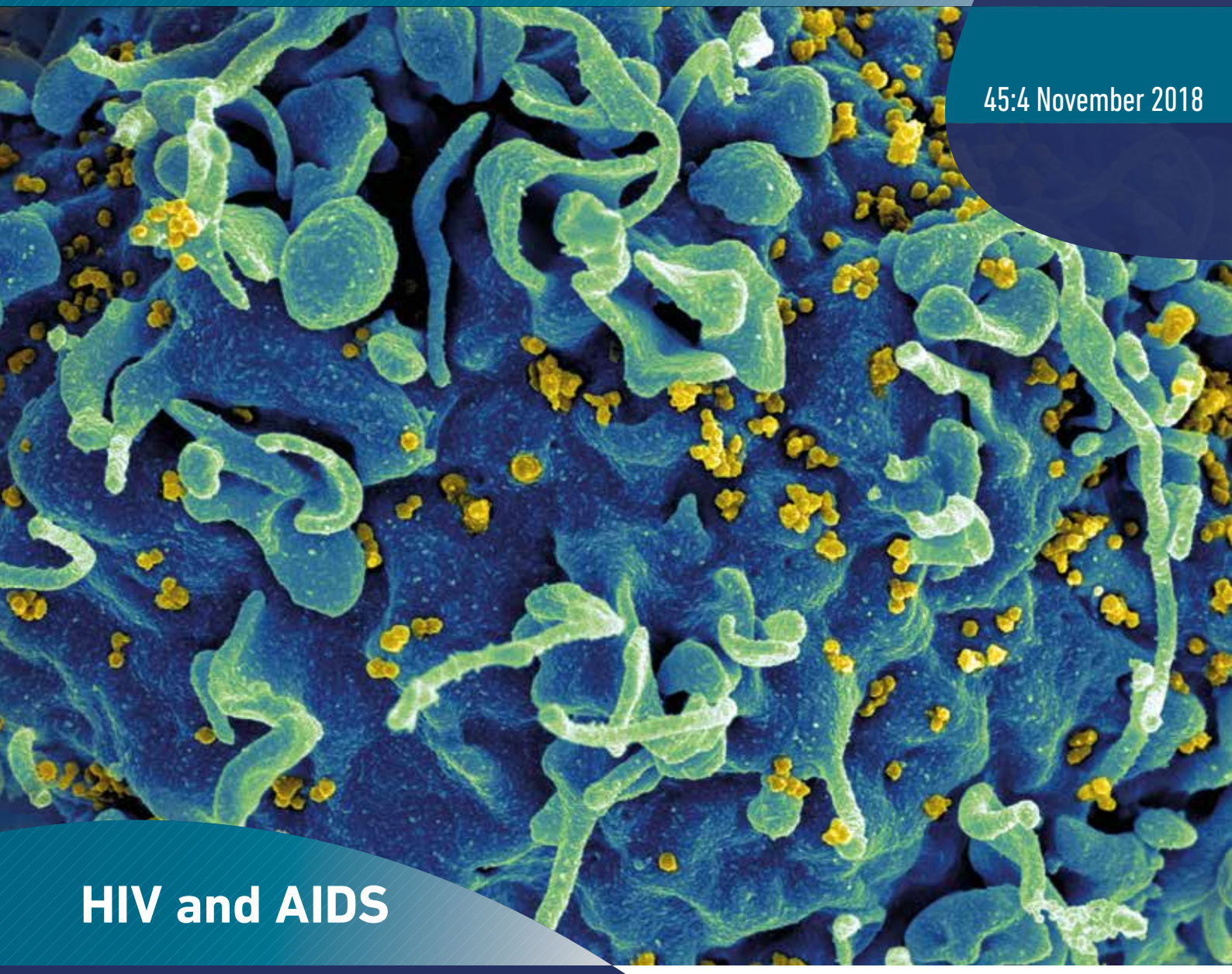
Microbiology TODAY

45:4 November 2018



HIV and AIDS

HIV worldwide in 2018
Atypical HIV test results – a need for vigilance
HIV and HCV co-infection
Cryptococcus – a deadly threat
HIV in pregnancy

MICROBIOLOGY SOCIETY

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ACCESS MICROBIOLOGY

The Microbiology Society announces the launch of *Access Microbiology*, a new open access journal publishing a variety of high-quality research outputs across the full spectrum of microscopic life forms.

Now open for submissions

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Editorial

Welcome to the November edition of *Microbiology Today*, an edition which considers how human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) impacts people across the world. HIV and AIDS are a major global health threat, affecting millions of people; however, with on-going research significant progress has been made in our ability to prevent, diagnose and treat HIV and AIDS. In this edition, our authors reflect on the ways in which the understanding of this virus and disease have changed across the years, the associated complications and what the future outlook might be.

Whole Picture

The issue opens with Paul Hine giving us an overview of the global HIV situation as it stands in 2018, explaining how advances in scientific research and understanding over the last decade have led to changes in preventing infection and treating HIV. Paul gives us an insight into how this disease can affect a wide variety of people and impacts on the lives of these individuals in diverse ways. He discusses the targets set by the Joint United Nations Programme on HIV and AIDS and provides a framework outlining what steps will need to be implemented to ensure we meet those goals by 2020.

Next, Gary Murphy, Colin S. Brown, Daniel Bradshaw, John Saunders and Noel Gill bring us up-to-date with the latest developments in pre-exposure prophylaxis. Discussing the issues surrounding atypical results caused by the increased use of this strategy, they highlight which of these atypical results could be indicators for retesting. They suggest that diagnostic methodology might need to adapt in the future to account for these new developments. They also emphasise that due to the changes in test results being seen, it will be essential to share experiences to find the testing strategies that lead to the best outcome for individuals moving forward.

Yvonne Gilleece explains how the advancements in available antiretroviral treatments, coupled with a series of interventions, such as opt-out for antenatal screening, have impacted on the outcomes of those who go through pregnancy with HIV. The use of these interventions has led to a huge drop in transmission of HIV from mother to child, with an undetectable viral load in the mother being a key determinant in reducing likelihood of transmission. The future outlook for pregnant mothers is an increasingly positive one; as evidence-based interventions continue to improve the outcomes for this population.

Discussing the challenges that the opportunistic fungal pathogen *Cryptococcus* can carry for those with HIV and AIDS, Xin Zhou, Robin C. May and Elizabeth R. Ballou outline which members of this genus are the biggest risks and explain how they invade. Our authors provide an insight into why this fungus is such a serious risk. In the wrong situation it can be fatal and lead to both cryptococcal pneumonia and cryptococcal meningitis. Resistance to anti-fungal agents can develop, and as research has now shown novel ways in which this pathogen can evade the immune system, it is clear that continued research will be essential to help improve our understanding of the diseases caused by this pathogen.

Another microbial risk for those with HIV is the possibility of co-infection with the hepatitis C virus. As dual infection with these two viruses is a common occurrence in those with HIV and AIDS, understanding the way in which they impact on health outcomes is imperative. Emma Thomson talks us through dual infection, outlining how these two viruses impact on the host immune system, and, in doing so, how they can potentially accelerate the progression to liver cirrhosis and cancer.

The Comment piece in this edition has been provided by Robin Weiss, and he evaluates where we are in our quest for a vaccine to HIV. Robin outlines some of the challenges that this virus presents in the on-going effort to design a vaccine. The development of a vaccine to successfully combat the ever-shifting antigenic profile of HIV is a complex process, but as research progresses there is hope that by utilising antibody and cellular immunity, some level of protection could be possible in the future.

Rowena Jenkins
Editor
r.e.jenkins@swansea.ac.uk

Contents

Microbiology TODAY

Articles

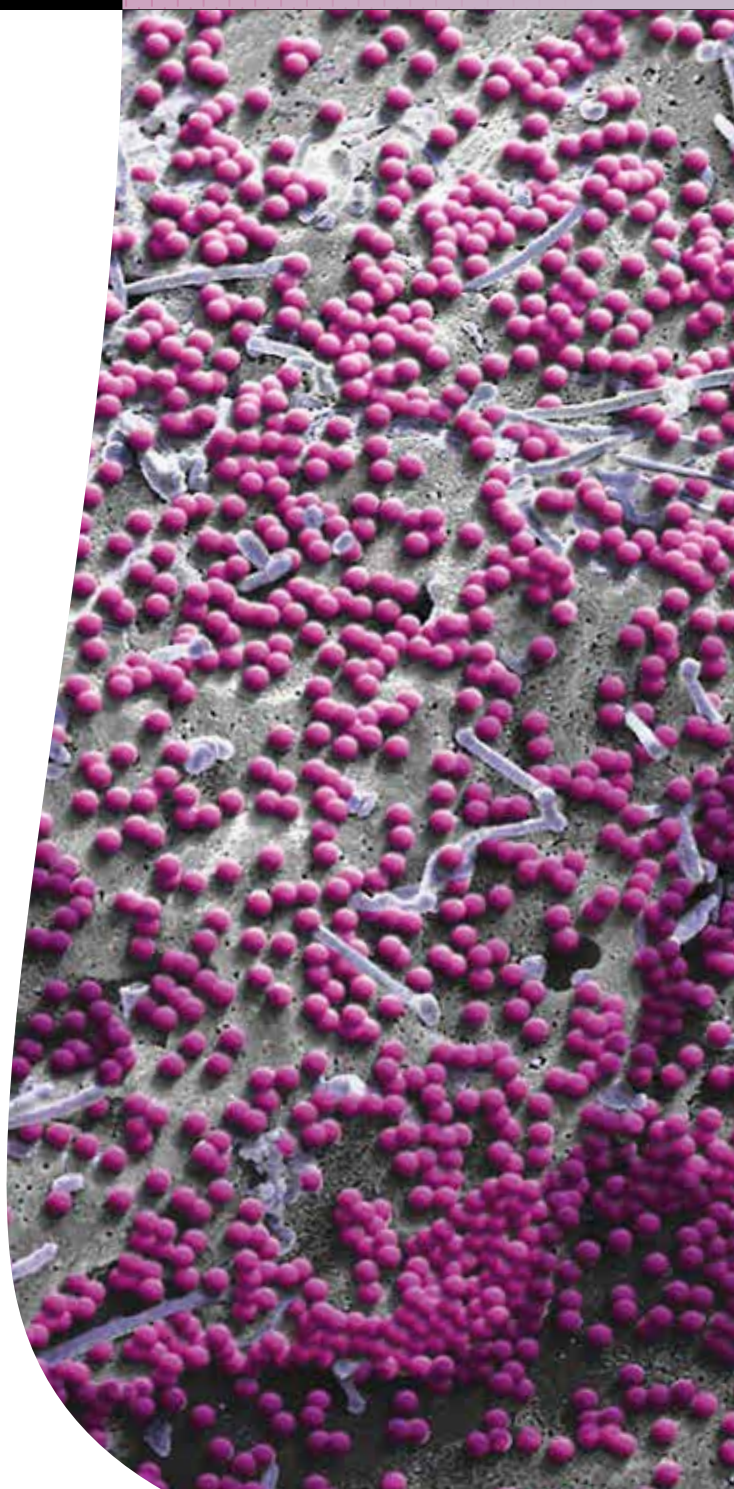
160 **HIV worldwide in 2018**
Paul Hine
Looking at the individuals behind the statistics.

164 **Atypical HIV test results when PrEP is prevalent – a need for vigilance in the laboratory**
Gary Murphy, Colin S. Brown, Daniel Bradshaw, John Saunders & Noel Gill
Challenges and responses associated with atypical HIV test results.

168 **HIV in pregnancy**
Yvonne Gilleece
Interventions involved in the reduction of vertical HIV transmission.

172 ***Cryptococcus* remains a deadly threat for those with HIV/AIDS**
Xin Zhou, Robin C. May & Elizabeth R. Ballou
The continuing threat to HIV-positive individuals.

176 **HIV and HCV co-infection – does it matter in the era of direct-acting antiviral therapies?**
Emma Thomson
Examining the impact and treatment of HIV and HCV co-infection.



45:4 November 2018

Features

159 **New President**
Introducing our new President.

159 ***Access Microbiology***
Our new journal.

184 **Society Showcase and AGM**
Highlights from the meeting and celebration of the Society's achievements.

186 **Think, Check, Submit**
How to choose a journal.

188 **Progressing Policy at the Society**
Prof. Paul Kellam and Dr Pat Goodwin reflect on ways members can engage.

190 **Society-Supported Conference Grants and FIS/HIS Conferences**
Events funded by Society-Supported Conference Grants, and FIS and HIS.

191 **FEMS Grants: make your Microbiology Society membership go further**
Members are eligible to apply to FEMS Grants.

192 **National Biofilms Innovation Centre (NBIC)**
A BBSRC and Innovate UK-funded Innovation and Knowledge Centre.

193 **ECM Forum update** – The inaugural ECM Summer Conference 2018
An interview with speakers Poppy Stevens and Ashley Otter.

194 **Membership Q&A**
Karen Buttigieg from Public Health England.

195 **Update your membership profile**
It's an easy three-step process.

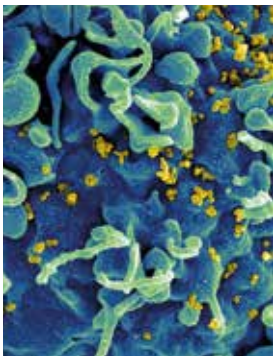
197 **Comment** – The quest for an HIV vaccine
Robin Weiss
A look at the problems and progress in development of a HIV vaccine.

Regulars

151 **Editorial**
154 **Council 2018**
155 **From the President**
156 **From the Chief Executive**
157 **News**
180 **Annual Conference 2019**
182 **Focused Meetings 2018 and 2019**
196 **Reviews**

Address **Microbiology Society, Charles Darwin House, 12 Roger Street, London WC1N 2JU** T **+44 (0)20 7685 2683** E **mtoday@microbiologysociety.org**
Design **Ian Atherton, Corbicula Design** (www.corbiculadesign.co.uk)
Printed by **Charlesworth Press, Wakefield**

ISSN 1464-0570



FSC Logo

Coloured SEM of HIV particles infecting a human T cell (blue). National Institute of Allergy and Infectious Diseases, National Institutes of Health/National Cancer Institute/Science Photo Library

MICROBIOLOGY SOCIETY

Council 2018

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Office of the Vice-Chancellor and Senior Executive, University of Exeter, Northcote House, The Queen's Drive, Exeter EX4 4QD; **president@microbiologysociety.org**

General Secretary – Professor Maggie Smith

Department of Biology, Wentworth Way, University of York, York YO10 5DD; **maggie.smith@york.ac.uk**

Treasurer – Professor Ian Roberts

School of Biological Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, Michael Smith Building, University of Manchester, Manchester M13 9PT; **i.s.roberts@manchester.ac.uk**

Chairs of Committees

Communications Committee – Professor Nicola Stonehouse (Interim Chair)

School of Molecular and Cellular Biology, University of Leeds, Leeds LS2 9JT; **n.j.stonehouse@leeds.ac.uk**

Early Career Microbiologists' Forum Executive Committee – Dr Helen Brown

Faculty of Health & Medical Sciences, School of Veterinary Medicine, University of Surrey, Daphne Jackson Road, Guildford, Surrey GU2 7AL; **helenlouise.brown@surrey.ac.uk**

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See 'Treasurer' above

Policy Committee – Dr Pat Goodwin

c/o Microbiology Society, Charles Darwin House, 12 Roger Street, London WC1N 2JU

Professional Development Committee – Dr Tadhg Ó Cróinín

Health Science Centre, University College Dublin, Belfield, Dublin 4, Ireland; **tadhg.ocroinin@ucd.ie**

Publishing Committee – Professor Jodi Lindsay

Institute of Infection and Immunity, St George's, University of London, Cranmer Terrace, London SW17 0RE; **jlindsay@sgul.ac.uk**

Scientific Conferences Committee – Professor Mick Tuite

School of Biosciences, University of Kent, Canterbury CT2 7NJ

Elected Members

Professor Paul Kellam

Imperial College London, Faculty of Medicine, St Mary's Campus, Norfolk Place, London W2 1PG; & Kymab Ltd; **p.kellam@imperial.ac.uk**

Dr John Morrissey

School of Microbiology, University College Cork, Ireland

Professor Stephen Oliver

Cambridge Systems Biology Centre & Department of Biochemistry, University of Cambridge, Sanger Building, 80 Tennis Court Road, Cambridge CB2 1GA

Professor Tracy Palmer

Centre for Bacterial Cell Biology, Baddily-Clark Building, Medical School, Newcastle University, Newcastle upon Tyne NE2 4AX; **tracey.palmer@newcastle.ac.uk**

Professor George Salmond

Department of Biochemistry, Hopkins Building, University of Cambridge, Tennis Court Road, Cambridge CB2 1QW

From the President

This is my last President's article after three happy years in the chair of the Microbiology Society. I would like to congratulate Judy Armitage on her election as our next President and I know that her passion for the discipline and tremendous managerial experience will serve the Society very well.

The manifesto that she gave to Council, describing the things that are of special interest to her, align very well with our five-year plan, and so I am sure that our strategic objectives will be strongly reinforced and underpinned under her leadership.

A word about this issue of *Microbiology Today* on HIV and AIDS. When I was a postdoc in the USA in the early 1980s, I recall writing home to tell my family and colleagues that a new disease, cause unknown, was going to emerge as one of the biggest health concerns of the age. Although HIV and AIDS has unfolded as one of the global tragedies of the last 30–40 years, it is also one in which the importance of the work of virologists and other microbiology-associated researchers has revolutionised the prospects for those who were and are infected with this virus. It is therefore important to recognise the value of investments made in basic and translational microbiological research and in a community of scientists that has an admirable track record in responding to major global challenges and threats.

It has been a wonderful and rewarding experience being President of one of the largest and most influential societies in the biosciences. The relationship between our Chief Executive, Peter Cotgreave, and all of our Charles Darwin House staff and Council has been collegiate and friendly, but also business-like, efficient, energetic and focused. I think the Society has been able to harness and support the talents of its community in delivering great conferences, efficiently managing a portfolio of excellent journals and creating a strong and clear voice in our policy work. I have been delighted to see the Early Career Microbiologists' Forum shoot out of the blocks and quickly become an integral and vital part of our structure. I've heard some thrilling science related to antimicrobial resistance (AMR) and disease, microbiomes and biodiversity, pollution and bioremediation, cell biology and bioengineering, and many other fields besides. I have had the pleasure of meeting hundreds of extraordinary and talented people who have discovered amazing things and made enormous contributions to the field.

There have been only a few problems to solve – but each one was addressed quickly and resolved, I believe, to the best possible outcome. The sum of these observations and experiences reinforces my own career-long conviction that the extraordinary world of microbes deserves its place at the head of the scientific table, because it impacts so directly (positively and negatively) on the lives of all of us, but also because it delivers resources, solutions and hope for the future. It really has been one of the greatest privileges to share these three years with colleagues who have worked and served the Society so well, and I would like to end by thanking them, and all of our members, who have contributed to the activities of this society.

Neil Gow
President
president@microbiologysociety.org

From the Chief Executive

For the past five years, the Microbiology Society has shared its premises in London with a group of other Societies. If you have been to the AGM or a Committee meeting, you have probably bumped into colleagues from one of the other biological charities at Charles Darwin House or our second building, Charles Darwin House 2, which is just around the corner.

The trustees of the six co-owners recently decided that the time is right to sell these buildings and make new arrangements for our headquarters.

There are several reasons for the decision. Firstly, the complexity of joint ownership has proven very difficult and, critically, has affected the day-to-day running of the Society. As a charity, the Society has to follow relevant laws, and they can sometimes be complex, especially when more than one organisation is involved. Even the Law Commissioners, a group of very eminent and learned judges, barristers and solicitors, admit that they are not entirely sure what some of the legislation actually means! Ensuring that we stay on the right side of the rules is time consuming and can be expensive. At the same time, changes to business rates mean that it would be increasingly expensive to stay in the current buildings. Secondly, the buildings are worth quite a lot more than we paid for them, and when they are sold we will be able to plough that money back into activities that support the careers of you, the members of the Society.

Our aims are all about helping to unlock the power and potential of the unique depth and breadth of your knowledge and experience. The scale of opportunity is clear from the first sentence of the strategic plan: "microbes are everywhere and affect almost all aspects of our lives". To match that ambition, we need a relentless focus on helping you to develop, expand and strengthen your networks, so that you share knowledge about microbes with one another and with other communities.

In pursuit of that goal, we collaborate with many organisations. There is no need to be in physical proximity with other organisations that we work with to be effective partners. Next year's Annual Conference will include sessions held jointly with Protistology-UK and the Irish Fungal Society. Our policy work in antimicrobial resistance is given extra impact by our work with an organisation called LeSPAR, a collection of scientific membership bodies, including the Royal Society of Chemistry and the Biochemical Society. We had a successful joint collection of journal articles with the British Society for Immunology earlier in the year. What is important about these activities is not where the staff or the partners happen to have their desks, but how the work delivers benefits for our members. We will of course continue to cooperate with our friends in the other five Societies that currently cohabit at Charles Darwin House, but we will do so without the unnecessary distractions that co-ownership brings.

We are lucky to have welcoming, dedicated and professional staff working at the Microbiology Society. I know that many of you greatly appreciate us, because you are kind enough to let me know. We also enjoy working with you. Staff greet you at meetings, help you through the process of publishing in the journals, keep you informed about what's going on, and support you in getting the most out of your membership. The decision to find our own bespoke offices will give us complete freedom to organise our working environment in ways that best support the staff of the Microbiology Society to deliver opportunities and benefits for you.

As always, one of the most obvious ways in which the Society's staff support the microbiology community is through our Annual Conference, which next year will be in Belfast from 8–11 April. Giving a talk or presenting a poster is a great way to get your science the attention it deserves. The deadline for abstracts is 10 December, so you still have a few weeks to submit yours. I look forward to seeing what you are working on this year.

Peter Cotgreave
Chief Executive
p.cotgreave@microbiologysociety.org

News

Abstract submission open for Annual Conference 2019

Abstracts are now being accepted for the Society's Annual Conference 2019, which is taking place on 8–11 April 2019 in Belfast. The flagship event is designed to cover the breadth of microbiology research, and its oral abstracts and posters reflect this comprehensive scientific programme. Submissions close on 10 December 2018, so don't miss out on this opportunity to showcase your microbiological work and research. See the website for more details: **microbiologysociety.org/annualconference**.

Harry Smith Vacation Studentships

Applications for support for undergraduate research projects during Summer 2019 will open on 3 December. Applications should be submitted by the supervisor, and successful applicants will receive support for their research project in the form of a stipend, as well as the chance to apply for a bursary to present the results of their projects at the Annual Conference 2020.

New ECM Forum Representatives

New representatives have joined the ECM Forum Executive Committee, and some representatives will be leaving after two years' service.

Welcome to incoming representatives Prerna Vohra, Roslin Institute, University of Edinburgh (Professional Development), Angharad Green, University of Liverpool (Policy), Omololu Fagunwa, University of Huddersfield (International), Alison MacFadyen, University of Edinburgh (Conferences) and Hermione Webster, University of Liverpool (Undergraduate).

Thank you and farewell to Andy Day, our outgoing Policy Representative, Grace Russell, outgoing Undergraduate Representative, Linda Oyama, outgoing International Representative, and Helen Brown, outgoing Chair.

Amy Richards will also be leaving her post as Conferences Representative to serve as the Chair from January 2019.

2019 Prize Lecture winners

We are delighted to announce the 2019 Prize Lecture winners, who will all be presenting at the Annual Conference in Belfast. Congratulations to the following awardees:

2019 Prize Medal: Professor Jennifer Doudna
University of California, Berkeley, USA

2019 Peter Wildy Prize: Professor Laura Bowater
University of East Anglia, UK

2019 Fleming Prize: Dr Peter Fineran
University of Otago, New Zealand

2019 Marjory Stephenson Prize: Professor Gordon Dougan
University of Cambridge, UK

Note: the Unilever Colworth Prize was not awarded for 2019.

Grant deadlines

Date	Grant
1 December 2018	Travel Grants for members presenting at conferences from 1 January.
31 January 2019	Society Conference Grants for early career members presenting at the Annual Conference. Also for technicians or retired members, and members requiring support for caring costs.
10 February 2019	Harry Smith Vacation Studentships to support undergraduate research projects during Summer 2019.

Check the website for details about applying for grants: **microbiologysociety.org/grants**.

Mi Society updates

We've been working hard over the last few months to create new content for Mi Society. Features include guidance on how to find a mentor and a round-up of current member opportunities across the Society in one easy-to-find place. Login to explore: **microbiologysociety.org/login**.

Annual Conference 2018 and Focused Meetings

Thank you to all who took part in Annual Conference 2018 and the Focused Meeting series. The Divisions and Scientific Conferences Committee define the events programme and these members support the microbiology community to make our meetings engaging and current. We hope you enjoyed the events that took place this year.

Stanley Hughes turns 100

Dr Stanley Hughes, mycologist and Order of Canada recipient best known for his work on 'sooty moulds' and other microfungi, turned 100 on 17 September. Congratulations to Stanley.

Changes to Divisions and Council

For 2019 there will be a number of new Division Representatives and Council members, and the Society would like to thank those who will be stepping down this year. The full list of changes can be viewed on the website: **microbiologysociety.org/news**.

Society Shadowing Scheme

Did you know that you can shadow any Microbiology Society Committee, to find out more about our work? Find out more by contacting **appointments@microbiologysociety.org**.

Microbiology is now publishing graphical abstracts

We're pleased to announce that *Microbiology* will now be accepting graphical abstracts which will be published as part of the final manuscript online. Authors will have the option to provide a high-quality image, summarising key elements of their paper, to enhance their publication. Find out more on our website: **microb.io/2NgfAJk**.

Contributions and feedback

The Society welcomes contributions and feedback from members. Please contact **mtoday@microbiologysociety.org** with your ideas.

Get the latest updates, follow the Microbiology Society on:

twitter facebook LinkedIn YouTube Google+

Professor Judith Armitage FRS
to be new Microbiology Society President

Professor Judith Armitage FRS from the University of Oxford will be the new President of the Microbiology Society, beginning 1 January 2019, when the current President, Professor Neil Gow FRS, steps down. Her presidency will run for three years.

Incoming President Judith Armitage with Outgoing President Neil Gow (left) and Chief Executive Peter Cotgreave (right).

Judy is a bacterial physiologist using interdisciplinary approaches to study bacterial behaviour. She joined the Society in the early 1970s as a PhD student, and was the editor of the *Journal of Bacteriology* for 10 years. She is one of the two Editors-in-Chief of *Current Opinions in Microbiology*, a member of EMBO, and a Fellow of the American Society of Microbiology and the Royal Society of Biology.

ACCESS MICROBIOLOGY
is now open for submissions

The Society's new Open Science journal, *Access Microbiology*, is now open for submissions.

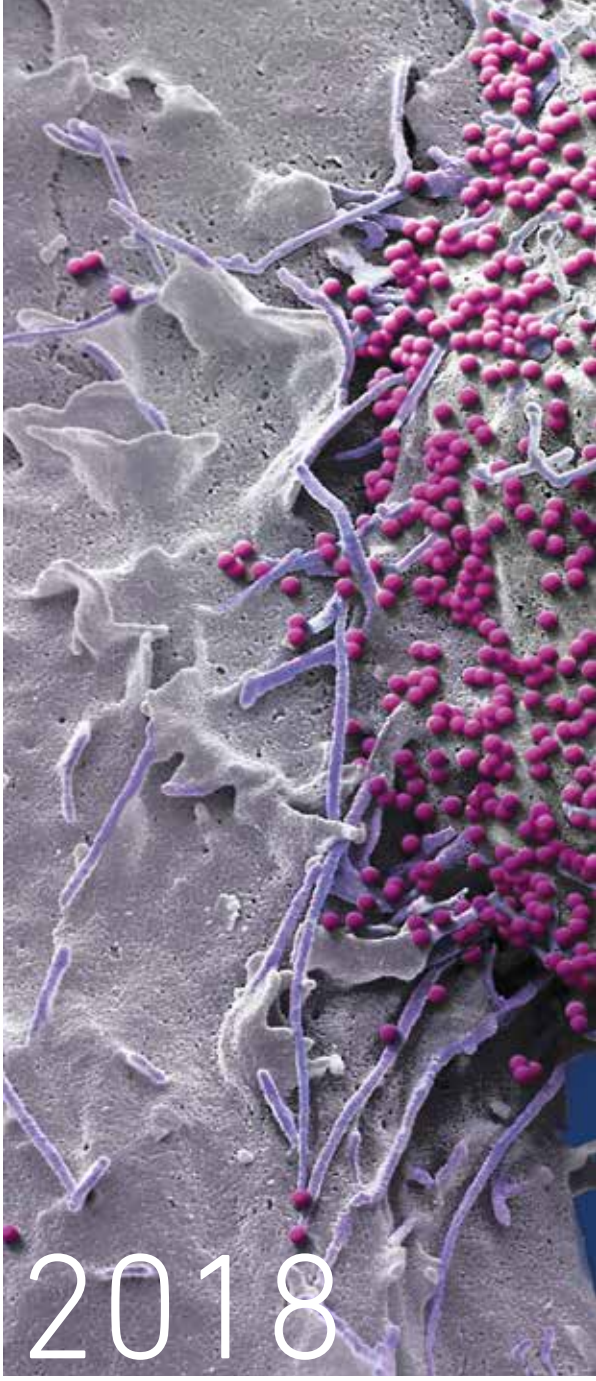
Wladimir Bulgar/Science Photo Library

The journal is our response to concerns about research reproducibility and research waste, encouraging the publication of valuable research outputs which have historically been lost because they are not seen as 'high impact', creating a situation in which research is re-done in multiple labs for no gain. The journal is open access and fully compliant with all funder mandates, and members are encouraged to take advantage of the APC-free launch offer. So, dig out that unpublished paper reproducing other work, delivering negative results, or adding to an established method, and support your Society while adding to your publication record.

For more information, please contact **acmi@microbiologysociety.org** or visit **microbiologyresearch.org**.

HIV worldwide in 2018

Paul Hine



Coloured scanning electron micrograph of a 293T cell infected with HIV (pink dots). Steve Gschmeissner/Science Photo Library

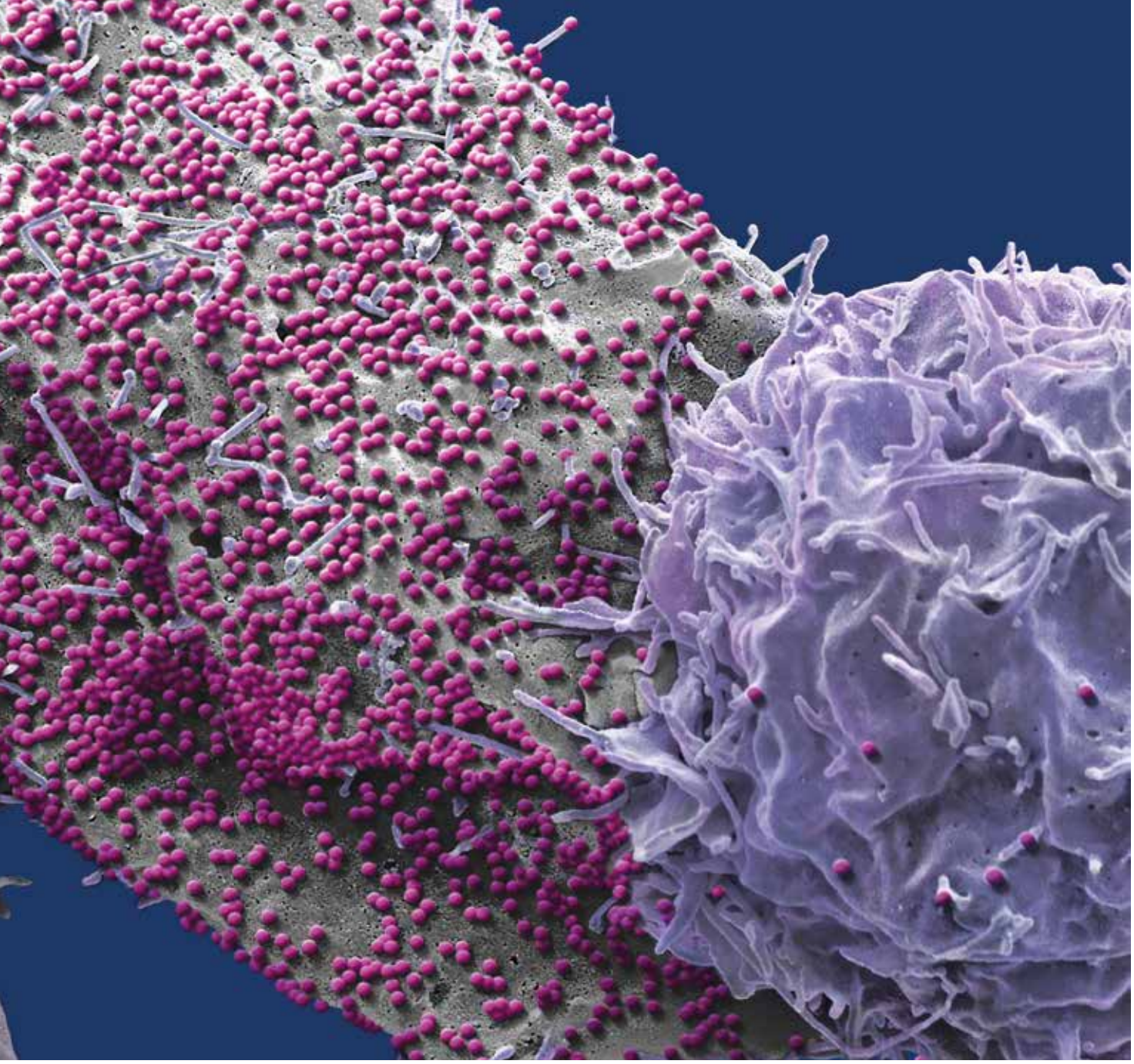
36.7 million people have HIV. The number is so large as to be incomprehensible, and the oft-used term 'epidemic' becomes almost reductionist. Behind the figures are the stories of individuals.

Imagine Tima, an 18-year-old Kenyan woman whose husband is admitted to hospital with tuberculosis and receives a new diagnosis of HIV. Tima is faced with the fear of raising their child alone.

Imagine Bindiya, a 30-year-old 'hijra', an Indian transgender woman, who sells sex in a park near Mumbai railway station; she knows she has HIV but fears discrimination if she seeks treatment.

Imagine Nikolai, the 24-year-old Russian man who injects heroin and does not know he is HIV positive; he does not access drug treatment services as he fears being branded an addict.

These vignettes, based on true accounts, remind us that HIV is a diverse disease which often affects the most vulnerable amongst us. This article describes the global fight against HIV and argues for the importance of remembering the rights of individuals such as Tima, Bindiya, and Nikolai.



Seismic changes

The last 10 years have brought seismic changes in the science behind HIV treatment and prevention. We now understand that 'undetectable equals untransmissable': a person with HIV who has an undetectable viral load does not transmit HIV to partners. We understand that starting treatment soon after diagnosis (or possibly immediately), regardless of their CD4 count, reduces morbidity and increases life expectancy. We understand that antiretrovirals can be used as pre-exposure prophylaxis (PrEP) to greatly reduce the risk of acquiring HIV sexually. HIV drug treatments are available as single tablets, and modern combinations have fewer side effects and greater robustness against treatment failure than ever before.

Against this backdrop, the international community has adopted a series of ambitious goals that would previously have been unthinkable. In 2015, the United Nations adopted 17 Sustainable Development Goals; the third of these sets the goal of ending HIV as a public health threat by 2030. This goal was reaffirmed in 2016, with the United Nations General Assembly Political Declaration on Ending AIDS, subtitled 'on the fast track', and promising to intensify efforts towards ending the AIDS epidemic. This seeks to reduce new HIV infections from 1.8 million in 2016, to fewer than 500,000 by 2020. The Joint United Nations Programme on HIV/AIDS (UNAIDS) also set a 90:90:90 target, which covers what is known as 'the cascade' of HIV care. By 2020, 90% of people with HIV will be

aware of their status, 90% of these will be on treatment, and 90% of those on treatment will be virally suppressed. How well are we doing?

Prevention

In the early 2000s, HIV prevention was seen to be as 'easy as ABC': to avoid acquiring HIV, people simply had to abstain from sex, be faithful to one partner and use condoms. The complicated reality was that people at risk of HIV might not want or be able to adopt these behaviours, and policies based on an ABC approach overlooked the sexual and reproductive rights of the individual. The exemplar is now 'combination prevention'. This approach combines biomedical interventions (including condoms, treatment, PrEP and voluntary medical male circumcision) and behavioural interventions (for example, sex education, infant feeding education), but also incorporates structural changes. Structural changes address underlying human rights issues, including decriminalisation of sex work, gay sex and individual drug use, and empowering women and girls.

In July 2018, UNAIDS warned of an emerging 'prevention crisis'. It argues that the partial success of programmes to date has weakened the sense of urgency required to meet 2020 targets. Relatively few health systems can launch combination prevention packages at sufficient scale. Therefore, most progress is made in high-income cities, and districts in eastern and southern Africa that act as research hubs. It also warns of the ongoing detrimental effect of stigma and discrimination in HIV prevention efforts.

Blood test cassette, positive result. Cordelia Molloy/Science Photo Library

The first '90': knowing your status

At the end of 2017, three quarters of people with HIV knew their HIV status. This represents vast progress in HIV diagnosis. In the early days of the epidemic, a positive result meant a terminal diagnosis, stigma and social exclusion, giving rise to a 'voluntary counselling and testing' model, in which a person actively attends a testing unit and receives counselling about the test. Since the publication of WHO/UNAIDS guidelines in 2007, there has been a huge paradigm shift and vast scale-up. HIV tests are now offered in integration with other healthcare services on an

> **As our world sees a resurgence of populism, nationalism and isolationism, we must not forget the utmost importance of respecting the rights of the most vulnerable individuals in our society in effectively fighting HIV.**

'opt-out' basis, the most successful example being the testing of pregnant women. Novel approaches make testing more accessible, including point-of-care tests, outreach testing and self-testing kits.

There remain considerable challenges. Globally, men are less likely to be offered or to accept an HIV test, and masculine norms may dissuade men from taking up testing. Younger people are also less likely to get tested due to unwelcoming healthcare facilities, and in some instances requiring parental consent for testing. Key populations such as gay men may still be dissuaded from testing due to fear of discrimination.

The second '90': receive treatment

At the end of 2017, 79% of people diagnosed with HIV received treatment. To achieve the 90% target, two things must happen: people with new diagnoses must be linked to care, and then they must be kept in care. The first of these is perhaps simpler, and, increasingly, diagnostic services are linked to rapid initiation of cheap and effective antiretroviral treatment. The second is a trickier proposition: the same barriers that may dissuade individuals from seeking testing may also affect their engagement in care, such as fear of stigma, discrimination or loss of income via attending care facilities.

The third '90': achieve viral suppression

At the end of 2017, 81% of people receiving treatment for HIV had suppressed viral loads. With modern antiretroviral treatment, the main reason for treatment failure is non-adherence to therapy. Treatment failure must be detected early to prevent emergence of resistance, and this depends on readily available viral load measurement. The question of adherence will be the final frontier in HIV medicine and reaching the third '90'. This challenge is much less attractive than the quest for a cure or a vaccine, and far less likely to lead to a Nobel Prize. The reasons people who are in care do not take their medicines are myriad, and often defy the rationalism of a scientist. There are many proposed technological solutions, for example electronic monitoring systems to detect non-adherence, or text-message reminders. However, there is unlikely to be a 'magic bullet', and as with prevention, the winning formula will likely need to address underlying structural factors also.

The future

Moving forward, we must remember that the great successes of the global community in fighting HIV to date have hinged on protecting and promoting human rights. It is easy to assume that international progress in human rights will continue unabated, and HIV treatment and prevention programmes will continue to flourish in this environment. However, as our world sees a resurgence of populism, nationalism and isolationism, we must not forget the utmost importance of respecting the rights of the most vulnerable individuals in our society in effectively fighting HIV.


Paul Hine

Paul Hine

Tropical and Infectious Disease Unit, Liverpool and Broadgreen University Hospital Trust

e **paul.hine@lstmed.ac.uk**

@doc_phine

Paul Hine is a Specialist Registrar in Infectious Disease and General Medicine at Liverpool Royal Hospital. He also works with the Cochrane Infectious Diseases Group developing evidence synthesis.

What is the most rewarding part of your job?

I'm extremely fortunate to work with amazing and inspirational teams in Liverpool Royal and the Liverpool School of Tropical Medicine

How did you enter this field?

I have always been interested in both public health and hands-on clinical work – infectious diseases is a great specialty to combine these things!

Atypical HIV test results when PrEP is prevalent – a need for vigilance in the laboratory

Gary Murphy, Colin S. Brown, Daniel Bradshaw, John Saunders & Noel Gill

Since the first diagnostic test for HIV was licensed in 1985, sensitivity and specificity has improved enormously, shortening the time taken to identify someone as having acquired HIV.

Typically, HIV infection leads to a high-titre viraemia within two to three weeks of infection, and within a few days of the virus becoming detectable, a protein component of the virus core, p24Ag, is usually detectable. The presence of p24Ag stimulates the humoral immune response to begin developing IgG and IgM responses. The IgM response falls after one to two weeks, but IgG increases in intensity over many months, until years later there is degradation of the overall immune response associated with progressive HIV-related disease. Using 'Fiebig' staging, the maturation of the HIV-specific immune response following initial infection can be used to categorise individuals as acutely infected, or having a longer-term antibody response.

Antiretroviral therapy and HIV antibody response

Very early initiation of effective antiretroviral therapy (ART) may inhibit the performance of diagnostic assays during the initial course of infection. As the maturation and maintenance of an antibody response is strengthened by sustained antigenic stimulation, such early use of ART can inhibit this response by very quickly reducing the amount of virus. This leads to less antibody production, and less time for antibodies to mature. Therefore, the diagnostic test results seen in these infections may be 'atypical'. Responses may happen later, not at all, or at levels lower and more fragmented than usually seen. Reactivity on two or more consecutive samples may not change or may stay discrepant while remaining on PrEP or after stopping. In rare cases, early treatment can lead to sero-reversion where, although still infected, there is no detectable antibody response on serum testing. These diagnostic

issues need consideration when testing specimens from those exposed to, or confirmed as acquiring, HIV infection while also receiving ART as either post-exposure prophylaxis (PEP) or very early treatment initiation.

Pre-exposure prophylaxis and scale-up

Pre-exposure prophylaxis (PrEP), which currently involves individuals taking a tenofovir preparation combined with emtricitabine, has been shown to be highly effective at protecting against acquiring HIV-1 infection. Infections that do occur will usually happen when PrEP has been used inconsistently, very rarely during consistent use, or may appear to happen if infection is acquired shortly before PrEP beginning but is recognised later. In each case the stimulus to the immune response may be altered, producing an atypical antibody response.

Opportunities for accessing PrEP have multiplied across the UK since 2015, leading to an accelerating scale-up of the numbers of gay men using the intervention. Although data on atypical results has not been centrally collated, it is probable that there has been concomitant increase in the likelihood of atypical HIV test results. PrEP is available on private prescription, can be bought directly at low price from one London clinic or from overseas, and publically funded PrEP programmes have begun in Scotland, Wales and Northern Ireland. In England, the PrEP Impact Trial, a pragmatic health technology assessment, is addressing outstanding questions on PrEP eligibility, uptake and duration of use, and impact on HIV and other STIs. Since beginning in mid-October 2017 and June 2018, almost 7,900 participants, mostly gay men, were enrolled at 140 clinics, and another 5,100 trial places are available. While 9,854 PEP courses following sexual exposure were begun by gay men in England in 2017, it is probable that over 10,000 gay men are now taking PrEP regularly. There is increasing evidence from a variety of groups, particularly those who test large volumes of blood donors, and from recent data from PrEP trials that PEP, PrEP and ART initiation during acute infection can cause blunting of the HIV-1 antibody response. Both non-reactive HIV serology and non-progressive Fiebig profiles have been seen, in a situation where detectable virus in the blood is also unlikely.

Technician holding a multi-well sample tray as he tests blood for HIV. Tek Image/Science Photo Library

The diagnostic challenge for those taking PrEP with atypical test results

Diagnosing 'breakthrough' HIV infections, therefore, may be a complex task. In analysing a sample from someone taking PrEP, it will be critical to consider all atypical results (Box 1) as indicating potential infection and to manage this accordingly. It will take time and multiple tests, including Western blot antibody analysis, as well as RNA and proviral DNA molecular assays to determine whether these patients with 'atypical' or discrepant antibody profiles have acquired HIV. It is too soon and the data are too sparse for reaching a consensus on which diagnostic assays, if any, will perform better in the era of PrEP. The number of reported breakthrough infections while on PrEP (four by March 2018), and incomplete recording to date

of those with any form of 'indeterminate' antibody result while taking PrEP, means very few platforms and assays have been assessed. This July at AIDS 2018, a session was held to highlight the importance of the topic and emphasise the work that needs to be done.

The decision about whether an individual with an atypical HIV test result should remain on PrEP or receive additional ART to treat a potential infection is important for individual management, but may compromise the opportunity to confirm a diagnosis. Atypical results may also contribute to a patient with HIV-1 beginning a potentially less efficacious treatment regimen. It is also important to consider the interpretation of the HIV-negative results that these individuals receive. Is the result truly negative, or could it be a consequence of the blunting of the immune response? Any sudden increase in the level of reactivity in a repeat sample in a diagnostic assay, even if still below the negative cut-off, should be considered suspicious and monitored. Clinicians managing individuals with atypical HIV test results (Box 1) while taking PrEP should be advised of the need for repeat testing with combined antigen/antibody assays, or with molecular methods, on cessation of PrEP to ensure HIV infection has not occurred. These atypical testing cases should be discussed with a regional expert and investigated further for possible seroconversion. Follow-up testing should take account of the 'high-risk' testing window, i.e. retest at both 4 and 8 weeks following discontinuation of PrEP.

The Clinical Services Unit of Public Health England (PHE) Colindale would welcome information of such cases (via an email without personal identifying information sent to **csuqueries@phe.gov.uk**). If requested, the Unit will liaise with the regional expert, provide expert advice, and collate information on the frequency and details of these events. PHE, in collaboration with colleagues at Imperial College, already investigate individuals who demonstrate unusual immune responses to HIV (Box 2). This service for managing individuals taking PrEP who have atypical test results will continue as PrEP scale-up proceeds further, testing specimens on a variety of diagnostic assays. These tests will cover a range of HIV-specific antigens to help determine if there is preferential reactivity against any individual antigen. Such evidence may guide the make-up of diagnostic assays that should be used in PrEP monitoring or screening programmes.

If a seroconversion event is suspected while taking PrEP, current best practice is to intensify ART while continuing laboratory investigations. If an atypical result is first detected after PrEP has been stopped, then it is advised that no further PrEP is prescribed until an expert consensus is reached regarding the individual's HIV status.

Laboratory request forms submitted with samples for further virological investigation (including HIV viral load testing or combined antibody/antigen testing) should contain information on whether the patient has been taking either PEP or PrEP, and if so, when and for what duration, to allow for better interpretation of atypical results.

Conclusion

The PrEP era marks a potential paradigm shift in HIV testing, where for a small population of cases persistent or one-off low-level antibody reactivity will require more follow up and consideration. International consensus and experience sharing will be key to highlight the best testing strategies for this group of at-risk individuals, and to ensure they have the best information about what any indeterminate result may mean.

BOX 1: Atypical HIV results: what to look for

1. Low signals near to cut-off in screening assays (including either just below or below cut-off).
2. Sero-reversion on follow-up specimens.
3. Discrepant results between assays.
4. Slow development of antibody/antigen signal in subsequent samples.
5. Weak and/or incomplete banding patterns on Innolia or Western blot.

BOX 2: HIV Reference Laboratory Services at PHE Colindale

1. Wide range of assays (non-standard commercial and in-house ELISAs, proviral DNA, novel sequencing).
2. Western blot to determine antibody-specific responses.
3. Collation of test results from a variety of platforms to determine PrEP interference with particular assays.
4. Referral to clinic specialising in atypical serological responses to HIV infection (difficult diagnoses).

Further reading

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Gary Murphy
National Infection Service Laboratories, Public Health England, 61 Colindale Avenue, London NW9 5HT, UK
e **gary.murphy@phe.ac.uk**
PublicHealthEngland
@PHE_uk

Gary Murphy is Joint Scientific Lead of the PHE Clinical Services Unit. He has an interest in HIV incidence and laboratory diagnostics which stemmed from watching Quincy as a child and wanting to be just like Sam, the trusted lab scientist.

Colin S. Brown
National Infection Service Laboratories, Public Health England, 61 Colindale Avenue, London NW9 5HT, UK
e **colin.brown@phe.ac.uk**
PublicHealthEngland
@PHE_uk

Colin S. Brown is a consultant microbiologist. Colin was inspired to work in the field of HIV given the opportunity to make a difference at individual, population and policy levels. His varied interests mean when not in Colindale he can often be found supporting projects in West Africa.

Daniel Bradshaw
National Infection Service Laboratories, Public Health England, 61 Colindale Avenue, London NW9 5HT, UK
e **daniel.bradshaw@phe.gov.uk**
PublicHealthEngland
@PHE_uk

Daniel Bradshaw is a consultant in the PHE Virus Reference Department. He trained as a sexual health physician before undertaking a post-CCT fellowship in virology. His main interests are HIV and viral hepatitis.

John Saunders
Public Health England STI & HIV Department, 61 Colindale Avenue, London NW9 5EQ, UK
e **john.saunders@phe.ac.uk**
PublicHealthEngland
@PHE_uk

John Saunders is a sexual health and HIV clinical academic working at Public Health England, University College London and The Mortimer Market Centre in central London. He has a wide range of scientific interests and is Clinical Champion of the National Chlamydia Screening Programme.

Noel Gill
Public Health England STI & HIV Department, 61 Colindale Avenue, London NW9 5EQ, UK
e **noel.gill@phe.gov.uk**
PublicHealthEngland
@PHE_uk

Noel Gill is Head of the HIV and STI Department at Public Health England, Colindale and has a special interest in HIV. His paper 'The hazard of infection from the shared communion cup' gave him the knowledge base and confidence to enter the HIV field in late 1987.

On a typical day in this position, what do you do?
Our day jobs include seeing patients, managing a high-throughput diagnostic laboratory, interpretation of lab results, service development and extracting information from carefully constructed tables summarising data. These are all done with the aim of improving HIV diagnosis and reducing the burden of HIV disease – a topic which unites us all.

What do you love most about your job?
Working closely together we are able to bring expertise from different disciplines into focused actions that bring benefits on individual and population levels.

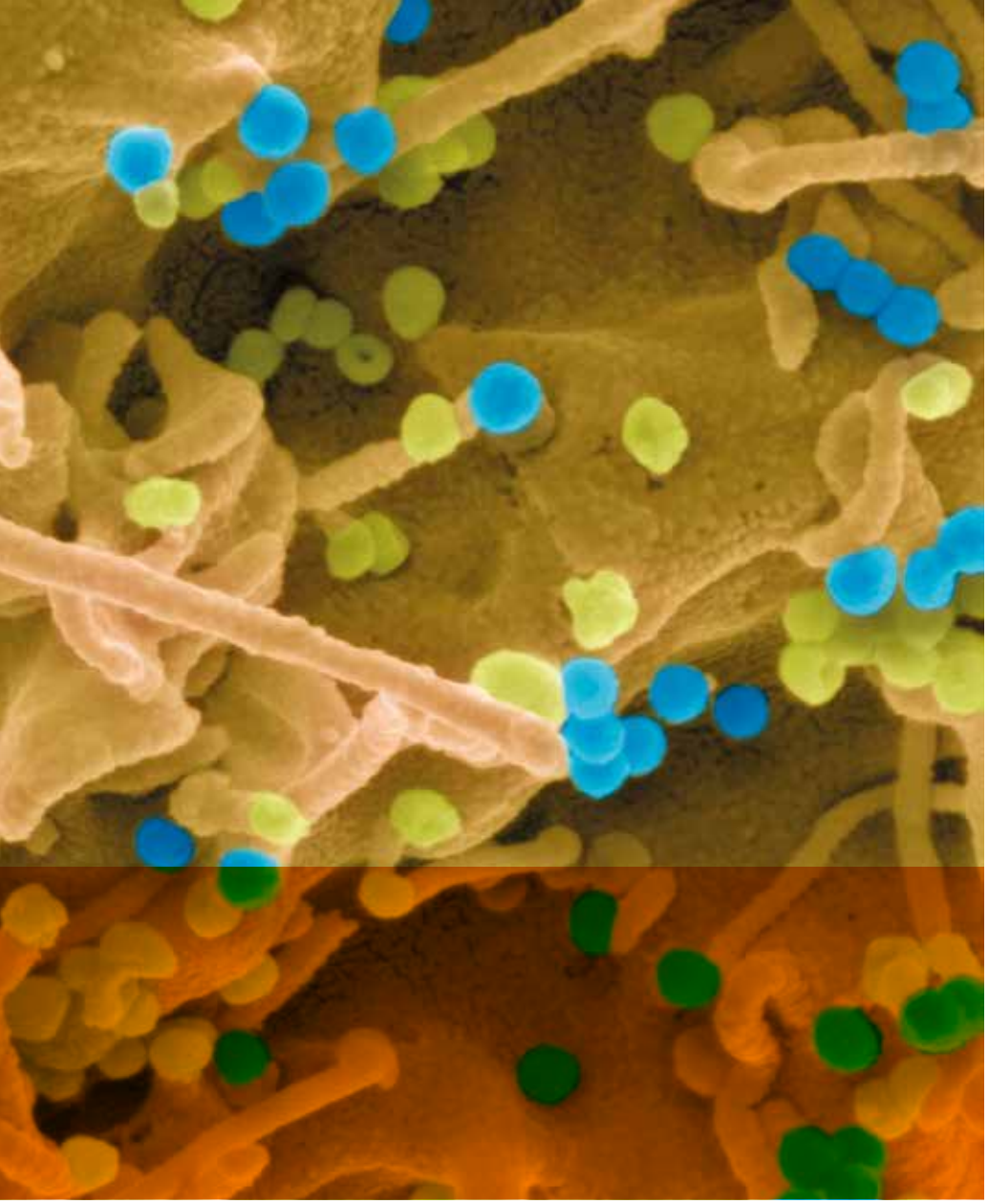
HIV in pregnancy

Yvonne Gilleece

The long-term outlook for people living with HIV has been revolutionised by early and lifelong use of combination antiretroviral treatment (cART). Effectively treated individuals with plasma HIV RNA <50 copies ml^{-1} ('undetectable') can have a normal life expectancy.

In 2015 in the UK, 88,769 people were seen for HIV care, 25,564 of whom were women, half of whom were of child-bearing age. The passing of HIV from a woman to her foetus is called vertical transmission and is largely preventable. Vertical transmission will most often occur in the perinatal period. With no intervention, the vertical transmission of HIV can be as high as 25–30%. The incidence of vertical transmission of HIV in the UK is at its lowest ever at 0.27% for all women with HIV and even lower at 0.14% for women with HIV on effective cART.

This is because of the following interventions:



Coloured scanning electron micrograph of a 293T cell infected with HIV (cyan). Magnification: x20,000 at 10 cm wide. Steve Gschmeissner/Science Photo Library

1. Antenatal HIV testing to diagnose pregnant women living with HIV.
2. Effective cART for the woman.
3. Management of labour.
4. Avoidance of breastfeeding.
5. Post-exposure prophylaxis for the baby.

Antenatal HIV testing

Routine opt-out antenatal HIV testing in the first trimester was introduced in 2000 in the UK, following a successful pilot programme. The number of pregnant women testing for HIV during pregnancy is very high at >90%. As a result, the number of women presenting with HIV for the first time in pregnancy or in labour has fallen dramatically. Since 2015, 89% of pregnancies in HIV have been in women diagnosed preconception. This is important because the highest risk of transmission is in women undiagnosed at delivery.

It is also important to note that even women presenting in labour with untreated HIV can have many of the interventions below to reduce vertical transmission. Therefore, any woman in labour without a documented HIV test should be urgently tested.

Effective cART for the woman

Maternal HIV viral load (VL) is the most important determinant of vertical transmission of HIV. The first published data on the effective use of antiretroviral therapy to prevent vertical transmission of HIV appeared in 1994. It showed that pregnant women treated with zidovudine monotherapy, which was standard treatment at the time, versus women not on any treatment, had a 67% reduction in vertical transmission. Since then, HIV treatment has advanced. cART consisting usually of three antiretroviral agents (ARVs) is standard care and should be started on diagnosis of HIV regardless of CD4 count, a marker of immune function. Therefore, a woman living with HIV may conceive while already on cART or may be started on cART if diagnosed in pregnancy. Pregnant women with HIV remain a special group with specific guidelines for HIV treatment based on teratogenicity and toxicity data on cART use in pregnancy from published data, national HIV in pregnancy databases and international databases such as the antiviral pregnancy registry. For example, earlier ARVs stavudine and didanosine caused very significant toxicity to both woman and baby and

A woman living with HIV on effective cART can have a normal vaginal delivery if there is no obstetric reason not to.

are no longer used either in pregnancy or in non-pregnant adults.

When starting treatment, as with any medication, the first trimester is avoided if possible, but started by 24 weeks gestation with the aim of getting HIV VL to undetectable by 36 weeks. Since 2015, 80% of women living with HIV in the UK have conceived on cART. The most common toxicity with cART is preterm delivery and this is particular to a class of ARVs called protease inhibitors. Pregnant women with HIV are monitored more frequently than non-pregnant adults. Women on cART without adequate safety data in pregnancy may be switched to agents with which we have more experience, such as efavirenz and boosted ataznavir, but should see their HIV physicians when they become pregnant to discuss this. All women should take folic acid preconception and for the first 14 weeks of pregnancy.

Management of labour

A woman living with HIV on effective cART can have a normal vaginal delivery if there is no obstetric reason not to. Labour should be managed in the standard way. Forceps or vonteuse may be used, and foetal scalp monitoring or blood sampling can be performed if clinically indicated in this group. Early pre-cART evidence suggested that rupture of membranes (ROM) greater than four hours caused a highly significant increase in risk of vertical transmission. Current evidence suggests that duration of ROM up to 24 hours is safe but only in women with HIV RNA <50 copies ml^{-1}. Elective caesarean section (C-section) as late as possible and after 39 weeks is recommended in women with an

A pregnant woman taking a tablet containing folic acid. Ian Hooton/Science Photo Library

> **Women living with HIV and receiving good care and effective cART are very likely to have a HIV-negative baby.**

HIV RNA >400 copies ml^{-1} even if she is on cART to minimise vertical HIV transmission.

Rates of vaginal delivery in the UK, including trial of normal delivery after a previous C-section, are increasing (40%). In 2016, an elective C-section was performed only in 10% of women living with HIV, down from 70% in 2000. Unfortunately, emergency C-section rates remain high but may be explained in part by lack of data on duration of ROM >24 hours and failure of vaginal delivery after a previous C-section.

Avoidance of breastfeeding

The risk of HIV transmission from breast milk was first identified in 1992, with the risk from breastfeeding reported as 15–25%. Even now with women on effective cART, whether or not to breastfeed remains controversial. There is no randomised controlled data in a UK-type setting assessing risk from breastfeeding when a woman is on cART. There are data from developing countries to suggest the risk is probably very low, at 0.1–5%. However, there are a number of issues to consider. The only certainty we have is that avoidance of breastfeeding will have zero transmission risk to the infant. A woman may be supported to breastfeed her baby, if her HIV VL is undetectable on cART and remains this way each month she is seen with her baby. Her HIV transmission risk may change if she develops mastitis or gastroenteritis or if her baby becomes unwell with vomiting and diarrhoea. Therefore, multidisciplinary input and support at this time is hugely important for both mother and baby.

Post-exposure prophylaxis (PEP) for the baby

All babies born to women living with HIV will receive PEP. What they receive and for how long depends on how the woman's HIV is controlled. For a woman on effective cART, the baby will only need 14 days of zidovudine monotherapy. But for a woman presenting late, in labour or with a detectable HIV RNA, her baby may need longer treatment and/or the addition of more ARVs to prevent HIV. The baby will be tested at birth and twice more after finishing PEP, usually by three months. Although there is still a final test at 18 months the HIV status of the baby can usually be confirmed by the first three tests.

In summary, women living with HIV and receiving good care and effective cART are very likely to have a HIV-negative baby. The multidisciplinary team of HIV, Obstetrics and Paediatrics work together with peer mentors to support mother and baby through this journey, but with evidence-based interventions the outlook is extremely good for both.

Further reading

BHIVA HIV Guidelines in pregnancy 2018 to be published September 2018 **www.bhiva.org/PrEP-guidelines**. Last accessed 23 October 2018.

The Antiviral pregnancy registry **www.apregistry.com**. Last accessed 23 October 2018.

The National Study for HIV in Pregnancy and Childhood **www.ucl.ac.uk/nshpc**. Last accessed 23 October 2018.

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Yvonne Gilleece

Brighton & Sussex University Hospitals NHS Trust

e **yvonne.gilleece@bsuh.nhs.uk**

@DrYGilleece

Yvonne Gilleece is Honorary Senior Lecturer and Consultant in HIV and Sexual Health Brighton & Sussex University Hospitals NHS Trust, Chair of the British HIV Association HIV in Pregnancy Guidelines and Chair of SWIFT, supporting information and research for women living with HIV.

What advice would you give to someone starting out in this field?

Get involved in research from early on in your training as you will be learning and trying to improve patient outcomes for the rest of your career.

What do you enjoy most about your job?

When I see a really complex patient, whether they have medical or psychosocial problems, and knowing I was absolutely the right person for that patient to have seen.

Cryptococcus remains a deadly threat for those with HIV/AIDS

Xin Zhou, Robin C. May & Elizabeth R. Ballou

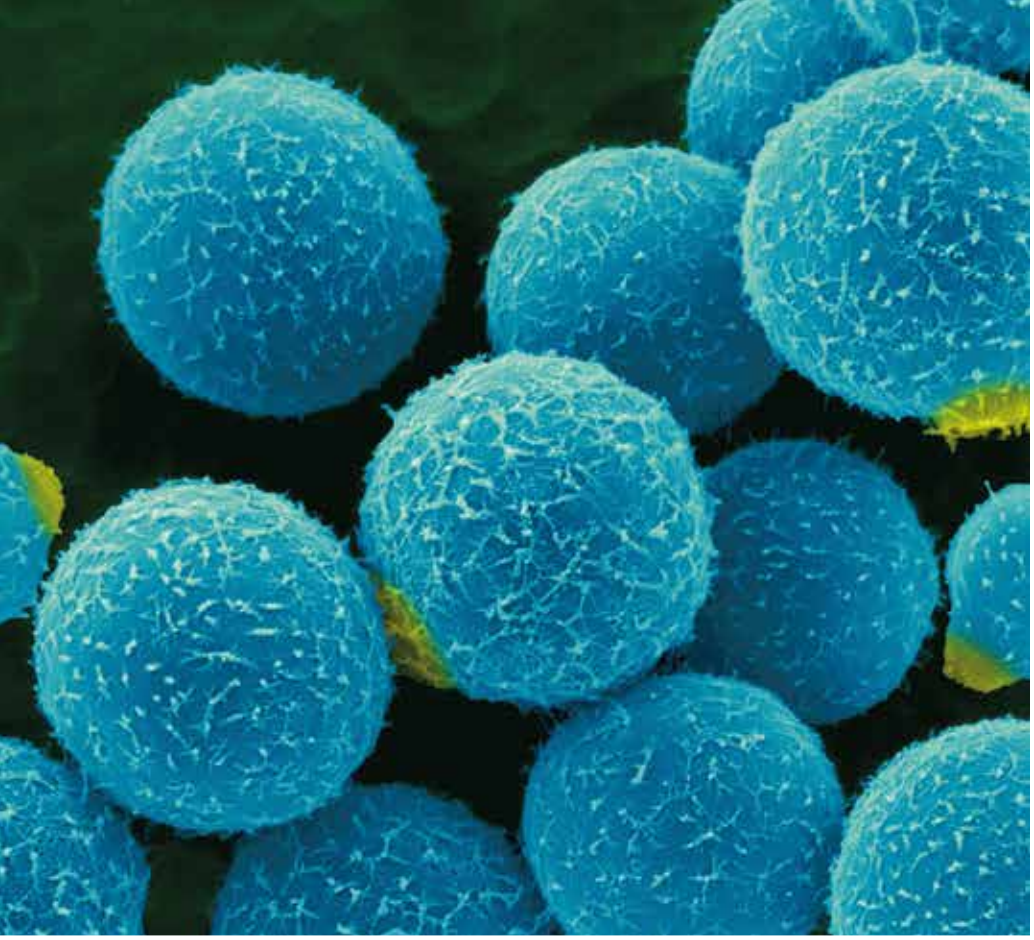
Cryptococcosis is an opportunistic fungal disease that causes life-threatening meningitis, particularly in the immunocompromised. Over the last three decades, the prevalence of cryptococcosis has increased because of the wide use of immunosuppressive drugs, the increasing number of organ transplant recipients and the HIV/AIDS epidemic.

While the majority of cases occur in sub-Saharan Africa, it remains a threat to immunosuppressed patients worldwide. Among all HIV-related deaths, 15% are caused by cryptococcal meningitis. This year, the WHO estimates that 223,100 cases of cryptococcal meningitis occurred in HIV-positive patients, with 181,000 deaths, or 81% mortality. Overall, cryptococcosis has unacceptably high morbidity and mortality rates. However, like other fungal diseases, it is underestimated and neglected despite having an alarming impact on global human health.

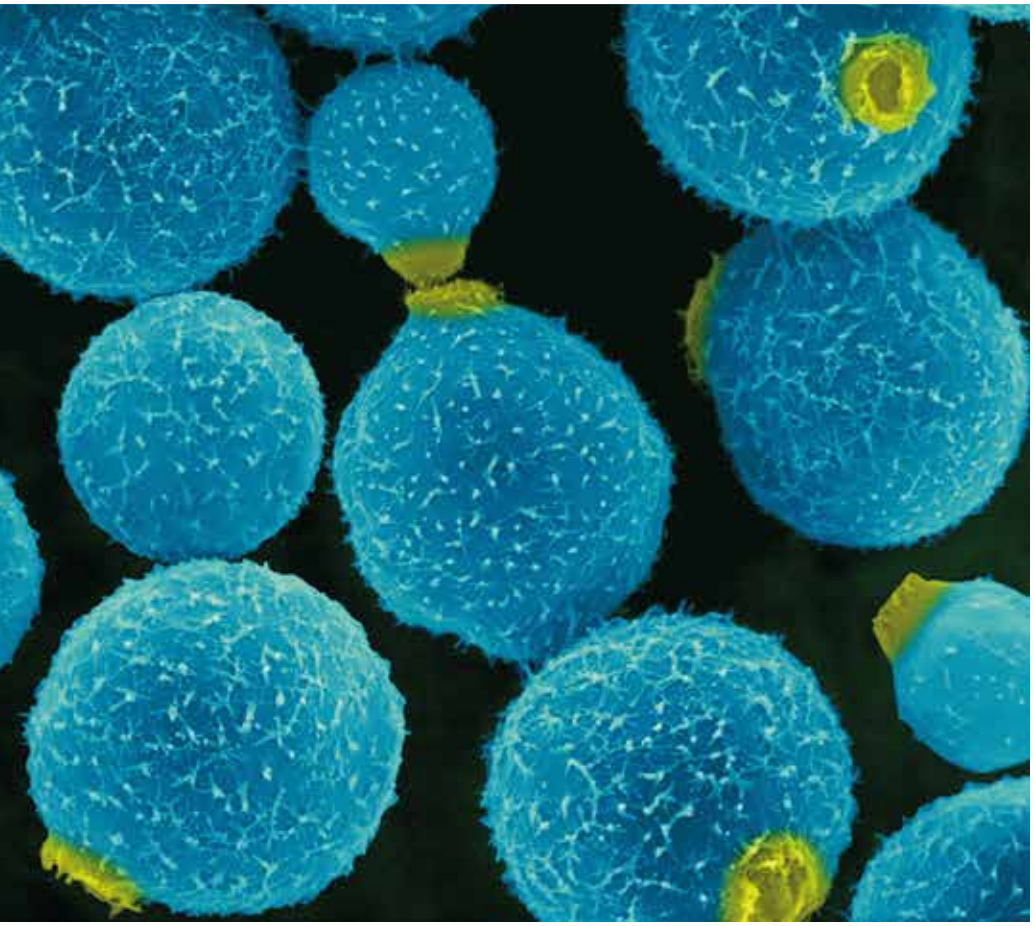
Cryptococcosis is attributed to several members of the genus *Cryptococcus*: the closely related sister species *Cryptococcus neoformans* and *Crytococcus deneoformans,* and the more distantly related *Cryptococcus gattii* species complex, which mostly causes infections in hosts with fully functioning immune systems. *C. neoformans* is the most common cause among immunocompromised patients, even in areas where *C. gattii* predominates. Cryptococcal infections present as a complex syndrome that can be challenging to diagnose. Symptoms include fever, fatigue, dry cough, headache, blurred vision and confusion. Diagnosis must be confirmed by laboratory evaluation, and early diagnosis is important for positive outcomes for patients.

Challenges to diagnosis and treatment

Cryptococcal infections start with inhaled spores or desiccated yeast cells, which grow in the lungs, causing cryptococcal pneumonia. This presentation can be difficult to distinguish from other lung diseases, and can therefore go unappreciated or unrecognised in the clinic. Cryptococcal pneumonia can be fatal, and there are increasing reports of cryptococcal pneumonia in HIV-negative patients. However, in most patients, pneumonia progresses to dissemination of the fungus into the central nervous



Coloured scanning electron micrograph of *Cryptococcus neoformans.*
Dennis Kunkel Microscopy/Science Photo Library



system (CNS), resulting in cryptococcal meningitis. Treatment requires combination therapy with the nephrotoxic antifungal amphotericin B (two weeks) and either flucytosine or fluconazole, followed by long-term monotherapy, representing a further continuing burden on patients and the healthcare system.

In the past, cryptococcal meningitis was uniformly fatal, but now, with more accurate diagnostic strategies and effective treatment, it has become a curable disease. Effective antiretroviral treatment (ART), to deal with the underlying HIV infection, combined with aggressive antifungal treatment has significantly improved survival. However, the high toxicity and challenging route of administration for anticryptococcal treatments mean that new treatment strategies are urgently needed. Recent clinical trials have demonstrated the value of shorter initial antifungal treatment regimens and alternatives such as itraconazole for monotherapy, and potential new drugs like VT-1129 and sertraline. Despite these improvements, we are still facing challenges: amphotericin is toxic and unaffordable, and *Cryptococcus* becomes rapidly resistant to the frontline antifungal fluconazole, which remains highly prescribed despite its low efficacy. These challenges demand further research into both the clinical and basic biological aspects of this human fungal pathogen.

Determinates of cryptococcal pathogenesis

C. neoformans is widespread in soil contaminated with avian excreta, particularly that of pigeons, possibly because the excreta is rich in xanthine, creatinine, urea and uric acid: nutrients that support *Cryptococcus* growth. *C. neoformans* has also been isolated

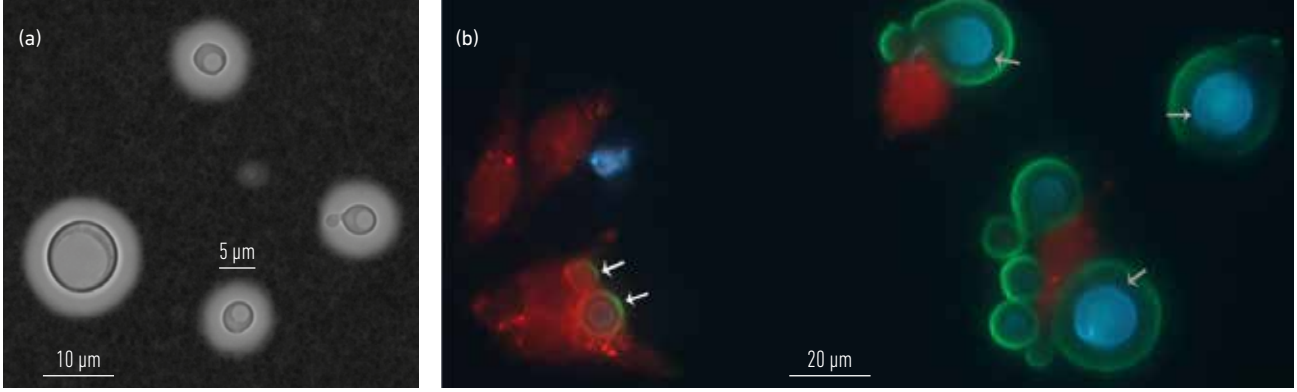


Fig. 1. **(a) India ink staining of *Cryptococcus neoformans* grown under Titan cells induction conditions (cells >10 µm, Titan cells, cells around 5 µm, yeast cells). (b) Murine macrophages (J774) infected with cryptococcal cells. Red, macrophages; blue, cryptococcal cells; green, capsule structure; white arrows, engulfed yeast cells; grey arrows, unengulfed Titan cells.** Xin Zhou

from non-avian sources such as vegetable, fruit and dairy products, and the very first isolation of *C. neformans* was from peach juice in 1894. *Cryptococcus* expresses membrane-bound phenoloxidase enzymes which can convert phenolic compounds into melanin, a black pigment in the cell wall and a major pathogenicity factor. Melanin production is rare among non-pathogenic *Cryptococcus* species, and it has been proven to protect cryptococcal cells from attack by host immune effectors cells.

C. neoformans yeast cells are around 5 µm in diameter, with a round-to-oval shape. In patients, it reproduces by budding. In the environment, it can also form mycelia when mating, with formation of basidiospores at the end of invasive hyphae. Under certain conditions, including within patients, or growth in low glucose with 5% carbon dioxide and serum, it can produce a characteristic structure at the outer layer of the cell wall, the polysaccharide capsule (Fig. 1a). This capsule can extend from the cell, ranging from 1 to 30 µm in diameter, and is a defining feature of the disease.

Many diagnostic tests are specifically designed to identify the presence of the capsule. Classic identification has been through India ink staining (pictured), in which ink reveals the polysaccharide capsule around cryptococcal cells. This method allows the rapid and easy identification of cryptococcocal cells from cerebrospinal fluid, although it lacks sensitivity at the early infection stage and may miss around 20% of patients with culture-positive cryptococcal meningitis. More recently, the CrAg latex agglutination and lateral flow assays detect the presence of capsule antigen in the blood. In terms of the sensitivity of diagnosis, these tests offer specificity close to 100%, although cases can occasionally still be missed. Unlike the conventional culture and microscopy methods, CrAg-dependent tests require only minimally specialised laboratory facilities and low costs.

Titan cells influence disease progression

Cryptococcosis starts when small cells – like desiccated, encapsulated yeast cells or basidiospores – are inhaled. In order to penetrate deeply into the lung parenchyma, cells must be smaller than 2 µm, while normally yeast cells are around 5 µm in diameter. It is therefore postulated that basidiospores are the infectious propagule, due to their small size (1.8–2 µm in diameter) and inherent stress resistance. *C. neoformans* has several intrinsic features, such as a melanin coat and capsule, that enable survival within the host environment. Inhaled cells will also encounter host immune cells including macrophages, neutrophils and dendritic cells among others, which all can kill the fungus directly or indirectly. However, cryptococcal cells can escape from host defenses via several mechanisms, including hijacking host phagocytes or evading uptake through an unusual change in cell size: the switch from yeast to Titan cells. This yeast-to-Titan transition happens during the earliest infection stage. During this transition, cryptococcal cells dramatically increase in size and repeatedly replicate their DNA, ending with formation of very large (more than 10 µm, up to 100 µm diameter) and highly polyploid Titan cells (Fig. 1b). These Titan cells were recognised as a specific *in vivo* phenomenon only in the last decade, but their importance in disease is becoming increasingly clear. Titan cells are thought to mediate pathogenicity through several distinguishing features: an altered cell wall structure, highly compacted capsule and viability under high antimicrobial stress. Very recently, *in vitro* models for Titan cells have been reported, and this innovation opens up important new avenues of study for pathogenicity and drug development.

As a novel virulence factor, the importance of Titan cell production in disease progression has become well recognised. Titan cell formation can help *C. neoformans* establish infection in lungs rather than being cleared by host immune cells, as Titan cells are more resistant to phagocytosis (Fig. 1b). Meanwhile, these enlarged cells also protect small cells from being engulfed and killed, resulting in an overall increase in fungal burden. These small cells are also more drug resistant, and this together with their small size is thought to help them further disseminate into the CNS. In addition, the production of Titan cells activates a non-protective type 2 helper T (T_H2) cell response in the host, further contributing to fungal pathogenesis.

Conclusion

Cryptococcosis is a serious, widespread fungal disease that causes unacceptably

high mortality in HIV patients every year. Refinements in diagnosis and treatment raise the possibility of improving outcomes for patients, but significant challenges remain. We urge further research into the basic biology of this pathogen, including improved understanding of the role of the yeast-to-Titan switch in disease progression and drug resistance.

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Xin Zhou

Institute of Microbiology and Infection, School of Biosciences, University of Birmingham, Birmingham, UK

e **XXZ773@student.bham.ac.uk**

@Phoebezhou07

Xin Zhou is a first year PhD student working in Dr Elizabeth Ballou's lab. Her research focuses on the mechanisms of Titansation in *Cryptococcus neoformans* and its effects on host and pathogen interactions.

Robin C. May

Institute of Microbiology and Infection, School of Biosciences, University of Birmingham, Birmingham, UK

e **r.c.may@bham.ac.uk**

Robin C. May is Professor of Infectious Diseases and Director of the Institute of Microbiology & Infection at the University of Birmingham, UK. His research interests focus on host-pathogen interactions and, in particular, in understanding how some fungal pathogens are able to subvert the innate immune system.

Elizabeth R. Ballou

Institute of Microbiology and Infection, School of Biosciences, University of Birmingham, Birmingham, UK

e **e.r.ballou@bham.ac.uk**

@BallouLab

Elizabeth R. Ballou is a Lecturer in Cellular Microbiology and Wellcome Trust Sir Henry Dale Fellow at the University of Birmingham. She studies how fungi respond to environmental signals to cause disease, focusing on the molecular mechanisms of the yeast-to-Titan transition by *Cryptococcus neoformans*.

What does a typical day (or week) involve for you?

Robin: I really enjoy the fact that no two days are ever the same.

Xin: As a first year PhD student, every day I start by planning my lab work, and then follow my list in the lab.

Liz: One of my favourite things about being a scientist is that there is no such thing as a typical day.

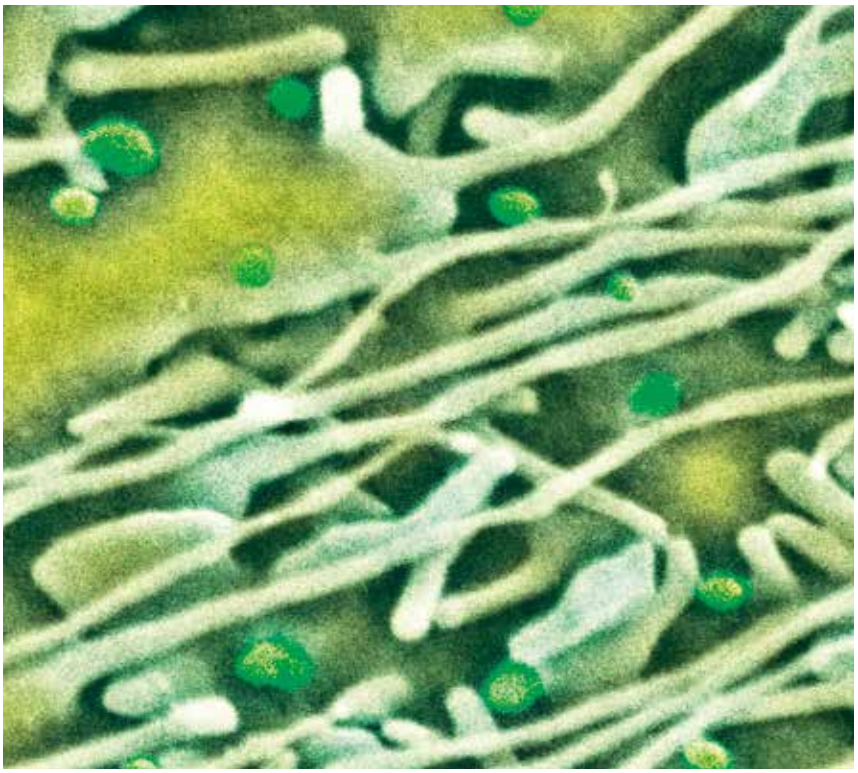
What inspired you to become a microbiologist?

Robin: I blame children's television! I have a memory of watching a TV programme which had a special episode on 'germs'. I was so captivated that I spent an hour hanging over a bucket, thinking that if I vomited I'd be able to spot some evil cartoon bug!

Xin: I first encountered different kinds of microbes as an undergraduate. I was attracted by these beautiful organisms, and later, during a lab training programme, started to realise how important microbes are for our lives.

Liz: I was lucky to grow up around microbiologists. They cemented my belief that through research we have an enormous opportunity to improve human health.

HIV and HCV co-infection – does it matter in the era of direct-acting antiviral therapies?

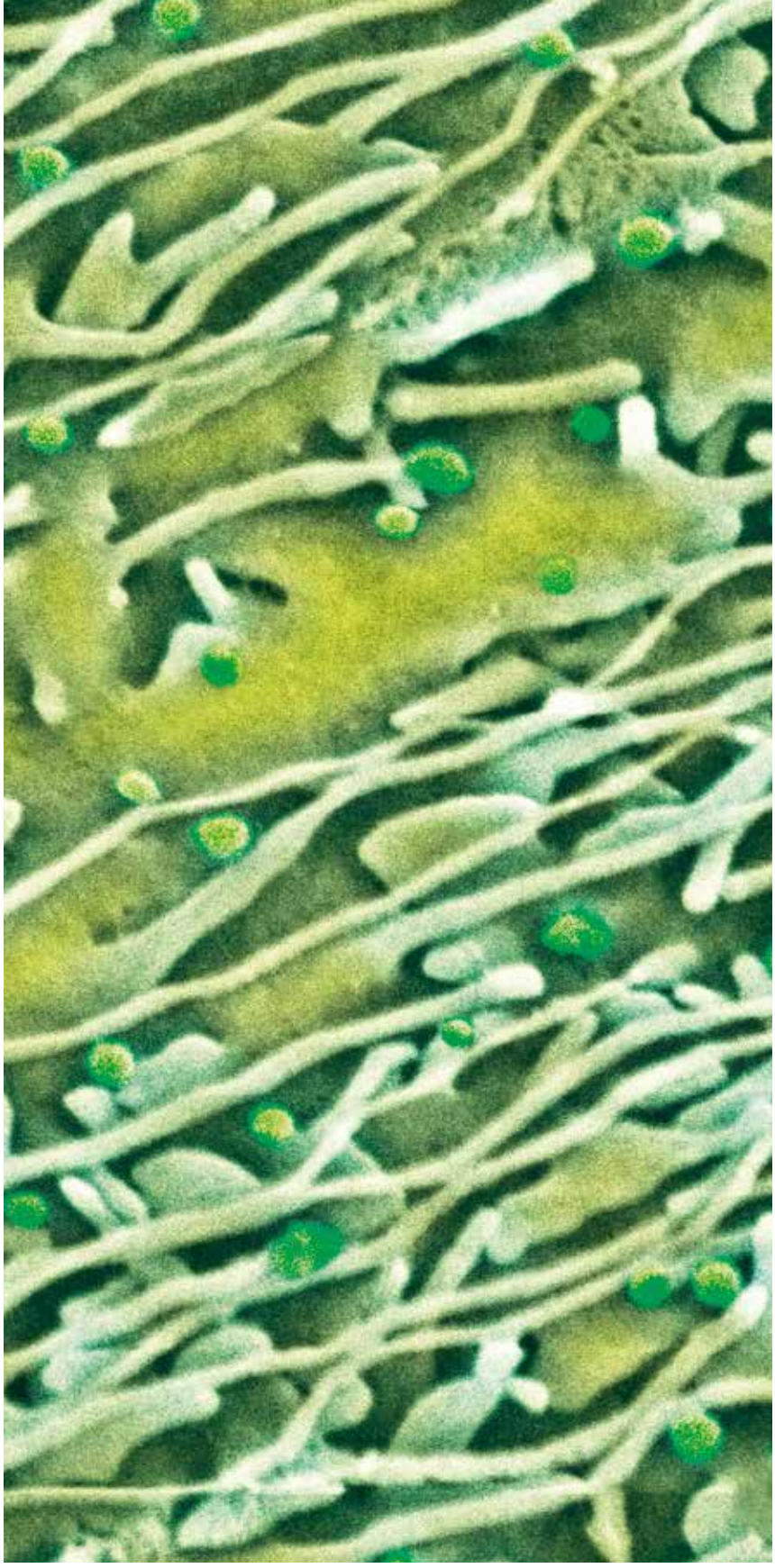


Coloured transmission electron micrograph of hepatitis C virus particles (green) infecting cultured liver cells (yellow). Magnification: x20,000 at 10 cm wide. Thomas Deerinck, NCMIR/Science Photo Library

Emma Thomson

Transmission of the human immunodeficiency virus (HIV) and hepatitis C virus (HCV) occurs within similar populations and therefore dual infection with both viruses is common, affecting more than two million people around the world.

Half of such infections occur in HIV-infected people who inject drugs (PWID), in whom the global HCV seroprevalence is as high as 82%. Iatrogenic infection via infected



blood products or medical instruments also occurs frequently in low-income countries (LICs). A notorious example of nosocomial transmission of HIV and HCV affected 418 children admitted to the Al-Fateh Hospital in Benghazi, Libya, in 1998. Foreign healthcare workers were initially blamed for these infections (and threatened with the death penalty) but the onset of the outbreak clearly predated their arrival in the hospital, where transmission had been occurring for many years due to poor medical practices.

Transmission of HCV and HIV in medical facilities is very likely to have been underestimated in other LICs and may have underpinned much of the transmission of HIV as it spread in sub-Saharan Africa during the 20th century. Sexual transmission of HCV also occurs frequently in HIV-infected men-who-have-sex-with-men (MSM), in whom the HCV seroprevalence is 6.4%. The incidence of HCV in this group increased by 18 times in the Swiss cohort study between 1998 and 2011. It is less common in HIV-infected heterosexual individuals (4.0%). Vertical transmission of HCV is significantly higher in HIV-infected versus uninfected mothers.

Does dual infection with HIV and HCV impact on outcome in infected individuals?

Dual HIV/HCV infection is important because HIV-infected individuals are less likely to clear HCV spontaneously and once chronically infected are at higher risk of progression to cirrhosis and primary hepatocellular carcinoma (HCC). Encouragingly, despite wide differences in sustained virological response (SVR) rates to interferon-based treatments, management of HCV infection using direct-acting antiviral therapies (DAAs) is as efficacious in HIV-positive as HIV-negative individuals, leading some to suggest that HIV-infected patients no longer need to be prioritised as a separate 'hard-to-treat' group. However, liver disease, including HCV-related liver disease, remains a leading cause of mortality and morbidity in HIV-infected people and while co-infected patients with optimally managed HIV are less likely to progress rapidly than those who are not maintained on antiretrovirals (ARVs), they are still at greater risk of complication than HCV mono-infected

individuals. HIV-infected patients develop HCC at an earlier stage of cirrhosis and at a younger age, and are more likely to develop multi-focal disease. Markers of bacterial translocation, a feature of both HIV and HCV mono-infection, are markedly increased in dual infection. Management of liver transplantation in HIV-infected patients, while feasible, is more challenging due to drug–drug interactions and the risk of infective complications.

Why do co-infected individuals progress more rapidly to liver cirrhosis and cancer?

The mechanism of accelerated progression to cirrhosis and to HCC in HIV/HCV co-infection relates at least in part to the role of the adaptive immune response in control of HCV infection, in particular, the central role of the CD4+ T cell (Fig. 1). The innate immune response to HCV is also altered via direct interactions with both viruses and depletion of innate lymphocyte subsets.

The adaptive T cell response is central to the control of hepatitis C infection

CD4 and CD8 T helper and T cytotoxic cells are critical in the control of HCV infection in infected individuals. In chimpanzees, depletion of either CD4 or CD8 cell subsets is associated with progression to chronicity, and in humans, class I and class II HLA associations with spontaneous clearance highlight the role of antigen presentation to T cells. Curiously, the class I HLA B27 and B57 alleles are protective in both infections, likely via presentation of structurally unrelated antigens. Depletion and loss of function of CD4 cells as a consequence of HIV infection impacts the HCV response both directly and indirectly. In HIV-infected individuals, HCV viral loads are higher than in mono-infected individuals and have been shown to correlate directly with CD4 count. CD4 cells classically maintain CD8 cytotoxic responses; these are impaired in both infections, in HCV infection at a more immature stage of development than HIV. As well as providing help to CD8+ cells, CD4 responses have been shown more recently to exert direct cytolytic effects on infected cells and are also key in the control of bacterial translocation from the gastrointestinal tract, a site where massive depletion of CD4 cells occurs early on in HIV infection. Upregulation of T cell exhaustion markers such as PD-1 and TIM-3 is associated with both HIV and HCV infection and may be increased in dual infection, resulting in a less effective adaptive response to HCV.

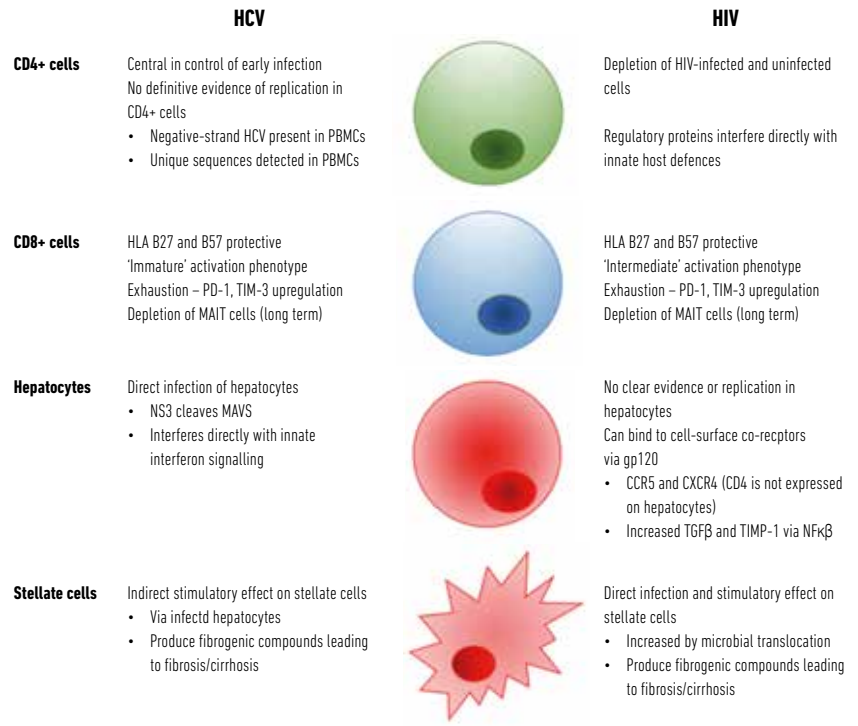


Fig. 1. Mechanisms leading to fibrosis in HCV- and HIV-infected cells. E. Thomson

Mucosal-associated invariant T (MAIT) cells are irreversibly depleted in HIV infection

Mucosal-associated invariant T (MAIT) cells, characterised by the semi-invariant T cell receptor (TCR) Vα7.2-Jα33, recognise vitamin B metabolites from bacterial and fungal pathogens presented via the major histocompatibility complex class I-related molecule, MR1. They express the transcription factors RORγt and PLZF, secrete IL17 and IL22, express CD161 and are highly enriched in the liver where they represent as much as 50% of the lymphocyte population. They may be activated via the TCR or in a non-TCR dependent manner by cytokines. Activation in response to HCV occurs via an IL18-dependent, TCR-independent cytokine pathway.

Importantly, MAIT cells are depleted in HCV infection in peripheral blood and the liver and are associated inversely with lower fibrosis and inflammation scores. Partial restoration of MAIT cell numbers and a decrease in activation occurs during effective antiviral DAA therapy but the response to cognate antigen remains impaired functionally and absolute numbers do not reach the level seen in uninfected controls. In patients infected with HIV, the MAIT cell population is dramatically decreased and

this is not replaced following successful ARV therapy. It is very likely therefore that a lack of MAIT cells in the liver may contribute to accelerated fibrosis in co-infected individuals.

Direct effects of HIV and HCV on hepatocytes and stellate cells

Hepatocytes do not support the entry of HIV (due to lack of the CD4+ receptor) but binding of the virus to the CXCR4 and CCR5 co-receptors which are present on hepatocytes may occur via gp120, resulting in an increase in intracellular signalling via NFκβ and an increase in expression of TGF-β1. This may result in accelerated fibrosis and increased replication of HCV within infected hepatocytes in the absence of hepatocyte entry. Expression of profibrotic proteins such as tissue inhibitor of metalloproteinase 1 (TIMP-1) is also increased by NFκβ and may contribute to accelerated fibrosis.

While hepatocytes are not infected by HIV, hepatic stellate cells, the cells central to hepatic fibrogenesis, can be infected by HIV (although not by HCV – stimulation of stellate cells is thought to occur via cytokine release from infected hepatocytes). Stellate cells directly infected by HIV may express higher levels of monocyte chemoattractant protein-1 (MCP-1) and TIMP, thereby increasing fibrosis.

Other cell types such as monocytes or B cells could in theory harbour both viruses, although this has not been shown conclusively either *in vitro* or *in vivo*. Within the same cell, multiple interactions between viral proteins that regulate the innate immune response to HIV and HCV could theoretically impact on HCV replication also, but such interactions have not yet been described.

Summary

In summary, HIV and HCV co-infection is common and is associated with a higher risk of progression to fibrosis and cancer, an effect only partly attenuated by antiretroviral therapy for HIV. This is likely to be related to immune perturbation of innate and adaptive immune responses in infected individuals. There is a rationale for early treatment of HCV in HIV-infected patients, even in the era of highly effective DAA therapies.

Further reading

Bolte, F. J. & others (2017). Intra-hepatic depletion of mucosal-associated invariant T cells in hepatitis C virus-induced liver inflammation. *Gastroenterology* **153**, 1392–1403. e2. doi:10.1053/j.gastro.2017.07.043

Cosgrove C. & others (2013). Early and nonreversible decrease of CD161++/MAIT cells in HIV infection *Blood* **121**, 951–961. doi:10.1182/blood-2012-06-436436

Faria N.R. & others (2014). The early spread and epidemic ignition of HIV-1 in human populations. *Science* **346**, 56–61. doi:10.1126/science.1256739

Hengst J. & others (2016). Nonreversible MAIT cell-dysfunction in chronic hepatitis C virus infection despite successful interferon-free therapy. *Eur J Immunol* **46**, 2204–2210. doi:10.1002/eji.201646447


Emma Thomson

Emma Thomson

MRC-University of Glasgow Centre for Virus Research, Bearsden Road, Glasgow G61 1QH, UK

e **emma.thomson@glasgow.ac.uk**

www.gla.ac.uk/researchinstitutes/iii/cvr/staff/groups/thomsongroup

Emma Thomson studied medicine in Glasgow before specialising in infectious diseases and general medicine in London. She carried out a PhD in viral immunology (hepatitis C) at Imperial College London and Oxford University and now runs a research lab at the MRC-University of Glasgow Centre for Virus Research.

How did you enter this field?

I was inspired by reading the *Origin of Species* and later other books by Charles Darwin (amazed that he was able to draw the first phylogenetic tree without even knowing about the existence of DNA) and *The Selfish Gene* by Richard Dawkins. I became fascinated by the host–pathogen arms race as an undergraduate. I also wanted to learn a multi-system speciality and was inspired by senior colleagues that aimed to challenge health inequalities. This led me into infectious diseases as a speciality and later into research.

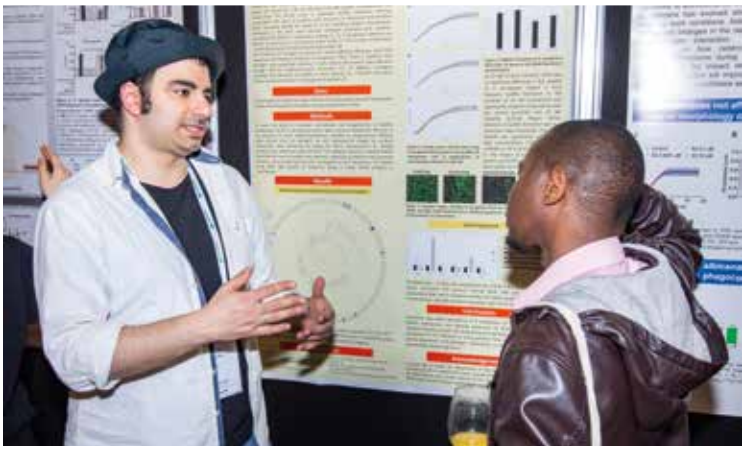
What do you see as your greatest achievement to date?

I had the opportunity to draft the first treatment guidelines for hepatitis C for the World Health Organization in 2014 – it was exciting to be able to contribute in a small way to the plan to eliminate the virus by 2030. I was also really excited when my lab team were able to sequence whole HCV genomes (and other viruses) for the first time using next-generation sequencing.

Annual Conference **2019** #Microbio19

8–11 April 2019 – Belfast Waterfront

The Annual Conference is the Microbiology Society's flagship event. The next meeting takes place in Belfast over four days on 8–11 April 2019 and consists of symposia, workshops, forums, poster sessions and a trade exhibition. You can find out all the information you need to know by visiting our website: microbiologysociety.org/annualconference.



Destination Belfast

Belfast is the capital of Northern Ireland and home to the conference venue – the Belfast Waterfront. This landmark venue stages the best in arts and entertainment as well as hosting major conferences and business events.

Belfast itself is a city rich in culture and history, so whether you're looking to visit its historic landmarks and attractions or experience new culinary delights, there's a lot waiting to be discovered. Visit the visit Belfast website to discover more **www.visitbelfast.com**.

Registration

Registration is open for Annual Conference, which attracts over 1,400 attendees for the UK's largest annual gathering of microbiologists.

To ensure the meeting remains of value for this broad microbiology community, ticket prices have not increased from last year beyond the rate of inflation and a new 10% discount is available for anyone registering for all four days of the meeting. As with all of our Society events, Microbiology Society members will receive a substantial discount.

Abstracts

Abstract submissions are also live on the website.

As always, Annual Conference is designed to cover the breadth of microbiology research developments and its abstracts reflect this comprehensive scientific programme.

Submissions close on **10 December 2018**, so don't miss out on this opportunity to showcase your microbiological work and research. More information and tips on writing abstracts can be found online.

Notifications of acceptances will be made from **15 January 2019**.

For those abstracts that are awarded a poster, the Annual Conference provides an excellent platform for emerging scientific research. Following feedback from last year's event, all posters will be displayed within the same space within the convention centre. Posters will also be rotated to ensure relevance to the content of the day's live programmed sessions.

Early career microbiologists

Annual Conference has a number of opportunities for early career microbiologist members to get involved. If you're eligible, don't forget to indicate your interest in participating in the Sir Howard Dalton Young Microbiologist of the Year Competition, or the Early Career Microbiologists' Forum Co-chairing scheme when submitting your abstract. More information can be found under the Grants and Professorial Development tab.

Access Microbiology

In 2019 the Society is launching a new journal, *Access Microbiology*, which will publish posters presented at Annual Conference alongside other high-value, but often hidden research.

If your work is accepted as a poster, the Society will contact you about publishing your work in the journal. All published articles are freely available to read, and as article processing charges are currently waived, it's free for authors to publish.

surangaw/Thinkstock

To get the latest Annual Conference news and updates, follow us on Twitter **@MicrobioSoc** using the hashtag **#Microbio19**.

Social Programme

Annual Conference is designed to offer ample opportunities for formal and informal networking for both early career and established microbiologists. This year we have arranged two low-cost, separately bookable events which you can book when registering for the Conference.

Crumlin Road Gaol. Crumlin Road Gaol

Crumlin Road Gaol Social

Monday 8 April – Tickets £25

HMP Belfast, also known as Crumlin Road Gaol, is a former prison situated on the Crumlin Road in north Belfast. It is the only Victorian-era prison remaining in Northern Ireland and is affectionately known as the Crum.

On the first night of Annual Conference, the jail will be opened exclusively for ticket holders. Over the years the jail has housed murderers, suffragettes and loyalist and republican prisoners. It has witnessed births, deaths and marriages and has been the home to executions, escapes, hunger-strikes and riots. Guests will receive a glass of prosecco and canapés on arrival before going on a 70-minute guided tour to experience what life was like for these prisoners.

Lavery's Bar. Lavery's Bar

Society quiz and games night

Wednesday 10 April 2019 – Tickets £15

The annual quiz night will be taking place at Lavery's bar with its roof terrace and a private floor for Society members.

The ever-popular annual quiz will start at 20:30 with prizes up for grabs. Following the quiz, you can make use of Northern Ireland's largest pool room with 22 high-quality and well-maintained pool tables.

Grants

Society Conference Grants are available to support eligible members wishing to present at the Annual Conference. The grants deadline is **31 January 2019**. Grant notifications will go out before **21 February 2019**. Full information is available on the Society Conference Grant page: **microbiologysociety.org/societyconferencegrants**. If you are a member who is not eligible for a Society Conference Grant, please apply via the Travel Grant scheme: **microbiologysociety.org/travelgrants**.

Accommodation and travel

If you're planning on joining us at this important event, we highly recommend you secure your accommodation and make your travel plans as early as possible. Belfast is a popular destination whose hotels fill up quickly.

To support you in securing your accommodation, go to the Annual Conference website where we provide links to our booking and accommodation services via Reservation Highway: **microbiologysociety.org/annualconference**.

Call for Annual Conference Sessions Proposals for 2020

The deadline to send your session ideas for our 2020 Annual Conference is **14 December 2018.**

We welcome session suggestions from members in any field of microbiology. If you have an idea for a session and would like it to be considered by our divisions at our next Conference planning day, we want to hear from you. The divisions meet in January of every year, and if your suggestion is accepted, the Scientific Conferences Committee (SCC) will appoint experienced session organisers to finalise the session programme. Visit our website to download the suggestion form: **microbiologysociety.org/proposals**.

Focused Meetings **2018** and **2019**

Focused Meetings 2018

The Conferences and Events Team delivered three successful Focused Meetings throughout September and October, rounding off the 2018 programme. The Focused Meetings are key events in the Society's calendar, presenting opportunities for microbiologists with shared interests to explore new scientific research, form new connections and hear from a varied line-up of distinguished invited speakers.

Molecular Biology and Pathogenesis of Avian Viruses

3–4 September 2018, St Catherine's College, University of Oxford

Following a successful meeting in London in 2016, the Molecular Biology and Pathogenesis of Avian Viruses meeting took place at University of Oxford from 3–4 September. Featuring a stimulating programme of expert speakers and showcasing scientific posters from the field of avian virology, the meeting attracted a range of delegates from all over the world.

Delegates enjoyed a drinks reception and conference dinner on Monday evening, which provided further opportunities to form new connections with fellow microbiologists and to expand professional networks.

9th International Symposium on Testate Amoebae (ISTA9)

10–14 September 2018, Riddel Hall, Queen's University Belfast

Taking place in the UK for the first time, The Microbiology Society worked with the International Society of Testate Amoeba Researchers (ISTAR) to deliver the 9th International Symposium on Testate Amoebae (ISTA9) in Belfast from 10–14 September.

The meeting attracted a diverse audience of international delegates, bringing together researchers working in the wide range of environments where testate amoebae occur.

With a full programme featuring over 60 abstracts and a range of social activities each day, the symposium presented the delegation with a unique opportunity to meet scientists with shared interests and to strengthen links within the research community.

Microbiomes Underpinning Agriculture

1–2 October 2018, Rochestown Park Hotel, Cork

The final Focused Meeting of the year, Microbiomes Underpinning Agriculture, took place between 1–2 October in Cork, Ireland. This meeting focused on the diverse roles played by micro-organisms in agricultural systems and explored what microbiome research can offer to agriculture.

Delegates were able to catch up with colleagues and establish new connections during the conference dinner, allowing for continued discussions in a more relaxed atmosphere.

The Society collaborated throughout this meeting with Teagasc (The Irish Agriculture and Food Development Authority) and, on the final day of the event, delegates attended a tour of the genomic sequencing and microscopy facilities in the Moorepark Research Centre.

Thank you to all who took part in these events during 2018, including all of the session organisers, sponsors, exhibitors and delegates who came together to make these events such enjoyable experiences. Visit our website (**microbiologysociety.org/events**) to find out how you can be involved in our future Focused Meetings programme.

Keep up-to-date with events, follow the Society on Twitter: **@MicrobioSoc**

Focused Meetings 2019

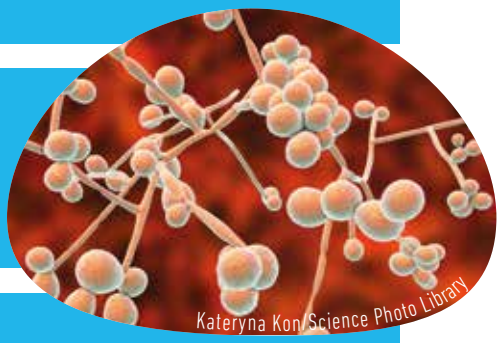
We are pleased to announce our programme of Focused Meetings for 2019, submitted by our members for our members and the wider microbiology community. You can find more information on each event by visiting our website (microbiologysociety.org/events) and by following our social media channels for announcements and updates in the build-up to the events.

Anaerobe 2019: Changing perceptions of anaerobic bacteria: from pathogen to the normal microbiota and back

#Anaerobe19

A symposium on topical aspects of anaerobic microbiology

June 2019, Cardiff, UK*



British Yeast Group: Discovery to Impact

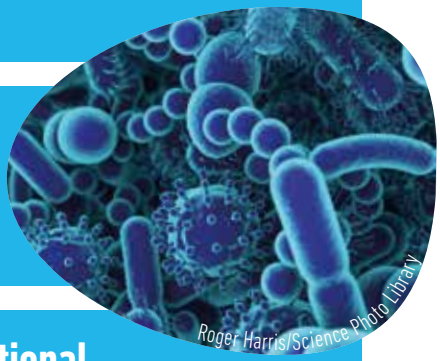
#BYG19

June 2019, Newcastle, UK*

IMAV 2019 – International Meeting on Arboviruses and their Vectors

#IMAV19

September 2019, Glasgow, UK*



Microbes in medicine

#MicroMed19

October 2019, Dublin, Ireland*

Antimicrobial drug discovery from traditional and historical medicine

#AMRmeds19

October 2019, Oxford, UK*

**Subject to confirmation. Please check the website.*

As our meetings are developed, please visit our website **microbiologysociety.org/events** for more information and follow the Microbiology Society on social media for updates.

Society Showcase and AGM: celebrating the achievements of the membership

Each year the Society hosts a showcase event before our Annual General Meeting for early career members of the Society to come together, meet each other and learn from other members of the Society who are further on in their careers. The event allows us to recognise the excellent work these Committee members, Champions and prize winners have accomplished over the past year.

Courtney Kousser receives the Sir Howard Dalton Young Microbiologist of the Year Competition Prize from Professor Neil Gow.

This year, guests had the opportunity to engage in a networking game that showed them just how much they had in common, before moving on to a session hosting some of our recent Prize Lecture winners and Society Committee members sharing what they wish they had known when they were starting out on their undergraduate degrees. Learning from others who have gone down the path can be so helpful for early career scientists, with one early career microbiologist commenting that it was "great to hear Dr Tansy Hammarton talking frankly about the challenges of career breaks from having children. It's not

Guests at the reception held at the Foundling Museum.

something you hear much about and it's so useful to early career women in STEM."

Guests were then invited to view posters from the Annual Conference poster prize winners during lunch, before the final of the Sir Howard Dalton Young Microbiologist of the Year (YMOY) Competition began. The eight finalists, who were shortlisted from over 600 abstracts across our Annual Conference and Irish Division Focused Meetings, gave fantastic presentations of their research in another hard-fought competition. The winners of the competition were announced at the reception at the Foundling Museum. Congratulations to Courtney Kousser, from University of Birmingham, for winning first prize for '*Pseudomonas aeruginosa* inhibits *Rhizopus microsporus* germination via the sequestration of iron', and to second- and third-prize winners Rute Maria Pinto, Roslin Institute, University of Edinburgh and Stephen Dolan, University of Cambridge.

Courtney said, "it's really nice to be recognised for something that I really enjoy doing. I enjoy communicating science and talking about science with people. So it's a big honour to be recognised for that."

After the business of the AGM, the final celebration of the day was Senga Robertson-Albertyn's Microbiology Outreach Prize talk, 'Microbe Motels: how to make a healthy poo'. Senga's entertaining talk displayed her passion for science communication and fantastic approach to teaching students about microbiomes.

Maria Fernandes
Head of Professional Development and Evaluation

Watch interviews with Courtney and Senga on our YouTube channel: **microb.io/29hqRA8**.

Senga Robertson-Albertyn receives her Outreach Prize from Professor Neil Gow.

Think, Check, Submit: how to choose a journal

Speak to any editor or publisher and they will tell you that *their* journal is the best place to publish, but that isn't always true. In this article we'll give you some tools to help you think a little more critically about your options, starting with a campaign called *Think, Check, Submit* (**thinkchecksubmit.org**). It was built by publishers, librarians and researchers in response to so-called "predatory publishers" – commercial organisations claiming to be Open Access publishers and charging authors for publication, but without proper peer review, Editorial Boards, indexing, and so on. *Think, Check, Submit* has a great checklist for assessing whether a publisher or a journal is trustworthy, and we encourage you to use it whenever you are submitting an article. Beyond trustworthiness, however, you need to consider a few other things before submitting work for review.

1. Scope

You probably have a list of preferred journals, and your instinct might be to start at the top of the list for every paper. Before you do that, consider the scope of each journal. Editors are busy people and will reject out-of-scope papers before peer review. By making sure your work is within scope before you submit it, you decrease the possibility that the paper will suffer a pre-screen reject. If you aren't sure, then get in touch with the journal: any decent journal will answer pre-submission questions, though it's likely to take a few days to consult the relevant editor. If you don't get a reply, you should ask yourself how responsive the journal is likely to be during peer review and publication.

2. Reputation

You need to be confident your chosen journal has a profile among your peers that will enhance your professional profile and help you progress in your career. The check step of *Think, Check, Submit* talks about knowing the Editorial Board, but what about other authors? Do your peers publish in the journal? What about more senior people? Do they have good things to say about it? Your professional networks are a valuable resource and might well be able to help you in your search for the 'right' journal.

Fig. 1. What makes a journal 'right'?

3. Profile and metrics

If you have been following the Microbiology Society you will know that we have signed the San Francisco Declaration on Research Assessment (DORA; **sfdora.org**). We are among hundreds of institutions, funders, societies and publishers worldwide who are committed to using metrics that are appropriate to a situation, not simply relying on the Journal Impact Factor (JIF). A good journal will show you article-level metrics like usage stats and Altmetrics (a measure of social impact), and will be transparent about things like acceptance rates – though the latter is often on-request, rather than on the journal website.

When you are thinking about the profile of a journal, be ambitious but remember that a good-quality journal in your specialist area might be more appropriate than something like *Nature*. This will help you avoid the cycle of submitting to a high-profile journal, being reviewed and rejected, and having to start again.

4. Support

Different publishers handle operations in different ways. Particularly for less experienced authors, having a single point of contact to take you through peer review and production is a real benefit. Small publishers like the Microbiology Society often run their operations in-house, where the larger entities may outsource everything.

5. Openness

Last but certainly not least, think about Open. If your funder or institution has an Open Access (OA) policy, is the publisher compliant? This could be immediate OA for the version of record (gold OA), in which case there might be an article processing charge to pay, or policies which allow you to deposit the accepted version of your article (green OA) free of charge, potentially some months after publication. For articles in traditional subscription journals, there's the related question about copyright – does the publisher require you to transfer copyright to them, or do they ask you to sign a license to publish, which means that you, the author, retain copyright and can reuse your own work without having to request permission first?

If in doubt, remember that the Microbiology Society, like many others, has a portfolio of journals and that publishing in our journals helps to support the Society, which in turn means we can support you, our community, now and in the future.

Journal links

Microbiology
mic.microbiologyresearch.org

Journal of General Virology
jgv.microbiologyresearch.org

Journal of Medical Microbiology
jmm.microbiologyresearch.org

Microbial Genomics
mgen.microbiologyresearch.org

International Journal of Systematic and Evolutionary Microbiology
ijs.microbiologyresearch.org

Access Microbiology
acmi.microbiologyresearch.org

Progressing Policy at the Society

Dr Pat Goodwin (Chair) and Professor Paul Kellam (Chair-Elect) of the Microbiology Society's Policy Committee reflect on progress in enabling members to engage with policy-makers and champion microbiology.

It is increasingly evident that scientists have an important role to play in informing and interacting with government, politicians and other key stakeholders involved in making and implementing policies. Brexit, science funding, antimicrobial resistance and food security are just some of the issues we have come across in our roles as Chair and Chair-Elect of the Microbiology Society's Policy Committee.

Putting our expert members at the heart of policy activities

The Society recognises that it has a vital role to play in providing a voice for microbiology and enabling members to connect and communicate with decision-makers. Indeed, policy work is fundamental to progressing the Society's strategic vision of 'a world in which the science of microbiology provides maximum benefit to society'. To help deliver this vision the Society will:

- **empower members to engage in science policy**, providing opportunities to stay up-to-date with policy developments, become involved in policy activities and build networks relevant to their work;
- **inform policy**, using the collective expertise of members to ensure that policy-makers are aware of the need for, and take account of, microbiological evidence in addressing policy issues;
- **champion microbiology**, increasing awareness and understanding of the public value of microbiology, our members' work, and the role of microbiology in addressing global challenges.

Engaging in science policy

Empowering members to input into our policy work is essential for the Society to have the authority and breadth of expertise to speak on behalf of the microbiology community and effectively inform policy. Our first Engaging in Science Policy session at Annual Conference 2018 attracted a lot of interest, and we aim to follow this up with further events and resources.

In June, we both attended Parliamentary Links Day in the Houses

It has been a privilege to chair the Policy Committee and it is great to see how the Society's influence in policy circles is growing. None of this would have been possible without help from many members of the Society.

of Parliament, together with several other members and our guest, the Head of the Parliamentary Office of Science and Technology. Events like this raise the profile of microbiology and enable members to engage directly with policy-makers.

Informing policy

Policy workshops, allowing face-to-face discussions between members and stakeholders, are another way we enable members to inform policy activities and expand their networks. This approach proved very successful in producing our Unlocking the Microbiome policy report. We connected scientists, funders and other stakeholders spanning areas such as health, agri-food and biotechnology, and made 10 recommendations to help the research community communicate the practical, educational, industrial and policy aspects of microbiome research. Feedback from funders indicated that they found the report useful, and it was discussed in a parliamentary POST Note on *The Microbiome and Human Health* and in *Science in Parliament* magazine – evidence that we are having an impact.

The Society has also been active in responding to policy consultations, thereby informing reports which make recommendations to Government. Notably, this year we were invited to give evidence at Parliamentary Select Committee hearings on the Life Science Industrial Strategy and Science, and Brexit. At both hearings, Paul presented the views of the Society, based on input from members.

Championing microbiology

Antimicrobial resistance (AMR) is an important policy issue which demonstrates various ways in which the Society can champion microbiology. First, it is the subject of one of our policy briefings . Second, as a member of the Learned Society Partnership on AMR we have supported several interdisciplinary events, including a workshop for early career researchers; and thirdly, we have a representative on the Chief Medical Officer's AMR Health Stakeholder Group which informs the development of the UK AMR strategy.

Looking forward to the Society's 75th Anniversary, Policy Committee will be overseeing a project exploring how microbiology can contribute towards implementing the Sustainable Development Goals (SDGs) and we hope that many members will be able to input into this.

Further information

More information about our policy activities can be found at **microbiologysociety.org/policy**. If you wish to become more involved please sign up to the science policy mailing: (**microbiologysociety.org/policymailing**) or contact the Policy Team at **policy@microbiologysociety.org**.

Microbiology Society Strategy 2018–2022
microbiologysociety.org/strategy

'Engaging in Science Policy' article
microb.io/2Q8BFYb

Microbiome Policy Project
microbiologysociety.org/microbiome

Antimicrobial Resistance Policy Project
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Learned Society Partnership on Antimicrobial Resistance
microbiologysociety.org/policy/lespar

Consultation responses
microbiologysociety.org/consultationresponses

Science in Parliament: Unlocking the Microbiome
microb.io/2wOqXOg

The Microbiome and Human Health POSTnote
microb.io/2wIwq8C

I look forward to taking over as Chair of Policy Committee in 2019 and working with members and staff to further develop the Society's policy activities to address the many challenges microbiology can help tackle.

Society-Supported Conference Grants

The Microbiology Society provides financial support for events held by members in different areas of microbiology. Numerous events have received funding through our Society-Supported Conference Grants, helping them cover the costs of invited speakers. More information about the full eligibility criteria and the application form can be found on our website: **microbiologysociety.org/ssconferencegrants**. Below are some of the events which have received funding through our Society-Supported Conference Grants.

Society-Supported Conferences 2018 and 2019

- 5th Midlands Molecular Microbiology Meeting (M4)
  13–14 September 2018, Coventry, UK
- Influenza Update Meeting 2018
  18–19 December 2018, Cambridge, UK
- Microbial Molecular Ecology Group (MMEG) Meeting 2018
  17–18 December 2018, Swansea, UK
- Recently Independent Virology Researchers (RIVR)
  7–8 January 2019, Leeds, UK
- e-Bug 10-year Anniversary International Meeting
  17–18 January 2019, London, UK
- Pseudomonas 2019: The 17th Biannual Conference
  22–26 July 2019, Putrajaya, Malaysia.
- British Mycological Society Annual Scientific Meeting 2019: Fungal Interactions
  17–19 September 2019, Aberdeen, Scotland

The deadline for the next round of applications for a Society-Supported Conference Grant is **14 December 2018**. Members can apply for a grant of up to £2,000 towards covering the costs of invited speakers, travel and accommodation.

The Federation of Infection Societies (FIS) Annual Conference 2018: Action on Infection

FIS 2018 will be hosted this November by the British Infection Association (BIA) at Sage Gateshead in Newcastle, on 13–15 November.

The Microbiology Society are delivering a session at this year's event, in collaboration with the Society of Anaerobic Microbiology, which will take place on the morning of 14 November between 9:30 and 11:00. The session will be on 'Lethal clostridial infection: from diarrhoea to septic shock' and will be chaired by our FIS representative, Professor Sheila Patrick. We will also have a stand in the exhibition hall promoting the Society.

Please visit the conference website, **fis2018.co.uk**, for more information on the programme and registration.

The 11th Healthcare Infection Society (HIS) International Conference 2018

The 11th HIS International Conference takes place at the ACC in Liverpool, 26–28 November.

Dr Esther Robinson, Lead Public Health Microbiologist, Public Health England, and Dr Adam Witney, Research Fellow, St George's University of London & St George's Healthcare NHS Trust, will be presenting 'Bringing genome sequencing and bioinformatics into hospital epidemiology' at 8:00–9:00 on Wednesday 28 November as Society representatives.

Please visit the HIS website for information **his.org.uk/training-events/his-2018**.

FEMS Grants: make your Microbiology Society membership go further

You probably already know that your membership of the Microbiology Society makes you eligible to apply for our grants programme, which offers funding for many different activities that can support your professional development and career prospects. Did you know that your Society membership also makes you eligible for a range of grants from the Federation of European Microbiology Societies (FEMS)?

Members of FEMS Member Societies are eligible to apply to FEMS for research grants and support for organising or attending meetings. The FEMS Grants on offer can help you to reach collaborators across the world, and host meetings of relevance to your colleagues, to facilitate network building. FEMS places an emphasis on supporting early career scientists, who they define as active microbiologists within five years of the highest academic degree earned, or current postgraduate students.

Microbiology Society member Conall Holohan won a FEMS Research Grant to visit Diana Sousa, Wageningen University, in April 2017, saying of the award: "Ultimately, this FEMS Research Grant ensured my research was comprehensive and efficient, gaining a more in-depth microbiological insight with [my host's] microbial methods, thus allowing our research and results to inform the field in a greater manner than before this visit."

FEMS Grants

Meeting Organiser Grants

Provide up to €15,000 to support selected European training courses, scientific conferences or laboratory workshops – 60% of the award should be spent on supporting the attendance of early career scientists.

Deadline: 1 December for events taking place between 1 April 2019 and 31 January 2020.

Meeting Attendance Grants

Provide up to €600 to support early career researchers to attend a microbiology meeting anywhere in the world.

Deadlines: 1 March and 1 September for events taking place within a year of the following 1 May or 1 November, respectively.

Research and Training Grants

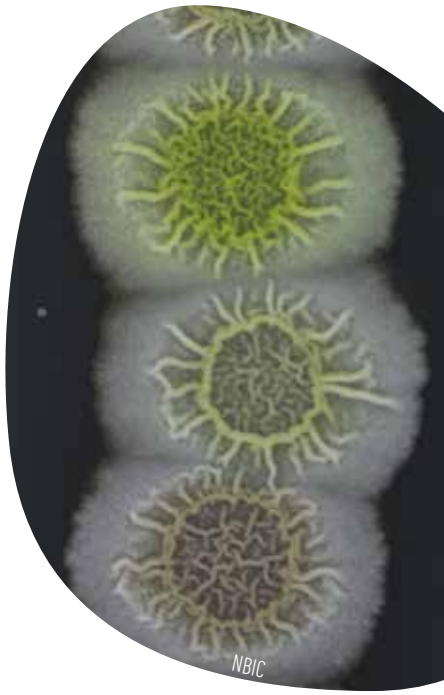
These grants offer up to €4,000 to early career researchers to visit a European host in a country outside of their country of residence, in order to conduct a research project or to gain some training.

Deadlines: 1 January and 1 July for projects starting within a year of the following 1 March or 1 September, respectively.

Conall additionally received a Microbiology Society Research Visit Grant later that year, showing that the initiative to apply for funding to visit collaborators can greatly enhance the research experience of early career researchers.

There are many benefits available from FEMS that you are eligible for via your Microbiology Society membership. You can find out more via the website: **microbiologysociety.org/grants**.

National Biofilms Innovation Centre (NBIC)



Biofilms are communities of microbes that occupy surfaces or environmental niches and encase themselves in a polymeric matrix that protects them from chemical and physical insult. A recent survey estimated that up to 75% of microbes live in these collaborative communities and that microbes are more often multicellular communities rather than unicellular loners.

Often polymicrobial, biofilms have an impact on every aspect of our everyday lives, from the water we drink to the food we eat, as well as the success or failure of medical interventions. They have impact on the oil and gas industry, waste-water treatment facilities, the crops we rely on, our shipping industries and the design of the urban environments many of us occupy. Their influence can be malevolent, benign or actively beneficial, but biofilms are everywhere.

The National Biofilms Innovation Centre (NBIC) is a new UK-wide centre set up to marry the best of fundamental academic research on microbial biofilms with the needs of end-users. Given the ubiquitous nature of biofilms, the challenge requires a multidisciplinary approach. At its heart, NBIC aims to bring the state-of-the-art in medical, biomedical, microbiological and systems approaches together with cutting edge physical sciences research across engineering, physics and maths. As a soft matter physicist who studies biological systems, I have been fascinated by the complex and beautiful architectures formed by these communities, and the complexity of the interactions that take place between these apparently simple organisms. It is intriguing that these communities show emergent behaviour: working together, microbes achieve remarkable things beyond the capacity of any single cell or any single species, and we are only now beginning to tease apart the complex web of collaborations, communications and competitions.

A core part of NBIC is to work closely across industry and with the healthcare sector to understand how best we, as academic researchers, can have an impact. We believe that academic researchers can be inspired by the challenges that end-users face. For example, the build-up of microbial and higher organisms on ship hulls has an enormous financial impact on the global shipping industry as it causes drag, meaning greater fuel costs to transport goods between ports. This apparently simple and even prosaic problem has complex and fundamental questions at its heart, which range from the physical (what properties of the surface promote attachment?) to the ecological (what impact does transporting these communities around the globe have on local environmental niches or on the spread of antimicrobial resistance?).

Our aim is not to drive or delimit the research taking place in academic laboratories, but to facilitate conversations that ensure useful findings are captured, and communicated appropriately and effectively to those who might benefit. We appreciate and celebrate the importance of blue skies research, while also recognising that our findings often have wider, and sometimes unforeseen, implications. NBIC also aims to open the academic research base up to industrial partners to enable collaborative and contract research, accelerating the delivery of technologies and interventions where appropriate.

NBIC is led by four Universities (Edinburgh, Liverpool, Southampton and Nottingham) with a wider partnership of 26 academic institutions across the UK. Together we are building a thriving community that aims to advance frontiers in biofilms research by working in partnership.

Cait MacPhee
National Biofilms Innovation Centre
cmacphee@staffmail.ed.ac.uk

NBIC is a BBSRC and Innovate UK-funded Innovation and Knowledge Centre co-directed by Jeremy Webb (Southampton), Rasmita Raval (Liverpool), Miguel Cámara (Nottingham) and Cait MacPhee (Edinburgh). The CEO of NBIC is Mark Richardson.
www.biofilms.ac.uk
@ukbiofilms

Early Career Microbiologists' Forum Update:

The inaugural ECM Summer Conference 2018

When he took office, a key aim for outgoing President Neil Gow was to bring early career scientists to the forefront of the Society. The ECM Forum Summer Conference, held in June at the University of Birmingham, came at a great time for this. It highlighted the work that the Society puts in to benefit those at all career stages, as well as showcasing the research being conducted by early career microbiologists.

Poppy Stevens and Ashley Otter are both early career researchers who gave talks at the Summer Conference. I caught up with them to get their views on the inaugural event.

Why did you decide to submit an abstract to the Summer Conference?

Poppy Stevens (PS) I had only ever given flash talks outside of my university and really wanted to get some experience presenting to an audience in a supportive environment. I also wanted to increase my visibility as a researcher within my peer group and get feedback on my ideas from other fresh-faced early career researchers!

Ashley Otter (AO) I have attended similar events run by the Society for Applied Microbiology and found it really useful. It was great to build connections to other microbiologists at similar stages in our careers.

What were you expecting from the event? Did it meet these expectations?

PS I was expecting it to be a bigger and more formal event, which is a professional way of saying I thought it would be scarier! In the welcome talk it was pointed out that the only principal investigator (PI) in the room was the keynote speaker Adam Roberts, which was a good move – the atmosphere instantly felt more relaxed, helping people get involved in the discussions.

AO I expected lots of other ECMs there and it was great to see so many from across the UK.

What did you take away from Adam Roberts' keynote session?

AO It was great to hear from Adam that you don't need to follow the unwritten rules of moving around or have consistently positive results to have a successful academic career. The Q&A was really useful, with lots of really helpful insights from Adam.

Do you have any advice to early career researchers who might consider submitting an abstract for the Summer Conference 2019?

PS Do it! Even if you don't have many results and just want some feedback on your methods, it's a great place to give your first conference talk and ask your first conference questions. I also found that giving a talk made networking easier, as people came up to ask me about my work.

Did the Summer Conference change your opinion of the Society?

AO Yes, but in a good way. It's great to see the Society starting events focused around ECMs, as many of us want to stay in academia. At some big conferences, ECMs can sometimes find it difficult to find others at similar stages of their career, whereas through events like this, collaborations can easily develop in the future.

Would you recommend the Summer Conference to other early career microbiologists?

PS Absolutely – particularly if you're quite intimidated by the process of conferences and networking, and as a safe forum to ask people who have been in your position (and who don't know your supervisors) questions about their different career paths.

Finally, what were your personal highlights from the event?

PS I have two – firstly, getting to know other PhD students at the poster session and barbecue. Talking about the joys and difficulties of doing a PhD with other people going through the same thing, without just talking about the science, was really great. My second highlight was the keynote from Adam Roberts and the Q&A session after, which went on far longer than it was supposed to because the discussion was so good!

AO I personally enjoyed presenting my work, and it was great talking with many other ECMs about the work I've done and what they are doing. I came back from the conference with lots of new ideas to try as a result of bouncing some ideas with other ECMs.

Did you attend the Summer Conference? Do get in touch with us if you have any feedback or suggestions for 2019.

Rebecca Hall
Communications Representative,
ECM Forum Executive Committee

To get in touch with the ECM Forum Executive Committee, please email us on **ecm@microbiologysociety.org** or tweet us using **#ECMForum**.

Membership Q&A

Karen Buttigieg

This is a regular column to introduce our members. In this issue, we're pleased to introduce Karen Buttigieg.

Where are you currently based?

I work for Public Health England, at Porton Down.

What is your area of specialism?

Viruses.

And more specifically?

I lead the National Collection of Pathogenic Viruses. We supply viruses to the scientific community all over the world for biomedical research and diagnostic development. It's important that scientists work with quality reagents that they can rely on, so as not to lose time and money trouble-shooting unnecessarily, or coming to the wrong conclusions.

My role is very varied. I'm responsible for predicting which viruses are likely to be in demand; encouraging scientists to deposit new isolates into the Collection; prioritising different projects; ensuring work is carried out safely, and that records are kept proving this; setting up systems to ensure the quality of the products; responding to customers' technical enquiries; managing the team and enabling their personal development.

Tell us about your education to date, and where did your interest in microbiology come from?

After finishing school, I studied Biology at Southampton University. My first 'proper job' was at Imperial College in London, in HIV research. I moved back to Southampton to work in cancer research, but there I realised that actually I wanted to work on viruses again, but without doing a PhD at that stage. So I funded myself to complete an MSc in Molecular Biology and Pathology of Viruses at Imperial College. I really enjoyed the course, and got a published paper from my project. That gave me the confidence to go for a PhD, also at Imperial. My MSc and PhD both involved making recombinant poxviruses to study transgene function. After my PhD I started working at what is now Public Health England, setting up a recombinant poxvirus capability to develop vaccines for emerging diseases.

What are the professional challenges that present themselves, and how do you try to overcome them?

Finding time to do everything. And Civil Service bureaucracy can slow things down. I stay calm and have a lot of patience. I'm quite autonomous in choosing which tasks to do each day, so I can be flexible if priorities change. I also have great colleagues, so it feels like I'm part of a team.

What is the best part about 'doing science'?

That there is an ethos of excellence, integrity and honesty. I love the sense of doing something that no one else has done before. Of making even a small contribution to improving lives somewhere. That I'm always learning, even if it's simply the result of the latest experiment.

Who is your role model?

I don't have one. I prefer to be my own person and just do my best.

What do you do to relax?

When I get the chance, I enjoy playing strategic board games with friends, such as '7 Wonders', or of course 'Pandemic'. I've recently started enjoying gardening too.

What one record and luxury item would you take to a desert island?

Rackwick Bay by Phamie Gow. I had this playing during the birth of my first child so it would remind me of my family. And cake.

Tell us one thing that your work colleagues won't know about you.

I bought my first house when I was 19.

If you weren't a scientist, what would you be?

Probably a vet.

If you would like to be featured in this section or know someone who may, contact Paul Easton, Head of Membership Services, at **p.easton@microbiologysociety.org**

Update your membership profile

It's now easy for you to update your details, to ensure the information we do hold is accurate and reflects your wishes.

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- Do your interest and expertise settings accurately reflect your current situation?

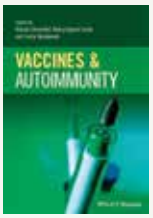
It's an easy three-step process:

1. Log into the Mi Society area of the website by clicking the 'Login' button on any screen.
2. Click on the drop-down menu next to your name.
3. Go to 'Update my details'. Update your details and save them, including your Member Directory information so other members can find you.

Paul Easton
Head of Membership Services
p.easton@microbiologysociety.org

Reviews

Vaccines and Autoimmunity



Edited by Y. Shoenfeld, N. Agmon-Levin & L. Tomlijenovic
Wiley-Blackwell (2015)
£136 ISBN 978-1118663431

Vaccines and Autoimmunity explores the role of vaccine adjuvants in inducing autoimmune or inflammatory response in genetically susceptible individuals, and the need for alternative adjuvants for ensuring vaccine safety. The authors specifically focus on aluminium-based adjuvants that can trigger a syndrome known as autoimmune/inflammatory syndrome induced by adjuvants (ASIA).

The book has been divided into three broad sections. Part I focuses on types and mechanisms of adjuvants; suitable animal models for testing adjuvant effects; the role of metals in development of autoimmune responses; factors that influence autoimmune response; silicone and vaccine-induced autoimmune response in susceptible individuals; as well as safety, efficacy and recommendations of vaccines in patients having rheumatic diseases such as ARD and AIRD. Part II reviews literature on autoimmune conditions induced by MMR, HBV, HPV, meningococcal and pneumococcal vaccines. This section also covers vaccine-induced conditions such as antiphospholipid syndrome. Part III discusses diseases in which vaccines are known to be solicitors for certain diseases such as systemic lupus erythematosus, and whether they can be induced by vaccines such as MMR, HBV, etc.

The authors suggest that a preliminary screening including patient history is required for individuals prone to develop autoimmune diseases following vaccine administration. In such cases a benefit-risk assessment may be made. Besides, newer alternative adjuvants with fewer side effects should be developed. While in some cases, certain vaccine adjuvants do seem to trigger rare autoimmune response, in the majority of cases vaccines do not seem to mediate any inflammatory response. The authors also reiterated the fact that rare side effects post-vaccination do not undermine the safety and protection offered by vaccines in general. In many instances, the causal relation is not evident, while in others there have been only a very limited number of studies, which precludes any conclusion. The benefit of vaccination still outweighs the rare risk of vaccination, if any. This book will serve as an excellent resource for students and researchers interested in vaccine safety.

Arindam Mitra
Adamas University

For more reviews, please visit the online issue of *Microbiology Today* at **microbiologysociety.org/microbiologytoday**

Comment

The quest for an HIV vaccine

Robin Weiss

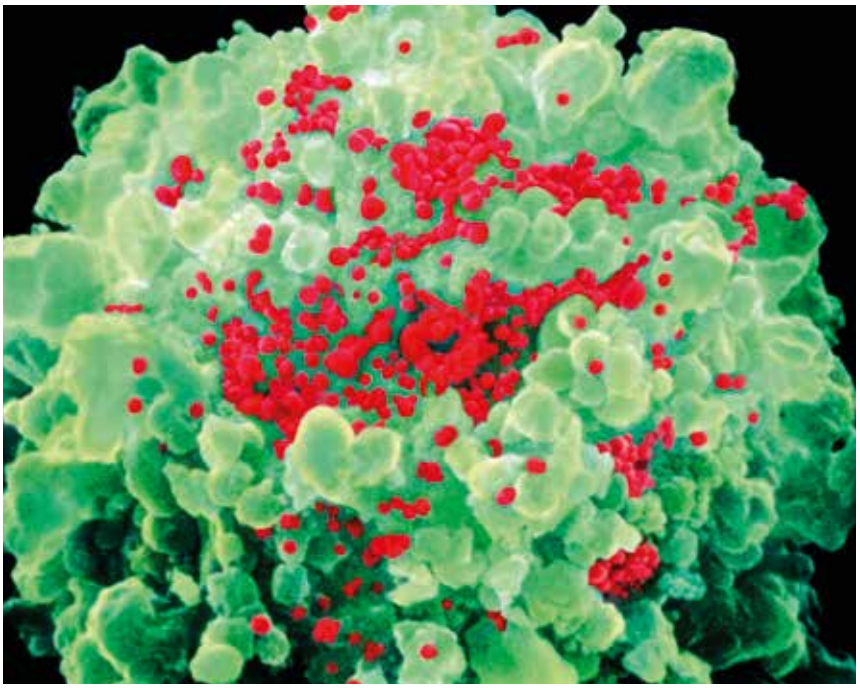
"Ever tried. Ever failed. No matter. Try again. Fail again. Fail better."

Samuel Beckett, *Worstward Ho*

The problem

The old adage that 'prevention is better than cure' still holds for human health. For HIV, there are several approaches to prevention, such as condoms and the use of drugs originally developed to treat HIV infection for pre-exposure prophylaxis, discussed in this issue of *Microbiology Today* by Noel Gill. However, unlike antiretroviral drugs, vaccines should not require healthy 'at risk' individuals to take them for life. Vaccines are our 'weapons of mass protection' with the eradication of smallpox and the huge reduction of yellow fever, polio, measles and cervical cancer to name a few viral diseases. So why don't we have an efficacious HIV vaccine, 35 years after the discovery of the virus?

With 1.5 million new infections by HIV each year, this failure is not due to want of effort by researchers, pharma and funding agencies. One major problem is the enormous genetic and antigenic variability of HIV strains across the world. It is like having to cope with 1,000 strains of influenza virus all at once – and we know how difficult it is for the World Health Organization to make the right call each year for seasonal 'flu vaccines. A second problem is that the surface of HIV particle has a 'glycan shield' that blocks potentially protective antibodies from reaching their targets. A third point is that HIV is a chronic, persistent infection that targets the CD4 lymphocytes of the immune system itself (as well as macrophages). Moreover, the virus inserts its genome into our own DNA, so that once infection has become established it is a formidable problem to eliminate it.



Coloured scanning electron micrograph of a T-lymphocyte blood cell (green) infected with HIV (red), causative agent of AIDS. NIBSC/Science Photo Library

The vaccines that have been developed since Edward Jenner's smallpox vaccine 220 years ago generally mimic the body's own immune response to infection. They act by preventing infection through antibodies with an immunological memory, supplemented by cellular immunity to clear up the pockets of virus-infected cells that might become established if 'sterilising' protection cannot be achieved. This doesn't work for HIV. As José Esparza, former head of HIV immunity at the Bill & Melinda Gates Foundation, pointed out, we need to 'do better than nature'.

Antibody immunity

Despite these daunting problems, I feel less despondent about the ultimate success of HIV vaccine development than I did 10 years ago. Monoclonal antibodies (mAbs) have been isolated from a small proportion of HIV-positive people which are both potent and neutralise almost all strains of HIV of different subtypes. They target conserved sites on the virus envelope; for instance, all HIV strains bind to the CD4 receptor on T-cells and thus antibodies that block receptor interaction prevent the initiation of infection.
Other potent and broadly neutralising antibodies recognise epitopes on the viral surface which include the glycan structures that otherwise prevent access, providing a sort of Achilles heel on the virus. These mAbs have been exploited to select recombinant antigens composed of HIV trimeric glycoproteins that maintain their native state. If used as immunogens, they ought to elicit a polyclonal humoral immune response with similar potency and breadth. Unfortunately, most immunisation tests to date resulted only in strain-specific neutralisation, yet improvements to immune responses using better immunogens and adjuvants are in the pipeline.

The potent, broadly neutralising mAbs are also being exploited in passive immunity; they can act as a form of pre-exposure or immediate post-exposure protection. This is reminiscent of the administration of anti-toxin to diphtheria (for which Emil von Behring won the first Nobel Prize in Medicine in 1901), and of post-exposure protection against rabies – but uses 21st century technology to deliver sufficient levels of mAb.

Cellular immunity

For cell-mediated immunity, vaccine design has focused on internal proteins of the virus, especially the major core antigen, p24. Again, HIV variation is a problem but this has been approached by analysing viral peptides that bind to the major histocompatibility antigens most frequent in the human population and modifying p24 to include them. Bioinformatics has helped to design 'conserved' and 'mosaic' immunogens to elicit broadly protective T-cell responses to candidate vaccines. Such immunogens are being tested pre-clinically in non-human primate studies and in clinical trials expressed by viral vectors including adenovirus, modified vaccinia virus and human cytomegalovirus. Clinical trials have shown moderately promising results. However, we should beware of premature optimism and hype when protection is claimed at, say, a 30% level, but the statistical confidence limits also encompass a possible null result. Complete protection through vaccination alone is unlikely to be achieved for HIV, but even a partially efficacious vaccine could be included as a component of our prevention strategy.

Further reading

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Brady J. M., Baltimore, D. & Balazs, A. B. (2017). Antibody gene transfer with adeno-associated viral vectors as a method for HIV prevention. *Immunol Rev* **275**, 324–333. doi:10.1111/imr.12478

Corey, L. & others. (2015). Immune correlates of vaccine protection against HIV-1 acquisition: a review. *Sci Transl Med* **7**, 310rv7. doi:10.1126/scitranslmed.aac7732

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Ndung'u, T. & Weiss, R. A. (2012). On HIV diversity. *AIDS* **26**, 1255–1260.

Robin Weiss

Division of Infection & Immunity, University College London, WC1E 6BT, UK

e **r.weiss@ucl.ac.uk**

Robin Weiss FRS is Emeritus Professor of Viral Oncology at University College London. He has been a member of the Microbiology Society for 50 years and was President 2006–2009.

What advice would you give someone starting out in this field?

(a) Perseverance.

(b) Choose a project that will yield publishable results of good science even if it doesn't hit the jackpot of a successful vaccine.

What inspired you to become a microbiologist?

I slid into it by chance. I was offered a PhD place by developmental biologist Michael Abercrombie to study cell transformation induced by Rous sarcoma virus and gradually became as interested in viruses as in the cancers they caused. Then, with the onset of AIDS, I became interested in epidemics. Now, in retirement, I am interested in the history of microbiology.

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31 January 2019

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