Microbiologist

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a science frozen in time

INSIDE

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editorial

Lucy Harper explores the developing world of interactive online networking

In this editorial I'd like to set you a challenge: think back to a time when mobile phones weren't commonplace; when we didn't have the ability to send a last-minute text message to rearrange a meeting; a time before we could access the internet on the go; before we could download podcasts, vodcasts, rss feeds or meet online in a virtual world or social networking website. That time is far removed from today's world and in my humble opinion as Communications Officer of the Society one of the best ways in which we can communicate is to embrace these emerging technologies and use them to their full potential.

I expect a number of you are registered with the social networking site 'Facebook'. Until recently I would have expected most of our members who are on Facebook to be younger members who would share an interest in the work of our PECS subcommittee (see page 13 for the regular article from our postgraduates and early career scientists). However, I was recently informed that there is a SAGA group on Facebook, so it seems that online networking is no longer a phenomenon which is limited to those born in the 1980s. For those of you who are unfamiliar with the concept, Facebook is an online networking website which allows users to sign up, keep in touch with their friends, join groups, connect with like-minded people and form networks of contacts who interact, share messages and useful information and generally keep up to date with recent events in any area of interest.

Facebook is just one of a number of ways in which we are all communicating with one another and I am pleased to announce that S*f*AM now has a presence on Facebook. To join the S*f*AM group, contact and chat with other S*f*AM group members and keep up to date with S*f*AM events, go to: http://www.facebook.com/group.php?gid=7338994879

Facebook is just one example of Web 2.0 — a growing interactive form of networking on the internet (see page 20 for an article from Med-Vet-Net which describes these new technologies in more detail). Blogs are another great example of this. For those who've not entered the blogosphere before, a blog is a website which is designed to allow people to post comments, diaries and an opinion on any number of topics. Podcasts can also form the initial talking point for a blog topic which can generate some very interesting discussion and debate.

Technology is moving fast and I can verify that I have travelled one step further in cyberspace to an example of Web 3.0 technology — Second Life. This is a virtual world where visitors can interact with each other in every way that we interact in the real world (without the physical presence). I attended a lecture recently in Second Nature, (the 'Natures' area of Second Life) on the epidemiology of Bluetongue disease. The whole experience was much more 'real' than any other internet based meeting I've attended and I think it is only a matter of time before we are all creating avatars and having virtual meetings in a virtual world.

We here at S*f*AM have every intention of embracing these new technologies as a way of keeping in touch with our members and meeting new ones. We hope to see you in cyberspace soon!

All that there is left for me to say is I hope you all have a lovely festive season and a happy and healthy 2008.

contribute

We are always looking for enthusiastic writers who wish to contribute articles to the magazine on their chosen microbiological subject.

For further information please email the editor, Lucy Harper at:
lucy@sfam.org.uk

Lucy Harper

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Information about advertising in *Microbiologist* and how to submit advertisements are can be found on the Society website.

Website: our website **(www.sfam.org.uk)** is a timely source of up-to-date information on all Society matters and maintains a comprehensive archive of articles and reports on a variety of microbiological topics.

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benefits

The Society for Applied Microbiology is the voice of applied microbiology within the UK and was founded in 1931. Society members play a leading role in shaping the future of applied microbiology, and enjoy many benefits, including:

- Many generous grants and awards
- Substantially reduced rates for attendance at Society meetings and conferences
- Access to the members areas of the Society website
- FREE access to four acclaimed journals

Detailed information about all these benefits and more can be found on the Society website at: www.sfam.org.uk

GRANTS & AWARDS: Many grants, awards and prizes are available to members including the W H Pierce Memorial Prize and Prizes for Student Oral Presentations and Posters at the Summer Conference. In addition to these substantial awards, the Society has funds to assist members in their careers as microbiologists. These include The President's Fund, Conference Studentships, Sponsored Lectures and the popular Students into Work Scheme.

Full details of all the Society's grants and awards can be found on the website together with PDF downloadable application forms from the members area. Look out for many new grants to be launched very soon.

JOURNALS: The Society publishes two monthly journals: *Journal of Applied Microbiology* and *Letters in Applied Microbiology*. We also produce this quarterly colour magazine, *Microbiologist*, which contains features, topical news stories and full details of our meetings. The Society is also a partner with Blackwell Publishing in the monthly journal *Environmental Microbiology* and we are launching a new journal for 2008; *Microbial Biotechnology*.

Synergy is an online service provided by Blackwell Publishing that gives Full and Student Members FREE access to the online versions of the Society's four journals: *Journal of Applied Microbiology*, *Letters in Applied Microbiology*, *Environmental Microbiology* and *Microbial Biotechnology*. Members can register for this service at http://www.blackwell-science.com. Members can also submit papers directly to our journals via an online submission service. For more information about Synergy or online manuscript submission, please visit the website.

MEETINGS: We hold three annual meetings. The Winter Meeting is a one-day meeting with parallel sessions on topical subjects. The Spring Meeting is a one-day meeting tailored for personnel in clinical microbiology. The Summer Conference is held every July and comprises a main symposium, a poster session, the AGM and a lively social programme. We also hold occasional joint ventures with other organisations on topics of mutual interest.

WEBSITE: The website is the best source of detailed information on the Society and it's many activities. It has fully interactive membership areas where you can book your place at Society meetings, find exclusive *Sf*AM documentation and much more.

membership options

■ **Full ordinary membership** gives access to our many grants and awards, online access to the *Journal of Applied Microbiology*, *Letters in Applied Microbiology*, *Environmental Microbiology* and *Microbial Biotechnology* for 2008, copies of *Microbiologist*, preferential registration rates at Society meetings and access to the members areas of the website.

■ **Full student membership** confers the same benefits as Full Membership at a specially reduced rate for full time students not in receipt of a taxable salary.

■ **Associate membership** is only open to those with an interest in applied microbiology without it being a prime aspect of their job. For example, school teachers and those taking a career break; on maternity leave, or working temporarily in other areas. It does not provide access to any journals or Society grants and awards.

■ **Honorary membership** of the Society is by election only and this honour is conferred on persons of distinction in the field of applied microbiology. Honorary members have access to our online journals.

■ **Corporate membership** is open to all companies with an interest in microbiology.
Corporate members benefits include:

- Quarter page advertisement in each issue of *Microbiologist* (which can be upgraded to a larger size at discounted rates)
- the opportunity to publish press releases, company news, etc., in each issue of *Microbiologist*
- FREE banner advert on the Society Website with a direct link to your company site.
- Up to three members of company staff attending Society meetings at members' rate (This means a 50% discount on non member registration rate).

■ **Retirement membership** is available to Full Members once they have retired from their employment. Retired members are entitled to all the benefits of Full Membership except grants and access to the Society's journals.

JOIN US!

You can apply for membership on, or offline. To apply offline, please contact the Membership Co-ordinator, Julie Wright on **+44 (0)1234 326846**, or email **julie@sfam.org.uk.** Alternatively, write to her at:

The Society for Applied Microbiology, Bedford Heights, Brickhill Drive, Bedford MK41 7PH, UK

www.sfam.org.uk

Congratulations to **Mark Fielder** who won last issues caption competition with the caption below:

microbreak

This issue's competition is based upon caricatures of delegates at the last two S*f*AM summer conferences. See if you can guess which members of S*f*AM are pictured here. Clue: all are members of either the S*f*AM main committee, subcommittees or staff. Please send your answers in an email to the Editor at lucy@sfam.org.uk **no later than 18 January 2008.**


A

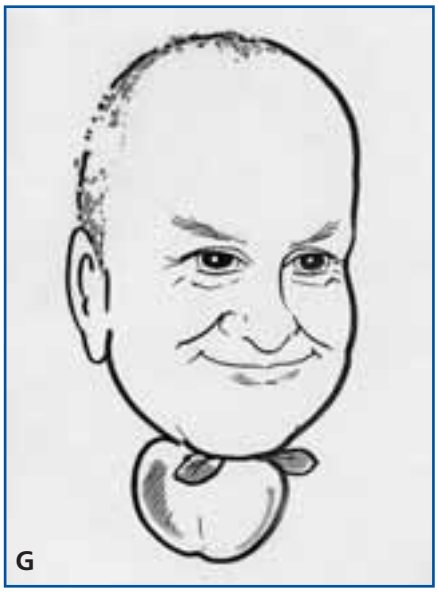

B


C


D


E


F


G

president's column

Margaret Patterson talks about the importance of communicating sound science in an appropriate way to the general public

It seems that every day there is at least one item in the news related to applied microbiology. As I write this article at the start of October we are hearing about new cases of Bluetongue and Foot and Mouth disease in the south east of England as the control and protection zones are being expanded. The Government has recently announced a programme to "deep clean" hospitals as a way of controlling MRSA (which in my view is not a solution to the problem!) Also, the elderly and those with other risk factors are being urged to get their flu vaccination as soon as possible.

The S*f*AM web site is an excellent resource for monitoring microbiology in the news and I checked back to discover that we have over 60 stories listed in the first nine months of 2007. The year started with avian flu and we have covered a wide variety of stories ranging from the problems of MRSA and *Clostridium difficile* in hospital patients, *Listeria monocytogenes* in a recall of smoked salmon, norovirus on cruise liners and the microbiology of finger nails (this last offering was as a result of work done by Dr Anthony Hilton, our Honorary General Secretary). The majority of articles in the media focus on the negative aspects of microbiology. However, there are a number of good news stories, including the fact that scientists have found that bacteria can survive in 'permafrost' and that a wide variety of bacteria, including extremophiles have been found in NASA cleanrooms, providing possible clues as to potential microbial life in space. Another good news story came from Professor Geoff Hanlon (our Vice-President) and colleagues, who are working on bacteriophage therapy as a method for treating infectious disease, such as MRSA. Geoff wrote an excellent article about this in the March 2007 issue of *Microbiologist* (page 30) and the story was included in a Press Briefing for science journalists organised by the Science Media Centre in London. The journalists picked up a number of stories from this briefing and these were widely reported, including an interview with Professor Hanlon on the BBC Radio 4 news at 6 pm, as well as the story appearing in numerous of the daily newspapers.

I think it is excellent that journalists are making good use of the services of organisations such as the Science Media Centre. It is my impression that balanced coverage of science issues is increasing, and we are hearing less about the MRSA "virus". S*f*AM is also gaining a reputation as a good source of information. For example we were contacted directly by *The Times* for a comment on a survey that "Bugs are Bad" (featured in *The Times* 'Body and Soul' Supplement, September 29th 2007).

In recognition of the importance of communicating sound science in an appropriate way to the public in general, S*f*AM Committee are considering a number of new initiatives, which we hope to launch in early 2008. These include a new grant which aims to bridge the gap between scientists and the general public (see page 11 for more details). This grant is among a number of new grants which we will soon be launching as additional benefits of S*f*AM membership. In the coming months look out for details of these new initiatives and as always, let us know what you think. With very best wishes for 2008.

Dr Margaret Patterson
President of the Society

ceo's column

Philip Wheat reports on the latest developments within the Society

It is 25 years since Blackwell Scientific Publishers (Wiley-Blackwell as they are now known) began publishing the Society's journals. Recently the Society gained a stake in the journal *Environmental Microbiology* which has proved to be a popular journal with a very competitive impact factor. I am pleased to announce that the President has recently signed a contract which commits the Society to remain with Wiley-Blackwell for the next seven years. I look forward to continuing to work with colleagues at Wiley-Blackwell, developing an already good working relationship further to the mutual benefit of both organisations. In particular I look forward to the launch of the new journal *Microbial Biotechnology* in January 2008. I am sure it will be as successful as the three other *Sf*AM Journals. Infact a number of articles from this journal are already available online — see page 15 for details.

The launch of the new journal is just one of a number of new initiatives that the Trustees and myself have been working towards. Other new initiatives include new grants which will be available exclusively to members. One new grant (New Lecturers Grant) was launched during 2007 and has proved to be very popular with the first awards being made in the final quarter of 2007. Other new grants will be launched during 2008 so watch this space for details!

A further initiative was the Spring one day meeting specifically targeting personnel in the field of Clinical Microbiology. This was launched during 2007 and proved to be very successful. Details of the second in this series of meetings to be held at Aston University, Birmingham on 9 April, 2008, can be found in this issue of *Microbiologist*. Finally, another initiative which further enhances membership of the Society is the regular monthly email news bulletin which is created by Dr Lucy Harper here in the office. I encourage members to forward any information which you think would benefit the *Sf*AM membership directly to Lucy (lucy@sfam.org.uk).

I can also report a small but definite increase in all categories of membership during 2007. In particular, the number of Corporate Members of the Society has risen significantly. As I write this column the Society has 26 Corporate Members (compared to 10 in 2005) and the companies represented cover a wide variety of areas associated with applied microbiology. I would like to thank the Corporate Members in their assistance with promoting awareness of the Society to their customers in the field of microbiology. This support is invaluable in helping the Society achieve our aims and objectives. Should any individual members like to promote the Societies activities (including recruitment of new members) in their own workplace please don't hesitate to contact the office and we will send you relevant promotional materials.

We have had a very good response to the promotion of our next Winter Meeting (9 January, 2008 Royal Society, London, see page 23). Please ensure if you are proposing to attend you book your place as soon as possible, as places are limited.

All that remains for me to do is wish you all a happy and peaceful Christmas and a prosperous New Year.

Philp Wheat
Chief Executive Officer

Under the Microscope

Letters in Applied Microbiology is looking for short review articles on specific micro-organisms or microbiological techniques. These reviews aim to give an up to date picture of a particular aspect of the micro-organism in question, for example, genetic advances, epidemiological data, novel virulence factors, novel usage (fermentation, bioremediation), novel detection processes or novel techniques and applications of an established technique. The reviews are concise at not more than 4000 words, including references, tables and figures. They contain a short summary, an introduction, a main section describing novel data and advances, a short conclusion and a short future prospect section. Information about the journal, including Guidance for Authors can be found at:
www.blackwellpublishing.com/lam

For further information, contact Chief Editor, **Jean-Yves Maillard** at: maillardj@cardiff.ac.uk.

membership matters

New Committee members

Louise Fielding

I graduated from the University of Reading with a Bachelor's degree in Food Technology (1990) and a PhD in food microbiology (1995). I am the Head of Department of Applied Life Sciences, which incorporates biomedical sciences, food science, nutrition and dietetics, in the Cardiff School of Health Sciences. I am also a Reader of the University of Wales and my research interests include novel methods for decontamination of bioaerosols and surfaces and implementation of food safety management systems. I also teach in the area of food and general microbiology, biotechnology, research methods and processing technology. I am a Fellow of IFST and a member of the International Association for Food Protection and have been a member of S*f*AM (then SAB) since my PhD studies. I am also a member of the Welsh Food Advisory Committee and the Foodborne Disease Strategy Consultative Group of the Food Standards Agency.

Andrew McBain

I am delighted to be the given the opportunity of serving on the S*f*AM committee. In order to introduce myself to those members that don't know me personally, I am a Lecturer in Microbial Physiology and Ecology at the University of Manchester. After graduating in Microbiology in 1993 from the University of Liverpool, I moved to the University of Cambridge to study for my Ph.D. at the MRC Dunn Clinical Nutrition Centre, focusing on the effects of pro- and pre-biotics on bacterial communities of the large intestine. After a short postdoctoral period with George Macfarlane at Cambridge, I moved to Peter Gilbert's research group at Manchester to study the impact of the biocide triclosan and other antimicrobial compounds on complex bacterial communities present in the general environment and in association with humans.

My role at Manchester includes teaching microbiology and immunology to pharmacy students and I maintain a keen research interest, particularly concerning the interaction of microorganisms colonising the skin, nasopharynx, oral cavity and intestine with the human host in health and disease. I also study the efficacy of antimicrobial formulations on biofilms. I very much enjoyed the four years that I served on the committee of the Biofilm Club as the senior book editor and I have maintained an involvement with the Club by coordinating the production of the book that accompanies the bi-annual general meeting. In my spare time, I play squash and am an enthusiastic photographer, still sometimes using film and printing in a darkroom.

Steve Davis

I have worked the majority of my professional life as a microbiologist within the NHS in Sheffield, although I did have a brief spell as a medical representative. I am currently Bacteriology Departmental Manager at the Northern General Hospital, which is part of the Sheffield Teaching Hospitals Foundation Trust. I am also an external lecturer for both Sheffield Hallam and Hull University on a variety of different subjects.

I have publications on many different organisms, but my current favourite is MRSA. I am a Chartered Scientist and have recently started my PhD on the effect of silver in wounds, as I feel chronic wounds are an area that many microbiology departments appear to ignore. As the former national Specialist Advisor to the IBMS and still current committee member of the Microbiology Advisory Panel, my main objective is to break down some of the professional barriers that still exist in the NHS. I hope to aid in the introduction of Biomedical Scientist Consultants in Microbiology, in a similar vain to that in the nursing profession. I hope my extensive clinical microbiology knowledge will be an asset to the *Sf*AM committee.

Andrew Fox

Currently I am Clinical Scientist at the Regional Health Protection Agency North West and Food, Water and Environmental Services, Preston Microbiology Service, and Professor of Biomedical Science at the Manchester Metropolitan University.

My professional and research interests are centred upon Public Health Microbiology and specifically the molecular epidemiology of infectious diseases. Most recently I have been involved in the development and application of Sequence-based typing including Multi locus Sequence Typing for the molecular characterisation of *Neisseria meningitidis* and *Campylobacter jejuni* and pathogenic *E.coli* and adaptation for non-culture strain characterisation.

New Grants soon to be launched

We will soon be launching some new grants for members of the Society. These will be varied in nature, ranging from a **Hardship Grant** for members who are studying an MPhil/PhD in applied microbiology to a **Research Development fund** for consumables to an **Innovative Project Grant** for projects which bridge the gap between research and the general public. All these grants will be launched in 2008, so look out for announcements in the e-bulletin and future issues of *Microbiologist* for more details.

mailbox

From: John Lowe
Subject: Biofuels

You asked for comment in your editorial in the June 2007 issue of *Microbiologist* and your questions certainly focused my attention on the two interesting articles.

I think the first thing to say, though, is that whatever non-renewable materials we are talking about (coal, oil, gas, sand & gravel ["Coast", BBC2, No. 6]), we should not be wasting them, global warming or not!

I must admit that the two articles made me think about my initial position, viz. that our primary concern must be to feed the world. Comments by the authors did move me towards being in favour of using land for biofuel production; but finally I hold to my original position, probably as a result of Stephen Smith's identification of the valid doubts that exist, particularly with respect to the proportion of land used for fuel or food.

I am aware that in many parts of the world land can be more intensively cultivated. On the other hand, the price of food is rising, partly at least because of the increasing wealth of some nations and the wish of their citizens to have a more varied diet than traditionally enjoyed.

As to the use of biofuels, I think I favour their use for transport because of the amount of energy they have in a small volume and would like to see, for example, clean coal technology developed and used more widely for heating and the like. So, as I said earlier, let's feed the world as our over-riding priority.

From: Brendan Gilmore
Subject: Another happy student

Pauline Conway conducted a 'Student into Work' project in my laboratory last summer. I will of course keep the *Sf*AM informed of the future progress of the work and would like to thank you again for the funding for Pauline. She was an excellent student and hopefully will rejoin us after her pharmacy pre-registration year as a graduate student.

Sponsor a new Member of the Society and win a £50 Voucher of your choice!

If you feel you could be our next winner for 2007, and would like some promotional material to help you recruit new members please contact Julie Wright, Membership Co-ordinator on 01234 326661 or email julie@sfam.org.uk.

Membership Changes
New Members

We would like to warmly welcome the following **new members** and hope that you will participate fully in the activities of the Society.

Italy

R De Philippis

Nigeria

C L Emerenini

Norway

A Krajete

South Africa

H Bok

United Kingdom

H H Abruquah; S Al-Baba; T Brocklehurst; K E Cheeseman; A Del Casale ; S Easton; A K Goodhead; R P Horsman; M A Ishfaq; M A Javed; L Lehtovirta; M Loughlin; G Manning; H Natto; J O'Donnell; N Oldfield; J L Roberts; C J Warren

USA

J Awong-Taylor; K Colacino; H Gill; R Gonzalez; M Hughes; K Weideman

CORPORATE

Q Chip Ltd, UK; Synbiosis, UK; Technopath, UK

Student member wins Communication Prize

We would like to congratulate *Sf*AM student member, **Vicki McCune** of the Health Protection Agency, Newcastle, for winning the Institute of Food Research sponsored prize in Communication at the SGM meeting in September. Well done from all at *Sf*AM!

In the loop

pecs

News from the S*f*AM Post-Graduate and Early-Career Scientist Committee

Surviving your PhD viva

VIVA... As a PhD student we constructively place this inevitable event to the back of our minds. Fearfully we anticipate the unavoidable looming prospect that at the latter part of three years we will end up trapped in a small room defending our very life and scientific soul! Arggghhh. I did it, I survived and I even enjoyed it. Here are my top tips...

thanks

Thank you to all the student members that showed an interest in the committee at the summer conference. We look forward to working with you all and remind you that any contributions to this section are welcomed and can be sent to:

j.heaton2@lancaster.ac.uk.

victoria.mccunes@hpa.org.uk

Be proud

Realistically judge your thesis. If you have worked hard for three years and your supervisor is pleased with your achievements, then you have every right to feel confident going into your viva examination. Confidence in your work will make your thesis a lot easier to defend.

Prepare for battle

Read your thesis thoroughly and know it inside out as you will be expected to defend all aspects of your work i.e. methods chosen, data analysis, results and conclusions drawn. Ensure you can concisely state your key research findings chapter by chapter and how these may relate or differ to current opinion. Your examiner is likely to refer to recent literature, so make sure you are up to date with the latest publications. Don't skim over your introduction; an examiner may spend a lot of time discussing this chapter to determine the breadth of your background knowledge.

What aspects make your thesis unique?

Identify what contribution you have made to your scientific field and the possible applications of your research findings.

Examine the examiners

It's a good idea to briefly study the examiners publications, as this may help you to identify points they may focus on during your viva. A well

chosen examiner will already have an interest in your research field and will challenge your work fairly.

Exam aids

Taking a copy of your thesis into the exam will help you follow the direction of the interview. You can make notes to aid you in your examination so ensure you read your thesis thoroughly and add annotations and diagrams where you feel you may need them. In particular a list of anticipated questions and responses may be a useful.

Nobody's perfect

Remember, a PhD is the start of your research career. Understanding and accepting flaws in your work will only credit your scientific development and judgment. Be prepared and don't be ashamed to discuss the weaknesses and limitations of your research with the examiner.

Under the spot light

Listen to questions carefully and take your time answering. If you don't understand a question, do not be afraid to ask for clarification and if you can't answer a question, be honest. Treat vague questions as an invitation to elaborate and demonstrate the breadth of your knowledge in your research field.

Look good to feel good

Dressing to impress may increase self confidence and pride in appearance will reflect pride in your work.

Know the process

A PhD viva usually lasts about 2 hours (try to ignore the 12 hour horror stories). Attending your viva will be an internal examiner, an external examiner and an independent chair to ensure that your examination is fair. Your supervisor may also be present if you wish, but they are not permitted to talk or respond to any discussions.

You are not alone

Don't suffer in silence; seek advice and support from friends and colleagues who have been in your position. Use the knowledge and the experience of your supervisor and if you feel you will benefit, arrange a mock viva.

Relax

Try to chill out the night before and avoid last minute cramming. You're nearly there and this time tomorrow you may be inebriated, asleep or in my case both.

Enjoy yourself

Remember you are the expert so be confident; be yourself and enjoy the experience. This is your chance to exhibit yourself and your research in the company of two respected peers, who have dedicated their own time to take an interest in YOUR work. Go for it!

Jess Rollason
Aston University

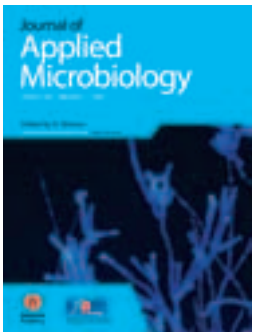
Summer conference student session

Building on the success of last year's student session, this year Dr Kate Exley presented a session on *'Managing your PhD'*. Kate demonstrated that a PhD is not purely an academic venture and gave student members the opportunity to assess their skills base, identify any gaps and learn how to promote their skills.

As a final year student I am all too aware that the focus on data publication can distract from the many other aspects that a PhD can offer, from teaching opportunities to scientific communication and even financial planning and time management. Kate reminded us that when applying for postdoctoral positions, all applicants have a PhD, and it is those extra diverse skills that really make an application stand out from the crowd. We were encouraged to identify skills we considered important and those we felt we had acquired. In a mock job interview we gave examples of how we could demonstrate those skills and identified any gaps. The session was valuable for all the attendees, alerting us to the need for skills away from the lab bench and allowing discussion between students to identify opportunities to acquire these skills and exchanging of advice.

Any students that are looking for activities to broaden their range of skills may be interested in becoming involved in S*f*AM's Postgraduate and Early-Career Scientist Committee (PECS). We are looking for contributions for this page in *Microbiologist* on any aspect of microbiology, from write-ups of activities you are involved in, to top tips and perhaps even cartoons. If you would like to be involved in the committee in any way, please email Jo, the committee chair at j.heaton2@lancaster.ac.uk.

Jo Heaton
Lancaster University



Top 5 most downloaded articles published in *Journal of Applied Microbiology* in 2007:

Microbial biofilms in the human gastrointestinal tract. S. Macfarlane, J.F. Dillon. Vol. **102**, No. 5, May 2007.

The microbiological quality of hot water-washed broccoli florets and cut green beans. S.C. Stringer, J. Plowman, M.W. Peck. Vol. **102**, No. 1, January 2007.

Intestinal bacteria and ageing. E.J. Woodmansey. Vol. **102**, No. 5, May 2007.

Understanding the effects of diet on bacterial metabolism in the large intestine. P. Louis, K.P. Scott, S.H. Duncan, H.J. Flint. Vol. **102**, No. 5, May 2007.

journal**Watch**

News about the Society's journals

Comparative analysis of environmental DNA extraction and purification methods from different humic acid-rich soils. F.M. Lakay, A. Botha, B.A. Prior. Vol. **102**, No. 1, January 2007.

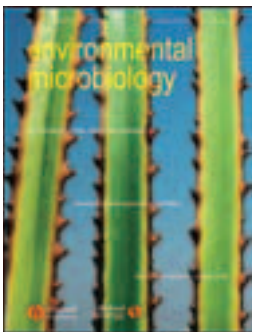
Top 5 most downloaded articles published in *Letters in Applied Microbiology* in 2007:

Screening and mutagenesis of a novel *Bacillus pumilus* strai. H.Y. Wang, D.M. Liu, Y. Liu, C.F. Cheng, Q.Y. Ma, Q. Huang, Y.Z. Zhang. Vol. **44**, No. 1, January 2007.

Antifungal activity of thyme (*Thymus vulgaris L.*) essential oil and thymol against moulds from damp dwellings. M. Segvic Klaric, I. Kosalec, J. Mastelic, E. Pieckova, S. Pepeljnak. Vol. **44**, No. 1, January 2007.

Vanillin production from simple phenols by wine-associated lactic acid bacteria. A. Bloem, A. Bertrand, A. Lonvaud-Funel, G. de Revel. Vol. **44**, No. 1, January 2007.

Evaluation of two viral extraction methods for the detection of human noroviruses in shellfish with conventional and real-time reverse transcriptase PCR. L. Baert, M. Uyttendaele, J. Debevere. Vol. **44**, No. 1, January 2007.



In vitro growth control of selected pathogens by *Lactobacillus acidophilus*- and *Lactobacillus casei*-fermented milk. M. Millette, F.M. Luquet, M. Lacroix. Vol. **44**, No. 3, March 2007.

Top 5 most downloaded articles published in *Environmental Microbiology* in 2007:

Key role of selective viral-induced mortality in determining marine bacterial community composition. T. Bouvier, P. A. del Giorgio. Vol. **9**, No. 2, February 2007.

Theory and the microbial world. Tom Curtis. Vol. **9**, No. 1, January 2007.

The human microbiome: eliminating the biomedical/environmental dichotomy in microbial ecology. Ruth E. Ley, Rob Knight, Jeffrey I. Gordon. Vol. **9**, No. 1, January 2007.

Interactions and competition within the microbial community of the human colon: links between diet and health. Harry J. Flint, Sylvia H. Duncan, Karen P. Scott, Petra Louis. Vol. **9**, No. 5, May 2007.

Environmental predators as models for bacterial pathogenesis. Hubert Hilbi, Stefan S. Weber, Curdin Ragaz, Yves Nyfeler, Simon Urwyler. Vol. **9**, No. 3, March 2007.

microbial biotechnology

Microbial Biotechnology — first articles online now!

Microbial Biotechnology is pleased to announce the publication of its first articles online. The article titles are listed below and are freely available to download from Blackwell Synergy: **www.blackwell-synergy.com/loi/mbt.**

Brief Report: Rhizoremediation of lindane by root-colonizing *Sphingomonas*. Dietmar Böltner, Patricia Godoy, Jesús Muñoz-Rojas, Estrella Duque, Silvia Moreno-Morillas, Lourdes Sánchez, Juan Luis Ramos.

Review: The application of Tet repressor in prokaryotic gene regulation and expression. Ralph Bertram, Wolfgang Hillen.

Metabolic engineering to enhance bacterial hydrogen production. Toshinari Maeda, Viviana Sanchez-Torres, Thomas K. Wood.

Pseudomonas aeruginosa PAO1 virulence factors and poplar tree response in the rhizosphere. Can Attila, Akihiro Ueda, Suat L. G. Cirillo, Jeffrey D. Cirillo, Wilfred Chen, Thomas K. Wood.

Activity and viability of polycyclic aromatic hydrocarbon-degrading *Sphingomonas sp*. LB126 in a DC-electrical field typical for electro-bioremediation measures. Lei Shi, Susann Müller, Norbert Loffhagen, Hauke Harms, Lukas Y. Wick.

Bacterial decolorization of textile dyes is an extracellular process requiring a multicomponent electron transfer pathway. Ann Brigé, Bart Motte, Jimmy Borloo, Géraldine Buysschaert, Bart Devreese, Jozef J. Van Beeumen.

book reviews

reviewers

The Society receives several new books every week from publishers around the world and we are always looking for enthusiastic additional reviewers who have an interest in the subjects covered.

There is an up-to-date list of titles available for review at the Society Office.

To make an offer to review any book simply email the Editor of *Microbiologist* at: lucy@sfam.org.uk. In return for your efforts you get to keep the book!

Titles for review and book reviews published in *Microbiologist* will soon be available on the website.

Management of Multiple Drug-Resistant Infections (2004)

Stephen H. Gillespie
Humana Press. pp. 403 + xii
ISBN 1-58829-230-4
Reviewed by Max Sussman

Childhood memories are often precious, even if not at the time understood. One of mine is of my mother handing to the doctor, when his visit was coming to an end, a crisply ironed clean towel with the implicit invitation that he wash his hands. That was in the country where in the 19th century Robert Koch held sway and taught the world important lessons that are now a staple of microbiology. In modern Britain it seems difficult to persuade health care staff to wash their hands. This, in environments where antibiotics are as endemic as the bacteria they are intended to combat, is responsible for the development of antimicrobial drug-resistance and the ready spread of microbes with nasty potentialities.

This useful book deals with bacterial, fungal and viral pathogens. It is, therefore, important to note that the title informs the reader that it deals with 'management'. This is a much broader remit than just treatment and though the main focus of the individual chapters is antimicrobial resistance, attention is given related matters, including pharmacodynamics and epidemiology. As a result this volume is even more useful than its title at first suggests.

The collection of papers begins with three on resistant pneumococci, which are becoming more troublesome. Two chapters deal with glycopeptide-resistant staphylococci and other Gram-positive organisms. The last chapter in the section on Gram-positive organisms considers the value of isolation in the control of methicillin-resistant *Staphylococcus aureus* and, after a systematic computer-based literature review, concludes that isolation still retains its place in MRSA control, in spite of the suggestion that stringent controls are no longer feasible in the face of its epidemic spread. Amongst the Gram-negative pathogens, *Acinetobacter*, *Helicobacter*, the gonococcus, *Salmonella*, *Burkholderia pseudomallei* and the pathogens of urinary tract infection each get their airing. Two chapters are devoted to multiple drug-resistant tuberculosis and one to non-tuberculosis mycobacteria. The final two sections of the book are devoted to fungal and parasitic infections and viral infections, particularly HIV and human cytomegalovirus. Drug-resistance is a widespread problem, which, to coin a phrase, has become an issue — indeed a political issue.

The contributors come predominantly from the United Kingdom and this shows in the style of writing, which is generally very accessible. The information is up to date and supported by reference to a good selection of literature.

Manual of Clinical Microbiology 9th Edition

Eds: Patrick R. Murray, Ellen Jo Baron, James H. Jorgensen, Marie Louise Landry, Michael A. Pfaller.
American Society for Microbiology
Publication Date: 2007 (pp. 2256)
ISBN-10: 1-55581-371-2
ISBN-13: 978-1-55581-371-0
Price: £140.00
Reviewed by Christianne Micallef

An ideal reference book for busy clinical microbiologists, infectious disease specialists, medical, pharmacy and microbiology students – this text is available as a set of two hardback volumes with an optional CD. It is updated with the latest techniques in the field (which includes molecular-based techniques) and contributors to this edition number more than 200 world experts.

Volume one comprises five sections. Initially, it includes an introductory section (Section 1) on common procedures and practices in place, in a typical clinical microbiology laboratory. A specific chapter provides detailed information on how the laboratory should be managed and another separate chapter on how a typical laboratory should be designed, including the type of equipment which must be present. Such information would be fundamental to new recruits and students intending to become clinical microbiologists.

Section 2 deals with infection control issues and also contains a very interesting chapter on the 'Laboratory Detection of Potential Agents of Bioterrorism'. This chapter includes detailed diagrams of the individual agents and how to correctly treat samples suspected to contain organisms such as *Bacillus anthracis*, *Brucella* spp., *Francisella tularensis* or *Yersinia pestis*. The authors state that positive samples should be reported to Laboratory Response Network, which is a US-based network, however no information is provided about how this should be done in laboratories which are not US-based and this would have indeed been an asset to scientists who are not working in the US.

Section 3 gives a detailed overview of the diagnostic techniques and methods used to detect and identify micro-organisms. This includes an entire chapter on molecular detection and identification. Here, the authors discuss target amplification techniques such as PCR (Polymerase Chain Reaction), RT-PCR as well as others, such as probe amplification techniques, including cleavase-invader probe-based technology. All the techniques are adequately supplemented with explanatory figures. However, the use of colour in these diagrams would have been a great bonus.

Section 4 is the largest section in this volume and includes detailed information on bacteria which may be isolated from patients and hence, encountered in a typical clinical microbiology setting. Initially, this section includes an introductory part where algorithms are presented showing how to correctly identify different bacteria. This is indeed very helpful to students who need to revise, or refresh their memories and provides a quick reference for newly-employed laboratory personnel. Two additional subsections on curved and spiral-shaped Gram-negative rods, *Mycoplasma* spp., and obligate intracellular bacteria are also provided.

Section 5 includes antibacterial agents and susceptibility test methods and this is strategically placed, right after the Bacteriology section.

Volume 2 includes another six sections. Section 6 deals with Virology and as for the Bacteriology Section, an introductory part with algorithms for the correct identification of viral pathogens is present, prior to discussing individual types of RNA and DNA viruses.

Chapter 97, covers arboviruses and includes an impressive table containing the different arboviruses, typical disease manifestations and geographical location. This table is four pages long but all the information is displayed in a very reader-friendly format. This is followed by Section 7 which deals with Antiviral agents and susceptibility testing. A section on Mycology (Section 8) and another on Antifungal agents (Section 9) follow. The Mycology section in particular, includes some excellent illustrations, such as the ones on page 1817 of *Aspergillus* spp., and those of dermatophytes on page 1892. The last part of this volume is dedicated to Parasitology (Section 10) and Antiparasitic agents (Section 11).

Each chapter, throughout the entire text, is supplemented with very clear diagrams and illustrations and consists of clearly defined sub-sections which typically include: Taxonomy and Description, Epidemiology and Transmission, Clinical Significance, Collection, Transport and Storage of specimens, and Direct Detection. This format is consistent throughout both volumes. The sections are written in a clear and easy-to-read manner and the presence of flow diagrams facilitates reading and understanding of the text and concepts. Also, the use of algorithms throughout the entire book, enable a better understanding of the scientific content and could be easily used as a reference in lectures and tutorials. The sections on antibacterials, antivirals, antifungals and antiparasitic agents include tables which provide essential and easily accessible information, not only pertaining to the individual chemotherapeutic agent but also on important drug interactions, mode of action and major side-effects. This would be of great help to a physician working in an infectious disease ward or a pharmacist working in clinical pharmacy or drug information units.

This book is an essential investment for anyone who is seriously pursuing, or wishes to start a career based in clinical microbiology.

Voice of Young Science

Andrew Hall reports on the Voice of Young Science — Standing Up for Science media workshop

our policy on the media

We will:

- always do our best to provide facts, information and explanation.
- if speculation is required, explain the rationale behind that speculation.
- desist from hyping a story—whether it is the journalist or the scientist doing the hyping.

In recent years microbiology has increased in prominence within the media with reports on MRSA, *C. difficile* and avian flu making front page headlines and occupying the news channels. Scientists from all disciplines are increasing in demand for comment and analysis, so it is important that we know how to liaise with the media to ensure that the reporting is accurate and the correct message is given to the public.

The Voice of Young Science (VoYS) programme was set up in 2004 to help postgraduates and early career scientists get involved with public debates on science and to give advice on dealing with the media. The programme includes the highly successful "Standing Up for Science" media workshops, which bring together young scientists, journalists, media savvy scientists and media experts. Programme manager Ellen Raphael told me; *"Sense About Science runs this workshop because we feel it's really important that early career researchers have the tools to stand up for science in public, especially in areas of controversy and when the scientific evidence is at risk of being lost."* The most recent workshop was held at the Institute of Biology, London, on the 18th May 2007. The workshop was attended by four S*f*AM members: Jonathan Caddick, Andrew Hall, Tarja Karpanen and Laura Wheeldon thanks to funding from the Society. The workshop was divided into three sessions giving scientists, journalists and media experts a chance to give their take on science communication. The first session brought together a panel of respected, media savvy scientists to talk on the changing image of science in the media and the role of scientists. Dr Stephen Minger from Kings College London spoke about his recent media exposure regarding the government's change of heart on the issue of human-animal embryos for research. Having spent the previous day giving 30 interviews to TV, radio and print media he spoke passionately about the need for scientists to develop a working relationship with the media to ensure the correct message is reported. Dr. Minger and the other panellists (Dr. Azra Ghani from the London School of Hygiene & Tropical Medicine and Dr. Steve Keevil from Guy's and St. Thomas' NHS Foundation Trust) discussed how scientific announcements can go wrong, key facts distorted and discussions polarised. The key messages from the session were to be prepared when speaking to the media and use the expertise of the Science Media Centre or Sense about Science. It is important to get good science into the public domain and this is ultimately the responsibility of the scientist.

With the media world set to rights, it was the turn of the journalists to have their say. Dr. Anjana Ahuja from The Times, Rachel Buchanan from BBC News, Alok Jha from The Guardian and Fiona MacRae from the Daily Mail discussed how they approached stories, dealt with accusations of misrepresentation and why they wanted scientists to become more engaged with the media. One frequent grievance from scientists is the simplification of science and omission of detail from reports. The journalists' response was simple; it is their job to make the information interesting, accessible and even exciting to the wider audience. It became apparent that, with their scientific background, the journalists are as passionate about good science as the scientists. Their advice for young scientists? Be accessible, explain things clearly, but above all, don't be afraid to speak about your research. This session was especially interesting to me, but what do the media get out

media**watch**

microbiology in the news

If you have any views on science in the media which you think should feature in this column, please send them to the Editor at: **lucy@sfam.org.uk.**

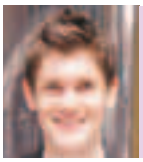
of it? Dr. Ahuja explained *"I immediately thought the workshop was a great idea. These young scientists are the communicators of the future, and journalists need to hear their views on how the media operates, even if it makes for unpleasant listening."*

The final session allowed us to quiz some experts from the field of scientific media. Dr. Claire Bithell from the Science Media Centre, Elsevier's Adrian Mulligan and Ellen Raphael from Sense About Science each gave short presentations about their roles, the role of peer review and practical guidance on how young scientists can get their voice heard. This inspired a lively debate, which continued into the evening at a local bar, where we were joined by some of the earlier panellists.

The VoYS workshop was a fantastic opportunity to speak to journalists about the reporting of scientists and challenged my misconceptions about their motivations when writing articles. It was also clear about what we, as scientists, can do to ensure that science is reported properly — Stand Up for Science! This includes talking about your research, commenting on stories, writing letters, speaking to journalists about the background to scientific stories and by joining the Evidence Base at http://www.senseaboutscience.org.uk/index.php/site/about/39

Thanks to Sense About Science and S*f*AM for the opportunity to attend the workshop. I left with increased confidence about talking to the media and how they would report on what I said. All that remains is to put what I've learned into practice.

Photographs by kind courtesy of ***Sense about Science***



Andrew Hall
University of Wales in Cardiff

MED•VET•NET

Web 2.0 tools for scientific collaboration

The main aim of Med-Vet-Net is to facilitate collaboration between scientists located in many different institutes. Workpackage 3 works to assist our scientific colleagues to undertake successful communications, much of which can now take place in a virtual environment, a "virtual institute." Virtual Communications was the topic of the Med-Vet-Net fourth module in the Science Communication Internship, which aims to give scientists working in the field of zoonoses and food safety essential communications skills. In October 2007, we spent two weeks examining recent advances and uses for mobile and online resources, including creating and writing web pages, podcasting, image manipulation and Web 2.0 technologies. Such resources can be used to communicate our science between colleagues and externally to stakeholders.

What is Web 2.0?

What does "Web 2.0" mean to you? An upgraded version of the web? According to Wikipedia, Web 2.0 refers to *"a second generation of web-based communities and hosted services — such as social-networking sites, wikis and folksonomies — which aim to facilitate collaboration and sharing between users."* You may already be familiar with websites such as MySpace and Facebook. These free sites allow users to share their ideas, photos and news with friends and family online. You have probably also read a "blog" — following the regular posting of news and opinion on a particular topic. I am sure you have heard about online messaging services such as Skype, MSN Messenger or Yahoo Messenger where you can chat in real-time to others who are sitting at their computers and even view that person using a webcam.

Web Conferencing

The Med-Vet-Net Communications Unit has been promoting the use of interactive tools. We have been running successful WebEx™ meetings online between our scientific colleagues spread across Europe and beyond. These allow participants to join in a meeting via a teleconference or VOIP (voice-over Internet protocol – in other words using a headphone and microphone plugged into your computer) while at the same time viewing a website where the meeting host is showing a PowerPoint® presentation, a working document or even performing training with a new software program. Their desktop can be shared and manipulated remotely by other users attending the meeting when permission is given. With our ever-increasing global working environment, these tools are enabling even greater communications across borders and around the world. The Internet and mobile technologies are continually evolving. In reality, you are never really "not contactable" anymore because now you can receive emails and instant messages direct to your mobile phone.

RSS feeds — news and podcasts

In the past, we used to receive news via email by subscribing to bulletins on topics of our choice. Now most generators of news bulletins have the ability to add an RSS (really simple syndication) feed. This is a web feed format used to publish frequently updated content such as blog entries, news headlines or podcasts. The RSS feed makes it possible for people to keep up with their favourite web sites without having to check them manually. The content of RSS feeds can be read using software called an RSS reader or an aggregator (such as iGoogle, My Yahoo or FeedDemon). This technology is making it possible to download regular podcasts and listen to them on iPods or MP3 players on the train or car journey to work. It is possible to subscribe to the RSS feed for Med-Vet-Net News by visiting: www.mynewsletterbuilder.com/rss/rss.php?user=medvetnet.

Using Web 2.0 tools for scientific collaboration

How can we then make these collaborative

internships

As part of its overarching 'Spreading Excellence' Workpackage 3, Med-Vet-Net is required to train people in scientific communication. The Med-Vet-Net Science Communication Internship runs as a course of four modules, each module running between 2 and 2.5 weeks and is open to any current student, researcher or staff member of the Med-Vet-Net partner institutes, as well as fee-paying external participants. Visit **www.medvetnet.org/cms/templates/doc.php?id=82** for more information.

information

For more information about Met-Vet-Net, visit: **www.medvetnet.org/** or contact Teresa Belcher on: **+44 (0)1234 271020**

tools useful in the workplace? Ideally, we can use Web 2.0 technologies to help scientists communicate with each other. We can meet online with our colleagues and see them at their computer in a web conference. We can chat to them online with instant messaging services. We can create a wiki so that a number of people can collaborate in the writing of documents such as proposals. We can download scientific podcasts and listen to the latest news during our journey to work. We can access our emails and websites while travelling. Many of us can work from home by remotely accessing our work server. Many of our institutes may also have an intranet which allows "social networking" between scientists within that institute.

Social networking with scientists globally

What about "social networking" with scientists external to our organizations, with our scientific peers located globally? There is certainly great potential in this type of resource being available. Nature Publishing Group have now joined the Web 2.0 revolution and come up with a solution by creating Nature Network . As part of Module 4 of the Science Communication Internship, we met with Matt Brown, Editor of Nature Network (London), an online companion to the journal Nature which aims to connect scientists globally and locally: *"It is free to join and helps scientists everywhere to meet like-minded researchers, hold online discussions, showcase their work via personal homepages, write blogs, share information with groups (open or private) and tag content,"* Matt explained: *"At the heart of the site, there are several networking tools, to help users find like-minded scientists, ask questions, and share experiences. The site is underpinned with tagging technology, allowing individuals to cut across the various sections and pull out items of interest to them."* As an initiative to encourage science collaboration online, we have already created a group for foodborne zoonoses (http://network.nature.com/group/zoonoses) so that we can begin to build an online network of like-minded people in this field. Please feel free to visit the Nature Network (http://network.nature.com), register and begin exploring and discussing topics with your colleagues.

The future: Web 3.0

So where do we go from here? Well, web 3.0 is already with us! Again, according to Wikipedia, *"Web 3.0 is a term that is used to describe various evolution of Web usage and interaction along several separate paths. These include transforming the Web into a database, a move towards making content accessible by multiple non-browser applications, the leveraging of artificial intelligence technologies, the Semantic Web, the Geospatial Web, or the 3D Web."*

One such example is Second Life, an Internet-based virtual world launched in 2003, developed by Linden Research, Inc. A downloadable client program called the Second Life Viewer enables its users, to interact with each other through motional avatars (created cyberspace characters), providing an advanced level of a social network service. Residents can explore, meet other Residents, socialize, participate in individual and group activities, create and trade items (virtual property) and services from one another. Initiatives with science networks include virtual talks and projects that can be undertaken online by organizations such as Nature, the Science Museum in London, and the Exploratorium in San Francisco, to name just a few.

Some of these new technologies might sound daunting at first, and virtual meetings won't replace face-to-face ones entirely. Sharing preliminary results over coffee with a colleague might seem more natural than chatting in an online forum. But, as we adapt to these tools, we have the potential to make information sharing faster, more open and free of geographical constraints. Imagine how this could increase the rate of new discoveries and techniques, as well as how they can be exploited for the benefit of humankind.

Teresa Belcher and **Jennie Drew**

med-vet-net

Med-Vet-Net is a European Network of Excellence that aims to improve research on the prevention and control of zoonoses by integrating veterinary, medical and food science research. Comprising 16 European partners and over 300 scientists, Med-Vet-Net will enable these scientists to share and enhance their knowledge and skills, and develop collaborative research projects. Med-Vet-Net officially commenced on 1 September 2004, and is funded to the value of €14.4 million for five years.

BIOSCIENCES FEDERATION

bio **focus**

Richard Dyer discusses the need for a full portfolio of bioscience skills

The Biosciences Federation is a single authority representing the UK's biological expertise, providing independent opinion to inform public policy and promoting the advancement of the biosciences.
For further information visit:
http://www.bsf.ac.uk/default.htm

There are frequent reports and comments about the shortage of skills in the biosciences: shortages that are important and potentially damaging to the prosperity of our country. However "skills" do not exist in some semi-independent context. It is always necessary to define what the "skills" are needed for, and this can produce conflicts for those responsible for the delivery of our bioscience skill base.

The first skill that we all need is the skill to be a good and productive citizen. In a knowledge driven economy, scientific skills should be part of the skills portfolio of as many citizens as possible, even though they do not themselves pursue a career in science. For me, it is highly desirable that we have more citizens who understand the scientific method, who appreciate the difference between probabilities and absolutes and who make decisions on the basis of evidence and not Luddite prejudice. With this training, public discussion about climate change, biodiversity or disease will be better informed and there will be greater understanding of the contribution that practicing scientists are making to the debate. In time, the public trust in scientists, which is already quite good, might improve further. The knowledge driven economy demands a scientifically literate population. Delivery of this essential skill is an important responsibility of our schools and universities.

However more usually, a skills shortage is used to describe a more specific problem than the generic need to have science as part of our everyday cultural base. The BSF, together with the ABPI, has just published a report entitled "*In vivo* sciences in the UK: sustaining the supply of skills in the 21st century" (the report is available at www.bsf.ac.uk). One of our recommendations is that a small number of Masters Programmes could be introduced to help alleviate a shortage that is already with us and is having important effects in the pharmaceutical sector. We propose 36 dedicated studentships for this Programme for each of the next three years. This is an important area and yet the solution involves really small numbers: *in vivo* skills are definitely not required in all life science graduates. Of course, practical skills are very definitely required because most science and most biology are intensely practical subjects.

There are many other areas of the biosciences where skills are being lost and yet the solution needs relatively small numbers of practitioners. Take for example the field of systematics and taxonomy. There is no doubt that we are losing the capacity to identify precisely some of our native species — for example lichens. Yet we need really expert individuals in this area today perhaps even more than in the past: we cannot monitor the effects of climate change on our flora and fauna unless we can identify species correctly! Perhaps we will end up relying on the "gifted amateurs" who already contribute much in this area – but in this case the academic subject will be lost.

The production of modest numbers of high level experts in many areas of the biosciences is predominantly the responsibility of our universities and, to a lesser extent, the Research Councils. I write "lesser extent" because some disciplines — for example taxonomy — can be internationally excellent without relying on large grants: and this leads to a second problem. Much biology today is rightly "big science" — big grants and big teams. The business of running a University means that these big science teams are financially more attractive than those individuals virtually grant free. Furthermore, individuals without grants are likely to find it difficult to meet the charges that Open Access brings. The result of course is that there is real pressure on systematics and taxonomy (and many other minority skills) as a profession. However the country needs these skills.

Clearly the skills landscape is complex and varied. The question to face is whether or not the delivery of highly specialised skills can continue to be left to the vagaries of the market place. This essay is not leading to a conclusion that, for example, all Universities with a life science degree have Masters Programmes for *in vivo* skills, or that all plant science departments have top level taxonomic skills. That would be absurd! But the question to answer is how we produce those experts that the country requires – and in sufficient numbers.

Not everyone will like the last sentence! Some will have a wider view, especially in the context of their own expertise! But that can be left to the market place. What we need is confidence that the UK will have the full portfolio of bioscience skills that will be essential if we are to maintain our strong global position in this area. These are skills that would be difficult to "buy in" if our own skill base was lost.

What is needed is top down management, coupled with inducements, in order to build a few excellent teams in minority subjects that are nonetheless essential. Let funding be ring fenced and Universities/Institutes compete for the money to provide leadership in these areas. This is not a new idea: it happens often. For example if you want capital equipment for structural biology from the BBSRC you have to apply from one of about ten Universities. What is new is the argument that this should be done to sustain skills — and there is the key word. Any initiative must be sustainable in the long term. These are not arguments for five years and then the money can be recycled into some other project. These are arguments for a generation — and, sadly, as a consequence they will not seem very dynamic where it matters!

Richard Dyer
Chief Executive
Biosciences Federation

Winter meeting 2008

A one day meeting on

Quality Assurance and Alcoholic Beverages

Royal Society, Carlton House Terrace, London
Wednesday 9 January 2008

CPD ACCREDITATION

A TOTAL OF 6 CREDITS HAS BEEN AWARDED FOR THIS MEETING

For the latest programme please visit us online at **www.sfam.org.uk**

including

The Denver Russell Memorial Lecture

Prevention of biomaterial-based medical device-related infection

Delivered by **Sean Gorman**, School of Pharmacy, Queen's University of Belfast

Programme

Quality Assurance and Alcoholic Beverages

10.00-10.30 **Tea, coffee and registration**

Chair: **Margaret Patterson**

10.30-11.15 **The Denver Russell Memorial Lecture: Prevention of biomaterial-based medical device-related infection**
Sean Gorman, School of Pharmacy, Queen's University of Belfast.

11.15-11.45 **Quality assurance in the university laboratory — is it necessary?**
Sandy Primrose, Business & Technology Management, High Wycombe.

11.45-12.15 **Systems approaches to optimise lager fermentations**
Katherine Smart, University of Nottingham.

12.15-13.15 **Lunch**

Session A. Quality assurance and accreditation issues in microbiology

Chair: **Andrew Sails**

13.15 -13.45 **Getting your food and environmental laboratory accredited — some common problems and misconceptions**
Andy Martin, Microbiology Accreditation manager, UKAS, Middlesex..

13.45-14.15 **Quality control in molecular diagnostics**
Paul Wallace, General Manager, Quality Control in Molecular Diagnostics, Glasgow.

14.15-14.45 **Quality control in food, water and environmental microbiology**
Julie Russell, Head of the Food and Environmental Proficiency Testing Unit, HPA Centre for Infections, Colindale.

14.45-15.05 **Tea and coffee**

15.05-15.35 **Internal quality auditing in clinical and food microbiology laboratories**
Ian Sharp, Quality Systems Unit, HPA Centre for Infections, Colindale.

15.35-16.05 **Living with the known unknowns — Uncertainty of measurement in food and environmental microbiology**
Melody Greenwood, Wessex Environmental Microbiology Services, Southampton

Session B. The Microbiology of alcoholic beverages

Chair: **Martin Adams**

13.15-13.45 **The microbiology of Belgian lambic beers**
Hubert Verachtert, University of Leuven, Belgium

13.45-14.15 **The malo-lactic fermentation in the maturation of wine and cider**
Bob Lovitt, University of Swansea

14.15-14.45 **Bacterial and yeast contributions to Scotch Whisky production**
Derek Jamieson, Heriot Watt University

14.45-15.05 **Tea and coffee**

15.05-15.35 **Wine yeast — transcriptional profiling of wine fermentations**
Bruno Blondin, INRA, Montpelier, France

15.35-16.05 **The role of the barley microflora in premature yeast flocculation during fermentation.**
Barry Axcell, SAB Miller, South Africa

For the latest information please visit the website at: www.sfam.org.uk/winter_meetings.php

BOOKING FORM and INVOICE

SfAM WINTER MEETING WEDNESDAY 9 JANUARY 2008

Only ONE person per form please. CLOSING DATE FOR REGISTRATIONS: Friday 21 December 2007
EARLY BIRD DISCOUNT of £30.00 is applied to all bookings made before **Friday 7 December 2007**

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IBD members	£75 ☐	£105 ☐

YOUR INTERESTS

Please indicate which of the two afternoon parallel sessions you wish to attend

Session A: Quality assurance and accreditation issues in microbiology ☐ **Session B:** The microbiology of alcoholic beverages ☐

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Spring meeting 2008

A one day meeting on

Broadening Microbiology Horizons

Aston University, Birmingham
Wednesday 9 April 2008

Programme

10.00-10.30 **Tea, coffee and registration**

10.35-11.05 **Latest developments in the detection and isolation of MRSA**
Steve Davies, Northern General Hospital, Sheffield

11.05-11.35 **The Fusobacteria and human disease**
Mike Wren, The Windeyer Institute of Medical Sciences,London

11.35-12.05 **Necrotising fasciitis**
Gus McGrouther, University of Manchester

12.05-12.35 **An infusion of Gram negatives (case study)**
Rob Townsend, Northern General Hospital, Sheffield

12.35-14.00 **Lunch**

14.00-14.30 **An update on Syphilis**
Penny Goold, Whittall Street Clinic, Birmingham

14.30-15.00 **Value of typing *C. difficile***
Val Hall, University Hospital of Wales, Cardiff

15.00-15.30 **PVL producing *Staphylococcus aureus***
Angela Kearns, Health Protection Agency, London

15.30-16.00 ***Mycoplasma pneumoniae* the hidden cause of RTIs**
Mark Fielder, Kingston University, Kingston-upon-Thames

14.45-15.05 **Tea and coffee**

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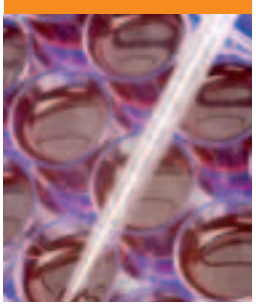

For the latest programme please visit us online at: **www.sfam.org.uk/spring_meetings.php**

BOOKING FORM and INVOICE

SfAM SPRING MEETING WEDNESDAY 9 APRIL 2008

Only ONE person per form please. CLOSING DATE FOR REGISTRATIONS: Friday 28 March 2008
EARLY BIRD DISCOUNT of £30.00 is applied to all bookings made before **Wednesday 5 March 2008**

Cancellation policy: Up to 30 days prior to the event all cancellations will be subject to a 10% cancellation fee, up to 14 days prior to the event there will be a 50% cancellation fee, and no refunds will be given on cancellations made within 7 days of the event.

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Bacterial anti-cancer vaccines:

a science frozen in time

illustration: Stephen Pollard

Peter N Green and **Stephen A Hoption Cann** re-examine the mechanisms and methodologies associated with Dr William Coley's famous toxins

Dr William Coley

As Curator of a major national culture collection, my main purpose is to propagate and maintain a wide range of bacterial species as reference material for the scientific community. However, in the health care professions, doctors, nurses, surgeons and other health care personnel view bacteria somewhat differently, in the clinical environment at least. Bacteria are viewed as the enemy: they cause wound infections, septicaemia, post-operative trauma, and on occasion can and do kill patients. Seen in this context, they are most definitely bad news. Indeed, in hospitals throughout the world most of the focus on bacteria, from the clinician's viewpoint, is geared towards prevention of the infective agent finding a niche in which it can survive and proliferate; and ultimately its destruction.

With Lister and the advent of antiseptics at the end of the 19th century, the fight against bacteria as infective agents began in earnest. By the 1930's and 1940's with the discovery and introduction of modern antibiotic therapies, the bacterial war was seen as being largely won. Sir Alexander Fleming and his successors were to open a Pandora's box of anti-infective agents which were to form a major component in the front line of infectious disease control.

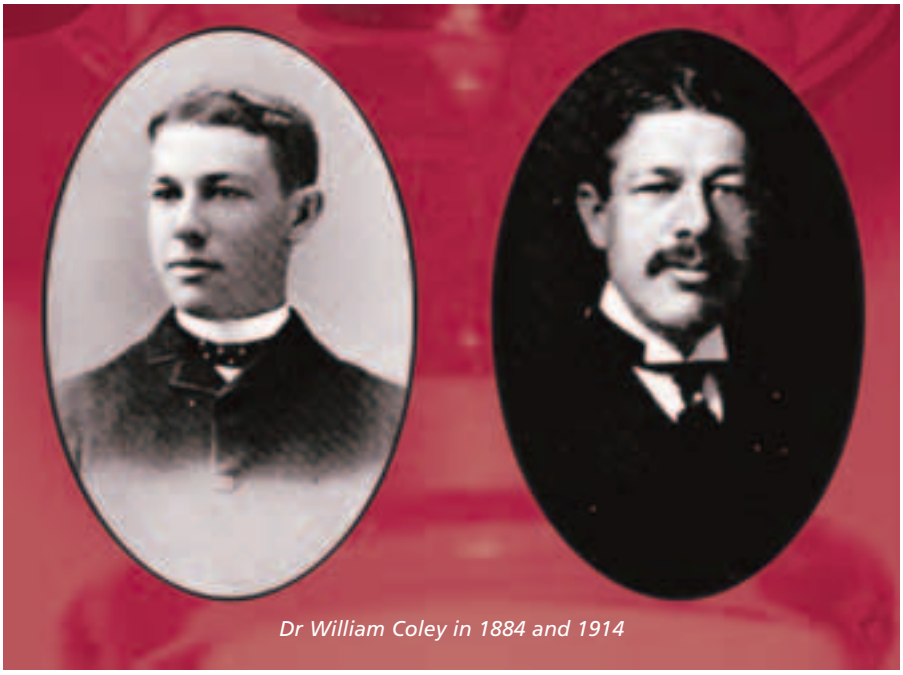
However, one should perhaps pose the question: was there a price to pay for this victory over infective agents in the hospital environment, apart from the obvious multi-drug resistance we see developing in the community today? Did anyone stop to ask themselves the simple question: are all infections by definition, bad? This article is aimed at convincing you that on some occasions they are not.

If I were to tell you that sometimes dangerous or pathogenic bacteria can benefit mankind and possibly even save lives many would think me crazy. Why? Because this is contrary to all we have been taught as scientists in terms of infection and disease control. However, every once in a while, it would be wise to have the courage to rip up the rule book and throw it away, to engage an open mind and examine new ideas. The man I am going to talk about in this article, had that courage, but like many who stray from the conventional teachings and beliefs of his peers, his efforts were scorned and largely ignored by the establishment of the day.

In the early 1890's Dr William Coley was a young surgeon at the New York Cancer Hospital (Later to become the Memorial Sloan-Kettering Cancer Center) in New York. Even at that young stage of his career, he was becoming disillusioned with the conventional medical treatment of cancer and wondered whether nature had its own cure. The first patient he was to lose as a young doctor was indirectly to lead to a huge change in his life as a practicing clinician. A young woman of 17 had injured her right hand and presented with persistent inflammation and pain. She was diagnosed as having sarcoma of the bone and her arm was amputated below the elbow. Despite no clinically evident metastases, the patient died 2.5 months after surgery. Shaken by his failure, Coley searched the hospital records for previous cases to learn more about her disease. Serendipitously, he came upon the record of an immigrant patient who presented with an egg-sized sarcoma on his left cheek. The sarcoma was operated on twice but recurred. The extensive wound after surgery could not be closed and skin grafts were unsuccessful. Ironically, this failure to close the wound was to play a crucial role in the patient's eventual recovery. The tumour progressed and a final operation only partially removed the growth. His case was considered hopeless. However, after the last operation, the wound became infected and the patient developed a high fever. The infective agent was shown to be *Streptococcus pyogenes* or erysipelas as it was known at the time. Little could be done to stop the infection, yet surprisingly, after each attack of fever, the ulcer improved, the tumour shrank and finally disappeared completely and the patient was fully discharged some 4.5 months later. Coley, eager to find this patient, spent weeks searching throughout New York's lower east side. His efforts were not in vain. The patient, still bearing a large scar from the previous surgery, had no trace of cancer and claimed excellent health since his discharge – seven years previously (Coley 1891).

During his investigations, Coley discovered a common theme. For hundreds of years, doctors had reported many cases where tumours had disappeared, apparently

spontaneously (Coley 1893). He researched more and more cases of spontaneous regression involving cancer patients and found that many of these people had something in common apart from their miraculous recovery. Most had been struck down by an acute infectious disease. It might have been flu or measles, malaria, smallpox or syphilis; or like the man in New York, erysipelas. In most cases, their fever subsided, their tumours had broken down and been absorbed or sloughed off. Indeed, infection seemed to be the key to many of these so called "miracle cures." Patients of pre-20th century surgeons, without antibiotics or antiseptics almost inevitably picked up infections from dirty hands, dirty instruments and unhygienic dressings. However, even by Coley's time, cleanliness and hygiene were the order of the day and surgeons would not



Dr William Coley in 1884 and 1914

entertain his seemingly bizarre notions of deliberately infecting patients. Occasionally though, a patient caught an infection by accident. Gradually, Coley began to reason with the few of his colleagues who would listen. He argued that it seemed fair to presume that if accidentally acquired infections of erysipelas could get rid of a tumour, then an artificially induced infection of the same agent would result in the same outcome. Convinced by his logic and determined to prove his sceptics wrong, Coley single-mindedly decided to inoculate the first case of inoperable sarcoma that should present itself. In May 1891, only a few months after losing his first patient, he found a willing volunteer. The man had tumours in both his neck and tonsils and despite recent surgery they had reappeared and were growing fast. Coley injected a streptococcal soup directly into the tumours, every day or two for the next two months. The tumours shrank and the man began to feel much better. In August, Coley stopped the injections and the tumours began to grow again. Coley acquired a more potent culture of streptococci and tried again. This time the patient developed a full blown fever. *"The disease ran its course and I made little effort to check it,"* reported Coley. After two weeks the tumour had completely disappeared. Almost two years later, when Coley reported his results, the tumour in the neck had not returned. Encouraged, Coley tried his treatment on more patients. His sixth patient was a middle aged cigar maker with a lumpy skin tumour on his back and a second tumour in his groin, the size of a goose egg. Surgery failed and both tumours soon grew back. Coley injected them with his streptococcal culture. They shrank but showed no sign of breaking down. He tried again with a different culture. Almost immediately, the cigar maker grew feverish and his temperature hit 40°C. The lump on his back responded immediately. A few days later, the second tumour began to break down as well. Three weeks from the start of his treatment, both tumours had entirely disappeared. Clearly, Coley had made another key discovery; namely that the infective agent had to induce a high fever in the patient to sufficiently stimulate the immune system to attack the tumours vigorously and to have any chance of resulting in their complete removal.

Indeed, it is worth noting that fever is a highly conserved physiological response to infectious stimuli. It is more than just a rise in body temperature and not analogous to hyperthermia (that is a mechanically achieved increase in temperature). Febrile thermogenesis (e.g. chill, shivering etc.) is associated with an increase in metabolic rate of 2-3 times, while maintenance of a fever has been associated with a 30-50% increase in metabolic rate (Baracos *et al.*, 1987). It is unlikely that such a response would be conserved unless it had considerable use or adaptive value.

Historically, Coley was not the first medical practitioner to see a positive role for infective agents in wound management. Centuries beforehand the use of septic or deliberately infected bandages was practised by a few in the profession, the logic being that they either killed the patient or improved the healing of their wound (Hoption Cann *et al.*, 2003). Indeed, the earliest example of such cancer immunotherapy may be thousands of years old. In the writings of Papyrus (ca. 1550 BC), he cited the great Egyptian physician Imhotep (c 2600 BC) who recommended that the treatment for swellings (including tumours) was a poultice followed by incision. Such a regime would inevitably lead to an infection at the tumour site. Nevertheless, using live bacteria to initiate an infection was a precarious gamble between life and death.

In the pre-antibiotic era, the problems associated with Coley's initial approach, as with the medieval practices before him, soon became apparent. Erysipelas was not that easy to control once it began and, perhaps surprisingly, it was not that easy to induce in the first place. Some patients required repeated injections and others never developed a fever. To begin with, Coley believed he needed live bacteria

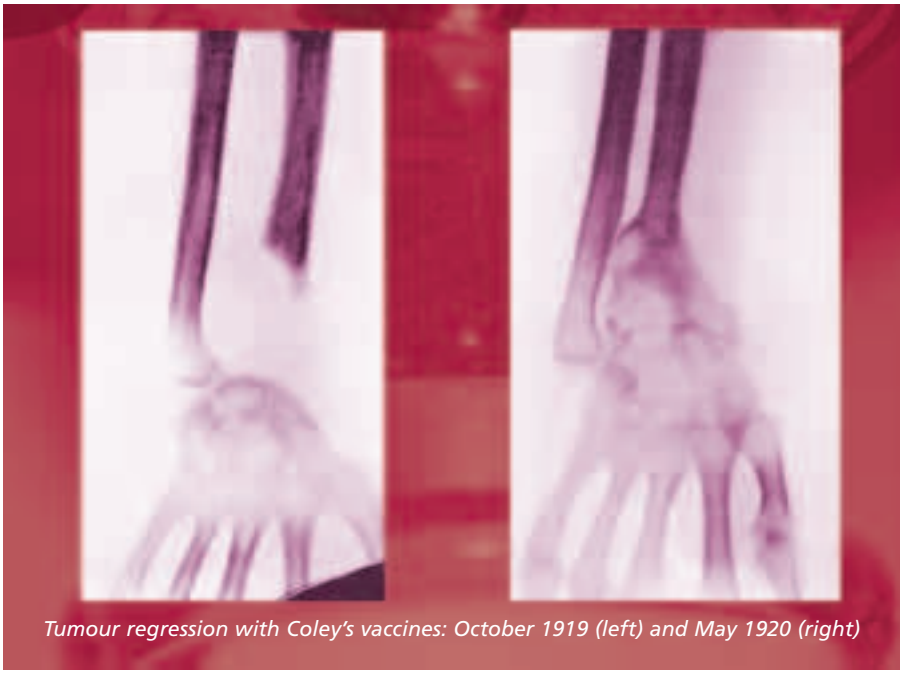
to elicit a patient response, but even daily injections sometimes failed to produce a fever, while in other patients the infection ran out of control. Coley decided that the key factors in his streptococcal soup were bacterial toxins or metabolites produced by the growing culture and that indeed dead bacteria or heat killed preparations may work just as well. After much painstaking work, he finally settled on a mix of dead erysipelas (*Strep. pyogenes*) and another bacterium, *Serratia marcescens*. This "vaccine" became known as "Coley's toxins." These had the advantage of eliciting the same response as live bacteria; importantly the fever, but without the risk of an actual infection. This was to prove a key breakthrough. Indeed, although most of his subsequent work was with Coley's toxins, he often held the view that the identity of the bacteria was less important than the method of use and the fact that they produced a febrile response in his patients. It was also highly desirable, (but not essential) to inject the toxins directly into the tumour as often as necessary to cause fever and to keep this up for weeks or even months (Hoption Cann *et al.*, 2002). It was almost as if the very high fever or "crisis" induced by Coley's toxins produced a greatly enhanced response from the body's immune system: one which, in addition to attacking the bacterial inocula, also attacked and destroyed the tumour cells.

Before summarizing Coley's remarkable work, it is perhaps worth looking in detail at some of the more important factors in Coley's treatment regimes as these are key to the success of anyone who revives his techniques in modern day medicine. Coley's work had not gone unnoticed, despite the sceptics, and his published papers on cancer regression associated with his mixed bacterial vaccine stimulated others to explore the underlying mechanisms of this phenomenon (Nauts *et al.*, 1953). Specifically, researchers strived to identify the "active" component of Coley's vaccine. This also led to investigations to determine which host factors produced in response to the vaccine could induce tumour regression. Cytokines such as tumour necrosis factor (TNF), interleukins and interferons were considered as possibilities. However, the answer is far more complex than ascribing the response to one or another of these factors. Any immune response to pathogens is associated with a multitude of cytokine cascades and a diversity of cellular responses. This immune response was readily evoked through the use of Coley's crude bacterial vaccine, but difficult to reproduce with single cytokine therapy.

After Coley's vaccine is administered, a wide range of cytokines become detectable in the urine including Interleukins 1,2, 6, 8, 10, 12 and 18; gamma-interferon, inducible protein 10, macrophage stimulating factor and TNF (Hoption Cann *et al.*, 2003). Many more cytokines are up-regulated and others down-regulated to varying degrees throughout the course of treatment, yet, this illustrates the point that individual immunomodulating cytokines are in fact only a small facet of this complex immunological response to infection, and correspondingly, tumour regression. That said, there are undoubtedly key cytokines that play a big part in the immune response to Coley's vaccine; principally Interleukin 2 which is produced by Th1 cells (a specific group of lymphocytes or specialised white blood cells often referred to as T helper cells which play an important role in all immune responses). In particular, they help activate and direct other cells within the immune system such as cytotoxic T cells and macrophages. One theory to explain the success of Coley's vaccine centres on its ability to enhance leucocyte and lymphocyte proliferation, maturation and activation. In particular, some think that lymphocytes and in particular macrophages, have a dual role in both cell and tumour production or repair and also similarly in their destruction, depending upon the cytokine expressions being exerted upon or by the immune system (van Netten *et al.*, 1992; Oleszczuk *et al.*, 1994).

Another aside perhaps worth making at this point, concerns the paradoxical influence of acute and chronic infections on tumour formation (Hoption Cann *et al.*, 2006). It is now well established that some malignancies arise in association with chronic infections of one type or another. *Helicobacter pylori* and gastric cancer, *Schistosoma haematobium* and bladder cancer and human papilloma virus (HPV) and cervical cancer are some examples. These infectious diseases generally afflict the organ where the cancer later develops. However, unlike the acute febrile response, a chronic infection generally represents a failed immune response to disease.

Acute infections, exemplified by opportunist post-operative infections or those induced using Coley's vaccine, in contrast, stimulate the immune system



Tumour regression with Coley's vaccines: October 1919 (left) and May 1920 (right)

Figure 1. Cancer: 5-Year Survival

American Cancer Society - 2004				Coley Vaccine
Type	**Localized**	**Regional**	**Distant**	**Inoperable**
Breast	**97%**	**79%**	**23%**	**65%**
Colorectal	**90%**	**66%**	**9%**	**46%**
Melanoma	**97%**	**60%**	**14%**	**60%**
Ovarian	**95%**	**72%**	**31%**	**67%**
Uterine	**96%**	**65%**	**26%**	**73%**

Figure 2. The importance of Clinical Protocol

Dependence of length of treatment on survival: 137 cases of inoperable soft tissue sarcoma

No. of Patients	Length of Therapy	Percentage 5-year survival
3	1 week	0%
7	2 weeks	14%
13	4 weeks	23%
24	2 months	42%
32	4 months	48%
15	6 months	80%
20	12 months	75%
8	24 months	50%
7	> 2 years	71%
8	unknown	63%

Figure 3. Historical case study (1999)

Cancer: 10 years survial rates

Cancer	NCI -SEER group	Coley vaccine group
Kidney	23%	33%
Ovarian	29%	55%
Sarcoma	38%	50%

to target and destroy the infective agent.

Although Coley's toxins were easiest to administer and observe on surface or easily accessible tumours by direct injection into cancerous tissue, the toxins could also be used systemically by intramuscular injection (IM) into the buttock, by intra-peritoneal (IP) injection and also by intravenous (IV) injection, although the last method was more difficult to control and monitor. Thus the beauty of Coley's vaccines, crude though they were, was that they could attack remote tumours, different types of tumours, as well as advanced metastatic progression of the disease.

There are countless other examples of success stories and also of failures as Coley strove to obtain a better understanding of his vaccine and its usage. Coley's success is all the more remarkable in that he was continually fighting the medical establishment who were highly sceptical of his non-conformist therapy. Even Coley's boss, the eminent pathologist James Ewing, became bitterly opposed to his use of the vaccine; seeing radium as the new utopian cure for cancer. In one hostile letter to Coley 1917, Ewing wrote *"gradually we shall get enough cases (treated with radium) with better results, and other institutions will report other good results, so that you will be discredited in the end."* (Hall 1997). However, continuing lacklustre results with radium stirred Ewing to later state (after Coley's death) that *"in some recoveries…there is substantial evidence that the toxins played an essential role"* (Ewing 1940). Coley died in 1936 and for a time his toxins died with him. However, Coley had a remarkable daughter; Helen Coley Nauts, and she developed a passionate desire to devote her life to proving her father's early beliefs and efforts were not to be in vain. During her life time, Helen Coley Nauts researched and documented countless numbers of her fathers' cases and forced the medical world to begin to give his work the credit it deserved (Nauts 1990). There was to be a further setback to the use of Coley's vaccine. In 1962 the FDA passed legislation outlawing the use of therapies it considered ineffective and this included Coley's toxins. This was put into place despite the fact Coley's daughter had presented evidence to show that of nearly 1000 patients treated by her father around 50% had survived in excess of five years (Nauts 1984). A quite remarkable statistic given the advanced state of many of the cancers he treated (See figure 1).

After his death in 1936, interest in Coley's toxins waned. Radiotherapy and later chemotherapy both became standard treatments. Both knock out the immune system and so infection became something to be avoided at all costs. Current researchers have focused resources on ways to trigger the production of specific types of anti-cancer cells or particular tumour suppressing molecules. But Coley's vaccine worked precisely because it was so crude and non-specific and thus stimulated a heightened general immune response. More importantly, the immune system works at its best during a fever, as many would now accept. In 1950, Dr M.J. Shear, an oncologist at the Children's Hospital in Boston, examined a large series of children with untreated acute leukaemia. In those that experienced spontaneous remissions, three quarters of these remissions were preceded by acute infections (Shear 1950). He made the following comment, namely: *"are pathogenic and non-pathogenic micro-organisms one of nature's controls of microscopic foci of malignant tissue? In making progress in the control of infectious disease, are we removing one of nature's controls of cancer?"* (Shear 1950). Think of it for a moment. What treatment are you offered in present

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day medicine if you seek help for a bacterial infection? You are offered antibiotics to kill the bacterial agent which is challenging the immune system and antipyretics to suppress unpleasant symptoms, like fever. The exact opposite of that which Coley's vaccine seeks to achieve; hence a possible explanation for the dramatic reduction in the number of spontaneous regressions observed today.

Although much of Coley's interest and work looked at bone sarcomas, his toxins were used to successfully treat carcinomas, lymphomas, melanomas and myelomas (Hoption Cann *et al.*, 2006). In a comprehensive evaluation of Coley's work involving 896 patients, looking at microscopically proven malignancies treated with Coley's vaccine up to 110 years ago, the five year survival for inoperable carcinomas (34% - 73%) was broadly similar to inoperable sarcomas (13 - 79%), the range varying with tumour sub-type (Nauts 1984). To determine comparable rates of 10 year survival for various cancer patients, in 1999 researchers compared Coley's vaccine patients with matched controls from the National Cancer Institute's Surveillance Epidemiology End Result or SEER database (Richardson *et al.*, 1999). The study found higher rates of 10 year survival for Coley's vaccine patients compared to modern patients in kidney cancer, ovarian cancer and sarcoma (figure 3).

When looking at treatment efficacies it is interesting to compare the effect of length of treatment on outcome or prognosis (figure 2). It is clear from much work that Coley's vaccine is not a one-shot wonder cure. It takes several months of sustained treatment to fully challenge the cancer being treated. Days, weeks, even months of repeated and sustained stimulation of the body's immune system with the vaccine.

Although clearly much more work needs to be done under controlled trial conditions on statistically larger groups of patients before these trends or findings can be more fully substantiated, in these and many other forms of cancer; the data of Coley and others cannot be dismissed out of hand. The phenomenon of spontaneous regression of a wide variety of cancers, linked to both the intentional and unintentional intervention of bacterial infective agents, is far too well documented over several decades, and indeed centuries to be dismissed (Nauts 1980).

The good news is that new small scale trials are now beginning with Coley's vaccine. A small Canadian Company MBVax has been set up and is in the process of conducting limited trials of a new vaccine based on Coley's original formulation. Treatment is at an early stage but initial results are very encouraging.

In conclusion, retrospective studies of Coley's work have shown that despite the billions of dollars spent on the development of modern conventional treatments, for many types of cancer, patients receiving current therapies fared no better than the patients receiving treatments initiated by Coley over 100 years ago. Indeed for some of the case histories I have shared with you, all that the patient would be offered in 2007 would be palliative terminal care. Ironically, had Coley been alive today, I suspect he would still have his sceptics within the profession. Nevertheless, the flame of hope, lit by Coley and indeed others who have argued that there may well be hidden mechanisms within the body's own immune system which can regress or cure many forms of cancer, was dimmed, but not extinguished by Coley's death. We may indeed rediscover what Coley had long known about the potential of the immune system. In a paper from 1920 "The Idea of Progress", Coley quoted the 1st Century Roman Philosopher Seneca who stated, *"The day will come when posterity will be amazed that we remain ignorant of things that will seem to them plain"* (Coley 1920).

The time is long, overdue to re-ignite and re-examine the mechanisms and methodologies associated with Coley's famous toxins which I earnestly believe can enrich, complement and advance modern cancer therapies.

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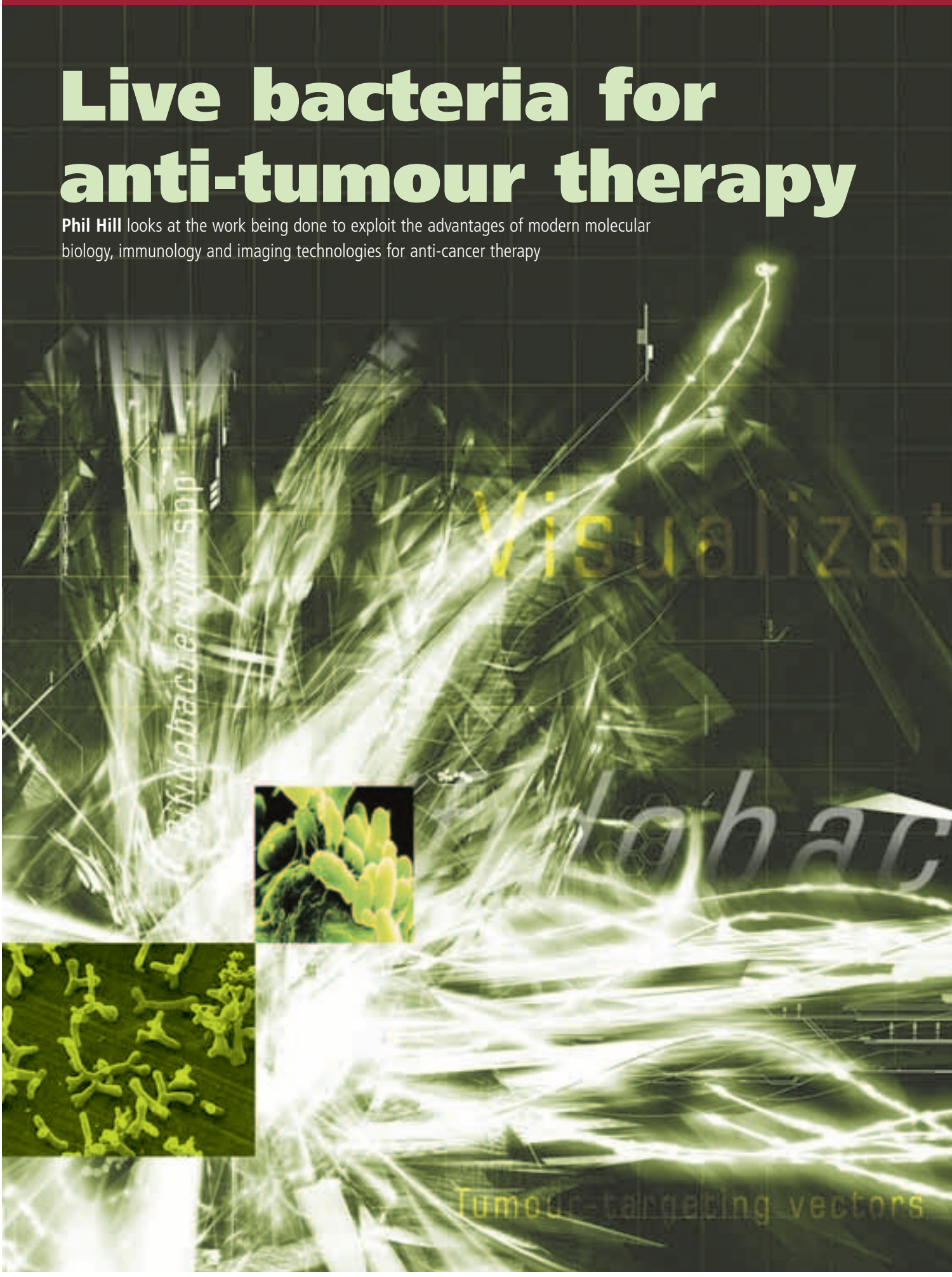
Live bacteria for anti-tumour therapy

Phil Hill looks at the work being done to exploit the advantages of modern molecular biology, immunology and imaging technologies for anti-cancer therapy



The numerous anecdotal reports of spontaneous tumour regression following infection and the fascinating story of Coley and his toxins described in the previous article by Peter Green and Stephen Hoption Cann (page 28), make it difficult to refute the possibility of using micro-organisms to directly treat cancer. Indeed it is the work of Coley and likeminded doctors who effectively initiated the field of cancer immunotherapy, which seeks to alter the body's own natural defences to fight disease. However, much modern immunotherapy tends to target the immune system to specific cells using monoclonal antibodies to cell surface receptors — for example the use of Herceptin against aggressive HER2+ breast cancer cells - rather than inducing a generalised immune response with a pathogenic microbe. Some non-specific immunotherapy using bacteria is currently in clinical use; the bacillus Calmette-Guerin (BCG) developed for vaccination against tuberculosis has been used since the 1970s for the treatment of superficial bladder cancers with significant success in prevention of tumour reoccurrence following endoscopic surgery. The treatment consists of instilling a suspension of BCG into the bladder. Although the specific mechanism of action is unknown, it is assumed that a local immune response is elicited with a variety of cytokines being found in the urine of patients undergoing treatment. Not all patients respond to this therapy, perhaps due to individual immune status, with reports of around 20% failure rate (Witjes, 2006).

While BCG is used as prophylaxis against cancer reoccurrence, a number of scientific groups are exploring the use of live micro-organisms, rather than immunogenic extracts, for tumour therapy due to their intrinsic 'tumour-targeting' properties. The precise mechanisms by which bacteria or viruses would preferentially colonise and replicate in tumours are unknown, however the reproducibility of colonisation has been established in a number of experimental animal models and provides great hope for new 'biologic' therapies. A perceived advantage of a self-replicating therapeutic agent is the continuous presence and increased localised concentration of the agent, removing the need for repeated doses and reducing the potential for toxic side effects. Some hypotheses suggest that hypoxic and/or necrotic regions found within tumours,, provide a niche within which anaerobic bacteria can replicate. To exploit this anoxic niche some groups have attempted to use obligate anaerobes such as *Clostridium* as oncolytic agents. Injection of *Clostridium tetani* spores into mice with implanted tumours resulted in death; however, tumourless mice cleared the bacteria and were seemingly unaffected. This experiment indicated that the spores were only able to germinate in the anaerobic region of the tumours and the vegetative cells were then able to express the tetanus toxins. Subsequent experiments with non-toxigenic strains established that spore germination and bacterial replication only occurred in tumours that were large enough to contain an anoxic/necrotic centre, while smaller tumours and metastases were uninfected (Barbé *et al.*, 2006). Subsequent to the initial *Clostridium* spore studies it has been shown that other obligate anaerobes such as *Bifidobacterium* spp. colonise and replicate preferentially in tumours while being cleared from the rest of experimental animals, though to date complete regression of the colonised tumours by unmodified anaerobes has not been reported.

As colonisation by obligate anaerobes seems to be limited to large tumours, the use of facultative anaerobes may additionally allow colonisation of smaller tumours and metastases, provided that the presence of anaerobic microenvironments is not the sole reason that growth of bacteria in tumours is possible. In 2004, Yu *et al.*, tagged a variety of bacteria and vaccinia virus with luciferases and Green Fluorescent Protein (GFP). They then used low-light imaging to track where these organisms located in anaesthetised animals following intravenous injection into tumour bearing mice. All of the micro-organisms used, even though not specifically modified for intratumoural growth, were shown to replicate in the implanted tumours and metastases. The bacteria used were all facultative anaerobes and could potentially just colonise the necrotic centre of tumours, however growth of bacteria was also noted in small metastases. This observation, together with the fact that vaccinia relies upon viable host cells located in the outer aerobic area of the tumour for replication, suggest that the tumour microenvironment is an immunological sanctuary, rather than simply a physiologically convenient site. Here, immune clearance or surveillance mechanisms are inhibited, therefore protecting colonising organisms from host defences. Subsequent studies in many laboratories appear to support this hypothesis, showing that after a few hours, systemically injected micro-organisms are cleared from most of the animal but some enter the tumour environment where they can replicate

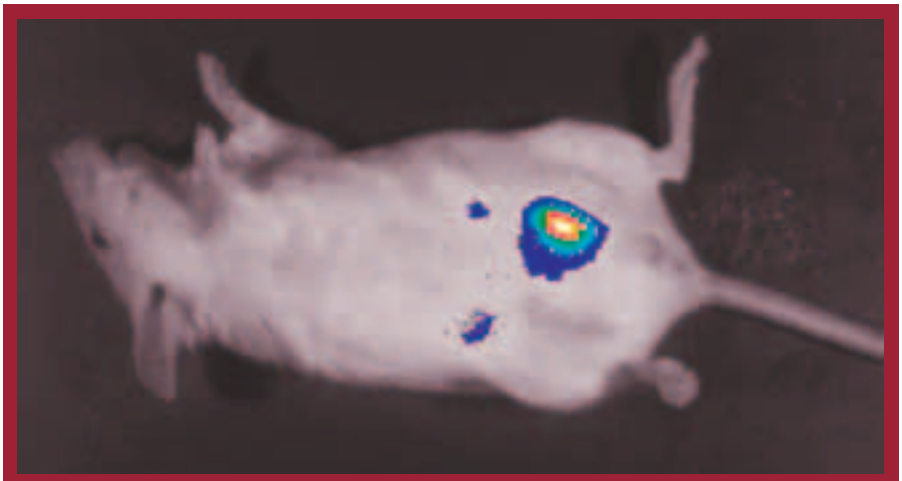


Figure 1. *Tagging bacteria with luciferases coupled with the use of low-light imaging allows researchers to follow bacterial location and thereby tumour colonisation non-destructively in live animals*

to high concentrations. In contrast to obligate anaerobic bacteria which grow in the necrotic centre of larger tumours, facultatively anaerobic bacteria appear to replicate at the border of live and necrotic tumour tissue (Stritzker *et al.*, 2007).

Since it was established that many organisms preferentially replicate in tumours, a number of groups have investigated the use of attenuated bacterial pathogens or viruses, and more recently probiotic bacteria, for tumour therapy. The idea is to facilitate clearance of the organisms from organs and tissues other than the tumour (Pawelek *et al.*, 2003, Stritzker *et al.*, 2007). Attenuated viruses including herpes simplex virus, adenovirus and vaccinia virus have been evaluated as oncolytic agents but lie outside the scope of this brief overview; a recent review of the field is available (Liu & Kirn, 2007). One current view regarding the way in which tumour-targeting bacteria and viruses can result in tumour regression or eradication, is that the replicating agents cause a degree of tumour-cell lysis which results in the release of tumour antigens into the blood. This alerts the immune system to the presence of the tumour, which is then eradicated due to the dual effects of oncolysis and immune clearance. Additionally, bacterial antigens could act as an adjuvant to increase the immunogenicity of tumour-associated antigens, which are often poorly immunogenic. The relative importance of bacterial oncolysis and immune system to tumour regression is unknown, however it is reasonable to speculate that a rate of oncolysis should exceed or at least match the replication rate of the cancer cells, for regression to occur.

Given that there are now 'tumour targeting' bacteria available or under development, and that most of those under consideration are well understood genetically, we can begin to consider engineering therapeutic agents. There are three main approaches currently being investigated by a number of groups. These are; the augmentation of any natural oncolytic activity, the addition of prodrug-converting enzymes and the inclusion of genes for direct immunomodulation.

Equipping bacteria with extreme oncolytic activity may initially seem an attractive approach, however as documented in early experiments using clostridia; if tumours are lysed very rapidly there is an accompanying acute toxicity which results in the death of most experimental animals. So unless the expression of the toxins/lytic proteins can be closely controlled *in vivo*, the side effects are likely to outweigh the benefits of this kind of therapy. Using tumour targeting bacteria which produce prodrug-converting agents has proved to be effective in some laboratories. The idea being that the tumour is firstly colonised by the bacteria, then a non-toxic prodrug is administered to the patient. The prodrug is converted to its active (toxic) form only in the immediate vicinity of the recombinant bacteria, so only the tumour cells close to the bacteria are killed. A widely reported prodrug-converting enzyme in animal models is the *E. coli* cytosine deaminase, which converts non toxic 5-fluorocytosine to the active anti-tumour agent 5-fluorouracil. A similar approach with recombinant bacteria which express heterologous genes, seeks to directly modify the tumour's development: for example, by producing anti-angiogenic proteins to prevent vascularisation of tumour tissue, thereby suppressing tumour growth, or by enhancing recruitment of immune cells to the tumour's location. For all of these approaches we must be able to control the expression of the heterologous genes within the tumour so they can be switched on or off as required. Some expression systems using harmless sugar or antibiotic inducers have been evaluated *in vivo* using optical reporter genes and these appear to give tight controllable expression of genes by tumour-colonising bacteria. Using live vectors to express therapeutic proteins, compared to targeting enzymes with tumour-specific antibodies, provides sustained high local concentration and continued production by bacteria. This is a significant advantage compared to the low amounts that may be delivered and the requirement for repeated administration using conventional delivery.

In the spirit of Coley and exploiting the advantages of modern molecular biology, immunology and imaging technologies, a number of groups have generated persuasive preclinical data to suggest live bacteria can safely be used for anti-cancer therapy. This can be done either alone or in combination therapy with chemo- or radio-therapy. Some are seeking approval for clinical trials whereas others have already embarked upon Phase 1 trials. If such studies prove safe, the intrinsic property of micro-organisms to preferentially replicate in tumours is likely to act as a platform for a variety of anti-cancer therapies.

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Silver wound dressings

Valerie Edwards-Jones looks at the history and current uses of silver as an antimicrobial agent

Figure 1. *An example of some silver dressings on the market*

Dressings have two major functions when applied to a wound. The first is to cover the damaged area and offer some physical protection to the injury; the second is to minimize infection risk. In addition, some sophisticated dressing materials offer additional benefits such as promotion of autolytic debridement, reducing odour, absorbing excess exudate, relieving pain and maintaining a moist environment at the wound surface. This allows the promotion of granulation tissue and the process of epithelialisation. Materials used in dressings vary from polyurethane, alginate, cellulose, starch and other gelable polysaccharides such as carboxymethylcellulose. These materials are incorporated into a plethora of products including films, foams, fibrous products, beads, hydrogels or hydrocolloid dressings. The choice of dressing selection by the wound care specialist is reflected by the requirements to effect wound healing, but cost is also a major consideration. The costs of the dressings vary considerably; especially some of the more sophisticated ones. For example, a recent audit undertaken by University of York has reported the cost for silver dressings in the UK has increased from £800K in 2004 to £23million in 2006 (Hermans 2007).

Wound healing is a dynamic process and is impeded by a number of factors including the patients' age, social factors, nutritional status, oxygen supply to the wound, glycation of growth factors (in diabetes), metalloproteases and other enzymes, and infection. Chronic wounds can persist for years and bacterial bio-burden has a role to play in this prolonged state. Topical antimicrobial agents such as iodine compounds, chlorhexidine, and silver are applied as lotions, creams or ointments or incorporated into wound dressings are used to reduce numbers of microorganisms thus minimising infection. Silver has been used since antiquity and is reviewed by Klasen HJ in 2000 (Klasen, 2000). Some examples of key uses, approximate date and scientist are shown in Table 1.

Table 1. History of silver as an antimicrobial agent

Key uses	Date and scientist
1% silver nitrate on neonates to prevent eye infection	1884 Crede
0.25% and 0.01% silver nitrate proven effective against	1887 von Behring
0.5% silver nitrate used in burn wounds	1965 Moyer and Monafo
1% silver sulphadiazine cream used for burns	1968 Fox

(modified from Dunn & Edwards-Jones, 2004)

Silver coins and silver jugs were used to cleanse water by the Romans and there are numerous reports of *lapis infernalis* (silver nitrate - 1 part silver / 3 parts nitric acid) used in the middle ages. A silver nitrate pencil was carried by physicians as a topical antimicrobial agent and used to manage eye infections. In 1965, Moyer and Monafo used silver nitrate to treat burn wound infections, but frequent dressing changes were required as the compound dissociated rapidly and deposits of insoluble silver chloride formed, causing blackening of the wound. The high concentration of silver needed caused some toxicity and in 1968, Fox (1968)

introduced silver sulphadiazine, a complex of silver and sulphadiazine (a sulphonamide), which dissociated more slowly therefore effecting a slower release of silver into the wound and allowing less frequent applications (up to 48 hours between dressing changes). This is not without problems however, as it forms a pseudo-eschar which makes inspection of the wound bed difficult. Also, high levels of silver are rapidly deposited onto the wound bed and cases of argyria, amongst other problems, have been reported (Lansdown 2006). It is known that the depth of penetration of silver sulphadiazine into the wound bed is limited and in recent years cerium nitrate has been added to the silver sulphadiazine (Flammercerium™) to enhance this (Garner 2005).

There has been an explosion of silver dressings released onto the market with different adjunct properties (see main picture). There are examples of absorbent, non-absorbent, hydrocolloid, alginate, adhesive and non-adhesive dressings. Different chemical forms of silver are incorporated into or onto the dressing fabric and after application release silver onto the wound bed (donating) or into the dressing (non-donating). Silver nitrate, silver sulphadiazine, metallic silver and nanocrystalline silver are currently used in dressings.

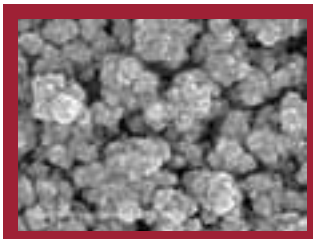

Figure 2a. *A thin film of nanocrystalline silver sputtered by vapour deposition onto a surface*

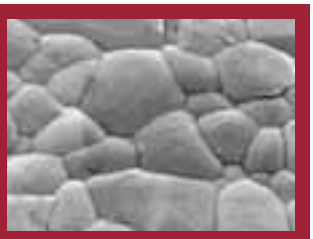

Figure 2b. *A thin film of normal metallic silver sputtered by vapour deposition onto a surface. Modified from Dunn & Edwards-Jones (3)*

Antimicrobial effect of silver

Silver is a broad spectrum antimicrobial agent showing activity against bacteria, fungi and viruses. It has also been shown to have anti-inflammatory properties acting as a metalloprotease inhibitor, which is known to inhibit wound healing. Silver ions bind to DNA and inhibit DNA replication, interfere with components of the electron transport chain, and interfere with the respiratory chain in the cytochromes. Like other antiseptics, silver is quickly inactivated by protein binding but this inactivation can also be caused by phosphates, sulphates and chlorides, all frequently found in tissues.

Biologically active silver is presented in a soluble cationic form, Ag+. Ionic silver is the familiar form seen in silver nitrate, silver sulphadiazine and other ionic silver compounds. Early silver formulations used in medicine had to compensate for the rapid release of silver as Ag+ from the compound and ultimate chemical complex formation, thus rendering it less active. This required frequent dressing changes by the practitioner, which was a time consuming process.

Ag0 clusters or Ag0 is the metallic silver form found in other silver structures and appears to have limited antibacterial action.

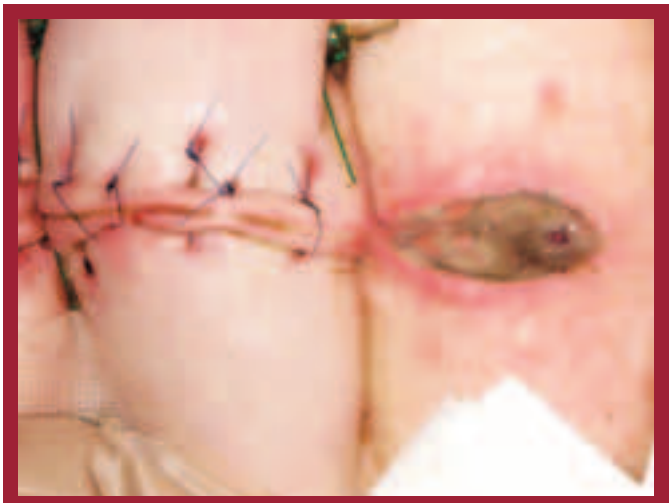

Figure 3a. *An abdominal wound infected with Pseudomonas aeruginosa prior to treatment of nanocrystalline silver dressing*

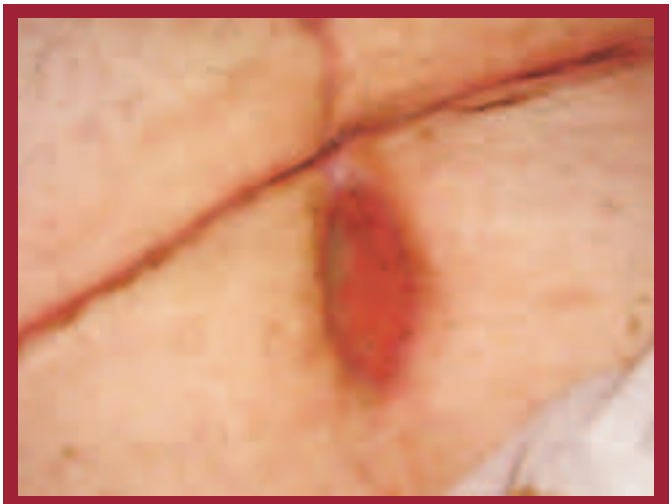

Figure 3b. *After three weeks treatment with nanocrystalline dressings*

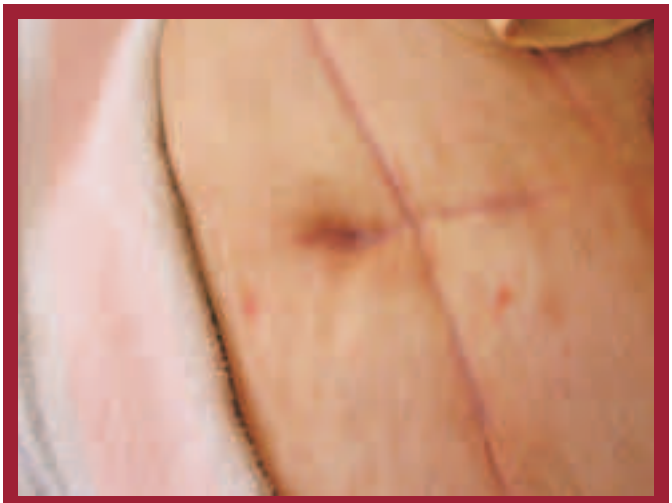

Figure 3c. *After twelve weeks treatment with nanocrystalline dressings.*

With the advent of nanocrystalline silver, the need for as many dressing changes has been minimised, which is cost effective in terms benefits to the wound, patient and practitioner. The average particle size of nanocrystalline silver is 20-120nm in size when sputtered by vapour deposition onto a surface, creating a larger surface area (see figure 2) and more availability of silver ions. Continual sustained release of Ag+ when exposed to water, occurs over 3-7 days from the Ag0 / Ag+ complexes and the reported levels remain at approximately 100 parts per million(Taylor *et al.*, 2005a and b). Examples of successful treatment of infected wounds using nanocrystalline dressings are shown in figure 3.

A number of studies have reported levels of silver released from the plethora of available dressings and these vary from 1p.p.m to 100 p.p.m. The levels do vary considerably depending upon the solvent used. However, it must be recognised that levels of available silver be different in a wound because of the protein levels and protein binding.

Sub-lethal levels of silver can inhibit metalloproteases (MMP's) produced by the host cells (Wright *et al.*, 2002) and also by *S. aureus* the commonest pathogen causing wound infection (Edwards-Jones 2002). The wound healing process is slowed by MMP's and inhibition of these at the wound bed could promote wound healing. Therefore silver dressings may be bi-functional depending upon concentration, with high levels exerting antimicrobial effects and sub-lethal levels inhibiting MMP's.

Reported levels of silver in the dressings often leads to confusion for a number of wound care practitioners. Many are using dressings to prevent or reduce colonisation in complicated wounds with high infection risk and others use them to reduce bioburden in chronic wounds with a view to improving smell, reducing exudate and hopefully helping the wound to heal. The number of silver dressings available is increasing almost by the month. Currently there are eighteen different silver dressings available (at the last count) where silver is incorporated into foams, alginates, hydrocolloids, and films.

Silver resistance

There have been reported cases of resistance to silver (Silver *et al.*, 2006). The resistance is usually intrinsic through prevention of entry into the cell or through efflux mechanisms, but these cases are sporadic and there do not seem to be large numbers of resistant strains emerging. This is good news in the current climate of increased numbers of multiple antibiotic resistant bacterial strains. With the high usage of silver it may be pertinent to monitor silver resistance among wound isolates, however, this would be difficult as screening is not common within diagnostic microbiology laboratories.

Silver toxicity

In vitro toxicity studies on keratinocytes and fibroblasts are difficult to relate to their effects on a healing wound. For example, heavily exudating wounds are difficult to reproduce, with the silver being potentially washed away. Also, the wound healing status may be different at every dressing change. There have been some cases of silver toxicity reported in the past with the use of silver nitrate, but very few cases have been reported in recent years with the use of products with more controlled release.

In summary, Silver dressing may have a place in the prevention of spread of infection in a colonised wound. Studies have shown that some wound dressings can actually prevent translocation of MRSA from the surface of a wound to the surface of the dressing (Strohal *et al.*, 2005) and this has been confirmed *in vitro* (Edwards-Jones, 2006). Using silver dressings as an antimicrobial barrier could help combat infection control problems.

Although this overview has focussed on silver in wound dressings it is only one of the numbers of antimicrobial agents currently used by wound practitioners. Other successful agents such as povidone iodine, cadexomer iodine, chlorhexidine and other topical agents have their role to play in wound care.

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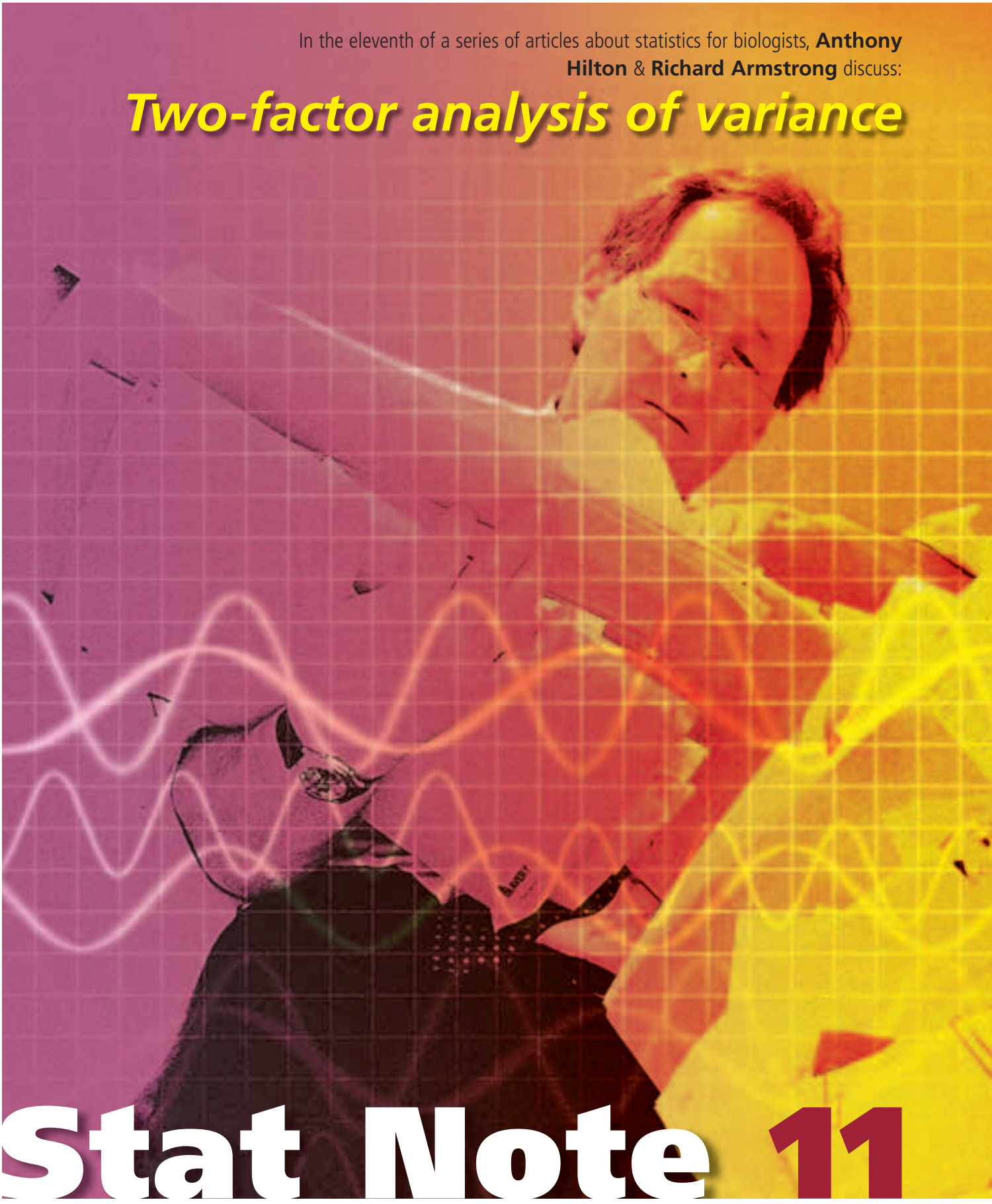
In the eleventh of a series of articles about statistics for biologists, **Anthony Hilton** & **Richard Armstrong** discuss:

Two-factor analysis of variance



Stat Note 11

The analyses of variance (ANOVA) described in previous articles of this series (Hilton & Armstrong, 2006; 2007) are examples of 'single factor' experiments. In its simplest form, the single factor experiment comprises two or more treatments or groups arranged in a randomized design, i.e., treatments are assigned at random and without restriction to the experimental units or replicates. An extension of this experimental design is the two-way design (Hilton & Armstrong 2007) in which the data are classified according to two criteria, i.e., treatment or group and the replicate or 'block' to which the treatment belongs. A factorial experiment differs from a single factor experiment in that the effects of two or more 'factors' or variables can be studied at the same time. Combining factors in a single experiment has several advantages. First, a factorial experiment usually requires fewer replications than an experiment that studies each factor individually in a separate experiment. Second, variation between treatment combinations can be broken down into components representing specific comparisons or 'contrasts' (Ridgman, 1975; Armstrong *et al.*, 2000; Armstrong & Hilton, 2004) and which reveal the possible synergistic or interactive effects between the factors. The interactions between factors often provide the most interesting information from a factorial experiment and cannot be obtained from a single factor experiment. Third, in a factorial design, an experimenter can often add variables considered to have an uncertain or peripheral importance to the design with little extra effort. This Statnote describes the simplest case of a factorial experiment incorporating two factors each present at two 'levels'.

Table 1. Influence of type of dishcloth and rinsing treatment on the number of bacteria transferred to a food preparation surface

Factor A	Cloth		Sponge	
Factor B	**Rinsed**	**Not rinsed**	**Rinsed**	**Not rinsed**
	1.0 x 105	7.8 x 107	3.9 x 105	8.0 x 106
	2.3 x 104	5.0 x 107	9.0 x 103	4.0 x 106
	3.9 x 105	4.1 x 107	8.5 x 104	2.0 x 106
Mean	**1.7 x 105**	**5.6 x 107**	**1.6 x 105**	**4.7 x 106**

The scenario

The kitchen dishcloth is increasingly recognized as a primary reservoir of bacteria with potential to cause widespread cross-contamination in food preparation environments. An investigator wished to study the influence of the material from which the dishcloth was manufactured (cloth or sponge) (Factor A) and the effect of rinsing the dishcloth in running water (Factor B) on the number of bacteria subsequently transferred to a food preparation surface (Hilton & Austin 2000). Dishcloths of each material type were inoculated with 1 ml of a 108 cfu ml^{-1} *E. coli* culture and after 10 min, the cloth was wiped over an appropriate area of sterile cutting board. Additional pieces of cloth were inoculated but rinsed in sterile running water before wiping. The cutting board was subsequently swabbed to recover *E. coli* that had been deposited from the wiping by the cloth. The data comprise the number of bacterial colonies obtained on nutrient agar from the two types of dishcloth, rinsed and unrinsed, and are shown in table 1. The objectives of the experiment were to determine whether the ability for bacteria to be transferred from the dishcloth varied with the type of dishcloth and with rinsing treatment and whether the two factors had an independent influence on the numbers of bacteria. Hence, there are four treatment combinations, i.e., two types of cloth each of which is either rinsed or not rinsed. This type of design is the simplest possible factorial experiment and is also known as a 2^2 factorial, i.e., two factors with two levels of each factor. In this notation, the superscript refers to the number of factors or variables included and the integer the number of levels of each factor.

Statistical model

Using the commonly used notation to describe the basic model of an ANOVA described in Statnote 9 (Hilton & Armstrong 2007) we can describe this model as follows:

$$x_{ijk} = \mu + a_i + b_j + (ab)_{ij} + e_{ijk}$$

In this model, x_{ijk} is the value of the 'kth' replicate of the 'ith' level of Factor A and the 'jth' level of factor B, a_i and b_j are the main effects and $(ab)_{ij}$ represents the two factor interaction between A and B.

ANOVA

As in previous examples, the total sums of squares (SS) can be broken down into components associated with differences between the effects of the cloth and rinsing treatment. In this case, the between treatments SS can be broken down into 'contrasts' which describe the main effects of 'A' and 'B' and the interaction effect 'A x B'. These effects are linear combinations of the means, each being multiplied by a number or 'coefficient' to calculate a particular effect. In fact, the meaning of an effect can often be appreciated by studying these coefficients (table 2). The difference between dishcloths is calculated from those replicates representing the cloth data (+) compared with those which represent the sponge data (-). Note that in a factorial design, every observation is used in the estimate of the effect of every factor. Hence, factorial designs have 'internal replication' and this may be an important consideration in deciding the number of replications to use. Each 'replicate' is actually providing two estimates of the difference between cloths and sponges. The main effect of 'rinsing' is calculated similarly to that of 'dishcloth'. By contrast, the two-factor interaction (dishcloth x rinsing) can be interpreted as a test of whether cloth type and rinsing treatment act independently of each other. A significant interaction term would imply that the effect of the combination of cloth type and rinsing treatment would not be predictable from knowing their individual effects.

Table 2. 'Orthogonal contrasts' for a two-factor experiment each at two levels

Dishcloth type (A)	Cloth		Sponge	
Rinsing (B)	**Yes**	**No**	**Yes**	**No**
Treatment Total	5.13 x 105	16.9 x 107	4.84 x 105	14 x 106
'Contrast'				
A	+1	+1	-1	-1
B	+1	-1	+1	-1
AB	+1	-1	+1	-1

In a 2^2 factorial, partitioning the treatments sums of squares into factorial effects provides all the information necessary for interpreting the results of the experiment and further 'post-hoc' tests (Hilton & Armstrong, 2006) would not be necessary. With more complex factorial designs, for example, those with more than two levels of each factor, further tests may be required to interpret a main effect or an interaction. With factorial designs, it is better to define specific comparisons before the experiment is carried out rather than to rely on 'post-hoc' tests which compare all possible combinations of the means. Factorial experiments can be carried out in a completely randomised design (Hilton & Armstrong, 2004), in randomised blocks (Hilton & Armstrong, 2007) or in more complex designs (Cochran & Cox, 1957). The relative advantages of these designs are the same as for the one-way design (Hilton & Armstrong, 2007).

Table 3. Analysis of variance of the dishcloth data in Table 1

ANOVA					
Source	**DF**	**SS**	**MS**	**F**	**P**
Cloth/Sponge	1	2002.83	2002.83	20.99	P<0.01
Rinsing	1	2760.42	2760.42	28.92	P<0.001
Interaction	1	2001.33	2001.33	20.97	P<0.01
Error	8	763.49	95.44		

Abbreviations: DF = Degrees of freedom, SS = Sums of squares, MS = Mean square, F = variance ratio, P = probability

Interpretation of the results

The resulting ANOVA (Table 3) is more complex than a one-way ANOVA because the between groups or treatments sums of squares is partitioned into three factorial effects, *viz.*, the main effects of dishcloth type and rinsing and the interaction between the two factors. In the present example, there is a main effect of dishcloth type ($F = 20.99$, $P < 0.01$) and of rinsing ($F = 28.92$, $P < 0.001$) suggesting significantly more bacteria were transferred from the cloth than the sponge and significantly fewer after rinsing both materials. In addition, there is significant interaction between the factors ($F = 20.97$, $P < 0.01$) suggesting that the effect of rinsing is not consistent for the two types of dishcloth. Examination of the treatment means suggests that the sponge transfers a smaller proportion of its bacterial load to the food preparation surface compared with the cloth. This effect is probably attributable to organisms being more exposed on the surface of the cloth and therefore more liable to be transferred compared with the more cavernous sponge (Hilton & Austin 2000).

Conclusion

Experiments combining different groups or factors are a powerful method of investigation in applied microbiology. ANOVA enables not only the effect of individual factors to be estimated but also their interactions; information which cannot be obtained readily when factors are investigated separately. In addition, combining different treatments or factors in a single experiment is more efficient and often reduces the number of replications required to estimate treatment effects adequately. Because of the treatment combinations used in a factorial experiment, the degrees of freedom (DF) of the error term in the ANOVA is a more important indicator of the 'power' of the experiment than simply the number of replicates (Hilton & Armstrong, 2006). A good method is to ensure, where possible, that sufficient replication is present to achieve 15 DF for each error term of the ANOVA (Ridgman 1975, Armstrong *et al.*, 2002). Finally, in a factorial experiment, it is important to define the design of the experiment in detail because this determines the appropriate type of ANOVA. We will discuss some of the common variations of factorial ANOVA in future Statnotes. If there is doubt about which ANOVA to use, the researcher should seek advice from a statistician with experience of research in applied microbiology.

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Rob Townsend describes a day in the life of a busy consultant in medical microbiology in a large teaching hospital

careers

A Day in the Life of Dr Rob

Finally getting back to my office at the end of a busy Friday and sitting down with a mug of tea I realised that this was probably the best time to think about writing this article on a typical day in the life of Dr Rob (as I seem to be known locally). So, I hear you cry, *"Who is Dr Rob and what does he do?"* Well, I am a Consultant in Medical Microbiology working for Sheffield Teaching Hospitals NHS Foundation Trust and I'm based at Sheffield's Northern General Hospital. The hospital I work at is a large adult hospital of close to 1200 beds and is a regional tertiary referral centre for specialities such orthopaedics, cardiology, cardiothoracic surgery and renal medicine to name but a few. I am one of three Consultant Microbiologists working at this hospital with three further consultants working across the city at the Royal Hallamshire Hospital and one at the Sheffield Childrens Hospital.

Before I begin telling you about a typical day I thought I'd spend a few paragraphs telling you about how I got here. The story starts with my A levels at which I didn't exactly excel. In fact as one supply chemistry teacher once said to me, *"Don't bother with higher education son, you haven't got what it takes."* I'm still not sure why he called me son (I am one obviously, but not his) but still, an interesting way of motivating a 17 year old. Even at this tender age I knew I wanted to "do microbiology" in some way but I still don't know how I came to this conclusion as we had never done any at school.

In 1988 I went to Sheffield City Polytechnic and took a degree in Biomedical Science, which is where I truly started to find science in general, and microbiology in particular, fascinating. We had some great lecturers especially Barry Davis and John Mills and another memorable one who had been in the foreign legion (or so he said) and knew 32 ways of performing random acts of violence with an army boot (16 with the left and 16 with the right was what he used to say).

I did my placement year in microbiology at the Royal Hallamshire Hospital and with grateful thanks to people like Phil Wheat, Trevor Winstanley and Dr Bob Spencer managed to write my first publication. I completed my degree with a 2:1 and returned to microbiology at the Royal Hallamshire to begin work as an MLSO (as it was then), completed my masters degree in pathological sciences (distinction this time!) then had a career changing moment and decided to head for medical school with Phil's advice ringing in my ears *"Do something different and don't come back to microbiology."* After working in infectious diseases for a while I decided that I'd follow Phil's advice to

the letter and duly returned to microbiology as a specialist registrar (you can take the boy out of microbiology etc., etc.)

Ultimately I was appointed to my current job of Consultant and took up post one freezing cold, snowy February morning this year, which I knew would be my destiny as Phil Wheat had said all those years ago: *"It'll be a cold day before he comes back to microbiology."*

So by now you're probably on the edge of your seat wanting to know about this Friday in the life of Dr Rob.

08.00. Turn pager on and head out of door to take small(ish) toddler to nursery, sing songs about scarecrows, rabbits, tractors etc whilst trying to wipe her breakfast off my shirt/tie/suit (delete as applicable).

8.20. Attend my newly created orthopaedic Multidisciplinary Team Meeting (MDT) (newly created by me to engage the surgeons and stress the importance of infection in general, and antibiotic prescribing in particular). Spend 40 minutes discussing various patients with infected hips and knees, surgeons now overcome with desire for breakfast (spent too long concentrating on infection in general and not enough on bones in particular) — head to canteen.

09.00. Canteen for bacon sandwich and mug of tea, continuing random policy discussions with surgeons (not discussing patients as we are in a public area!) Wipe brown sauce off my shirt/tie/suit (delete as applicable).

09.20. Head to the orthopaedic wards to review some difficult infections with one of the orthopaedic consultants, advise on assorted collection of patients and change said antibiotic regimes to something (relatively) less likely to give rise to MRSA or *C.difficile*.

10.00. Head to the Macmillan palliative care unit for another ward round, change or stop various antibiotic regimes to try ones less likely to lead to MRSA and *C.difficile*.

11.00. Rendezvous with one of the microbiology registrars on cardiac intensive care for the start of the ITU ward rounds. Review all the patients on the ward and start/stop/change a variety of antibiotic regimes and suggest a range of further investigations (much to the annoyance of radiologists/ cardiologists/ haematologists/ surgeons — delete as applicable).

11.30. Continue the ITU ward round by going to the general ITU. More of the above: Review all the patients on the ward and start/stop/change a variety of antibiotic regimes and suggest a range of further investigations (much to the annoyance of radiologists/ cardiologists/ haematologists/ surgeons — delete as applicable).

12.30. Return to microbiology via the deli bar for ham salad and mug of tea. Discuss the various issues of the morning with the team whilst having lunch. Wipe salad cream off my shirt/tie/suit (delete as applicable). Switchboard now change from paging me the whole time to phoning my office as I've foolishly let them track me down, continuing answering seemingly random questions from various junior doctors whilst trying to change their antibiotic regimes to ones less likely to lead to MRSA and *C.difficile*.

13.00. Medical authorisation! The highlight of the day — spend approx one hour signing out reports. (Do I really need to see all these coliforms from GP wound swabs?)

14.00. Off to the medical admissions unit to present an upcoming service evaluation aimed at improving blood culture taking in an attempt to reduce contamination. Have many conversations with many junior doctors about how you shouldn't take blood cultures from a cannula even if it is newly inserted. Got the ward to agree to take part in the evaluation of a new skin prep solution — success!

15.00. Back to microbiology, have a mug of tea whilst catching up with emails and correspondence (more letters from orthopaedic surgeons about complicated infected bones from all around the country), more seemingly random calls from assorted junior doctors whilst all the time change or stop various antibiotic regimes to try and prevent MRSA or *C.difficile*.

16.00. Microbiology clinical team meeting (the so called "4 o'clock meeting.") Discuss all the ITU patients from the ward round and any other interesting or difficult cases from the day with all the microbiology consultants, registrars and SHO's. This meeting is mainly for the benefit of the on-call person, but also a key educational meeting for the junior medical staff (and often the senior ones as well).

16.30. Have mug of tea, email the finished article for the trust newsletter (the 'Dr Rob's bug page') and start thinking about the article for S*f*AM.

17.15. Off to the nursery to pick up small(ish) toddler. Hear all about small persons day at nursery (running, playing, singing, shouting etc., etc.) Head for home singing songs about scarecrows, rabbits, tractors etc and trying to wipe her dinner off my shirt/tie/suit (delete as applicable).

18.00. Arrive home, not on-call so finally turn pager off, switch kettle on for a mug of tea and put bottles of assorted fermented products from a hard working *Saccharomyces* into the fridge for later.

Reflecting back now on what was a fairly full day I think it illustrates quite nicely some of the key roles of a medical microbiologist. Medical liaison plays a central role particularly with respect to advising on antibiotic prescribing, infection control and appropriateness of various clinical investigations — not just microbiology related ones. Many times the conversation will be: *"I think this requires a CT or ultrasound scan"* or "Needs an urgent surgical opinion," or; *"I think this is endocarditis — they need an echocardiogram."*

The role of a medical microbiologist is certainly a varied one and depending upon specialist interest areas within your job (orthopaedic microbiology for me, infection control or laboratory management roles for others), this will be reflected within your average working day. The route to becoming a medical microbiologist is usually not as long and winding as mine but always

requires a medical degree. Following medical school there is one year as House Officer (HO or Foundation year 1 as it is now) in various medical or surgical specialities then some will enter microbiology as a Senior House Officer (SHO or Foundation 2 as it is now) and having completed at least one year at SHO level (in microbiology or infectious diseases) will look for a registrar post (or specialist trainee as it is now) which lasts for five years. Some candidates enter microbiology having done several years in general medicine and have usually (although not always) obtained membership of the royal college of physicians (MRCP). Whatever pathway a trainee has taken into microbiology once they are a registrar they are required to complete their training portfolio and obtain membership of the Royal College of Pathologists (MRCPath). Obtaining MRCPath requires successfully completing two exams: the first (part 1) is usually undertaken after approximately one year as a registrar and is primarily multiple choice and extended matching questions. The second exam (part 2) is taken towards the end of training (from year four onwards) and is based over four days: the first day consists of four written papers and the remaining three days are based around a microbiology practical exam (extremely good fun — or perhaps that was the old MLSO in me!). Once they have completed their MRCPath and fulfilled a variety of additional training requirements, including the required courses and completion of a log book they then obtain their Certificate of Completion of Training (CCT) at the end of their five year training period. Armed with a CCT and an MRCPath an applicant can head off to look for a consultant position.

23.00. Cease jotting notes down for the S*f*AM article, put glass down and wipe remnants of said fermented products from dressing gown/pillow/bed (delete as applicable) and go to sleep.

further reading

- **www.rcpath.org.uk**

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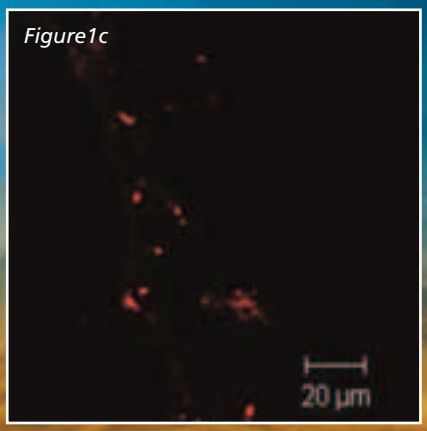
S*f*AM Laboratory Fellowship Article

Microbiology and biogeochemical cycling in the sea surface microlayer



Environmental interfaces are often biologically important places to be. At the point where the ocean meets the sky, the sea surface microlayer (SML) is a distinct ecosystem. It covers ~70% of the planet's surface yet it is only as thick as the full stop at the end of this sentence. For many years the SML, or neuston, has been shown to be physically, chemically and biologically distinct compared to sub-surface waters. Recent application of 'modern' molecular microbiology tools is now allowing a greater depth of ecological and biogeochemical understanding.

Microbial life in the sea surface microlayer

Microbial life in the SML has been known to be distinctive for some time. Early studies have shown elevated numbers of bacteria are present in the SML compared to sub-surface from a range of marine and freshwater sites. Furthermore these bacteria are highly active; consuming hydrophobic compounds produced by phytoplankton in sub-surface water. The mineralization of biogenic organic matter in marine ecosystems is a fundamental ➤

biogeochemical process. This is particularly important during periods of high activity, i.e. during phytoplankton blooms, when the water column becomes a dense soup of algae and their exudates. During phytoplankton blooms, surface slicks are often visible as a 'scum'.

Part of our current research at the University of Warwick is to investigate microbial community structure and function in the SML. Studies of bacterial and archaeal communities in the SML using denaturing gradient gel electrophoresis (DGGE) have shown that community structure is distinct compared to the corresponding sub-surface water in a range of marine habitats. We have detected populations of both archaea and bacteria in the SML that we cannot detect in the sub-surface water directly beneath the SML. It remains unclear what determines community structure in the SML, why SML-specific populations are present and what are the determinants of the SML-niche?

There is strong evidence to suggest that the microbial populations present in the SML have ecological qualities which may help them to grow in the SML-niche. These include the ability to produce and/or be resistant to antimicrobial compounds and therefore compete with other populations for resources and space. Also as the SML is exposed directly to UV radiation, populations that are resistant to UV-damage may have a competitive advantage. The presence of the biogenic film may mean that microbes present in SML are in effect a biofilm, as opposed to microbes in the water column below, which are planktonic. It is now widely established that the ecological pressures of microbes in biofilms are different to those existing planktonically.

The sea surface microlayer — a vanguard for trace gas transfer

There is strong evidence to suggest that the sea surface microlayer may influence the transfer of globally significant trace gases such as methane, carbon monoxide and nitrous oxide. The physical presence alone of an organic film influences gas transfer. However, mesocosm experiments taking place at the Ocean Research Group in the University of Newcastle in collaboration with the University of Warwick have shown that methanotrophic bacteria in the sea surface microlayer can further affect the flux of methane from surface water into the atmosphere. Understanding the interactions between marine ecosystems such as the sea surface microlayer, biogeochemical cycles and climate regulation is a major challenge for researchers today.

Who is doing what in the sea surface microlayer?

The ability to determine community structure – function relationships in microbial populations has relied upon techniques such as Stable-Isotope Probing (SIP) and Microauto-radiography combined with Fluorescent *in situ* Hybridisation (FISH-MAR) or microarray analysis. FISH-MAR relies upon the union of two methodologies. A microbial community is exposed to radioactive substrate (e.g. 14C-glucose, 3H-leucine). Microbes within that community which are able to utilise the labelled substrate will become radioactive as they are subsequently labelled themselves. The sample is prepared by covering it with a film emulsion which can determine which cells are radioactively labelled (Fig 1a). FISH uses oligonucleotide probes which have a fluorescent marker attached. The probes can be designed for specific ribosomal sequences to target specific microbial groups, e.g. *Alphaproteo-bacteria* or *Alteromonas* spp. (Fig 1b&c). The data sets are then combined: the identities of the populations which have utilised the labelled substrate can be determined (Fig 1d). The FISH-MAR images presented here were obtained on a training project funded by the **SfAM Laboratory Fellowship** which allowed me to visit the Department of Microbial Ecology at the University of Vienna, Austria, and work under the guidance of Dr. Holger Daims and Prof. Michael Wagner. These experimental approaches will allow us to identify and study microbial niches in the SML in order to establish what is determining community structure.

As with much of this planet, the microbial communities in the sea surface microlayer remain poorly understood to say the least. We are currently using a broad range of techniques to start to answer both fundamental and applied questions about the processes that take place in the sea surface microlayer. Understanding the sea surface microlayer and the role it plays in biogeochemical cycling will improve our knowledge of earth system processes in this current climate of change.

further information

The **SfAM Laboratory Fellowship** is available to Full members who work in private, academic or government laboratories. Grants of up to £1,000 per week (to cover travel, accommodation and consumable costs in the host laboratory) for up to four weeks are available to support staff wanting to visit another laboratory to be trained in a new technique or learn new skills..

To apply for this award, please contact the Society Office or visit the website at :

- **www.sfam.org.uk/grants.php**

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Students into Work Grant reports

information

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Characterizing the cell surface of several marine *Synechococcus* strains

I am entering the third and final year of a Microbiology and Virology BSc at the University of Warwick. I have a specific passion for Microbiology and am interested in pursuing a research career after graduating. Therefore, I was delighted to be offered an opportunity to gain practical experience in a ten week vacation placement in the Microbiology Research Group at the University of Warwick.

Oceans cover 70% of the earth's surface and are responsible for about 40% of the carbon fixed on this planet. The large central areas of the world's oceans, are responsible for most of this marine primary production, a function of the tiny (<2 um) oxygenic photoautotrophic microorganisms contained within. Prokaryotic cyanobacteria are the most abundant component of the picophytoplankton responsible for 20-40% of global chlorophyll biomass and carbon fixation. Amazingly these marine cyanobacteria comprise only two genera, *Synechococcus* and *Prochlorococcus*. These organisms are of particular ecological importance being at the edge of the physiochemical world (light, nutrients) and the biological world (food webs, ecosystems). Because of the tremendous ecological importance of these cyanobacteria, the complete genome sequences of several marine *Prochlorococcus* and *Synechococcus* strains have recently been completed. This includes six new marine *Synechococcus* genomes which this laboratory has been co-ordinating. Within these genomes, we have identified a group of 'giant' proteins whose function is unknown. The *Synechococcus* sp. WH7805 contains five open reading frames (ORFs) encoding polypeptides ranging in size from 182 kDa to 734 kDa which belong to this 'family', whilst strain RS9917 possesses two ORFs encoding proteins of 839 kDa and 2,724 kDa. Several other strains contain one to three proteins of this type. The proteins are similar to a protein characterised in another marine *Synechococcus* strain, WH8102, designated SwmB and which is known to be localised to the cell surface. The objective of this project was to gain an understanding of the function of these 'giant' proteins using biochemical techniques to assess their expression. The project thus aimed to characterise the cell surface of several marine *Synechococcus* strains, which is where we propose these 'giant' proteins reside.

Synechococcus strains WH7805, WH8102, RS9916 and RS9917 were grown in artificial seawater (ASW) medium and using both whole cell pellets and fractionated samples to perform SDS-PAGE to study protein expression in different strains. Having optimised the procedure using gradient SDS-PAGE, good overall protein expression profiles were obtained and the expression of proteins was studied under different growth conditions. Growing the strains in an enriched sea water medium (SOW), the expression of proteins was compared between ASW- and SOW-grown cultures and any differences detected. In ASW, *Synechococcus* strain WH8102 was found to be non-motile but, in SOW medium, it became motile, allowing the study of motility and the expression of giant proteins to investigate any potential link. To investigate even further, SOW-grown *Synechococcus* cells were nitrate- or phosphate-starved for four days and subsequently any

changes in expression were compared using SDS-PAGE. Proteins separated by SDS-PAGE were further characterised by mass spectrometry and by thrombin in-gel digestion. Results from SDS-PAGE suggest that phosphate-starved WH7805 and RS9917 expressed 4 and 3 high molecular weight proteins, between sizes 350 and 600 kDa, respectively. The identity of these bands is being confirmed by mass spectrometry. Further work is required.

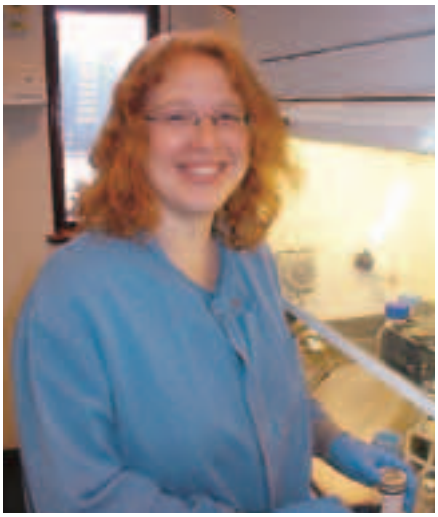
During the vacation placement, I gained important laboratory experience in handling equipment, carrying out experiments, managing my own research project and solving problems. I acquired an insight into how the scientific research process progresses. Experiments often raised more questions than they answered, and despite unexpected results and numerous set-backs, the process was fascinating. Having tried many different approaches, it was satisfying to gradually perfect the procedure and discover more and more. I was able to put theory into practise, and also learned independence in practical work. This research project gave me not only confidence and motivation, but also enthusiasm to continue studying microbiology at a postgraduate level after I graduate.

I would like to thank Dr. Ken Flint, Dr. David Scanlan and Dr. Martin Ostrowski for the supervision, guidance and support I received. I thank the Society of Applied Microbiology for giving me an opportunity to gain such a valuable experience.

Laura Lehtovirta

The efficacy of ultraviolet (UV) light treatment to inactivate *Mycobacterium avium* subsp. paratuberculosis (Map) in milk and buffer solution

After completing two years of a BSc Honours degree in Food and Nutrition, the opportunity arose to take advantage of an *Sf*AM Students into Work Grant and work for 10 weeks alongside Dr Irene Grant in Food Microbiology at Queen's University



Belfast. The Food and Nutrition course covers all aspects of food science and nutrition, including food microbiology so, as I am currently exploring all possible career options available to me after graduation, I was keen to take this opportunity to expand my knowledge and develop new skills in relation to practical food microbiology research.

The aim of the research project was to investigate the efficacy of ultraviolet (UV) light treatment to inactivate *Mycobacterium avium* subsp. paratuberculosis (Map) in milk and buffer solution. Map causes Johne's disease, a chronic inflammatory bowel disease, in ruminant animals. This bacterium may also have some role in the aetiology of Crohn's disease in humans. If this is the case, one possible route of transmission of Map to humans is via cow's milk. Previous research carried out by Dr Grant and others has shown that Map may not be completely inactivated by milk pasteurization. Hence, alternative methods of inactivating this bacterium in milk are being sought by the dairy industry and use of UV light is a possibility.

UV inactivation of Map was carried out using a laboratory-scale UV machine provided by Iatros Ltd., Dundee. The company provided me with training on correct operation of the machine. After initially establishing the UV sensitivity of Map in Middlebrook 7H9 broth, the second phase of experiments investigated the rate of UV inactivation of Map suspended in UHT whole and semi-skimmed milk. The inactivation kinetics of Map in both milk and buffer were determined by two different methods: colony counts on Herrold's egg yolk medium and plaque counts using the FastPlaque phage amplification assay (Biotec Laboratories Ltd, Ipswich). Conventional culture is extremely slow (4-6 weeks for colonies to appear) whereas the phage assay provided a viable count within 18h.

At the end of my 10 week placement, conventional culture was still in progress for many of the experiments conducted. Phage assay results indicated that some reduction in Map numbers was achieved by UV treatment. However, a much larger reduction in numbers of viable Map was observed in the 7H9 broth than in semi-skim or whole milk indicating that Map is more resistant to UV light when present in milk. Milk components such as fat and protein are known to reduce UV penetration and hence its germicidal action.

The 10-week project gave me the opportunity to experience all aspects of laboratory based research, from the initial experimental design through to the interpretation of data, while developing new practical skills and techniques. It also provided me with an insight into the ever evolving nature of research - experiments do not always work as planned and methodologies are continually being developed and refined. I enjoyed the challenge of developing and conducting the experiments and felt as if I experienced both the ups (when results obtained were better than expected) and downs (when we were left scratching our heads at incoherent results) of working in research. This experience will be invaluable as I begin my final year at university, during which I will undertake my 3rd year research project. It has also opened up another possible career path to consider after graduation.

I would like to express my sincere thanks to the Society for Applied Microbiology for the Students into Work grant. I would also like to thank my project supervisors, Dr Irene Grant and Dr Michael Rowe, for their knowledge, help and guidance during the work placement. It was a rewarding experience which I would recommend to anyone interested in microbiology or anyone considering postgraduate research.

Leslie Altic
Queen's University of Belfast

Getting down and dirty with the microbes on the farm!

Before my final year studying Microbiology at The University of Aberdeen I felt confident enough to try a summer placement, thinking it would be beneficial before going into my honours year. So when a placement became available to me working for Dr. Chris Hodgson at the Institute of Grassland and Environmental Research (IGER) –in Devon I decided that it would be the perfect opportunity to try something new. The microbiology I had being doing at Aberdeen had been based around the medical and molecular side whereas the placement at IGER was very much focused on applied environmental microbiology.

The Project

The project at IGER was a RELU (Rural Economy and Land Use) project. The RELU programme is sponsored by NERC, BBSRC and ESRC, and brings together social and physical scientists to address practical rural issues. The project has a rather grand title; ***Sustainable and holistic food chains for recycling livestock waste to land.*** In a nutshell it is looking towards the implementation of the tighter microbiological standards resulting from the revised Bathing Waters Directive and what farmers can do to reduce the risk of transfers of faecal indicator organisms (FIOs) from their land. Transfer of FIO to water could seriously impact on businesses reliant on clean water, e.g. tourism and shell fisheries.

The study is focussed on the Taw river catchment in North Devon. Up to 100 farmers have been interviewed regarding their farm management practice and attitudes towards manure and livestock management. Ten of these farms have been selected for routine monitoring of concentrations of FIOs, faecal coliforms and faecal streptococci in streams above and below the farm. The analysis of the questionnaires completed by these farmers has identified in the researchers minds the 'riskier' times of year on these farms in terms of the transfers of FIOs from farms to water courses. For example, when a dairy farm turns out the cattle in the Spring and when slurry is applied to the land. During these 'riskier' times pairs of farms are monitored more intensively, with up to ten areas of each farm being monitored.

Monitoring

During the ten weeks I was at IGER I was involved in the routine monitoring on the farms and monitoring during the intensive periods on a beef farm and a farm that is predominantly arable but has a small suckler herd. We carried out on-site testing, performing simple chemistry at different points of the streams surrounding the farms - testing the pH, temperature, turbidity and conductivity of the water. We also took 500 ml samples in a sterile bottles for microbiological testing back at the lab. Where possible we also determined the flow in the streams using a flow meter in order to estimate 'loads' of FIO transfers, but this proved very difficult because it was such a dry summer and many of the streams dried up. For the intensive sampling we had a mobile laboratory which allowed us to filter the water samples on site, ensuring that we were able to analyse all our samples within two hours. The water samples were analysed using the membrane filtration method where a known volume of water is filtered through a 0.47 ìm filter trapping the FIO's. The filter is then placed aseptically on a selective media; MFc agar for the faecal coliforms or thermotolerant coliforms and Slanetz and Bartley (S&B) agar for the faecal streptococci. The agar plates were then incubated at different temperatures, 44.5ºC for the MFc and 37°C for the S&B. After 24 hours the numbers of colony forming units on the MFc agar were enumerated, 48 hours for the S&B media.

Die-off experiment

While I was at IGER I was given the responsibility of setting up an experiment looking at the 'die-off' rate of faecal indicators in slurry which had been spread onto grassland plots. We simulated two different spreading techniques; surface broadcast spreading and shallow injection. We included control plots into our statistical design so that we could show what the 'residual' concentration of FIO's is in the soil. For the spreading we used watering cans, this was smelly, but great fun! In order to simulate the broadcast spreading we used a watering can with a spoon strapped at the spout end which resulted in the slurry splashing against the spoon and spreading in a similar manner to a farm-scale slurry spreader. It worked very well! In order to simulate the shallow injection, 5-6 cm deep slots were cut into the ground and we used a watering can (without the spoon attachment!) to pour the slurry into the slots.

The first time that we collected the slurry for the experiment we left it in a $1m^3$ container for several weeks prior to spreading it. When we tested the slurry after the application there were no FIOs in the slurry at all! We concluded that due to the very hot, sunny weather the slurry had pasteurised sitting in the one tonne container out on the experimental field. This was a disaster and put our experiment back by at least a week. Frantic phone calls and lots of cajoling of local farmers ensured we were able to source some new 'fresh' cattle slurry and the experiment was repeated on a new site on field called little burrows at IGER.

Once the slurry was spread for a second time (on to new plots) we used a 2cm corer and a 7.5cm corer to take samples from the plots. We used the 2cm corer to collect samples from the control plots and the plots where slurry had been surface spread. The 7.5cm corer was used to take samples from the shallow injection plots. As the slots were on average 5.5cm deep, the 7.5cm corer was used in the slot to retrieve a 2cm sample from the base of the slot, this meant that there were samples

taken from 2cm below the ground on all plots. Five soil cores were taken from each plot and the soil homogenized.

Five grams of soil was added to 45ml of Ringers solution, vortex mixed and then shaken for 60 minutes. After standing for 10 minutes the elution was analysed for faecal coliforms and faecal streptococci. Necessary dilutions were made which were reduced as the colony counts began to decline.

We sampled the plots every day for one week, then twice a week in weeks two and three, continuing to once a week thereafter. We increased the time between sampling because we were beginning to see a decrease in the number of FIO present in the samples. Although there was a decline, the 'die-off' rate of the faecal coliforms appeared to be quicker than the faecal streptococci. Thus far, there has been a significant decrease of the FIOs in both the shallow injection and the broadcast plots. Decline of FIO appears to be more rapid in the surface broadcast plots than the shallow injection plots. There was an interesting observation with the MFc plates, not only did we detect the distinctive blue colonies, the majority of which we identified as *E. coli*, using bioMerieux api® system, but a distinctive pink colony was also growing on the plates.

Thoughts about my placement at IGER

The atmosphere at IGER is very friendly and open and I found I always had someone to talk to. I found IGER incredibly multi-national, with people from all over the world. I learned how to drive Landrovers and if I had been there for longer, there were various additional courses that I could have taken such as off-road driving, tractor driving and forklift driving. I found it a very relaxed way of life and much less stressful than working in a laboratory. IGER incorporates science and agriculture and really is trying to make a difference. I made a lot of new friends and although I was apprehensive at first, I was made to feel welcome.

Working at IGER has been great, I learnt a lot during my ten week placement and I'm glad that I had the opportunity to visit the institute. This placement has completely changed my views on Microbiology, and because of this I have had to reassess my priorities for the future. Working at IGER has allowed me to see a lot of the countryside and feel that I am actually doing something to help make this a better country to live in. I enjoyed a more varied placement than constantly working in a laboratory, and I preferred it. I feel that if more people had this kind of opportunity to experience something different than staying in a lab all day then they would also feel this.

I would like to thank everyone who made me feel so welcome at IGER, especially my line manager Chris, who managed to secure the position for me, and everyone I worked with and (tried to!) play volleyball with. Finally I would like to thank S*f*AM for enabling me to undertake this valuable and rewarding summer project.

Rebecca Murray
University of Aberdeen

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Aerobic degradation of polychlorinated biphenyls: shattering the dogma of recalcitrance

Despite active research spanning more than three decades, extensive regulatory actions, and an effective ban on their production since the late 1970s, in the United States and mid 1980s in Europe and other nations, polychlorinated biphenyls (PCBs) remain a focus of research and environmental attention. Polychlorinated biphenyls consist of the biphenyl structure with two linked benzene rings in which one or all of the hydrogen atoms have been substituted by chlorine atoms. For approximately 50 years prior to 1976, PCBs were used extensively in industry. Their non-flammability, superhydrophobicity, excellent chemical and thermal stabilities, and electrical insulating properties made them ideal for a number of industrial and commercial purposes such as in electrical applications, heat transfer and hydraulic equipment; as plasticizers in paints, plastics and rubber products; in pigments, dyes and carbonless copy paper and many other applications. Unfortunately, the same properties, which made PCBs so useful to industries, make them some of the most serious and persistent environmental pollutants. More than one-third of the total global production of PCBs has been deliberately and/or accidentally released into the environment (Holoubek, 2001), and they are believed to be universally distributed throughout the world. The global distribution, potential for toxicity, mutagenic, teratogenic and carcinogenic effects on human and wildlife populations; and proven bioconcentration and bioaccumulation properties demonstrate PCBs to be of ecological and environmental health concern. Although the toxicity of PCBs to the biota is excessively exaggerated and usually bordered on the irrational, it should be remembered however, that PCBs were an important life saving invention. Prior to 1929, electrical equipment contained flammable fluids, which often ignited creating conflagrations that constitute serious risks to human health. The use of PCBs and other chlorinated organics as fire retardant fluids help create a safer environment for the fast growing industrial society.

Due to the hazards presented by these xenobiotics in the environment, information on their rates and extent of biodegradation is of great interest. If bioremediation and bioaugmentation of contaminated matrices are to be effectively used, isolation and characterization of organisms capable of degrading PCBs are necessary. Increased knowledge about physiological properties and substrate diversity will help determine the process conditions that should be used in the range of transformations that can be obtained in practical treatment systems. In spite of their thermodynamic stability, structural diversity and toxicity, it is somewhat amazing therefore, that many microorganisms and enrichment cultures have been obtained that are able to metabolise and utilize PCBs as carbon and/or energy sources under aerobic and anaerobic conditions. Ahmed & Focht (1973) reported the first evidence of microbial degradation of PCBs. They demonstrated co-culture of two different species of *Achromobacter* isolated from sewage to degrade several congeners of PCBs. They also showed in addition, that degradation of the unsubstituted aromatic ring was preferred, that no dechlorination occurred, and that this resulted in a built up in chlorobenzoic acids (CBAs). PCB congeners with chlorine on only one of the rings were degraded more easily than those with chlorine on both rings. Since this initial report, many naturally-occurring bacteria have been isolated and demonstrated to grow on one or more of the monochlorobiphenyls (CBs) (Furukawa *et al.*, 1978; Bedard *et al.*, 1987; Bopp, 1986). All these studies have resulted in elucidation of the PCB catabolic pathways.

PCB degradation is complicated because they are produced as complex mixtures, with individual congeners exhibiting varying effects on the scavenging organism. The range of PCBs transformed by the pathways is highly dependent upon the bacterial strain. Some organisms do not transform PCBs that contain more than three chlorines, whereas, other strains such as *Burkholderia xenovorans* LB400, *Rhodococcus* sp. RHAI and *Alcaligenes eutrophus* H850, transform up to hexachlorobiphenyls (Bedard *et al.*, 1987; Seto *et al.*, 1995; Bopp, 1986). Generally, the degradation rate of PCBs decreases as chlorine substitution increases, while congeners with more than five chlorine substitution in most cases, are practically recalcitrant to aerobic cometabolism.

The discovery in the mid 1980s that an aerobic degradation of PCBs by indigenous microorganisms occurred more often than was previously thought (Brown *et al.*, 1989) made bioremediation of these compounds seem a viable cost-effective and environmentally friendly alternative to the only available physical and chemical remediation strategies. As a general rule, highly chlorinated congeners are good substrates for anaerobic degradation, possibly via chlororespiration (the initial use of the PCB as an electron acceptor), but are poor substrates for aerobic degradation. As a result, the use of a sequential anaerobic-aerobic process is often proposed as a potential bioremediation for treatment of soils and sludges contaminated with PCBs. Using this scenario, an anaerobic treatment would be used to reductively dechlorinate highly chlorinated congeners. The lightly chlorinated congener products would then be degraded aerobically. One difficulty associated with such a sequential treatment is that aerobic biodegradation is thought to require a cometabolic substrate, e.g., biphenyl, since PCBs rarely serve as growth substrate for aerobic bacteria. But biphenyl is expensive and often subject to regulatory restrictions as well. The use of biphenyl as a cometabolic substrate might be circumvented therefore, if aerobic bacteria could be isolated that could grow on a range of dichlorobiphenyls (diCBs) or trichlorobiphenyls (triCBs) while cometabolically degrading more highly substituted congeners. Development of an effective sequential anaerobic-aerobic treatment is also impeded by other factors. Reductive dechlorination of PCBs rarely occurs at the ortho positions and generally results in the accumulation of ortho- or ortho- and

para-substituted congeners (Abramowicz, 1990). Unfortunately, ortho-chlorinated congeners elicit a wide range of toxic responses and are among the most recalcitrant to chemical and aerobic degradation (Abramowicz, 1990; Dai *et al.*, 2002). This may be a result of inhibition by ortho-chlorinated metabolites of the enzyme responsible for aromatic ring cleavage, 2,3-dihydroxybiphenyl 1,2-dioxygenase.

It is generally believed that only CBs functions as a sole source of carbon and energy for aerobic bacteria. Other workers were of the opinion that claims of isolation of diCB-utilizing organisms must be viewed as equivocal because the cultures are not available, the description of the growth media was insufficient for the media to be reproduced by others, the purity of PCBs (absence of biphenyl) was not determined, and no accompanying data on growth curves and chloride liberation were given. Potrawfke *et al.*, (1998) were the first to demonstrate unambiguous growth by a natural strain of *Burkholderia xenovorans* LB400 on 2,3- and 2,4'-diCB. Similarly, in a recent publication, Kim & Picardal (2001) described for the first time growth on a diortho-substituted chlorobiphenyl (2,2'-diCB) by a novel natural bacterium capable of mineralising both 4-CB and 2,4'-diCB. It should be noted that 2,2'diCB is rarely susceptible to aerobic cometabolic pathway. More recently, exotic tropical bacterial strains exhibiting fascinating metabolic diversity and possessing novel catabolic properties were reported. We documented growth of these isolates on a broad and unusual spectrum of PCB congeners including all CBs, 2,3-, 2,2'-, 2,4'-, 3,3'-, and 3,5-diCB and several congeners of di-and trichlorobenzenes (Adebusoye *et al.*, 2007a, b). Interestingly, growth of these tropical organisms was also sustainable on 2,2',4- and 2,2',5-triCB (Adebusoye S. A., Picardal F. W., Ilori M. O., Amund O. O. and Fuqua C., submitted for publication). It is noteworthy that these organisms were isolated from African contaminated soils where PCB contamination is widespread and indiscriminate discharge of hazardous waste into the environment is a regular occurrence, without appropriate efforts to clean up the mess. Included among the microorganisms was an enteric organism — *Enterobacter* sp. SA-2. The isolation of this strain is particularly significant. Growth of an enteric organism on PCBs is an uncommon phenomenon, thus suggesting that the genes for dissimilation of diCBs may be more widely distributed across microbial genera than previously believed for the last several decades and that novel or extensive degradative pathways may be evolving in response to selective pressure of long-term PCB exposure, or that the contaminated tropical soils we used as inoculum contained unique metabolic capabilities.

Since our studies showed that the presence of chlorine at the ortho position resulted in no obvious patterns of recalcitrance, these novel strains therefore, could be indispensable tools in preventing accumulation of ortho-substituted congeners in natural systems and offer the hope for development of effective sequential anaerobic-aerobic bioremediation strategies. Successful application of this sequential treatment may enable the cleanup of all types of PCB-contamination. Meanwhile, as years go by, it is believed that isolation and characterization of superior and novel PCB degraders with ability to grow on triCBs and even tetrachlorobiphenyls would be reported. This microbial expansion will greatly improve understanding of the breadth of PCB-degradative activity that exists naturally. Afterall, prior to the work of Ahmed & Focht, PCBs were perceived as immutable, and this perception lingered even into the late 1970s and early 1980s despite the early research. It was the extensive body of work on aerobic biodegradation that indeed shattered the dogma of PCB recalcitrance. It is now evident that it is not only CBs that can serve as growth substrate for aerobic PCB-degrading microorganisms.

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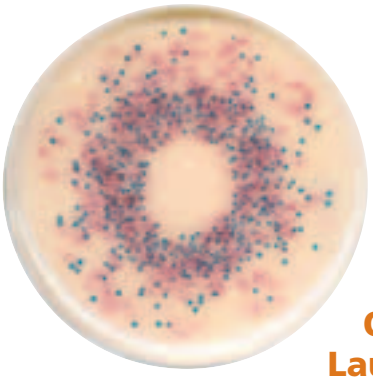

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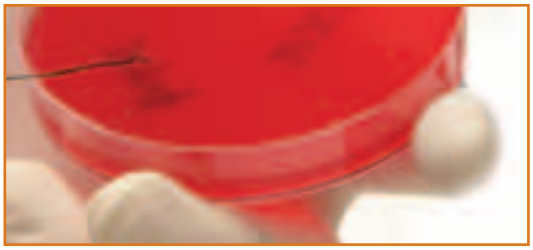

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Significant expansion of Lab M's ISO compliant media for food industry

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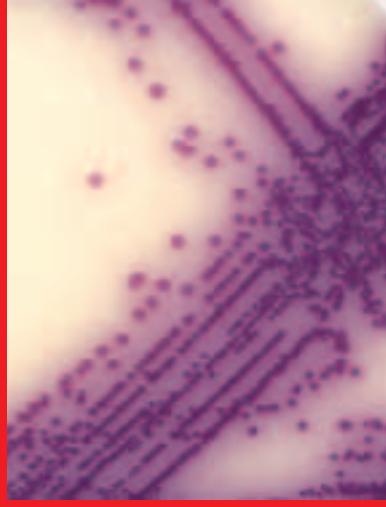

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Oxoid Salmonella Chromogenic Medium Mark II (OSCM II) is the first ever selective culture medium to incorporate Inhibigen™ technology, combining it with familiar chromogenic technology to provide excellent isolation and identification of *Salmonella* colonies.

The R&D team responsible for Oxoid's new Inhibigen™ technology

The Inhibigen™ used in OSCM II specifically inhibits the growth of *E. coli*, a common competing organism in *Salmonella* investigations, whilst novobiocin and cefsulodin at carefully selected levels, inhibit the growth of other competing flora, such as *Proteus* and *Pseudomonas*. Two chromogens are also added to the medium, allowing the differentiation of *Salmonella* colonies (bright purple) from other organisms, such as *Klebsiella* and *Enterobacter* (blue).

The combination of these principles makes it easier to identify *Salmonella* colonies and reduces the number of false positive results requiring follow-up investigations. With OSCM II you can experience a new level of efficiency in your laboratory. For more information please speak to your local Oxoid representative or contact Val Kane, Oxoid Ltd, on 01256 841144, email: val.kane@oxoid.com

Inhibigen™ technology - a new dimension in selective microbiology.

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