased, but with tremendous support from his wife Toek, he retained a sharp mind and enjoyed life until his last moments. His many students and co-workers will remember Hans Veldkamp with respect and gratitude as a self-willed and great scientist who possessed the skills to teach them the beauties of microbiology.

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SocietyNews

February Council Meeting

FEMS Award for our President

● Council warmly applauded the news that its nomination of **Professor Sir David Hopwood** for the Lwoff Medal had been successful. The medal lecture will be delivered at the 1st FEMS Congress in Ljubljana in early July.

European Society for Clinical Virology

● This society has recently become a company limited by guarantee and it has been agreed that its registered address for company law purposes will be at Marlborough House. SGM has provided a similar service to FEMS for some years.

Journals

● Council has agreed to the establishment of a Working Party to review the operations of the journals' Editorial Boards with a view to sharing best practice and where possible harmonizing procedures. It is hoped that it will report back to the July meeting of Council.

Biosciences Federation

● Council learned that the new Federation was launched at an informal event in London on 18 February and future plans include a more formal launch at Westminster in the autumn. The Federation plans to set up four standing committees, on Education, Animal Science, Bioethics, and Environment and Sustainability. There would also be three working groups focused on Biodefence, GM Crops, and Public Health Benefits from Pathogen Genome Sequencing. The last of these SGM considers important in relation to the Chief Medical Officer's recent report *Getting Ahead of the Curve* (see p. 224 of the November 2002 issue of *Microbiology Today* for background information on the report).

New Prize

● Council has decided that the new Communication Prize for postgraduates and early postdocs, details of which appeared in Gradline in our last issue, will be called the *Young Microbiologist of the Year*.

Publication policy re bioterrorism concerns

● Council discussed its policy on scientific publication, security and censorship in the light of recent worries about the potential use of micro-organisms and toxins for bioterrorism. It was agreed to prepare a written policy statement stressing the need to protect the integrity of the publication process, while recognizing that very rarely, a paper might give rise to specific concerns.

MAC in Scotland

● The Microbiology Awareness Campaign has taken a further step forward with the announcement of an event for members of the Scottish Parliament, to be held following the parliamentary elections in Edinburgh. Council hopes to build on initiatives north of the border to extend the campaign to other regions.

Postgraduate matters

● The results of a recent survey of postgraduate student members were reported to Council. Matters of concern included the amount of time spent teaching; the finding that nearly a quarter of respondents had received no induction training and the one third of respondents who said that they did not attend SGM meetings. Local representatives will be sent details of the survey and encouraged to provide further feedback to Council. It is hoped that dialogue can continue with a view to improving SGM's relevance to its younger members.

Joint Regional Meetings with SfAM

● Agreement has been reached between SGM and the Society for Applied Microbiology to run jointly two kinds of regional meeting: special topics meetings focused on a particular area of microbiology and local microbiology group meetings. The first of these has taken place in Plymouth, when the Peninsula Microbiology group based in the south west met in March.

International Research Grants

● In future, grants previously given as International Research Fellowships will be discontinued in their original form and have been replaced by International Research Grants. These, together with applications for the International Development Fund, will in future have a single common closing date in October (see p. 75 for details).

● *Alan Vivian, General Secretary*

E-mails to Members

SGM can now send members occasional emails about Society activities (definitely not spam!). If you have not received such emails, it means that we do not have a correct email address for you. If you would like to receive such messages, please send your address to **members@sgm.ac.uk**

Annual General Meeting 2003

The Annual General Meeting of the Society will be held on **Tuesday, 9 September 2003** at the Society Meeting at UMIST. Agenda papers, including reports from Officers and Group Conveners, and the Accounts of the Society for 2002 will be circulated with the August issue of *Microbiology Today*.

New Council Officers

Professor Hugh Pennington, Department of Medical Microbiology, University of Aberdeen, has accepted Council's invitation to be the next President of the Society. **Dr Sue Assinder**, School of Biological Sciences, University of Wales, Bangor has accepted the post of Education Officer. Both officers will start their term of office in September. Their profiles will appear in a future issue of *Microbiology Today*.

Staff News

Congratulations to former Staff Editor **Jo Couchman** on the birth of a son, Robert William Andrew, in February.

Congratulations also to Staff Editor **Natalie Wilder** on her engagement to James McGuire on 20 March.

News of Members

Professor Jim Lynch, Head, School of Biomedical and Life Sciences, University of Surrey, has been appointed Chief Executive of the Forestry Commission's Forest Research Agency. He will take up his new post in July.

Ernst Chain Prize to SGM President

Congratulations to **Professor Sir David Hopwood FRS**, the first recipient of the Ernst Chain Prize, in recognition of the tremendous impact that Sir David's work has had on the understanding of *Streptomyces* and the ability to use it to produce new and more effective medicines. This major scientific prize is awarded annually by Imperial College London, funded by the Kohn Foundation, to a career scientist who has made an original and substantive contribution in any field of science, which has furthered, or is likely to further, understanding or management of human disease. The winner receives a personal award of £10,000, and a commemorative medal. The prize-giving ceremony was on 19 March 2003 on Imperial's South Kensington campus, and was followed by Sir David's lecture on *Streptomyces* genes in antibiotic discovery and development.

Undergraduate Microbiology Prizes

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

One prize is available to each university in the UK and Ireland offering an appropriate microbiology course. The full rules and a form are on the SGM website The closing date for nominations is **29 August 2003**.

SGM Prize Lectures and Awards 2003

Procedure for nominations

A range of prestigious awards is made by the Society in recognition of distinguished contributions to microbiology. To facilitate nominations, the rules for each prize lecture due to be awarded in 2004 are provided on this page and a form is available overleaf. It is now also possible for self-nominations to be made for all awards. The award panel will consider the submissions in the autumn and their recommendations will be taken to November Council for approval. The outcome will be announced in the February 2004 issue of *Microbiology Today*.

Nominations are now sought for the 2004 prize lectures. Please complete the form overleaf and send it to **Professor Alan Vivian, c/o SGM HQ**. Professor Vivian will be pleased to discuss the criteria for nominations, should any queries arise.

The closing date for all nominations is **30 September 2003**.

Fleming Award

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

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

Marjory Stephenson Prize Lecture

This is the Society's principal prize, awarded biennially for an outstanding contribution of current importance in microbiology. The winner receives £1,000 and gives a lecture on his/her work at a Society meeting. The lecture is usually published in a Society journal.

The Marjory Stephenson Prize Lecture shall be awarded biennially for an outstanding contribution of current importance in microbiology, without restriction on the area of microbiology in which the award is made.

Nominations for the Marjory Stephenson Prize Lecture shall be made by any two members of the Society; the nominee need not be a member of the Society. Nominations should be accompanied by a statement of the contribution to microbiology made by the nominee, supported by reprints or other appropriate documentation. A brief CV of the nominee and a full bibliography of his or her work should also be included. Alternatively, candidates may submit all of the information listed above, together with the names of two members who are familiar with their work, who will be asked to supply the appropriate statement with regard to the candidate's contribution to microbiology.

There shall be no restriction by means of age or nationality of those eligible for the Marjory Stephenson Prize Lecture. Recipients of the Lectureship may not be nominated on a subsequent occasion.

The recipient of the Marjory Stephenson Prize Lectureship will be expected to give a lecture based on the work for which the Prize Lectureship has been awarded to a meeting of the Society, normally the Spring meeting following the announcement of the award. The recipient will be strongly encouraged to publish the lecture in either *Microbiology* or the *Journal of General Virology*, whichever is the more suitable. The choice will be at the discretion of the Editors of the journals.

Peter Wildy Prize for Microbiology Education

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

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

   Nominations should be accompanied by a statement of the contribution to microbiology education made by the nominee, supported by appropriate documentation if available. A brief CV of the nominee should also be included.
3. There shall be no restriction by means of age or nationality of those eligible for the Prize. Recipients of the Prize may not be nominated on a subsequent occasion.
4. The recipient of the Prize will be expected to give a presentation based on an aspect of educational work for which the Prize has been awarded to a meeting of the Society, normally within a year of the announcement of the award. The presentation may take the form of a lecture, workshop, audio/visual display or any other appropriate activity. The recipient will be strongly encouraged to publish an article based on the presentation in *Microbiology Today*.

Grants

New Rules for International Research Fellowships

This scheme, which began in 2000, has been reviewed by Council and the rules amended to make them more appropriate to the type and number of applications being received. There will now only be one closing date for applications in October, instead of three throughout the year as previously. Applications will be assessed at the same time and by the same panel as the International Development Fund. The minimum research visit period has been set at one month. Financial administration of the awards will now be the responsibility of the relevant UK institution. Maximum annual funding will be capped each year to promote a true competition and has been set at £25,000 for 2003. The name of the scheme has been changed to **International Research Grants**, to more accurately reflect its purpose. The full rules and an application form are available on the website.

The purpose of the grants is to allow scientists to travel to or from the UK and Republic of Ireland in order 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 is **10 October 2003**.

International Development Fund

The rules for this scheme have also been changed slightly in response to changing circumstances. The fund aims to provide help to countries where microbiology is inadequately developed, but where its further development may assist education or the economy of these countries. At present these include many places in the Far East, Africa, South and Central America, the Indian sub-continent and Eastern and Central Europe. Awards are made by competition to SGM members and support may be available for:

- running short lecture courses and laboratory training in microbiological subjects. Host laboratories are usually expected to provide some evidence of local support for the courses. Grants may cover travel and accommodation and allow the purchase of basic equipment essential for the needs of such training courses.
- assistance of national microbiological facilities, e.g. culture collections (which underpin microbiology), where these run into temporary difficulties.
- any other small project to assist in technology transfer from Western Europe to the areas mentioned above for which other sources of funding do not exist.

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

The closing date for applications is **10 October 2003**.

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).

Education Development Fund Awards

The following Public Understanding of Science grant has been made:

Sue Fryer, Bishop Burton College, has been awarded up to £500 towards the expenses of running a Year 10 GNVQ Science practical microbiology course.

Education Development Fund 2003

Members are invited to apply for small grants to fund either (a) initiatives to promote the public understanding of microbiology or (b) to support developments likely to lead to an improvement in the teaching of any aspect of microbiology relevant to secondary or tertiary (including postgraduate) education in the UK. There are different application forms for the PUS awards and the teaching aids. There is no closing date for applications; which will be considered on a first come, first served basis during the calendar year 2003.

Technician Meeting Taster Grants

These grants, which enable eligible technicians to sample an SGM meeting with expenses of up to £200 being met by the Society, are still available for the UMIST meeting. See SGM website for full details and an application form.

Retired Member Conference Grants

The scheme enables retired members to attend one SGM meeting per year. The grant covers en-suite accommodation and the Society Dinner. The maximum award is £250. It is hoped that the scheme will enable retired microbiologists both to keep up with their science and to share their knowledge with other members. Completed application forms must be submitted to the Grants Office before the meeting. Applications are now invited for grants to attend the Society's meeting at UMIST, 8–11 September 2003.

Seminar Speakers Fund 2003

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

The Watanabe Book Fund

Members who are permanently resident in a developing country are reminded that they may apply for funding to acquire for their libraries books, or possibly journals, relating to microbiology. These annual awards are available as a result of a generous donation from Professor T. Watanabe of Japan. The closing date for the receipt of applications, which should be made to the Grants Office at SGM Headquarters, is **3 October 2003**.

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. 92 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 Main Symposium 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. Each submission must be accompanied by a completed form also available on the website. Deadlines for submissions are published in *Microbiology Today* and on the web. For further information contact the Events Administrator.

Edinburgh Meeting April 2003

Microbial subversion of host cells
Symposium volume 62

This is now available from CUP at a special discount price for members. A review of the book appears on p. 88 and an order form is included in this issue.

Abstracts book

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

Future Meetings

AUTUMN 2003 – 153rd Meeting
UMIST, Manchester
8–11 September 2003

● Main Symposium
Exploiting genomes: bases to megabases in 50 years

Organizers: H.F. Jenkinson, D.J. Kelly, P.C.F. Oyston, J. Parkhill & I.C. Sutcliffe

● Speakers

G. WEINSTOCK (USA) *Genomes and beyond*

J. PARKHILL (Sanger Centre) *Comparative genomics of bacterial pathogens*

P. GHAZEL (Edinburgh) *Cytomegalovirus expression in human cells*

S. ANDERSSON (Sweden) *Genomics of Bartonella*

T. GAASTERLAND (New York) *Bioinformatics: making sense of megabases of data*

C. HUTCHISON (TIGR) *Minimal microbial genome*

P. KELLAM (UCL) *Global views of host/pathogen interactions; transcriptional changes in virally infected cells*

A. DAVISON (Glasgow) *Herpesvirus genomics*

D. USSERY (Denmark) *Prediction of highly expressed genes in sequenced prokaryotic genomes*

E. GARCIA (USA) *Comparative analysis of Yersinia*

P. BUTCHER (London) *Bacterial gene expression and infection: microbes, messengers and microarrays*

D. O'CONNOR (Southampton) *Proteomics*

B. WREN (London) *Genomics in Campylobacter jejuni pathogenesis*

P. RAINEY (New Zealand) *The secret life of Pseudomonas fluorescens SBW25*

P. RATHOD (USA) *Identification of novel targets for anti-malarial drugs*

R. RAPPUOLI (Italy) *Vaccine antigen discovery in silico*

DNA50

On April 25th 1953 James Watson and Francis Crick described the structure of DNA in the journal *Nature*.

This momentous discovery, which was the culmination of research by Maurice Wilkins and Rosalind Franklin in London, and James Watson and Francis Crick in Cambridge, was one of the most significant landmarks of 20th century science. To mark the 50th anniversary the Medical Research Council, the Royal Society and *Nature* have joined forces to coordinate a programme of events in 2003 (see **www.dna50.org.uk**).

Research into the structure and role of DNA has been underpinned by studies on microbes and SGM is delighted to take part in the DNA50 programme. Our contributions include the whole of the 153rd Meeting at UMIST. The main symposium addresses a wide range of microbial genomics and genomics-related topics and will duly acknowledge the Watson and Crick anniversary, whilst the Group symposia cover various aspects of microbial molecular biology. Cambridge historian of molecular biology Soraya de Chaderevian, will also be delivering a public 'History of Microbiology' lecture on the DNA theme at UMIST.

● Other symposia

● Microbial sensing and signalling
Cells & Cell Surfaces Group
11 September
Organizers: J. Armstrong (j.armstrong@sussex.ac.uk) & D. Devine (d.a.devine@leeds.ac.uk)

● Making sense of bioinformatics: seeing the wood for the trees
Education & Training/Systematics & Evolution Groups
10–11 September
Organizers: R. Goodacre (rrg@aber.ac.uk) & C. Jones (c.jones@mmu.ac.uk)

● Post genomics applied to processes: advances in eukaryotic microbiology
Eukaryotic Microbiology with British Mycological Society and British Society for Medical Mycology
10–11 September
Organizers: A.J.P. Brown (al.brown@abdn.ac.uk) & S. Purton (s.purton@ucl.ac.uk)

● Production of DNA and protein
Fermentation & Bioprocessing Group
10 September
Organizer: A. Weiss (amanda.weiss@cobrat.com)

● DNA-based detection methods
Food & Beverages/Environmental Microbiology Groups
8–9 September
Organizers: G.R. Gibson (g.r.gibson@reading.ac.uk) & I.P. Thompson (ipt@ceh.ac.uk)

● Bacterial gene expression *in vivo*
Microbial Infection Group
10–11 September
Organizer: N. Dorrell (nick.dorrell@lshtm.ac.uk)

● DNA 1953–2003: from structure to function
Physiology, Biochemistry & Molecular Genetics Group
10 September
Organizers: J. Hinton (jay.hinton@bbsrc.ac.uk), C.J. Dorman (cjdorman@tcd.ie) & R. Dixon (ray.dixon@bbsrc.ac.uk)

● *Young Microbiologist of the Year* finals

9 September

This competition is sponsored by the Society to encourage excellence in scientific communication by young microbiologists. Group Committees have now judged recent oral or poster presentations by members who are postgraduate students or postdocs who have gained their PhD in the past two years. The finalists from each Group go forward to compete for prizes at a special session of short oral presentations on their research. The best three entries win cash prizes:

- **1st:** £500
- **2nd:** £200
- **3rd:** £100

All finalists receive a year's free Society membership.

● 'History of Microbiology' Lecture

10 September

Origins and Birthdays: the double helix fifty years on

Speaker: Soraya de Chadarevian, University of Cambridge

This lecture will be open to the public and covers the fascinating story of molecular biology in the era of Watson and Crick.

Deadline for the receipt of titles and abstracts: **9 May 2003**

SPRING 2004 – 154th Meeting

University of Bath
29 March–2 April 2004

● Main Symposium (29–30 March)
Microbe–vector interactions in vector-borne diseases

● Other symposia and workshops

● Surface mediators
Cells & Cell Surfaces Group

● Imported infections
Clinical Microbiology Group/ British Infection Society

● Virology and occupational health
Clinical Virology Group
Organizer: B. Cohen

● Tailor made or off the peg? Teaching and learning resources for microbiology
Education & Training Group
Organizers: M.R. Adams & H. Sears

● Protein production using microbial systems
Fermentation & Bioprocessing Group
Organizers: M.G. Duchars & J. Miller

● Toxins
Microbial Infection Group
Organizers: O. Sparagano & N. Fairweather

● RNA–protein interactions
Physiology, Biochemistry & Molecular Genetics Group
Organizer: I. Stansfield

● Viruses and signalling (Symposium 1)
Virus Group
Organizers: W. Barclay & K.N. Leppard

● Viral hepatitis (Symposium 2)
Virus Group
Organizers: M. Harris, D.J. Rowlands & J. McLauchlan

● Workshops
Virus Group

Deadline for the receipt of titles and abstracts: **28 November 2003**

AUTUMN 2004 – 155th Meeting

Trinity College, Dublin
6–10 September 2004

● Main Symposium
Novel anti-microbial therapies

Irish Branch

Biocatalysis

UCD, 4–5 September 2003

Organizer: Kevin O'Connor (kevin.oconnor@ucd.ie)

Invited speakers: D. BOYD (Queens University Belfast), A. DOBSON (University College Cork), C. MURPHY (University College Dublin), F. HOEKS (Lonza AG, Switzerland), W. DUETZ (ETH Zurich) and C. KNOWLES (University of Oxford)

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

Other News and Events

● Bioinformatics Workshops

Following the success of the workshops held jointly by the SGM and The Sanger Centre in 2002 the following further events will be held this year:

Maynooth 13 June **Edinburgh** 25 July
Bristol 29 August **Birmingham** 19 September

Registration fees (to include lunch, refreshments and set of literature):

Company staff	£100
Academics (university & research institute)	£50
Postgrads/first postdocs	£20*

**Grants are available – see website*

Attendance is restricted to SGM members only.

Many members were disappointed last year because the available places filled so quickly. Register now to ensure your attendance. Full details of the workshops and a booking form are available on p. 84 and the SGM website (www.sgm.ac.uk/meetings).

● SfAM/SGM One-day Regional Meetings

A joint initiative to sponsor one-day regional meetings in the UK and Ireland has been launched by the SGM and the Society for Applied Microbiology. See the website of either society for the full rules and to download an application form: **www.sfam.org.uk** or **www.sgm.ac.uk**

The next Regional Meeting will be:

Transport of microbes through soils and the environment

University of Lancaster
18 September 2003

A short overview of the topic will be followed by a mixture of invited and offered presentations. Posters will also be displayed. There will be a prize for the best oral presentation by a microbiologist in the early stages of their career. If you would like to participate, please contact the organizers: Keith Jones (k.jones@lancaster.ac.uk) or Kirk Semple (k.semple@lancaster.co.uk).

Gradline

A job in... Science communication

SGM External Relations Office careers expert Jane Westwell takes a look at the opportunities for microbiologists in Science Communication.

If you would like to appear in a Job Profile, email **mtoday@sgm.ac.uk**

Other contributions for Gradline are always welcome on any topic relevant to microbiologists in the early stages of their careers.

Profile 1

Name Tracey Duncombe

Age 29

Present Occupation
Press and Communications Officer, Institute for Animal Health

Previous Employment
Public Affairs Administrator, SGM

Education
PhD, University of Liverpool, *The bioremediation of contaminated soil using mushroom compost*

BSc, University of Liverpool, *Microbial Biotechnology*

Q *How did you get into science communication?*

'I think it was a lucky accident. I attended a five-day residential course on personal development midway through my PhD. Afterwards I realized that if I was ever going to come across well during interviews then I had to practice speaking in public. Not long after I returned to the lab I saw an advert from NERC asking for PhD student volunteers to give a talk at something called the 'Stand up science show'. The show was part of the BA Festival of Science, which is the biggest UK science event for the general public. I'm not going to lie and say that I wasn't terrified of getting up in front of a packed theatre of 450 people, but once I'd given my talk I felt fantastic. Actually I think I got off lightly – one of the other students had to strip down to his boxer shorts! But it got me thinking that perhaps there were career options available to me other than research. I made it my priority during the remainder of my PhD to improve my communication skills and get more experience in this area.'

Q *How did you find the transition from lab based to administrative work?*

'Although I enjoyed research, I had the feeling that I was never going to be a brilliant scientist. Perhaps a small part of me regretted that I would not be running experiments ever again, but I was happy being able to do a job that played to my strengths, and that I found really enjoyable. One of my responsibilities was to write articles for *Microbiology Today*, in fact I was the previous Gradline Editor, so the tables have really been turned now!'

Q *What prompted your move to IAH?*

'My time at SGM gave me a taste of what it was like to work with 'the media'. We had some good news coverage too, of which I was very proud. But when I saw the advert for the job at IAH I knew that I couldn't let the opportunity pass me by. The media profile of the Institute has been very high over the last couple of years, perhaps most notably because of the UK foot-and-mouth disease outbreak in 2001, and our research on BSE and scrapie. Infectious diseases of farm animals are a continuing global problem, and as such research from IAH will always be of interest to the public, governments, and to the veterinary pharmaceutical industry. This was my chance to work more closely with scientists at the cutting edge of research, and also with journalists. But of course dealing with the press is not my only role. As communications officer I am responsible for organizing exhibitions at public events such as the Royal Show, as well as the annual competition for schools. I was also given the mammoth task of re-designing the Institute's website, which I am happy to say is now on-line.'

Q *What qualities make a successful science PR professional?*

'Being able to write (and speak) in plain English is a must. I would say the vast majority of scientific papers are inaccessible to the general public, and even to scientists from other disciplines. So the ability to 'translate' papers into a more accessible form is essential. Dealing with the press on a regular basis means that it is vital that you can work to short deadlines. Journalists usually need information before the end of the day, and you never know when they are going to call! You definitely have to be a 'people person'. I think it is important that, as well as being out-going, you listen to what people have to say. Above all I would say that you have to be dedicated. Science communication is a growing industry, and there are a number of MSc courses available now, so competition for jobs in this area is growing.'

Profile 2

Name Leigh Fish

Age 31

Present Occupation
eLearning Manager, Glasgow Science Centre

Previous Employment
2001–2003: Staff Scientist, Glasgow Science Centre

2000–2001: Exhibitions Coordinator, Glasgow Science Centre

1998–2000: Content Manager, At-Bristol Science Centre

1999 (secondment): Adult Education Science Tutor, University of Bristol

1997: Techfest (Aberdeen), Scitec (Derby) and Edinburgh International Science Festivals

1996: 'Genes Are Us' Exhibition Presenter

Education
PhD, University of Nottingham, *The role of N-acyl homoserine lactones in regulating secondary metabolism and virulence gene expression in Aeromonas species.*

BSc, University of Nottingham, *Applied Microbiological Sciences*

Q *What prompted you to leave research?*

'I've always been something of a communicator – and I started to enjoy facilitating public engagement with science sometimes a little more than doing the science itself! Throughout my undergraduate studies I had the opportunity to take part in university open days and also managed to do some work with the Wellcome Trust and MRC on genetics communication. As the events diversified, my experience grew, and the evaluation forms and feedback were positive. I knew communication was for me. During the remainder of my research career, I investigated ways of communicating science and getting paid for it. When a job offer came from the At-Bristol science centre (I'd badgered them incessantly) while I was writing up my PhD, I decided to leave research.'

Q *Did you have prior experience in science communication before applying for first job outside the lab?*

'Yes. Lots. Though I liked communication, I was not quite sure what my chosen career path would be after my BSc, so I found a fantastic PhD project and continued to consider my options during my research. I built upon my activities at open days and events during National Science Week, and gradually secured more and more senior and demanding roles. Science festivals and Science Week were among the most effective ways to get experience at the time, as there weren't many science centres around. Participation in lots of small projects worked for me, and is still one of the best ways into the field.'

Q *How did you find the transition from lab research to work in a science centre?*

'Very different. I joined a science centre in the early stages of creation where deadlines were tight and rapid results were needed. I didn't really get on there until I had submitted my PhD (never get a job while writing up – *never*). Once I could properly focus I moved rapidly from researcher, to exhibition developer, and eventually gained responsibility for the implementation of the *Get Connected* digital communications gallery. At opening it wasn't clear that there would be an on-going role in Bristol, but fortunately Glasgow chose to value my skills.'

Q *What aspect of your work gives you the most job satisfaction?*

'Simple – it's all in visitors' faces – when I help someone to find something on the internet, or when I do a demonstration or a talk, it's their look of understanding, seeing them smile, and the thank yous when we do something right. It's not always like that, but there are certain highs unattainable elsewhere when participating in a project that attempts to make science accessible to all – and succeeds most of the time.'

Q *What qualities make a successful science communicator?*

'Interpersonal skills, enthusiasm, sensitivity (to a visitor's needs), vitality and passion for the subject, flexibility (the job can involve unsocial hours), self-motivation and team working.'

Q *Do you have any advice for people thinking of a career in science communication*

'This can be a very difficult field to get into and it is sometimes necessary to take low paid or voluntary jobs just to get experience. The pay in science centres is relatively low (even with a higher degree and 5 years experience) and job security is rare. However, everyone in this field is committed, not in it for the money, and generally has a high level of job satisfaction (for as long as the post lasts) – it's a lifestyle choice.'

Further information about science communication careers

- ABSW (Association of British Science Writers) website (**www.absw.org**) features a list of science communication courses and a downloadable booklet *So You Want to be a Science Writer.*
- STEMPRA (The Science, Technology, Engineering & Medicine Public Relations Association) website (**www.stempra.org.uk**) features an on-line handbook *Practical Advice for Science Communicators* and a handy links page.
- The BA (British Association for the Advancement of Science) funds Media Fellowships for scientists with a minium of 2 years postgraduate experience. Information about this and other science communication activities from **www.the-ba.net.**
- Psci-com (**psci-com.org.uk**), sponsored by the Wellcome Trust, is a gateway to internet sites relevant to the public engagement with science. Psci-com also hosts a discussion list where many science communication posts are advertised.
- GEM (Group for Education in Museums) has a website (**www.gem.org.uk**) and discussion list, featuring job adverts.

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

Wanted...

Microbial menu items. We are going to post some microbial recipes on the web, such as ginger beer and yoghurt. If you have a favourite recipe that involves the use of microbes, please send it to us by email.

Enquiries:
education@sgm.ac.uk

Website:
www.microbiology online.org.uk

New Vocational Applied Science GCSE

Since September 2002 a new qualification has been available. The GCSE in Applied Science (Double Award) is one of several GCSEs in vocational subjects launched for students at Key Stage 4 and post-16.

These qualifications aim to: widen participation in vocationally related learning; increase progression routes to post-16 education and training; raise attainment levels; and clarify the equivalence between GNVQs and GCSEs.

Vocational GCSEs will appeal to students who:

- have an interest in vocational work-related qualifications as they provide the technical knowledge and understanding to equip students with some of the skills they will need in the workplace;
- wish to progress to other courses such as A/AS Levels, AVCE, BTEC National Diplomas, NVQs or modern apprenticeships;
- want variety in the way they work and are assessed at Key Stage 4 as it provides a range of teaching, learning and assessment styles;
- are encouraged by working independently.

Applied Science (Double Award)

This course helps to prepare a student for involvement in scientific issues in everyday life. To understand the nature of applied science the student must actively experience science in the work place environment. This can be achieved through approaches including work experience, links with local employers and research establishments, case studies and research. This qualification is accredited at Levels 1 and 2 (Foundation and Intermediate) of the National Qualifications Framework and provides candidates with a progression route to Foundation and Intermediate GNVQs, NVQ and VCE.

Examples of employment to which the Applied Science student might progress include: medical technician, pharmaceutical technician, and laboratory technician in industry, service sectors or education.

The course includes three mandatory units and microbiology is covered in some depth in all three.

- **Developing scientific skills**

The importance of health and safety in the work place; carrying out standard procedures; handling scientific equipment and materials; recording and analysing observations. Microbiology in this unit includes:

Microscopy

- set up a light microscope ready to use, choosing a suitable objective lens for the task;
- prepare samples for investigation, including making a temporary slide, using a staining technique

Working with micro-organisms

- understand the importance of aseptic techniques and be able use them to culture micro-organisms and dispose of them safely;
- investigate the effects of anti-microbial agents on micro-organisms;
- set up a culture, which will produce a useful product such as a food substance.

- **Science needs of society**

The application of science to benefit society. This includes exploring the use of living organisms. In this unit students study the beneficial role of microbes including production of beer, bread, wine, yoghurt and antibiotics as well as the harm that they cause to us, or to plants and animals. Students have to:

- describe the use of bacteria, yeasts and other fungi in food and in medicine production;
- know that diseases may be caused by micro-organisms and name some examples (limited to measles, mumps, rubella, polio, TB, foot-and-mouth, athlete's foot and skin infections due to *Staphylococcus aureus*;
- give examples of a range of methods of protecting against infection by harmful micro-organisms in food production (personal hygiene, sterilization, disinfectants, antiseptics);
- understand about the use of immunization to protect humans and other animals from infection by specific micro-organisms (limited to MMR, TB, foot-and-mouth, polio);
- know that antibiotics may kill some bacteria, but not viruses.

- **Science at work**

Explores practical skills and the roles scientists have in their workplaces; develops scientific skills through monitoring living organisms. Students have to:

- identify the types of scientific activity that are carried out and the job titles and qualifications of the people that perform them;
- find out what skills scientists need in addition to their qualifications;
- find out what careers are available in science and science-related areas.

The unit includes practical investigations.

● ***Dariel Burdass, Education Projects Administrator***

New resource – *Cold Wars*

Launched on Red Nose Day, this new factsheet for Key Stages 2 and 3 explains what the common cold is, what causes it, how colds are spread and how we can develop immunity to the strains of cold virus that we encounter throughout life. An exciting investigation called 'Stop that rhino in its tracks' reinforces how colds are spread through poor hygiene. This is safe and fun as glitter gel is used to simulate the virus – no laboratory conditions are required.

The factsheet can be downloaded in full colour from: **www.microbiologyonline.org.uk**. Just click on 'Red Nose' on the front page.

International Research Fellowship reports

Identification and epidemiological typing of *Legionella* species using genotypic methods

Laura Franzin

I was really very happy when the SGM accepted my application for a two-week research visit, hosted in January 2003 by Dr Norman Fry of the Respiratory and Systemic Infection Laboratory at the Central Public Health Laboratory (CPHL) in London.

Legionella is a respiratory pathogen, responsible for severe pneumonia. In my laboratory in Turin, we had obtained several isolates of *Legionella bozemanii* from a patient and the hospital environment that required further characterization. The SGM grant allowed me to carry out molecular typing of these strains.

The scientific objectives of my visit were: (1) to confirm the identity of the presumptive *L. bozemanii* clinical and environmental isolates from Turin by macrophage infectivity potentiator gene (*mip*) sequencing; (2) to epidemiologically type the isolates by amplified fragment length polymorphism (AFLP) and fluorescent-AFLP (f-AFLP) analysis; (3) to look for microbiological evidence of the source of the infection; and (4) to compare these data with those obtained from UK isolates.

Genotypic *mip* sequence-based identification (first described by Dr Rod Ratcliff, University of Adelaide, Australia) was carried out on 16 Turin isolates by PCR amplification, purification of the amplified products and sequencing. Nucleotide sequences were determined using the dideoxynucleotide method and by analysing the products on an automated fluorescent DNA analysis system (CEQ 8000; Beckman Coulter). Sequence analysis was performed using BioNumerics (Applied Maths) and data were compared to a comprehensive database of all available *Legionella mip* sequences. AFLP was performed using the Standard European Working Group on *Legionella* Infections Protocol. Agarose gels were photographed under UV transillumination, scanned and saved. The files were normalized and analysed using BioNumerics and clustered using the Pearson correlation similarity coefficient. The f-AFLP analysis was performed using a two enzyme and primer combination. One primer was labelled with Beckman Dye-4. The f-AFLP traces of the labelled fragments were analysed using a numerical character type with a simple matching similarity coefficient.

The *mip* sequence data confirmed the identity of all Turin isolates as *L. bozemanii*. To date there are at least five distinct *mip* gene sequences of *L. bozemanii* strains, and the *mip* sequence type of the Turin strains showed complete homology with one of these types found in strains from Australia and the UK. The AFLP method showed that all the clinical and environmental *L. bozemanii* Turin isolates were highly related to each other and that the AFLP profiles were distinct from the type strain (included as a reference). The f-AFLP method also showed a high level of similarity for the profiles obtained with clinical and environmental isolates tested, which were also distinct from the profile obtained with the type strain.

In conclusion, the *mip* sequence, AFLP and f-AFLP data support the hypothesis that the hospital contained a reservoir of a dominant clone of *L. bozemanii*. The clinical and environmental isolates showed a very high degree of similarity using three methods of analysis. However, to confirm that this clonal lineage of *L. bozemanii* is endemic to the hospital, we intend to seek further clinical and environmental isolates of *L. bozemanii* from unrelated sources in Italy and compare them with UK isolates.

I would like to thank the SGM for awarding the fellowship and Dr Jane Westwell for her helpful advice. My scientific visit at the PHLS Central Public Health Laboratory was very profitable and pleasant. I am very grateful for assistance and kindness from Dr Norman Fry, Dr Tim Harrison and Dr Baharak Afshar. I would also like to acknowledge the helpful support of Dr Robert George, Director of the Respiratory and Systemic Infection Laboratory and Frances Knight, Operations Manager, CPHL.

Laura Franzin, Infectious Diseases Unit, University of Turin, Amedeo di Savoia Hospital, Turin, Italy.

BELOW:
Laura and Dr Baharak Afshar (Bee), the *Legionella* Project Scientist.
COURTESY MEDICAL ILLUSTRATION DEPARTMENT, CPHL

TOP LEFT:
The author taking a moment out of the busy schedule at UCSF to blow up an inflatable cheetah!

BOTTOM LEFT:
The research group of Craig Cameron (Pen State). Craig is pictured fifth from the right with checked shirt and glasses.

PHOTOS COURTESY IAN GOODFELLOW

Analysis of RNA structures involved in poliovirus replication

Ian Goodfellow

Although poliovirus no longer poses a serious medical threat, its study has given virologists a much greater understanding of how positive-stranded RNA viruses interact with the host cell and how this interaction leads to genome replication. Poliovirus is arguably one of the best studied of all RNA viruses and has long been used as a model system for many of its more economically important relatives; examples of which are the common cold virus (Rhinovirus) and foot-and-mouth disease virus (FMDV). One of the major benefits of using poliovirus as a model system is the availability of a cell-free replication system capable of replicating *in vitro* transcribed RNA to form progeny virus particles. The cell-free replication also allows the dissection of the intricacies of the viral genome replication cycle – many features of which are currently impossible to dissect using cell-based systems.

Although over 10 years old, the cell-free replication system, which is based on cytoplasmic extracts from permissive cells, still remains something of a 'black box' as very few labs can consistently reproduce the system. One such lab at UCSF (San Francisco), headed by Raul Andino, has been at the pinnacle of poliovirus research for many years. They have had a long-term interest in vaccine development and more recently their work has focused on the role that RNA interference plays as an intracellular anti-viral defence mechanism. This lab was the obvious choice for me to gain the necessary experience to address the role that small RNA structures play in genome replication. Specifically, I was interested in two RNA structures, one located in the middle of the poliovirus genome and the other located at the 3′ end of the genome.

In total I spent six weeks at UCSF, beginning in September 2002 – one of the hottest months in California, which didn't seem to deter the San Francisco fog at all. During this time I prepared extracts from over 20 litres of highly permissive cells. Using these extracts we were able to address the role that a small RNA structure in the centre of the poliovirus genome played in genome replication, and also the role that an RNA structural element at the 3′ end of the genome plays in genome replication.

The second part of my research trip was made to the lab of Craig Cameron at Pen State University. Craig's lab is something of a newcomer to the RNA virus replication field, but in a short time they have made a major impact with a somewhat unique approach to their research. They have used highly optimized expression and purification schemes to purify viral RNA-dependent RNA polymerases. Their lab specializes in using highly quantitative enzyme kinetic analysis to study every feature of RNA-dependent RNA polymerases. In addition to their outstanding work on poliovirus and hepatitis C virus replication, one of their recent major findings was that the antiviral Ribavirin, often used in the treatment of hepatitis C infection, functions as an RNA virus mutagen essentially forcing the virus into error prone catastrophe.

The purpose of my visit to Pen State was to address the effect that a mutation in viral-RNA-dependent RNA polymerase, which suppresses a structural mutation in the 3′ end RNA structure, has on its various activities using highly quantitative enzyme kinetics. In the two weeks I spent at Pen State, I not only managed to purify the viral polymerase in sufficient quantities to address these problems, but also learnt the technologies to allow me to perform the technically difficult enzyme kinetic analysis back in Glasgow. Craig and the rest of his group went out of their way to make me feel very welcome and I was also privileged enough to get to see the Pen State American football team play at home – with the stadium holding around 110,000 screaming fans it was certainly an exhilarating experience, even if it was well below freezing!

The trip was a fantastic experience and I thank the SGM immensely for giving me this opportunity. It has left me feeling very enthused, but also exhausted. That said I would highly recommend such a research visit to anyone. The work carried out has added greatly to our understanding of the role of these small RNA structures in genome replication and has formed the basis of two research papers. I would particularly like to thank Raul Andino and Chanti Polacek (UCSF), Craig Cameron and Christian Castro (Pen State), as well as all the members of their labs for taking time out from their work to accommodate me in their labs and making my trip truly worthwhile.

For more information on the research groups mentioned above please see
http://www.polio.vir.gla.ac.uk
http://www.ucsf.edu/andino/
http://phonechatter.bmb.psu.edu/

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Hot off the Press

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

Witches' brooms

A new disease of almonds, an economically important crop in most Mediterranean countries, has emerged in the Lebanon in recent years. Bushy clusters of twigs with small yellowing leaves develop on the tree, called witches' brooms because of their unnatural appearance. No flowers or fruit develop on the tightly packed twigs and normal parts of the branches become starved. The witches' brooms themselves do not live long and after a few years the entire tree can die.

These disease symptoms are caused by several pathogens, but researchers at the Lebanese Agricultural Research Institute in Zahle, working with French scientists from the Institut National de la Recherche Agronomique at Villenave d'Ornon have discovered that this particularly devastating disease is caused by a phytoplasma. These are bacteria-like organisms except that they lack a cell wall and cannot be grown outside their host plants. Symptoms develop slowly, and are frequently spread by sap-sucking insects, so that once the symptoms are obvious, the pathogen may already have spread to many other, apparently healthy, plants. The European Union considers these infections so seriously that affected plants must be quarantined.

The researchers suspected that a phytoplasma caused the disease because they had detected typical phytoplasma genetic material within diseased almond trees. They have now reported a detailed examination of the pathogen, and a specific test for it in a recent issue of IJSEM. Electron microscopy revealed the characteristically small and irregular phytoplasma cells in the sieve tubes of petioles and midveins of infected leaves.

DNA was extracted from both symptomatic and healthy midveins and tested for DNA typical of phytoplasmas. This involved using two short pieces of DNA that should match all phytoplasmas, along with an enzyme to copy the DNA between the pieces. Phytoplasma DNA was consistently detected only in the diseased plants, and the sequence of the DNA copy was very similar, but not identical to other phytoplasmas. The nearest ones were members of the pigeon pea witches'-broom group, rather than phytoplasmas that infect other fruit trees. Worryingly, the sequence was virtually identical to one from a phytoplasma detected in Iran that was implicated in 'almond brooming disease', suggesting that the pathogen might be present and spreading across the Middle East. This new phytoplasma has been given the *Candidatus* designation (owing to its non-culturability) '*Candidatus* Phytoplasma phoenicium' sp. nov.

Verdin, E., Salar, P., Danet, J.-L., Choueiri, E., Jreijiri, F., El Zammar, S., Gélie, B., Bové, J.M. & Garnier, M. (2003). '*Candidatus* Phytoplasma phoenicium' sp.nov., a novel phytoplasma associated with an emerging lethal disease of almond trees in Lebanon and Iran. *Int J Syst Evol Microbiol* 53, in press.

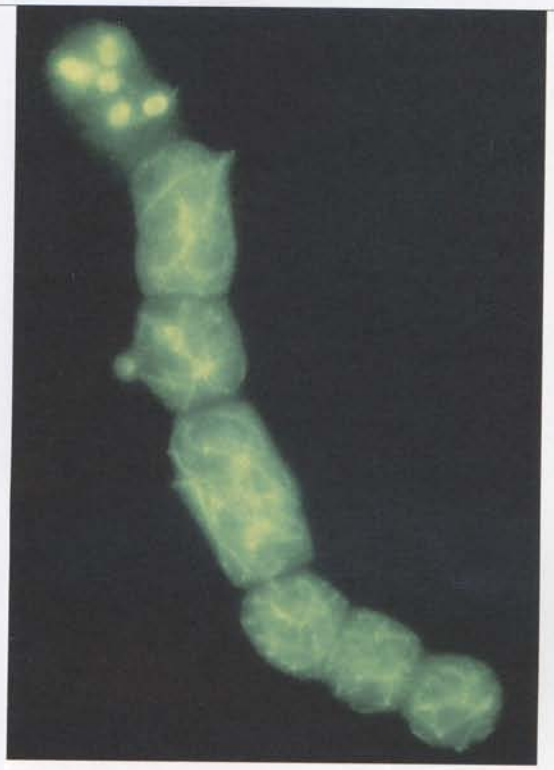
Sensitive test for hepatitis B

More than 350 million people across the world suffer persistent liver disease caused by hepatitis B virus (HBV) even though vaccination and antiviral drugs are reducing the number of new infections. The exact level of viral DNA in blood fluids is a useful way to monitor the progress of antiviral therapy, and there are several commercially available methods. One of the current favourites is the Hybrid Capture II HBV Test (HBII) from the Diagene Corporation. Although it is not as accurate or sensitive as some others, it beats them on technical simplicity, reproducibility and lack of susceptibility to contamination.

Researchers at Queen Mary Hospital in the University of Hong Kong have been comparing it with a new method that uses LightCycler real-time PCR (LC-PCR) from Roche Diagnostics to see if the latter offers any advantages. This exploits recent developments in the equipment for doing PCR, the Nobel Prize-winning technique used to make millions of copies of a specific sequence of DNA. The new instruments allow the build-up of DNA copies to be detected continuously, rather than only at the end of the reaction. This cuts out many of the time-consuming steps that used to be required when using PCR to amplify a DNA sequence. The Chinese researchers have been working on methods of HBV detection for almost a decade and have been able to use all their experience to design and conduct a comparison of the two methods.

Neither method yielded a positive result from 45 people who were free of HBV infection, indicating that they both had excellent specificity for HBV. However, of 120 people who were infected, LC-PCR correctly identified 95 % of them, while HCII only detected 56 %. The difference was primarily due to the sensitivity of the assays. LC-PCR could detect as few as 250 copies of the viral DNA per millilitre of blood, while the detection limit of HCII was almost 600 times higher. One other big difference between the methods was that, starting from blood serum, LC-PCR only took 2·5 hours to produce a result. The researchers concluded that LC-PCR certainly offers another option for both clinicians and researchers who want to monitor a patient's viral load.

Ho, S.K.N., Yam, W.-C., Leung, E.T.K., Wong, L.-P., Leung, J.K.H., Lai, K.-N. & Chan, T.-M. (2003). Rapid quantification of hepatitis B virus DNA by real-time PCR using fluorescent hybridization probes. *J Med Microbiol* 52, 397–402.



LEFT:
Fluorescent micrograph of *Aureobasidium pullulans* stained for microtubules using TAT1 monoclonal anti-tubulin antibody (yellow).
COURTESY K. GULL, MANCHESTER, AND M. GABRIEL AND M KOPECKÁ, BRNO, CZECH REPUBLIC

H. pylori defence systems

The bacterium *Helicobacter pylori* has been implicated in peptic ulcers and other stomach diseases. The bacteria persist in the stomach lining, despite the inflammation that their presence causes. Increasing numbers of host cells flood to the inflamed site, all with the objective of secreting toxic compounds to destroy the bacterial cells. Many of the toxins are reactive oxygen species, like hydrogen peroxide and superoxide anions. Scientists think that one of the secrets to *H. pylori*'s survival is its sophisticated and numerous defence mechanisms against these oxidants. Australian researchers have now demonstrated that two of these systems are indeed essential if the bacterium is to cause a persistent infection within mice.

The systems are a protein for an enzyme called KatA that acts as a catalase to remove hydrogen peroxide, and a second protein called KapA, for KatA-associated protein, whose function is unknown. However, its gene is located next to the one for KatA in the *H. pylori* genome and it has a role in protection against hydrogen peroxide *in vitro*, although not as a catalase. The researchers created strains of *H. pylori* that lacked the genes for KatA or KapA and then infected mice with these bacteria. After 8 days, 3 months and 6 months the researchers killed some of the mice and examined their stomachs for signs of both bacteria and inflammation. The control group that was infected with the parent strain of *H. pylori* with its full ability to remove oxygen radicals set up an infection in all the mice, and it became more acute as time went on. In contrast, by the end of 6 months, the strains without KatA, and particularly without KapA, had disappeared from many of the mice.

The researchers are confident that their results demonstrate that resistance to oxidative stress is essential for the long-term survival of this pathogen in an inflamed stomach, and that the KatA and KapA proteins form a crucial part of that defence.

Harris, A.G., Wilson, J.E., Danon, S.J., Dixon, M.F., Donegan, K. & Hazell, S.L. (2003). Catalase (KatA) and KatA-associated protein (KapA) are essential to persistent colonization in the *Helicobacter pylori* SS1 mouse model. *Microbiology* 149, 665–672.

Development of antifungals against the black yeast

The black yeast *Aureobasidium pullulans* is unusual. Although its usual habitat is decaying wood, it can be an opportunistic pathogen of plants, and also animals, including humans. It has been found in a number of very unpleasant infections, usually in patients who are already immunocompromised. Treating these conditions is difficult, because there are only subtle differences between a fungus and a human that can be exploited for antifungal therapies.

Researchers at Masaryk University in the Czech Republic have worked with colleagues at Chiba University in Japan to study the development and organization of *A. pullulans*, hoping to find clues for new antifungal drugs. Their observations are also intrinsically interesting because, unlike other yeasts, the cells in one culture can exist in a variety of sizes and shapes with variable numbers of nuclei. In optimal growth conditions, with ample nutrients and aeration, the cells grow as long, thin multi-nucleate hyphae. The nuclei are regularly spaced along the hypha, and thick bundles of microtubules line the cell walls. These microtubules, along with structures formed from the protein F-actin, make up the cytoskeleton that gives structure and shape to the cells. They are also essential in directing the flow of nutrients along the long cells. The researchers were particularly interested to see whether the cytoskeleton was different in various types of cells, or went through characteristic changes as the culture aged and began to produce spores.

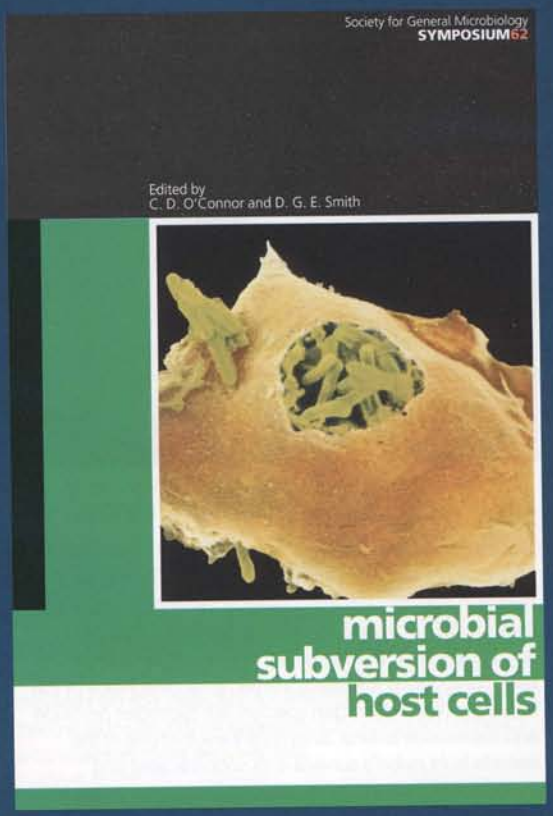
They spotted that F-actin was located only at the tip and in a few rings around young hyphae, and that these were the sites where cross-walls and spores appeared as the hypha aged. Other changes occurred to the microtubules in synchrony with division of the nuclei, indicating a possible role in positioning of the chromosomes. Their observations have laid the basis for further studies on the susceptibility of the fungus to antifungal agents, focusing attention on those that disrupt microtubules and thus a fundamental step in the life cycle of the fungus.

Kopecká, M., Gabriel, M., Takeo, K., Yamaguchi, M., Svoboda, A. & Hata, K. (2003). Analysis of microtubules and F-actin structures in hyphae and conidia development of the opportunistic human pathogenic black yeast *Aureobasidium pullulans*. *Microbiology* 149, 865–876.

SGM Symposium Vol. 62 review

Microbial Subversion of Host Cells
SGM Symposium Vol. 62

Edited by C.D. O'Connor & D.G.E. Smith
Published by Cambridge University Press (2003)
Non members: £75.00/US$125.00
Members: £30.00/US$50.00
pp. 258. ISBN: 0-521-82998-4



I have been asked to review this book pre-publication and indeed before the symposium around which it is based has been held. If the talks at the symposium are even half as good as the book then it will be one of the best SGM symposia for years. Quite simply it has been a pleasure to review this volume. Normally when asked to review a book with a short deadline the temptation can be to skate over bits of it that are maybe a little outside one's own knowledge or interests and to concentrate on the bits that one finds most comprehensible or most easily reviewed. In contrast I read this book avidly from cover to cover, every word of it.

The central subject matter of the book is the fast-moving and exciting field often called cellular microbiology. There are many excellent scientists working in this field, and this symposium brings together a varied selection from amongst them. I particularly like the fact that bacterial and viral research is brought together here, something that is always informative and interesting, and not done often enough. I would strongly recommend that bacteriologists and virologists reading this book do not stick to reading only those chapters directly related to their fields. There is something for everyone in each of the chapters. Perhaps a slight omission from the content of the symposium, and therefore from the book, is a presentation from the world of parasitology, which I am sure would have provided an excellent added dimension to the piece. Somebody would have had to have been replaced if this were to happen, however, and it is difficult to see which chapter could have been dropped to make room, as they are all of a very high quality.

I suppose that a book reviewer has to try to find something to be negative about, but I have to admit that it has been difficult to do with this one. If I were to be hyper-critical about the balance of the book, I would say that there is possibly too much emphasis on presentations about type three secretory systems (TTSSs), which could possibly have been condensed somewhat. But this does reflect the enormous interest in TTSSs in the scientific community at the moment, as well as their importance in the determination of virulence in diverse pathogens. The book might have been strengthened by the inclusion of chapters on other pathogens, especially *Neisseria* spp. and there is also a slight lack of coverage of cellular responses to non-protein virulence determinants. Finally, I would have liked an introductory chapter at the start of the book from a card-carrying cell biologist given a remit to produce an overview of the eukaryotic cell and its processes. This would have allowed those prospective readers new to the field to orient themselves from the start in the complexities of normal cell biology before considering how pathogens subvert these processes. However, all of this minor criticism is overwhelmed by the excellence of the contributions that have been included.

I think that the target audience for this book should include all research scientists involved in trying to understand the host–pathogen relationship, as well as anyone with an interest in how eukaryotic cells and pathogens have co-evolved such that many econiches and mechanisms within the cell are utilized. I would venture to suggest that the book might also be interesting for cell biologists who might not be aware of the massive strides being taken by those studying pathogenesis in concomitantly understanding particular aspects of normal cell biology. As far as students are concerned the book provides a useful and up-to-date review of many areas of interest for final-year undergraduate science students studying pathogenesis, and should be required reading for any PhD students working in this field. At the time of writing the review I do not have pricing information. I expect that the SGM's usual reasonable pricing policy will be applied, so that this book will be great value for money for individual purchasers, and that libraries in institutions with researchers studying pathogenesis should definitely buy the book.

To sum up, I think that this is a tremendous book, full of well-presented up-to-date information covering a wide range of subjects related to cellular microbiology. Books of symposia proceedings can often become curate's eggs with the bad bits not always outweighed by the good. This volume only contains good bits and I therefore have no hesitation in recommending it to all of my colleagues with any interest at all in this field.

■ ***Duncan Maskell, University of Cambridge***

An order form for Symposium Vol. 62 (and earlier volumes in the series) appears on p. 97.

Reviews

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

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

A list of publisher's website addesses is given on p. 91.

Viral Hepatitis: Diagnosis, Therapy and Prevention

Edited by S. Specter
Published by Humana Press (1999)
US$110.00, pp. 416
ISBN: 0-89603-424-0

This book gives a broad coverage of viral hepatitis, including virology, diagnosis, therapy and prevention. The first five chapters deal in alphabetical order with each of the five viruses known to be responsible for hepatitis in humans, while the sixth chapter concerns hepatitis G virus, which is now thought not to be associated with liver disease. These chapters cover the basic features of the agents, including such aspects as their genome structure and replication, epidemiology, pathology and immunology. They are followed by chapters on diagnosis and chemotherapy and separate chapters on vaccines for HAV and HBV, the only hepatotrophic viruses for which they are available. The general style of the book is comfortable and easy to read. It would be a useful addition to the book collections of gastroenterologists and for medical students with an interest in hepatology.

■ ***Dave Rowlands***
University of Leeds

Influenza in Practice

By R. Jennings & R.C. Read
Published by The Royal Society of Medicine, London (2002)
£14.95, pp. 56
ISBN: 1-85315-514-4

This is a brief guide on issues related to influenza, written mainly for general practitioners and the general public. Thus, description of the virology and immunology is short. There is more emphasis of pathogenesis, clinical assessment, immunization, specific treatment and general clinical management. The epidemiology chapter is too condensed, and specific influenza surveillance schemes, including the GP 'spotter practice' scheme, should have been covered in the text. The DH Pandemic Plan could have been outlined. The therapeutic applications of neuraminidase inhibitors are over-emphasized. Citations of the literature are generally up-to-date. The indication of relevant websites is very useful. On the whole, a useful guide for most practical purposes.

■ ***Ulrich Desselberger***
Cambridge

The Human Immunodeficiency Virus: Biology, Immunology, and Therapy

Edited by E.A. Emini
Published by Princeton University Press (2002)
£52.00/US$75.00, pp. 532
ISBN: 0-691-00454-4

This book is an in-depth and yet very readable overview of the current and potential future approaches to combat the global problem of HIV infection. It is written by leading researchers in the field and describes the molecular biology, immunology and pathogenesis of HIV in great detail. Strategies of antiviral intervention based on viral as well as cellular targets are explained. Furthermore, social approaches to prevention of infection, as well as drug- and vaccine-based ones are described. This book represents an excellent resource for both students and researchers in the field. Unfortunately, however, the cover price is such that it is likely to be out the reach of most students. My only real criticism of the book is that some of the figures could be a little clearer, benefiting from the use of colour.

■ ***Christopher Ring***
Glaxo SmithKline R&D

Gene Regulation: a Eukaryotic Perspective. Fourth Edition

By D.S. Latchman
Published by Nelson Thornes (2002)
£30.00, pp. 323
ISBN: 0-7487-6530-1

As with movies, there are the big American epics in the world of textbooks. And then there are the more modest English language productions which, to pursue the analogy with the world of cinema, are often British in origin. This book by David Latchman falls very definitely into the latter category. But, to return again to the movies, the product is often well crafted and deserves to enjoy popular success. The same can be said of Latchman's book.
In this fourth edition, Latchman has once again provided an excellent (and thoroughly updated) account of the process that leads from the gene to the gene product. Trying to understand the web of interconnecting threads that contribute to gene regulation can be quite a challenge, and students in biochemistry and molecular biology will find this book a valuable aid in learning. The illustrations are simple but elegant, and easy to assimilate.

■ ***Philip Meaden***
Heriot-Watt University

Human Microbiology. Lifelines Series

By S.P. Hardy
Published by Taylor & Francis (2002)
£15.99, pp. 261
ISBN: 0-415-24168-5

This book is divided into two parts, the first and largest of which covers the basics of bacteria, viruses and fungi, including structure, mode of growth and death. It tackles, in a very clear way, topics which students tend to find difficult, such as bacterial growth rate, redox potential and some of the basics of bacterial metabolism. These are well and simply explained making the topics readily accessible. This part of the text would be extremely useful for students studying any aspect of microbiology, not just human. The second smaller part of the book considers microbial infection almost exclusively from the point of view of the infecting agent with no emphasis on the immune response. Due to brevity, some aspects have been simplified to the point where, without reference to other texts, misunderstanding could creep in. Students requiring basic understanding of microbial–host interaction would therefore need to use this book in conjunction with other sources to obtain a clearer idea of the overall picture.

■ ***Sheila Patrick***
The Queen's University of Belfast

DNA Vaccines: Methods and Protocols. Methods in Molecular Medicine, Vol. 29

Edited by D.B. Lowrie & R.G. Whalen
Published by Humana Press (1999)
US$119.50, pp. 520
ISBN: 0-89603-580-8

This is one of the many Humana Press volumes devoted to 'methods in molecular medicine' and follows the usual format for books in this series. It comprises more than 40 short chapters, each dealing with specific practical aspects of DNA vaccination and providing detailed experimental protocols. It is little more than 10 years since the concept of naked DNA vaccination burst upon the scientific community and many of the contributors to this volume were intimately involved in the early discovery stages of the science. DNA vaccination has yet to fulfil some of the extravagant hopes that were expressed initially and, as is so often the case, it is far more complex than originally thought. Work on the development of DNA vaccines continues apace for a huge range of potential applications and this book will be invaluable for any laboratory involved in research in this field.

■ ***Dave Rowlands***
University of Leeds

Encyclopedia of Evolution, Vols 1 & 2

Edited by M. Pagel
Published by Oxford University Press (2002)
US$260.00, pp. 922
ISBN: 0-19-512200-3 (2-vol. set)

This intriguing pair of books truly deserves a place on the coffee table, as they comprise an excellent collection of short essays on almost every topic related to evolution. The essays vary in length, but are rarely more than a couple pages, making them a short stimulating read (who needs the caffeine?), with a splendid group of slightly longer overview essays at the beginning. The contributors list reads like a who's-who in evolution research. The topics are organized, in good encyclopaedic tradition, alphabetically, so this is a dip-in rather than cover-to-cover read. The only problem I found was the index, which did not include many of the concepts I tried looking up, so navigation was an issue.
I would guess the level to be suitable for undergraduates, but given the rapid developments in thinking, they are also a good catch-up for those of more mature years.

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

Polymicrobial Diseases

Edited by K.A. Brogden & J.M. Guthmiller
Published by American Society for Microbiology (2002)
US$115.95, pp. 446
ISBN: 1-55581-244-9

This is an interesting and informative volume bringing together polymicrobial and/or dual infections in both the human and veterinary world. Detailed discussion of the molecular mechanisms underlying pathogenicity of enhanced disease caused by multiple organisms is rather variably discussed, with some systems faring rather better than others. Although co-infections with human retroviruses are reasonably well covered, there are some significant gaps, in particular a chapter on human sexually transmitted diseases would have been appropriate in this book to consider bacterial and viral genital infections, particularly as they might impact on the transmission of blood-borne sexually transmissible viruses. Nevertheless, it is extraordinarily useful to have together in one volume diverse examples of multiorganism disease in different animal species and discussion of the ensuing pathology. This book is recommended for institutions and academic centres/laboratories with a strong interest in the pathogenesis of infectious disease and the study of microbial pathogenicity. It is likely to be beyond the budget of an individual researcher, but would be a welcome addition to human and veterinary clinical microbiology laboratories.

■ ***Maria Zambon***
PHLS, Central Public Health Laboratory, London

Hepatitis B & C: Management and Treatment

By T. Poynard
Published by Martin Dunitz (Taylor & Francis) (2001)
£19.95, pp. 120
ISBN: 1-84184-077-7

This little book summarizes the current status of the clinical perspectives on hepatitis B and C virus-related liver disease. The book is small, inexpensive and deals with the subject in a series of short 'bullet point' style chapters (some comprise a single paragraph). There are a number of clear tables and figures illustrating and summarizing information such as response rates to therapeutic regimes and the clinical consequences of infection. Much of the coverage of hepatitis B virus relates to the use of the antiviral drug lamivudine in comparison to interferon. For hepatitis C, results from clinical trials of interferon, native or pegylated, and of combination treatments including ribavirin are presented. The book includes comments on cost-effectiveness of treatment, goals of therapy and practical guidelines. It will be of value to practising hepatologists and medical students.

■ ***Dave Rowlands***
University of Leeds

Principles and Practice of Clinical Virology. Fourth Edition

Edited by A.J. Zuckerman, J.E. Banatvala & J.R. Pattison
Published by John Wiley & Sons (1999)
£175.00, pp. 800
ISBN: 0-471-97340-8

This is the latest update of the authoritative book *Clinical Virology* first published in 1987 and last updated in 1994. The book is a well established standard reference volume and this most recent edition will be a welcome addition to the infectious diseases section of any medical library. It might also be illuminating for some 'molecular' virologists to browse through its pages and wonder at the clinical importance of their favourite laboratory toys. It is authored by an impressive list of contributors, most of whom had provided chapters for earlier editions and have now brought these up to date. A few chapters are by new contributors who have maintained the high standards typical of the publication. Significant advances have been made in the diagnosis, prevention and treatment of viral disease in recent years and it is important that these have been included in a new edition of this book.

■ ***Dave Rowlands***
University of Leeds

Essentials of Antimicrobial Pharmacology: A Guide to Fundamentals for Practice

By P.H. Axelsen
Published by Humana Press (2001)
US$39.50, pp. 152
ISBN: 0-89603-842-4

For a book on pharmacology there is a great deal of microbiology included here. This is a very useful up-to-date text which summarizes antimicrobial agents in general as well as including a valuable chapter on Immunomodulators and immunizing agents. Its brevity means that the microbiological content is not presented in depth; nevertheless, it provides a simple user-friendly guide. Its usefulness is slightly impaired by some confusion over names of organisms, and by a printing error affecting sub-headings. However, its simple descriptions of antimicrobials and many useful figures mean that this book will be of benefit to any student trying to understand the properties of antimicrobial agents and its market should not be limited to medical students. Unfortunately, for its size, it is not cheap and its price may put off prospective purchasers.

■ ***Adrian Eley***
University of Sheffield

Clinical Virology, Second Edition

Edited by D.D. Richman, R.J. Whitley & F.G. Hayden
Published by American Society for Microbiology (2002)
US$159.95, pp. 1,338
ISBN: 1-55581-226-0

This large and comprehensive book, edited by eminent clinical virologists from the USA, is intended for practising clinicians. Clinical virology is a rapidly changing field, but every attempt has been made to make this book as up-to-date as possible. It is divided into three sections, viral syndromes and general chapters, the viruses which cause human disease and subviral agents (hepatitis D and transmissible spongiform encephalopathies). The virus chapters include virus structure and replication, pathogenesis, epidemiology, clinical manifestations, prevention and treatment. Recently discovered viruses, such as the zoonotic paramyxoviruses and TTV are included. Laboratory techniques are not described in detail, but each chapter is comprehensively referenced. The book contains many good diagrams, but some of the prints are not clear and would have been better in colour.
It would be a good buy as a reference book. However, European practices may sometimes differ from those described, especially for viruses such as rubella, which are close to elimination in the USA.

■ ***Jenny Best***
Guy's, King's and St Thomas' School of Medicine, London

Introduction to Modern Virology, Fifth Edition

By N.J. Dimmock, A.J. Easton & K.N. Leppard
Published by Blackwell Science (2001)
£27.50, pp. 449
ISBN: 0-632-05509-X

Since its publication in 1974 *Introduction to Modern Virology* has deservedly become a standard student textbook for many university virology courses. The book is written and produced with this objective in mind; the subject is clearly presented and well illustrated with simple cartoon-style figures. It is also reasonably priced. The authorship has changed since the publication of the fourth edition in 1994; Easton and Leppard having replaced Primrose, but the style of the book is unaltered. The text has been updated where necessary and there have been some relatively minor changes in the overall structure. For example, gene expression has been split into two chapters, one dealing with DNA and the other with RNA viruses. Towards the end of the book there is a chapter on future trends and it is interesting how many of the 'problem areas' mentioned in the fourth edition are still highlighted in the fifth.

■ ***Dave Rowlands***
University of Leeds

Nuclear Export of Viral RNAs. Current Topics in Microbiology and Immunology, Vol. 259

Edited by J. Hauber & P.K. Vogt
Published by Springer (2001)
60.95, pp. 131
ISBN: 3-540-41278-6

Increasingly, research of viral replication includes investigations of cellular proteins interacting with viral components (nucleic acids, proteins). During the last 10–15 years many such proteins with particular functions have been identified in different virus–host cell systems. This volume brings together data for herpes, adeno, and retroviruses for the circumscribed area of nuclear export of viral RNAs/mRNAs and also data on constitutive nuclear export and the nuclear pore complex. There is a useful chapter reviewing methods and assays to investigate nuclear export. The virus-specific chapters are written very competently and with great attention to detail. The references are up-to-date for 1999/early 2000. It is regrettable that corresponding data of other RNA viruses with nuclear replication functions like influenza viruses have not been included. In those viruses nuclear localization and export signals of viral proteins, as well as interacting cellular proteins, have also been well described and there was certainly space for such data in this slim volume.

■ ***Ulrich Desselberger***
Cambridge

Essential Fungal Genetics

By D. Moore & L.N. Frazer
Published by Springer (2002)
79.95/SFr133.00/£56.00/
US$69.95, pp. 357
ISBN: 0-387-95367-1

The publication of a general text devoted entirely to fungal genetics is a welcome, but not common event. Publication at this time has allowed the authors to cover traditional genetics, such as mutation and recombination, while including the latest molecular biology. The book contains a wealth of useful information and is written in quite a dense style, often demanding careful re-reading. Although the text has many diagrams, the reasons for particular choices are not always obvious and some difficult concepts are left unillustrated. Starting each chapter is an extensive list of 'revision concepts'; similar techniques have been used by other authors, but in this volume it seems less appropriate. The text is not directly referenced, but lists of publications and websites 'worth a visit' or 'worth knowing about' are given at the end of each chapter. Despite minor reservations, this is a valuable contribution on these fascinating and important organisms.

■ ***Roger Marchant***
University of Ulster, Coleraine

Structure–Function Relationships of Human Pathogenic Viruses

Edited by A. Holzenburg & E. Bogner
Published by Kluwer Academic/Plenum Publishers (2002)
US$190.00/£133.00/ 218.00,
pp. 528
ISBN: 0-306-46768-2

It is the declared aim of this book to illustrate the complexity of viral pathogenesis in a comprehensive yet concise way. It contains a series of reviews, each of which uses a well-characterized virus to illustrate the fundamental processes involved in viral life cycles. As a result, most readers are likely to dip into chapter(s) of interest rather than being exposed to a coherent synthesis of ideas. Only two chapters compare and contrast the mechanisms used by different viruses (if only more chapters were in the same style as these). Nevertheless, the volume brings together several interesting topics under one cover.
As often happens with multi-author books, there is some repetition between chapters. Some of the figures are of dubious quality and in some chapters there are a lot of typographical errors. The price of this volume is likely to restrict its purchase to institutions.

■ ***Janet Daly***
Animal Health Trust, Kentford, Newmarket

The Springer Index of Viruses

Edited by C. A. Tidona & G. Darai
Published by Springer (2001)
279.00/SFr451.00/£195.50/
US$295.00, pp. 1,511
IBSN: 3-540-67167-6

Edited entirely via the internet by an impressive list of virologists, this Index contains a comprehensive, but not exhaustive, list of viruses and their characteristics, all presented in a clear and concise, albeit unimaginative and not particularly informative, manner. Most interesting are the history sections provided for each virus, but, although interesting, these sections are an open invitation for controversy.
This work is also the first major publication to adopt the 19-digit decimal code for virus nomenclature and proposes its routine citation in publications. As a publisher, nothing horrifies me more! It will be interesting to see if this is in fact the first, and last, publication to adopt this system. Perhaps this Index will prove indispensable for its appendices on virus codes! Although this book purports to be nothing more than an index, it is, quite simply, just that. As such, I would not recommend it over other similarly priced issues of reference.

■ ***Catherine Tarbatt***
SGM, Marlborough House

Gene Probes: Principles and Protocols. Methods in Molecular Biology Vol. 179

Edited by M.A. de Muro & R. Rapley
Published by Humana Press (2001)
US$89.50, pp. 275
ISBN: 0-89603-885-8

This publication sets out to be a resource for those bench scientists in search of genes, although the bias towards microbiological applications is strong. The style is straightforward and instructive, with high production standards maintained across all 23 chapters. It is more protocols than principles, but none the worse for that, and most chapters finish with a valuable Notes section. There is just enough background and overview content to interest the casual reader, but it does not pretend to be anything other than a collection of molecular biological methodologies targeted at the practitioner. While I would have preferred more on generic techniques for the design, production and application of gene probes, there is plenty of general guidance to be found in the specific chapters. A final summative chapter would have been a useful addition, but this book is still worth having on the laboratory bookshelf.

■ ***Alan McCarthy***
University of Liverpool

Biotechnology – the Making of a Global Controversy

Edited by M.W. Bauer & G. Gaskell
Published by Cambridge University Press (2002)
£19.95/US$27.00, pp. 411
ISBN: 0-521-77439-X

The title promised an easy read of an exciting and engaging story: how biotechnology, the practical expression of the biological sciences, was faring in the varied environments of the world's rich and poor societies. It turned out not to be quite like that. This is an academic book written mainly by sociologists and probably as difficult for me (a microbial biochemist) as microbiology would be for them. It offers a wealth of detail and analysis although, for anybody used to the ordered and clear sequence of a natural sciences paper, it is often difficult to evaluate. Even the conclusions and summaries at the ends of sections and chapters sometimes failed to provide a clear message. But it really is all there: case studies, media treatments, Europeans compared with Americans, crops, foods, cloning, genetic profiling, drugs – the lot. Try hard: it may be tough going yet well worth the effort.

■ ***Vivian Moses***
King's College London

Publisher's website addresses

ASM Press	www.asmusa.org
Blackwell Science	www.blackwellpublishing.com
Cambridge University Press	uk.cambridge.org
Humana Press	www.humanapr.com
Kluwer Academic/Plenum Publishers	www.wkap.nl
Nelson Thornes	www.nelsonthornes.com
Oxford University Press	www.oup.co.uk
Princeton University Press	www.pup.princeton.edu
Royal Society of Medicine	www.rsm.ac.uk
Springer	www.springer.de
Taylor & Francis	www.tandf.co.uk
Wiley	www.wileyeurope.com

Diary

june 03

MICROBIOLOGICAL METHODS AND METHOD VALIDATION

Harrington Hall Hotel, London
26 & 27 June 2003

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)

june–july 03

LABORATORY HEALTH AND SAFETY

Loughborough University, Leicestershire
30 June–3 July 2003

CONTACT: Mrs Sandy Edwards, Centre for Hazard & Risk Management (ChaRM), Loughborough University, Loughborough LE11 3TU (Tel. 01509 222188; Fax 01509 223991; email s.p.edwards@lboro.ac.uk)

july 03

STRESS, SIGNALLING AND CONTROL. BIOCHEMICAL SOCIETY MEETING 679

University of Essex
2–4 July 2003

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

22ND ANNUAL SCIENTIFIC MEETING OF THE AMERICAN SOCIETY FOR VIROLOGY

Davis, California
12–16 July 2003

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

august 03

BIOFILMS IN INDUSTRY, MEDICINE AND ENVIRONMENTAL BIOTECHNOLOGY: THE TECHNOLOGY. EUROPEAN SUMMER SCHOOL

National University of Galway, Ireland, 9–14 August 2003

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

56TH HARDEN CONFERENCE. BIOLOGICAL ELECTRON AND PROTON TRANSFER

University of Plymouth
26–30 August 2003

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

september 03

CHRO 2003. 12TH INTERNATIONAL WORKSHOP ON *CAMPYLOBACTER, HELICOBACTER* AND RELATED ORGANISMS

Aarhus, Denmark
6–10 September 2003

CONTACT: CHRO 2003, c/o Kongreskompagniet (Tel. +45 8629 6960; Fax +45 8629 6980; email kontakt@kongreskompagniet.dk; www.chro2003.dk)

57TH HARDEN CONFERENCE. PROTEINASE STRUCTURE AND FUNCTION

Oriel College, Oxford
9–13 September 2003

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

BIOLOGY OF TYPE IV SECRETION PROCESSES. EUROCONFERENCE ON THE MECHANISMS AND APPLICATIONS IN BIOTECHNOLOGY

Giens, France
12–17 September 2003

CONTACT: Dr J. Hendekovic, European Science Foundation, EURESCO Unit, 1 quai Lezay-Marnésia, 67080 Strasbourg Cedex, France (Tel. +33 388 76 71 35; Fax +33 388 36 69 87; email euresco@esf.org; www.esf.org/euresco/03/mc03168)

4TH INTERNATIONAL CONFERENCE ON TULAREMIA

Assembly Rooms, Bath
15–18 September 2003

CONTACT: email Tularemia@indexcommunications.com; www.tularemiaconf.co.uk

JOINT MEETING OF INTERNATIONAL BIODETERIORATION AND BIODEGRADATION SOCIETY AND INTERNATIONAL BIODETERIORATION RESEARCH GROUP ON 'MANAGEMENT AND CONTROL OF UNDESIRABLE MICROORGANISMS'

Manchester Metropolitan University
15–18 September 2003

CONTACT: Dr Joanna Verran (email j.verran@mmu.ac.uk)

FEMS Young Scientists Grants are available for this meeting.

BIOTECHNOLOGY FOR THE NON-BIOTECHNOLOGIST

Rembrandt Hotel, London
25 & 26 September 2003

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)

sep 03–feb 05

POSTGRADUATE CERTIFICATE/DIPLOMA IN HEALTHCARE RISK MANAGEMENT – SPECIFICALLY FOR SENIOR MANAGERS IN HEALTHCARE UNITS

Loughborough University
September 2003–February 2005

CONTACT: Joyce Bostock, Centre for Hazard & Risk Management, Loughborough University, Loughborough, LE11 3TU (Tel. 01509 222175; Fax 01509 223991; email j.g.bostock@lboro.ac.uk)

sep–oct 03

11TH INTERNATIONAL CONFERENCE ON MICROBIAL GENOMES

Durham, North Carolina, USA
28 September–2 October 2003

CONTACT: Ms Kim Y. Smith (email smithky@ornl.gov)

december 03

13TH INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF THE ACTINOMYCETES

Melbourne, Australia
1–5 December 2003

CONTACT: Symposium Secretariat, c/o Conference Strategy Pty. Ltd, PO Box 1127, Sandringham, Victoria 3191, Australia (www.conferencestrategy.com.au)

january 04

HYGIENIC COATINGS & SURFACES. SECOND GLOBAL CONGRESS

Orlando, Florida, USA
26–28 January 2004

CONTACT: Janet Saraty, PRA, 8 Waldegrave Road, Teddington TW11 8LD (Tel. 020 8614 4811; Fax 020 8614 4812; email j.saraty@pra.org.uk; www.hygienic-coatings.com)

june 04

MANAGEMENT OF PLANT DISEASES AND ARTHROPOD PESTS BY BCAS AND THEIR INTEGRATION IN GREENHOUSE SYSTEMS (JOINT IOB/WPRS MEETING)

St. Michele, Trentino, Italy
10–13 June 2004

CONTACT: Yigal Elad, Convener (Current email during sabbatical: y.elad@sbc.bbk.ac.uk; www.agri.gov.il/Depts/IOBCPP/JGroup/IOBCWPRSintegration1st.html)

july 04

BIOSCIENCE2004: FROM MOLECULES TO ORGANISMS

SECC, Glasgow
18–22 July 2004

CONTACT: Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW (Tel. 020 7580 3481; Fax 020 7637 7626; email meetings@BioScience2004.org; www.BioScience2004.org)

12TH INTERNATIONAL CONGRESS OF IMMUNOLOGY/4TH ANNUAL CONFERENCE OF THE FEDERATION OF CLINICAL IMMUNOLOGY SOCIETIES (IMMUNOLOGY/FOCIS 2004)

Montréal, Québec, Canada
18–23 July 2004

CONTACT: Immunology/FOCIS 2004 Secretariat, National Research Council Canada, Building M-19, 1200 Montreal Road, Ottawa, ON K1A 0R6 Canada (Tel. +1 613 993 7271; Fax +1 613 993 7250; email immuno2004@nrc.ca; www.immuno2004.org)

Comment

Influenza – are we on the brink of a pandemic?

Is there another influenza pandemic coming – if so, when will it arrive and how bad will it be?

Spring 2003 is heralding a flurry of confirmed or suspected influenza activity. In February, H5N1 avian influenza virus was recovered from a father and son both hospitalized in Hong Kong. The family had travelled to Fujian province, China. The alert came when the 9-year-old boy was admitted to hospital in Hong Kong upon their return. Although he recovered, his father died. It transpired that the boy's sister had become ill during the visit to the mainland and died there in a local hospital, whereas the mother had recovered. It is not clear whether any of them might have acquired infection from each other rather than from an avian source. Human-to-human transmission is a prerequisite in the onset of a new pandemic. Preliminary reports confirm that the recovered viruses do not contain any human viral RNA segments, but whether there are any mutations that might enhance human transmission awaits experimental enquiry.

All this takes place against a background of hazy reports from China of hundreds of cases of an atypical pneumonia and some associated deaths, and a hospital-based outbreak of acute respiratory syndrome in Hanoi, Vietnam in which the index case had recently visited Hong Kong. More hospital-associated atypical pneumonias in Hong Kong are being investigated and a mystery respiratory disease is spreading quickly across air travel routes.

It is only 6 years since another H5N1 influenza virus outbreak in Hong Kong demonstrated for the first time the potential of influenza virus to transmit from birds to man without an intermediate host. In the 1997 incident, 18 people were infected and six died. After a mass poultry cull, the murmurs of pandemic panic ebbed away. But ever since, a close eye is kept on the genetic activity of influenza viruses in the South East Asian 'epicentre', and other regions of the world. This reveals an incredible promiscuity where genetic mutations and re-assortments are begot in the virus 'primordial soups' which are the lakes on migratory pathways, the live bird retail industry and the intensive poultry farming businesses of Europe, South America and Asia. Any of these arenas might nurture the next pandemic virus. Indeed, there is a current H7N7 outbreak in poultry farms in the Netherlands and Belgium with associated cases of human conjunctivitis. Although we don't know how many steps away from a pandemic virus we are when these sentinel zoonotic cases are picked up, the more frequently avian influenza viruses replicate in humans, the greater is the potential pandemic risk.

The impact of the next pandemic will depend on several factors which include our ability to control the virus, and the nature of the virus itself. The recent outbreaks of H5 and H7 influenza are worrying because both subtypes can transform into highly pathogenic 'fowl plague' viruses where virus tropism, usually limited to areas of the body in which trypsin-like protease can activate the HA protein into its fusogenic form, is extended because the multiple basic amino acids at the HA cleavage site render it susceptible to ubiquitous proteases. However, the surge of research into the molecular basis of virulence since the 1997 H5N1 outbreak has shown that influenza pathogenicity is also determined by mutations in viral genes such as polymerase and non-structural protein which increase replication in mammalian hosts and lead to inappropriate cytokine responses. Interestingly, despite all this new information, we still do not understand why the 1918 Spanish flu virus, which is painstakingly being pieced together from RT-PCR fragments, was so virulent that it remains the single biggest influence on mortality in recent recorded history. There are clearly many ways to skin a cat in the RNA virus world.

This year's influenza activity will undoubtedly stimulate more interesting research. There are many questions to be answered: It is tantalizing that the Hong Kong human cases are due once more to infection with an H5 virus. Is this subtype more prone to zoonosis than the other 11 which have not yet 'humanized'? H7 infection has been previously associated with human conjunctivitis – is this a hallmark of zoonosis by this subtype? And are the reports of increased zoonotic activity simply the result of better surveillance mechanisms or is the virus evolving, perhaps in the poultry host, in a way which enhances the probability of interspecies transmission?

Since the last influenza pandemic in 1977, our ability to respond has changed substantially because of new antivirals and massively increased vaccinology experience. How will we fare in the new millennium? The immediate response of the influenza community has been to launch a race to develop a suitable vaccine. The experience of 1997 suggests that this will not be straightforward. Working with viruses which are highly pathogenic in both birds and man hampers vaccine development and production. An avian virus, rather than the preferred traditional re-assortant, remains the only licensable H5 vaccine 6 years on. Newly developed reverse genetics techniques, which allow generation of recombinant influenza viruses to order, offer attractive solutions, but IP and regulatory issues may impede their practical implementation. And meanwhile the virus is out there, mixing, breeding, mutating. Given a little more time, or the opportunity to acquire an internal gene set optimized for replication and transmission in the mammalian host, the virus progeny of 2003 may constitute our next challenge to pandemic preparedness.

Wendy Barclay is a lecturer in virology in the School of Animal and Microbial Sciences at the University of Reading (w.s.barclay@reading.ac.uk). She has an active research group whose focus is on the understanding and control of influenza A and B viruses using a molecular approach.

Further reading

Hatta, M., Neumann, G. & Kawaoka, Y. (2001). Reverse genetics approach towards understanding pathogenesis of H5N1 Hong Kong influenza A virus infection. *Philos Trans R Soc Lond B Biol Sci* 356, 1841–1843.

Wood, J. (2002). Selection of influenza vaccine strains and developing pandemic vaccines. *Vaccine* 20, B40–B44.

Zambon, M. & Barclay, W. (2002). Unravelling the mysteries of influenza. *Lancet* 360, 1801–1802.

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