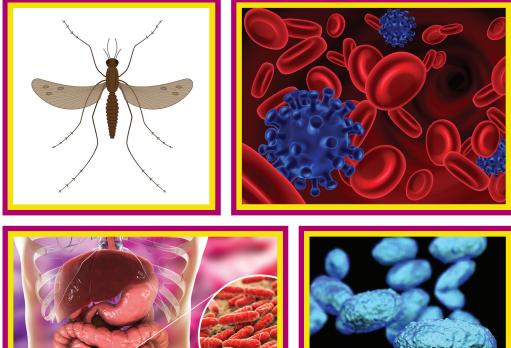


Trainees' Day & 21st Annual Scientific Meeting

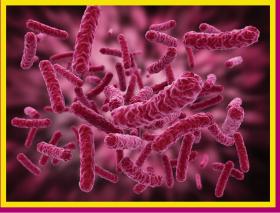
Wednesday 16th and Thursday 17th May 2018 Cavendish Conference Centre, London











Programme Book

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BRITISH INFECTION ASSOCIATION COUNCIL

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Professor Rob Read Sheffield Teaching Hospitals NHS Foundation Trust

AIMS OF THE ASSOCIATION

The Association aims to work to ensure the optimum delivery of healthcare to patients diagnosed with infection, and to represent the interests of its members.

Specifically:

- To provide expert opinions and represent the views of specialists in infection to anybody seeking advice relevant to infection or infection professionals. Groups who might be expected to consult The British Infection Association include, but are not limited to, the Department of Health and similar bodies in the devolved governments, the Royal Colleges, NICE, statutory medical bodies, House of Lords select committees and other professional bodies.
- To set and review standards in infection practice including the development of guidelines, working in collaboration where appropriate.
- To support members of the Association in the performance of their professional duties.
- To develop and provide education and training in infection for all and in particular to support training grades.
- To foster excellence in all aspects of infection-related research.
- To support all aspects of communication between different branches of infection and to work towards the development
 of an integrated voice for infection specialists.
- To provide a public face for infection and represent infection opinions to the general public and to patients.



There are four types of membership:

- Full membership (including overseas)
- Trainee membership
- Retired membership
- Associate membership

Full membership includes subscription to the Journal of Infection. Members in training may opt for free membership which includes the BIA Newsletter but not the Journal of Infection.

| Membership Type | Full | Full (Overseas) | Retired | Trainee/Associate |
|-------------------|------|-----------------|---------|-------------------|
| No Journal | Х | Х | £10 | Free |
| Electronic Online | £75 | £75 | £45 | £35 |
| Hard Copy Print | £90 | Х | £60 | £50 |

Online membership application and Direct Debit subscriptions at: http://www.britishinfection.org/

ENQUIRIES

Contact for enquiries relating to Journal subscriptions, payments and change of membership details:

Jo Wheeler, BIA Administrator Hartley Taylor Medical Communications Ltd Suite GC, Caledonian House Tatton Street, Knutsford Cheshire WA16 6AG

Email: BIA@hartleytaylor.co.uk Tel: 01565 632982

Data Protection

All membership details (as supplied by you) are stored on an electronic database. This database is used for legitimate BIA business only. We occasionally co-operate with other societies and organisations whose objectives are consistent with those of the Society by including material in BIA mailings. If you do not wish to receive such mailings please notify BIA Administration at the above address.

CORPORATE SPONSORS



ViiV Healthcare aims to take a deeper and broader interest in HIV/AIDS than any company has done before and takes a new approach to deliver effective and new HIV medicines, as well as support communities affected by HIV. For more information on the company, its management, portfolio, pipeline, and commitment, please visit www.viivhealthcare.com.



TRAINEES' DAY PROGRAMME WEDNESDAY 16TH MAY

Chair: Dr Rebecca Bamber (University Hospital of Wales)

| 09:00 | Registration & coffee | |
|-------|---|---|
| 09:40 | Welcome | |
| 09:50 | The Virtual Doctors | Dr Rebecca Bamber SpR in Microbiology University Hospital of Wales |
| 10:35 | Treating MDR-TB – what we know and what we need to know | Dr Francesca Conradie <i>Clinical Research Advisor</i> <i>University of Witwatersrand</i> <i>Helen Joseph Hospital</i> <i>Johannesburg, South Africa</i> |
| 11:10 | Coffee | |
| 11:30 | Selected Trainee Abstract Presentations: "My most inter | resting case to date" |
| | 1. It's all in the eyes | Dr Vivak Parkash |
| | Sometimes the hoof beats are neither horse nor zebra | Dr Susannah Jane Amina Froude |
| | 3. The first reported case of imported yellow fever in the UK | Dr Angela McBride |
| | 4. Old disease, new location | Dr Carlene Rowson |
| | Disseminated infection following intravesical instillation of Bacillus Calmette-Guérin for carcinoma in-situ of the bladder | Dr Eben Jones |
| 13:00 | Lunch | |
| 14:00 | HIV - PrEP and future prevention | Professor Charles JN Lacey Honorary Consultant Physician in GU/HIV Medicine University of York and York Hospitals Foundation Trust |
| 14:45 | Dysbiosis in the inflamed intestine – the rise to prominence of mucosa-associated <i>Escherichia coli</i> | Professor Barry J Campbell Department Director of Postgraduate Research University of Liverpool |
| 15:30 | Coffee | |
| 15:50 | Integrated Infection Services: the Hull experience | Dr Gavin Barlow <i>Consultant Physician</i> <i>Department of Infection</i> <i>Hull & East Yorkshire Hospitals NHS Trust</i> |
| 16:35 | Meeting close & drinks reception | |

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Speaker Biographies & Abstracts

Dr Rebecca Bamber Specialist Registrar in Microbiology University Hospital of Wales

Having trained at Downing College, Cambridge, I completed my Foundation Training in East Anglia before moving to a Microbiology training post at University Hospital of Wales, Cardiff in 2010 (currently I am a Less than Full Time trainee). I completed my FRCPath in 2016 and will achieve CCT in 2019. My current areas of specialist practice are in Infection in Oncology and Palliative Care and General Surgery.

I have been the BIA Trainee Representative for the last 2 years (May 2016-2018) and have volunteered with The Virtual Doctors for the last year.

The Virtual Doctors

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What if a smart phone could save a life? We think it can!

We provide a smart phone, loaded with our specially written app, to Clinical Officers working in remote clinics. When a patient with a complex or unusual condition appears, the Clinical Officer creates a patient file with examination notes and photos. This is uploaded to the cloud. A doctor in the UK reviews it and offers diagnostic and treatment advice.

Dr Francesca Conradie Clinical Research Advisor, Clinical HIV Research Unit University of Witwatersrand, Helen Joseph Hospital, Johannesburg, South Africa

Dr Francesca Conradie is a South African medical doctor and clinical investigator. She has over 15 years' experience in clinical in clinical trials, first in the field of HIV treatment. The pressure of the dual epidemic of HIV and TB, prompted a change into MDR TB clinical research in 2009. As a principal investigator of STREAM 1 and 2 and other pivotal MDR TB treatment trials, Dr Conradie is one of the leading experts in MDR TB treatment trials.

Treating MDR-TB - what we know and what we need to know

The WHO estimates that there are over 600 000 cases of Rif Resistant TB (RR TB) annually. While the diagnosis of RR TB has been vastly improved with the advent of new molecular tests, the proportion of patients who have a successful outcome remains dismally low. With the exception of the new drugs, the second line drugs are more toxic and are less effective that the first line options. This talk will cover the basics of the diagnosis of TB, the principles of the treatment of RR TB in composing a regimen with a focus on the Shorter Treatment Course endorsed by the WHO in August 2016 and outcome measures.

Professor Charles JN Lacey Honorary Consultant Physician in GU/HIV Medicine Hull York Medical School, University of York, and GU/HIV Medicine, York Teaching Hospital

I am an academic clinician practising in HIV/GU medicine, with ID and immunology interests. I have been involved in HPV and other vaccine research for ~ 30 years. I was a PI in the pivotal HPV vaccine phase 3 trials. We currently have Wellcome Trust, MRC, Bill and Melinda Gates Foundation, and EDCTP awards to support our HPV vaccine one dose studies in Tanzania, our Leishmania vaccine studies in Sudan, Ethiopia, Uganda and Kenya, and our development of a Leishmania human challenge model in York.

HIV - PrEP and future prevention

An early usage of the term pre-exposure prophylaxis (PrEP) was in the late 1970s in relation to the administration of Hepatitis B immune globulin to neonates born to Hepatitis B positive mothers. Later in 2003 Joel Gallant and colleagues showed that volunteers taking intermittent Nevirapine had protective anti-HIV blood levels and suggested that PrEP against HIV might be effective. Recently a series of studies (iPrEX, PROUD & IPERGAY) showed definitively that Tenofovir disoproxil fumarate + Emtricitabine was strongly effective as PrEP. I will discuss the increasing worldwide uptake of PrEP, the role it has played in the recent drop in HIV incidence in the UK, and the future of HIV prevention.

Professor Barry J Campbell Department Director of Postgraduate Research University of Liverpool

Barry Campbell started his scientific career in gut endocrine physiology at UCNW Bangor, receiving a BSc with Honours in Zoology in 1988, and a PhD in Physiology from University of Liverpool in 1991. Following an MRCfunded post-doctoral research position, he held a Wellcome Trust-funded lecturership in intestinal physiology, before being appointed to a full-time academic post in Medicine at Liverpool where his research led to specific understanding of the causes and consequences of altered intestinal mucosal glycosylation that occurs in intestinal inflammation and cancer. He now leads one of the key international research groups investigating bacteria-host epithelium interactions, particularly Crohn's disease- and colorectal cancer-mucosa associated Escherichia coli, including translational projects on effects of antibiotics, environment modulating agents and dietary components. He was awarded a Personal Chair within the University of Liverpool's Institute of Translational Medicine in 2013. He is a member of the UK Gut Microbiota for Health Expert Panel and the 'Scientists in Gastroenterology' lead for the British Society of Gastroenterology, supporting education, research and the annual meeting Translational Science Masterclass symposia.

Dysbiosis in the inflamed intestine - the rise to prominence of mucosa-associated Escherichia coli

There is now very strong scientific evidence that both a reduction in the diversity of the gut bacteria and increases in numbers of harmful bacteria living naturally in the gut are key factors in development of inflammationassociated bowel diseases. Several independent groups have consistently shown changes in both the faecal and mucosa-associated microbiome, with alteration in the dominant organisms, specifically a reduction in beneficial Firmicutes and an increase in Proteobacteria (including *Escherichia coli*). We and other groups have reported increase in mucosa-associated E. coli in both Crohn's disease (CD) and colorectal cancer (CRC) which have an adherent, invasive phenotype (AIEC). Some of the properties of these pro-inflammatory CD E. coli have been associated with specific genes which support epithelial adherence and invasion and ability to survive and replicate within host macrophages. Although there is no genotype that is consistent across all AIEC, mucosal E. coli isolates from CD tend to express long polar fimbriae (Lpf) relevant to translocation across M (microfold) cells overlying lymphoid follicles – the likely portal for initial invasion through the gut wall and the site of the earliest lesions in CD. The mucosal *E. coli* isolates from CRC and ulcerative colitis often possess the polyketide synthase (*pks*) gene complex that results in production of the genotoxic metabolite colibactin, relevant to cancer induction. A large body of data from *in vitro* and animal studies shows promise for therapeutic approaches that target mucosaassociated E. coli recruitment to the inflamed mucosa and those residing/replicating within the macrophage phagolysosome. Approaches include antibiotics, biological agents, probiotics, dietary supplementation with fermentable fibres (prebiotics) or 'contrabiotic' soluble fibres that block bacterial-epithelial adherence, and vitamin D supplementation acting via enhancement of innate immunity.

Dr Gavin Barlow Consultant in Infection at Hull & East Yorkshire Hospitals NHS Trust Hon. Senior Clinical Lecturer at Hull York Medical School

Dr Gavin Barlow qualified in Medicine at Leicester University and trained in infectious diseases and general internal medicine in Leeds, Sheffield and Dundee, including a two-year research training fellowship at the University of Dundee. His main clinical interests are orthopaedic infection, outpatient parenteral antibiotic therapy (OPAT), antimicrobial stewardship, and the management of complex bacterial and healthcare-associated infections.

Research interests are broad, but predominantly focus on the epidemiology and clinical care of infections commonly managed in the NHS. Gavin is the British Society for Antimicrobial Chemotherapy (BSAC) Officer for Stewardship and Surveillance.

Integrated Infection Services: the Hull experience

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Clinical microbiology and infectious diseases have historically been separate sub-specialties of infection in UK medical practice, often sited in different healthcare groups/directorates within a hospital's management structure, and, until recently, with differing training pathways. Increasingly, some hospitals have recognised the inefficiency of this situation, however, and departments are increasingly working together or formally merging. This talk will describe the experience of such a merger, sometimes driven by a priori planning, and sometimes by expediency and circumstance, at Hull and East Yorkshire Hospitals NHS Trust.

Selected Trainee Abstract Presentation 1

Title It's all in the eyes

Author Dr Vivak Parkash

Abstract

A 38-year-old female with a presumptive diagnosis of adult-onset Still's disease had worsening arthralgia, rash, persistent fevers and weight loss despite immunosuppressive therapy for 8 years. Due to ongoing gastrointestinal symptoms, gastroscopic biopsy was performed and proved highly suggestive of Whipple's disease.

Despite initially improvement with antibiotics, the patient went on to develop significant diplopia. MRI of her orbits revealed an infiltrative myositis of the extraocular muscles.

Biopsy of her extraocular muscles was performed but was PCR negative for *Tropheryma whipplei*. Due to the high degree of suspicion however, samples were tested in France and immunohistochemistry staining was highly suggestive of *T. whipplei*. Further evaluation locally using electron microscopy also revealed effete *T. whipplei* in macrophage lysosomes.

Her bilateral ocular myositis was treated with both a prolonged course of antibiotics and steroid therapy.

Selected Trainee Abstract Presentation 2

Title Sometimes the hoof beats are neither horse nor zebra

Author Dr Susannah Jane Amina Froude

Abstract

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A 57 year old gentleman receives a kidney transplant and is discharged following an uneventful post-operative recovery. He is readmitted a few days later with a fever and confusion which progresses into meningoencephalitis requiring critical care support.

Hours after he is re-admitted a 42 year old gentleman who has also received a kidney transplant starts to develop the same signs and symptoms. The illness in both patients follows a similar devastating course and they both have the same unexpected diagnosis.

These cases highlight the importance of multidisciplinary team working across different physical locations and are a reminder that when the possible and impossible have been excluded the improbable is all that is left. It is also a reminder that sometimes really strange things happen that only an autopsy can diagnose.

Selected Trainee Abstract Presentation 3

Title A cautionary tale about a Grande Holiday

Author Dr Angela McBride

Abstract

A 33 year old male German national presented to the Emergency Department in a London hospital. He described a 4-day history of fever, intense malaise and vomiting which began in the fourth week of his holiday to Rio de Janiero and Ilha Grande.

On examination he was febrile and jaundiced with 4cm hepatomegaly. Initial investigations showed a severe acute hepatitis and acute kidney injury. Serum and urine samples taken on day 4 of illness were positive for yellow fever RNA by real time PCR at the Rare and Imported Pathogens Laboratory.

The patients liver failure continued to progress with encephalopathy and worsening coagulopathy. He was transferred to ICU, followed by a specialist liver unit. Despite supportive care he died on day 11 of his illness.

This is the first reported case of imported yellow fever in the UK. Several other cases of yellow fever acquired in Brazil have been described in Europe this year, reflecting intense transmission in tourist hotspots, including Ilha Grande. UK clinicians should remember to include yellow fever in their differential diagnosis for a traveller with fever and hepatitis returning from an endemic region. Yellow fever is preventable by vaccination.

Selected Trainee Abstract Presentation 4

Title Old disease, new location

Author Dr Carlene Rowson

Abstract

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A previously fit and well 18-year-old student was referred to hospital with a 5-day history of fever, vomiting, diarrhoea, lethargy and right-sided abdominal pain. She had had a persistent intermittently productive cough for the preceding 5 weeks. She had travelled to Slovakia 4 months previously. She was treated initially for suspected gastroenteritis with intravenous fluids. However, over the following twenty-four hours she deteriorated, developing fevers of 40 degrees and subsequent septic shock with cardiovascular compromise. She was transferred to the Intensive Treatment Unit.

Blood investigations showed a mild neutrophilia, mild thrombocytopenia, markedly elevated C-reactive protein, acute kidney injury stage 2 and mildly elevated liver function tests (mixed hepatocellular and cholestatic picture). Initial plain chest x-ray demonstrated bilateral lower zone patchy shadowing. Ultrasonography of the abdomen revealed an ill-defined mixed echogenic area measuring around 60mm situated in the right lobe of liver. Contrast-enhanced CT depicted a 7cm lesion in zone 7 of the liver, with associated thrombus in the adjacent portion of a branch of the right hepatic vein. Thoracic CT imaging demonstrated extensive bi-basal consolidation with a pulmonary nodule in the right lower lobe, suspicious for septic pulmonary emboli. Transthoracic echo was unremarkable. The causative organism was identified on blood cultures collected on admission.

Selected Trainee Abstract Presentation 5

Title Disseminated infection following intravesical instillation of Bacillus Calmette-Guérin for carcinoma in-situ of the bladder

Author Dr Eben Jones

Abstract

We present the case of a 75-year-old man presenting with septic shock following intravesical instillation of Bacillus Calmette-Guérin (BCG) for carcinoma in-situ of the bladder. He was initially treated with intravenous fluids and broad-spectrum antibiotics. He was admitted to the intensive care unit where he was intubated and ventilated, received vasopressor support, and underwent haemodialysis for acute kidney injury (AKI) and pulmonary oedema. After an incomplete clinical response, the patient was empirically treated with anti-mycobacterial therapy for suspected disseminated BCG infection (BCG-osis), and this diagnosis was subsequently confirmed by molecular detection of Mycobacterium tuberculosis complex and positive sputum culture for Mycobacterium bovis (BCG strain). He continues to make a good clinical recovery and has been discharged home with outpatient respiratory clinic follow-up.

Our case demonstrates the potentially life-threatening nature of disseminated BCG infection, which is a recognised complication of this common treatment modality for carcinoma in-situ of the bladder.

ANNUAL SCIENTIFIC MEETING PROGRAMME THURSDAY 17TH MAY

08:45 to 09:10 **Registration, coffee/tea & poster viewing**

09:10 to 09:15 Welcome Dr Albert Mifsud, President of the BIA 09:15 to 10:40 Free Scientific Papers (14 minutes each)

> Chairs & discussants - Dr Chris Chiu (London) Dr Tristan Clark (Southampton)

- 1. Differences in the CSF host inflammatory response and clinical outcome in bacterial meningitis caused by *Streptococcus pneumoniae* and *Neisseria meningitidis* are unaffected by HIV-1 infection. <u>Emma Wall</u> et al. University College London
- Whole genome deep sequencing of HIV reveals extensive multi-class drug resistance in Nigerian patients failing first-line antiretroviral therapy. <u>Kate El Bouzidi</u> et al. UCL Division of Infection & Immunity, London
- 3. HIV-1 viral protein R (Vpr) causes a global change to gene expression in primary CD4+ T cells following infection. <u>Christopher Ward</u> et al. King's College London
- 4. Assessment of a malaria rapid diagnostic test compared with qPCR in healthy volunteers undergoing controlled human malaria infection. <u>Ruth Payne</u> et al. University of Sheffield
- 5. Polyspecific intravenous immunoglobulin in clindamycin-treated patients with streptococcal toxic shock syndrome: a systematic review and meta-analysis. <u>Tom Parks</u> et al. London School of Hygiene and Tropical Medicine, London
- 6. ARK-Hospital (Antibiotic Review Kit-Hospital) A complex behaviour change intervention in secondary care to safely and substantially reduce antibiotic use. <u>Elizabeth Cross</u> et al. Brighton and Sussex Medical School, Brighton

10:40 to 11:00 Coffee/tea & poster viewing

11:00 to 11:30 British Infection Association AGM

Dr Albert Mifsud, Dr Mike Kelsey, Dr Katie Jeffery, Dr Hiten Thaker

11:30 to 12:25 International Keynote Lecture

Current management and latest research on the management of drug resistant TB

Dr Francesca Conradie

Clinical Research Advisor, Clinical HIV Research Unit, Wits Health Consortium, Department of Medicine, University of Witwatersrand, Helen Joseph Hospital, Johannesburg, South Africa

Chair & discussant - Professor David Dockrell (Edinburgh)

12:25 to 13:15 Lunch & poster viewing

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13:15 to 13:45 UK State of the Art Lecture 1

Gut microbiome

Professor Barry J Campbell

Department Director of Postgraduate Research, Gastroenterology Research Unit, Department of Cellular & Molecular Physiology, Institute of Translational Medicine, University of Liverpool

Chair & discussant - Professor Martin Llewellyn (Brighton)

13:50 to 15:50 Associate Members Parallel Symposium

Antimicrobial Stewardship

13:45 to 14:35 Free Scientific Papers (15 minutes each)

Chairs & discussants - Dr Natasha Ratnaraja (Birmingham) Dr Peter Moss (Hull)

- 7. Direct contact with platelets modulates monocyte responses to *Mycobacterium* tuberculosis. <u>Daniela E. Kirwan</u> et al. Imperial College London
- First blood-stage *P. falciparum* malaria vaccine candidate to show clinical efficacy in a controlled human malaria infection model. <u>Angela Minassian</u> et al. The Jenner Institute, Oxford University, Oxford
- 9. The immunogenicity of live attenuated influenza vaccine in Gambian children: insights into reduced efficacy and effectiveness against pandemic H1N1. <u>Benjamin Lindsey</u> et al. Imperial College London

14:35 to 15:00 Coffee/tea & poster viewing

15:00 to 15:50 Free Scientific Papers (15 minutes each)

Chairs & discussants - Dr Hiten Thaker (Hull) Dr Alec Bonnington (Manchester)

- 10. Antimicrobial prescribing 'app' fails to improve adherence to guidelines in junior doctors. <u>Sheena Bhadresha</u> et al. Cambridge University Hospitals, Cambridge
- 11. Evaluating the use of a 25-pathogen TaqMan Array Card for rapid diagnosis of viral, bacterial, and fungal respiratory pathogens in adult intensive care patients. <u>Nick K. Jones</u> et al. Cambridge University Hospitals NHS Foundation Trust, Cambridge
- 12. Chronic pulmonary aspergillosis (CPA) complicating tuberculosis is an unrecognised global public health issue: a cross-sectional survey. <u>Iain Page</u> et al. The University of Manchester

15:50 to 16:20 UK State of the Art Lecture 2

Clinical implications of HPV infection

Professor Charles JN Lacey

Honorary Consultant Physician in GU/HIV Medicine Hull York Medical School, University of York, and GU/HIV Medicine, York Teaching Hospital

Chair & discussant - Professor Clifford Leen (Edinburgh)

| 16:30 to 17:30 | Clinical Papers (10 minutes each) Chairs & discussants - <i>Dr William Lynn (London)</i> <i>Dr Katie Jeffery (Oxford)</i> | | |
|----------------|---|---|--|
| | | | |
| | Α. | In sight and out of mind. Blessing Essang et al. Castle Hill Hospital, Hull | |
| | В. | Scratchings beneath the surface. <u>Phillip Simpson</u> et al. Sheffield Teaching Hospitals, Sheffield | |
| | C. | Acute neurological presentation in an ex-Kruger National Park ranger. <u>Thomas Boland</u> et al. Guy's and St Thomas' NHS Foundation Trust, London | |
| | D. | Bleeding oesophageal varices: common presentation, unusual aetiology. <u>Melanie Etti</u> et al. Royal Free Hospital, London | |
| | E. | A beast not from the East. Jennifer Tomlins et al. Bart's Health NHS Trust, London | |
| | F. | From silk roads to Meltemi winds. <u>Alanah Proctor</u> et al. National Aspergillosis Centre, Manchester | |
| 17:30 to 17:35 | Clo | se of proceedings | |

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Dr Albert Mifsud, President of the BIA

SELECTED **POSTER PRESENTATIONS**

- 01 Keeping an eye on the diagnosis. <u>Dinesh Aggarwal</u> et al. Imperial NHS Healthcare Trust, London
- 02 TB or not TB what is the infection? <u>Sakib Rokadiya</u> et al. Barts Health NHS Trust, London
- 03 Cross-reactive antibodies to dengue and Zika virus envelope protein: panacea or Pandora's box? Shannon Gunawardana et al. University of Oxford
- 04 Late presentation and missed opportunities: an 11 year audit of newly diagnosed HIV in Newcastle upon Tyne (2007-2017). Joti Ahir et al. University of Newcastle Medical School, Newcastle upon Tyne
- 05 Antimicrobial resistance: how fixed dose combinations could be India's biggest public health scare. <u>Vishaal Dovedi</u> et al. Bart's and the London
- 06 Review of *Mycobacterium tuberculosis* infection in HIV co-infected adults at Sarawak General Hospital, Malaysia. <u>Han Hua Lim</u>. Sarawak General Hospital, Kuching, Malaysia
- 07 Tricks of the trade: an unexpected case of prosthetic valve endocarditis. <u>Claudia Meyer</u> et al. Queen Alexandra Hospital, Portsmouth
- Vear of the dog. <u>Blair Merrick</u> et al. Royal Victoria Infirmary, Newcastle upon Tyne
- 09 Antimicrobial stewardship in haematology and oncology the effect of pharmacy and infection specialist input. <u>Patrick Lillie</u> et al. Hull and East Yorkshire Hospitals NHS Trust
- 10 Local antibiotic delivery systems: current and future applications for diabetic foot infections. <u>Hamed Sharaf</u> et al. Manchester Royal Infirmary, Manchester
- 11 Improving TB infection control in a regional hospital in the Eastern Cape, South Africa. <u>Ilsa Louisa Haeusler</u> et al. NHS Thames Valley and Wessex Leadership Academy, Winchester
- 12 Staphylococcal bacteraemia: finding the path of least persistence. <u>Nisha Ranganathan</u> et al. Imperial College London
- 13 The influences of demographics and departments on HIV testing in tuberculosis patients within Newcastle upon Tyne Hospitals, 2010-2017. <u>Thomas Jones</u> et al. Newcastle University Medical School, Newcastle upon Tyne
- 14 The importance of the organism: a cellulitic story. <u>Rohan Mehra</u>. Portsmouth Hospital Trust, Portsmouth
- 15 Barriers to and facilitators of antibiotic stewardship in secondary care: a qualitative interview study of manager and clinician views. <u>Emma Wiley</u> et al. University College London Hospitals NHS Foundation Trust, London
- 16 Initial management of community-acquired acute bacterial meningitis in a London teaching hospital. Arjun Chandna et al. University College Hospital, London
- 17 Things IRON what they seem. Akish Luintel et al. Whittington Hospital, London
- 18 Sepsis and hepatorenal syndrome after contact with sewage. <u>Christopher Smith</u> et al. Imperial College London
- 19 What factors influence the control of tuberculosis in Emergency Centres in the Western Cape, South Africa? A mixed methodology study based on a knowledge, attitude and practice framework. <u>Helen Casey</u> et al. University of Manchester
- 20 Pericardial tuberculosis: 9-year multicentre retrospective review. <u>Waleed Chaudhry</u> et al. London NorthWest University Healthcare NHS Trust

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- 21 Evaluating the utility of MRSA PCR in surgical patient flow; time for a rethink for hub-and-spoke laboratory models. <u>Matthew O'Hare</u> et al. Imperial College London
- 22 Molecular diversity of Scottish *Cryptosporidium* species reported in humans. <u>Lynne Ferguson</u> et al. Scottish Microbiology Reference Laboratories, Glasgow
- 23 No pressure ... <u>Helena Bond</u> et al. Royal Victoria Infirmary, Newcastle upon Tyne
- 24 An antibiotic headache. Thomas Locke et al. Sheffield Teaching Hospitals, Sheffield
- 25 How effective are we at preventing infections in immunocompromised patients? A multi-specialty audit. Laila Sayeed et al. James Cook University Hospital, Middlesbrough
- 26 *Strongyloides stercoralis* in Guatemala: seroprevalence studies of healthy rural and immunosuppressed urban populations. <u>Paul Arkell</u> et al. St George's University London
- 27 Acute meningitis investigation and initial management at a busy London teaching hospital. <u>Rebecca Stout</u> et al. St George's University Hospital Trust, London
- 28 Forgotten disease, found in new location. Carlene Rowson et al. Sheffield Teaching Hospitals, Sheffield
- 29 "TB or not TB....that is the question". Juliette Mutuyimana et al. Leicester Royal Infirmary Hospital, Leicester
- 30 Spots, clots and GCS drops. Jonathan Youngs et al. St George's Hospital, London
- 31 A perilous complication of plastic surgery. <u>Davina Sharma</u> et al. Guy's and St Thomas' NHS Foundation Trust, London
- 32 Severe presentation of atypical pneumonia associated pulmonary fungal infection. <u>Findra Setianingrum</u> et al. University of Manchester
- 33 The importance of the organism: a cellulitic story. <u>Rohan Mehra</u>. Portsmouth Hospital Trust, Portsmouth
- 34 Clinical utility of multiple mycology laboratory techniques in the management of patients attending the National Aspergillosis Centre. <u>Alanah Proctor</u> et al. National Aspergillosis Centre, Manchester
- 35 PrEP pathfinder. Chinonye Onyeocha. Homerton University Hospital, London
- 36 Utility of cytology and histology in the diagnosis of active TB. Aishwarya Pai et al. Imperial College London
- 37 Successful control of outbreak caused by clonally related pan-resistant *Acinetobacter baumannii* in an intensive care unit. <u>Bushra Sultan</u> et al. Armed Forces Institute of Pathology, Rawalpindi, Pakistan
- 38 Aetiology of lymphocytic meningitis in a London hospital with high TB prevalence. <u>Clare Thakker</u> et al. Northwick Park Hospital, London
- 39 The diagnosis, investigation and management of non-lactational inflammatory breast masses at a London hospital in an area with high tuberculosis incidence. <u>Alexander Keeley</u> et al. Northwick Park Hospital, London

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International Keynote Lecture

Dr Francesca Conradie Clinical Research Advisor, Clinical HIV Research Unit University of Witwatersrand, Helen Joseph Hospital, Johannesburg, South Africa

Dr Francesca Conradie is a South African medical doctor and clinical investigator. She has over 15 years' experience in clinical in clinical trials, first in the field of HIV treatment. The pressure of the dual epidemic of HIV and TB, prompted a change into MDR TB clinical research in 2009. As a principal investigator of STREAM 1 and 2 and other pivotal MDR TB treatment trials, Dr Conradie is one of the leading experts in MDR TB treatment trials.

Current management and latest research on the management of drug resistant TB

The Shorter Treatment Course was endorsed by the WHO in August 2016 and has been rolled out in many high burden DR TB countries. While this is a good move in the correct direction, there has to be more improvement in the treatment if the epidemic of DR TB is to be controlled. There are a number of new and repurposed drugs available for the treatment of DR TB. This talk will concentrate the latest research and implementation of these drugs in a variety of settings.

UK State of the Art Lectures

Professor Barry J Campbell Department Director of Postgraduate Research Gastroenterology Research Unit, Department of Cellular & Molecular Physiology, Institute of Translational Medicine, University of Liverpool

Barry Campbell started his scientific career in gut endocrine physiology at UCNW Bangor, receiving a BSc with Honours in Zoology in 1988, and a PhD in Physiology from University of Liverpool in 1991. Following an MRCfunded post-doctoral research position, he held a Wellcome Trust-funded lecturership in intestinal physiology, before being appointed to a full-time academic post in Medicine at Liverpool where his research led to specific understanding of the causes and consequences of altered intestinal mucosal glycosylation that occurs in intestinal inflammation and cancer. He now leads one of the key international research groups investigating bacteria-host epithelium interactions, particularly Crohn's disease- and colorectal cancer-mucosa associated Escherichia coli, including translational projects on effects of antibiotics, environment modulating agents and dietary components. He was awarded a Personal Chair within the University of Liverpool's Institute of Translational Medicine in 2013. He is a member of the UK Gut Microbiota for Health Expert Panel and the 'Scientists in Gastroenterology' lead for the British Society of Gastroenterology, supporting education, research and the annual meeting Translational Science Masterclass symposia.

Gut microbiome

Recent developments in DNA sequencing technology have allowed a very rapid expansion in our knowledge the gut microbiota and its importance for health. Established early in life, becoming fairly stable by 2-3 years of age, the human gut microbiota typically remains remarkably constant over time but is subject to important variations according to diet, antibiotic exposure, inflammation, and exercise. The faecal microbiome shows considerable diversity in health which is diminished in inflammation, with observed in inflammatory bowel disease (IBD), colorectal cancer (CRC), liver disease and other gut disorders such as irritable bowel syndrome (IBS). The gut microbiota is also implicated in obesity and metabolic syndrome. More specific changes that have been found consistently in the human mucosa-associated microbiota (i.e. below the adherent colonic mucus layer) in IBD and CRC include a reduction in beneficial Firmicutes and an increase in Proteobacteria, especially E. coli pathovars that are able to induce intestinal inflammation and CRC in mice. The potential of manipulating the gut microbiota in these disorders is emerging, with evidence supporting use of targeted antibiotics, probiotics, prebiotics, dietary modification/supplementation and faecal microbiota transplantation.

UK State of the Art Lectures

Professor Charles JN Lacey Honorary Consultant Physician in GU/HIV Medicine Hull York Medical School, University of York, and GU/HIV Medicine, York Teaching Hospital

I am an academic clinician practising in HIV/GU medicine, with ID and immunology interests. I have been involved in HPV and other vaccine research for ~ 30 years. I was a PI in the pivotal HPV vaccine phase 3 trials. We currently have Wellcome Trust, MRC, Bill and Melinda Gates Foundation, and EDCTP awards to support our HPV vaccine one dose studies in Tanzania, our Leishmania vaccine studies in Sudan, Ethiopia, Uganda and Kenya, and our development of a Leishmania human challenge model in York.

Clinical implications of the HPV infection

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Human papillomaviruses (HPVs) are ancient stable DNA viruses that have co-evolved with hominid species. HPVs cause a wide variety of benign epithelial infections and proliferations, which in a minority of cases progress to specific pre-cancers and cancers, including ano-genital, cutaneous, and oro-pharyngeal malignancies. Clinical implications for the generalist are thus the understanding and timely recognition of pre-invasive and invasive disease. In the last 10 years HPV prophylactic vaccines have been shown to be outstandingly effective. UK national HPV vaccine implementation will be reviewed, as well the obstacles to population based coverage in the developing world.

Free Scientific Paper 1

| Title | Differences in the CSF host inflammatory response and clinical outcome in bacterial meningitis caused by <i>Streptococcus pneumoniae</i> and <i>Neisseria meningitidis</i> are unaffected by HIV-1 infection |
|-----------|--|
| Authors | <u>Emma Wall</u> ¹ , Brigitte Denis ² , Gabriele Pollara ³ , Matthew Scarborough ⁴ , Katherine Ajdukiewicz ⁵ , Katharine Cartwright ⁶ , Mavuto Mukaka ⁷ , Queen Dube ² , Cristina Venturini ¹ , Veronica Mlozowa ² , Jennifer Cornick ² , Dean Everett ² , Theresa Allain ⁸ , Stephen Gordon ² , Mahad Noursadeghi ¹ , David Lalloo ⁹ , Robert Heyderman ¹ |
| Addresses | ¹University College London, United Kingdom ²Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi ³UCL, London, United Kingdom ⁴Oxford University Hospitals, Oxford, United Kingdom ⁵The University of Manchester Academic Health Science Centre, North Manchester General Hospital, Manchester, United Kingdom ⁶Sheffield Teaching Hospitals, Sheffield, United Kingdom ⁷Mahidol-Oxford Clinical Research Unit (MORU), Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand ⁸College of Medicine, University of Malawi, Blantyre, Malawi ⁹Liverpool School of Tropical Medicine, Liverpool, United Kingdom |

Abstract

Objective

Pneumococcal meningitis is associated with substantially worse clinical outcomes than meningococcal meningitis in adults and adolescents in all settings. We examined the CSF host inflammatory response in adults with proven pneumococcal (PM) and meningococcal meningitis (MM) in Malawi.

Method

Clinical, laboratory, CSF cytokine and transcriptomic data were compared between the two groups. Analyses were stratified by HIV sero-status and clinical outcome. CSF cytokines were measured by bead array. CSF transcriptomics was done with RNAseq.

Results

The acute host CSF inflammatory response in adults with PM (n=467) was markedly different to adults with MM (n=27). CSF WCC were significantly lower in PM compared to MM; median CSF WCC (cells/mm³) 375 (IQR 75-1623) in PM compared to 2320 (IQR 880-9800) in MM; OR per \log_{10} unit change 2.70 (1.4-4.9) p<0.001. Low CSF WCC on admission were strongly associated with non-survival in PM.

In contrast, acute CSF levels of pro-inflammatory cytokines (TNF-alpha, IL-1 and IL-8) were significantly higher in PM than MM. No correlation was observed between any CSF cytokine and CSF WCC.

No effect of HIV on CSF WCC or outcome in PM or MM was observed. The CSF transcriptome in a small number of patients shows important differences in the host responses to the pathogen.

Conclusions

The host CSF inflammatory response in PM substantially differs from patients with MM, and appears unaffected by HIV infection. Early attenuated recruitment of peripheral neutrophils into the CSF space in pneumococcal meningitis is strongly associated with mortality.

Free Scientific Paper 2

| Title | Whole genome deep sequencing of HIV reveals extensive multi-class drug resistance in Nigerian patients failing first-line antiretroviral therapy |
|-----------|--|
| Authors | <u>Kate El Bouzidi</u> ^{1,2} , Rawlings Datir ¹ , Vivian Kwaghe ³ , Sunando Roy ¹ , Dan Frampton ¹ , Judith Breuer ¹ , Obinna Ogbanufe ⁴ , Fati Murtala-Ibrahim ⁵ , Man Charurat ⁶ , Patrick Dakum ⁵ , Caroline Sabin ² , Nicaise Ndembi ⁵ , Ravindra Gupta ¹ |
| Addresses | ¹ UCL Division of Infection & Immunity, London, United Kingdom ² UCL Institute of Global Health, London, United Kingdom ³ University of Abuja Teaching Hospital, Abuja, Nigeria ⁴ U.S. Centers for Disease Control and Prevention, Abuja, Nigeria ⁵ Institute for Human Virology Nigeria, Abuja, Nigeria ⁶ Institute of Human Virology, University of Maryland School of Medicine, Baltimore, USA |

Abstract

Introduction

First-line antiretroviral therapy (1L ART) in resource-limited settings is often provided without routine viral load or drug resistance testing. We used whole genome deep sequencing (WGS) to investigate emergent resistance by revealing the distribution of mutations throughout the viral population.

Methods

Adults receiving 1L ART (two NRTI and one NNRTI) at the University of Abuja Teaching Hospital, Nigeria, were included if they had virological failure (HIV-1 RNA >1000 copies/mL, >6 months into ART, confirmed by cliniciandriven testing), and plasma available for WGS. Resistance mutations were stratified by frequency within the sample and by ART duration.

Results

Of 60 participants, 93% had CRF02_AG or G subtypes. Thymidine analogue mutations were present in 57%, 95% had other NRTI mutations and 100% had NNRTI mutations. The most common mutations were M184V, Y181C, G190A, K65R and K103N. Overall, 17% (61/367) of mutations were minority variants (2-20% of the intra-host viral population), which would not be detected by standard sequencing; 24% (88/367) were present at 20-90% frequency; and 59% (218/367) were dominant majority variants (>90% frequency). ART duration (median 28 months, IQR 18-41) was not associated with the prevalence of mutations.

Discussion

Nigerian HIV clades exhibit multi-class resistance at 1L ART failure. The predominance of high-frequency mutations suggests resistance was already fixed in the viral population. Routine viral load monitoring and adherence support are likely to be crucial from the outset to preserve therapeutic options. The effectiveness of second-line ART in this setting remains unknown in the context of extensive NRTI resistance.

Free Scientific Paper 3

| Title | HIV-1 viral protein R (Vpr) causes a global change to gene expression in primary CD4+ T cells following infection |
|-----------|---|
| Authors | Caroline Goujon ¹ , Helene Bauby ² , Reiner Schulz ² , <u>Christopher Ward²</u> , Rupert Hugh-White ² , Michael Malim ² |
| Addresses | ¹ CNRS Montpellier University, Montpellier, France ² King's College London, United Kingdom |

Abstract

Introduction

Transcriptomic analyses of viral infection can provide new insights into host-pathogen interaction. Such studies of HIV-1 infection in primary CD4+ T cells have demonstrated broad changes to gene expression profiles but failed to identify a cause. We endeavoured to determine whether this transcriptional response was virally mediated or a consequence of cellular anti-viral responses.

Methods

Primary CD4+ T cells were isolated from healthy, non-HIV-1 infected, volunteers and infected with HIV-1. Cells were harvested at 8, 10, 12, 24 and 48 hours following infection and gene expression analysed using microarrays. The same infection protocol was also used to test modified viruses.

Results

There was a profound change to gene expression in total CD4+ T cells following infection. This response was replicated in memory CD4+ T cells and for multiple different strains of HIV-1. We showed, using an HIV-1 virus deficient for Vpr expression, that cellular gene expression changes in the first 48 hours of infection were dependent on this viral protein.

Conclusion

We have shown for the first time that the HIV-1 Vpr protein has a profound effect on the gene expression profile of CD4+ T cells. Vpr's role in modifying cellular transcription may lead to increased viral gene expression and further investigation of this phenotype may lead to a better understanding of ways to reactivate HIV-1 from latency. This may, in turn, progress strategies for viral reservoir eradication and possibly a sterilising cure for HIV-1.

Free Scientific Paper 4

| Title | Assessment of a malaria rapid diagnostic test compared with qPCR in healthy volunteers undergoing controlled human malaria infection |
|-----------|---|
| Authors | <u>Ruth Payne^{1,2}</u> , Nick Edwards ² , Catherine Mair ² , Katherine Ellis ² , Georgina Bowyer ² , Duncan Bellamy ² , Sarah Silk ² , Jordan Barrett ² , Thomas Rawlinson ² , Simon Draper ² , Angela Minassian ² |
| Addresses | ¹ University of Sheffield, United Kingdom ² The Jenner Institute, University of Oxford, United Kingdom |

Abstract

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Malaria remains a significant disease worldwide, with an estimated 216 million cases in 2016. It is the most commonly imported tropical infection to the UK with roughly 1500 infections each year. The majority of cases are from individuals who have visited friends/ relatives in Africa, but malaria is an important differential diagnosis for many returning travellers presenting with a febrile illness. The 'gold standard' for diagnosis is considered to be thick and thin film microscopy, however the sensitivity and specificity of this test is dependent on operator experience. Current UK guidelines suggest that a rapid diagnostic test (RDT) alone cannot be used to diagnose or exclude malaria. RDTs have been shown to have a reduced sensitivity at low parasitaemias, but at what point they are reliable is unclear. During a controlled human malaria infection (CHMI) study in Oxford, we sought to define at what parasitaemia level the RDT used in our local NHS Trust became positive.

Twenty three healthy volunteers were recruited to a *Plasmodium falciparum* CHMI trial in which infection was administered intravenously. Seventeen of the participants had previously been infected with *P. falciparum* and completed treatment three months earlier. Six volunteers were malaria-naïve controls. Participants were monitored twice daily for symptoms, and a blood sample taken to assess parasitaemia by qPCR. From the fourth day post-CHMI the volunteers' blood was also assessed for malaria positivity using the Carestart[™] Malaria (Pan) RDT.

At the time of submission the study is ongoing. Results will be available by April 2018.

| Title | Polyspecific intravenous immunoglobulin in clindamycin-treated patients with streptococcal toxic shock syndrome: a systematic review and meta-analysis |
|-----------|--|
| Authors | Tom Parks ¹ , Clare Wilson ² , Nigel Curtis ³ , Anna Norrby-Teglund ⁴ , Shiranee Sriskandan ² |
| Addresses | ¹ London School of Hygiene and Tropical Medicine, London, United Kingdom ² Imperial College London, United Kingdom ³ Royal Children's Hospital, Melbourne, Australia ⁴ Karolinska Institutet, Stockholm, Sweden |

Abstract

Introduction

Streptococcal toxic shock syndrome (STSS) is a complication of invasive *Streptococcus pyogenes* infection (IGAS) associated with high mortality. While advocated by some experts, use of polyspecific intravenous immunoglobulin (IVIG) in STSS remains controversial, not least because of difficulty separating the effects of clindamycin in the published studies.

Methods

We identified prospective studies published 1980–2017 evaluating the relationship between IVIG and mortality in patients with STSS defined using the consensus criteria. Our primary measure of treatment effect was the risk ratio (RR) of death at 30 days calculated for the subgroup of patients who received clindamycin. Having evaluated risk of bias, we did a meta-analysis using random effects models.

Results

Of 412 articles identified through the search, we included one randomised and four non-randomised studies. Across the studies, IVIG was administered to 70 and not administered to 95 clindamycin-treated STSS patients. In association with IVIG, mortality fell from 33.7% to 15.7% (RR 0.46, 95% CI 0.26-0.83, p=0.010). The pooled result of the non-randomised studies (RR 0.43, 95% CI 0.23-0.81) was remarkably consistent with the effect size estimate of the randomised study (RR 0.42, 95% CI 0.05-3.28). This result implies as many as one additional death could be prevented for every six clindamycin-treated STSS patients administered IVIG.

Discussion

Our study provides evidence that administration of IVIG to clindamycin-treated patients with STSS is associated with a statistically significant reduction in mortality. Without sufficiently sized randomised studies, such a metaanalysis may be the best means available to evaluate this intervention.

| Title | ARK-Hospital (Antibiotic Review Kit-Hospital) - a complex behaviour change intervention in secondary care to safely and substantially reduce antibiotic use |
|-----------|---|
| Authors | <u>Elizabeth Cross</u> ¹ , Jasmin Islam ² , Fiona Mowbray ³ , Tim Peto ⁴ , Marta Santillo ³ , Katy Sivyer ³ , Sarah Walker ⁵ , Lucy Yardley ³ , Martin Llewelyn ¹ |
| Addresses | ¹ Brighton and Sussex Medical School, Brighton, United Kingdom ² Brighton and Sussex University Hospitals NHS Trust, Brighton, United Kingdom ³ University of Southampton, United Kingdom ⁴ Oxford Biomedical Research Centre, Oxford, United Kingdom ⁵ University of Oxford, United Kingdom |

Abstract

Introduction

ARK-Hospital is a complex behaviour change intervention developed to reduce antibiotic use safely by increasing early antibiotic stop rates for acute medical patients. The feasibility and acceptability of ARK-Hospital was assessed ahead of a multicentre stepped-wedged cluster randomised trial.

Methods

The intervention comprises: 1) An online learning tool. 2) A decision aid to apply to antibiotic prescriptions. 3) A leaflet for patients and carers. 4) A system for audit and feedback to clinical teams. Feasibility was assessed at one trust over 12 weeks from April-July 2017. Data on antibiotic prescribing was collected at baseline and weeks 1-4, 6, 8 and 12 of the intervention. Focus groups and interviews were conducted with healthcare staff and patients to determine the acceptability of the intervention.

Results

The decision aid was applied to the majority of antibiotic prescriptions (80%). The proportion of prescriptions reviewed and the proportion of prescriptions stopped within 72-hours increased substantially during the intervention period, 91% to 99% (p=0.0001) and 9% to 35% (p<0.0001), respectively. The intervention was highly acceptable amongst staff and patients. Refined intervention materials have been implemented in three additional trusts as part of a pilot trial. In light of encouraging findings relating to intervention uptake progression has been made to the main trial.

Discussion

ARK-Hospital has been shown to be feasible and is associated with a substantial increase in antibiotic stop rates for acute medical inpatients. This landmark study will determine the efficacy and sustainability of ARK-Hospital in dramatically reducing antibiotic use in acute hospitals.

| Title | Direct contact with platelets modulates monocyte responses to <i>Mycobacterium tuberculosis</i> |
|-----------|---|
| Authors | Daniela E. Kirwan ¹ , Katharine Fox ¹ , Ashley Whittington ¹ , Joanna C. Porter ² , Robert H. Gilman ³ , Jon S. Friedland ¹ |
| Addresses | ¹ Imperial College London, United Kingdom ² University College London, United Kingdom ³ Johns Hopkins University, Baltimore, USA |

Abstract

Background

Much of the morbidity and mortality from tuberculosis (TB) is caused by an exaggerated immune response resulting in enzyme-mediated tissue damage. Platelets modulate inflammation and are involved in many chronic inflammatory diseases. TB patients have increased platelet counts. However, the role of platelets in TB immuno-pathology remains unexplored.

Methods

Markers of platelet activity were measured in plasma from 50 TB patients pre-treatment and 50 age- and sexmatched controls. 25 patients were prospectively evaluated during treatment. A platelet-monocyte co-culture model was then developed: following infection with live virulent H37Rv *Mycobacterium tuberculosis (Mtb)*, secretion of monocyte-derived mediators was measured using ELISA and Luminex and gene expression by PCR. Transwells were then used to evaluate the effect of platelet contact on monocyte responses.

Results

Mean age of participants was 35 years, and 65% were male. Plasma concentrations of sCD40-L, PF4, PDGF-BB, and RANTES were upregulated in TB patients (all p<0.0001). Concentrations increased to treatment day 14 and normalised by day 60. Matrix metalloproteinase (MMP) gene expression, and secretion of MMP-1, -7 (both p<0.0001), -10 (p<0.001), -3, and -9 (both p<0.05), were increased in *Mtb*-infected monocytes co-cultured with platelets. This effect was significantly blunted when a transwell separated platelets from monocytes.

Conclusion

These data demonstrate that platelets may have a key regulatory role in immune responses in TB. Direct cell-tocell contact is important in platelet-driven activation of *Mtb*-infected monocytes. Platelet-monocyte interactions offer potential targets for interruption by host-directed therapies aimed at controlling harmful immune responses in TB.

Free Scientific Paper 8

| Title | First blood-stage <i>P. falciparum</i> malaria vaccine candidate to show clinical efficacy in a controlled human malaria infection model |
|-----------|--|
| Authors | <u>Angela Minassian</u> ¹ , Sarah Silk ¹ , Ian Poulton ¹ , Celia Mitton ¹ , Ruth Payne ^{1,2} , Tom Rawlinson ¹ , Megan Baker ¹ , Raquel Lopez Ramon ¹ , Fernando Ramos Lopez ¹ , Nick Edwards ¹ , Jordan Barrett ¹ , Catherine Mair ¹ , Katherine Ellis ¹ , Georgina Bowyer ¹ , Duncan Bellamy ¹ , Kazutoyo Miura ³ , Ababacar Diouf ³ , Pedro Folegatti ¹ , Daniel Silman ¹ , Mehreen Datoo ¹ , Robert Smith ⁴ , Eleanor Berrie ⁴ , Danielle Morelle ⁵ , Marc Lievens ⁵ , Amy Noe ⁶ , Lorraine Soisson ⁷ , Rebecca Ashfield ¹ , Carole Long ³ , Fay Nugent ¹ , Alison Lawrie ¹ , Simon Draper ¹ |
| Addresses | ¹ The Jenner Institute, Oxford University, Oxford, United Kingdom ² Sheffield University, Sheffield, United Kingdom ³ Laboratory of Malaria and Vector Research, NIAID/NIH, Maryland, USA ⁴ Clinical BioManufacturing Facility, Oxford University, Oxford, United Kingdom ⁵ GSK Vaccines, Wavre, Belgium ⁶ Leidos Life Sciences, Fredrick, Maryland, USA ⁷ USAID, Washington DC, USA |

Abstract

Introduction

The development of an effective blood-stage malaria vaccine holds significant promise for reducing the morbidity and mortality associated with clinical malaria. The reticulocyte-binding protein homologue 5 (RH5) is the most promising blood-stage *P. falciparum* candidate antigen to date. It is essential for erythrocyte invasion, and has shown *in vivo* efficacy in non-human primates. Protection was strongly correlated with anti-RH5 serum IgG antibody concentration and *in vitro* functional growth inhibition activity. We have recently shown the recombinant protein RH5.1 delivered with GSK's adjuvant AS01B to be safe and immunogenic in a dose-escalating Phase Ia study (NCT02927145, unpublished). Here we report on vaccine efficacy, assessed using a controlled human malaria infection model against both primary and secondary homologous *Plasmodium falciparum* challenge.

Methods

30 healthy malaria-naïve UK volunteers were recruited into the study. 15 received 3x 10 µg doses of RH5.1/ AS01 (4 weeks apart) and then received an intravenous injection of parasitized red blood cells in parallel with 15 control volunteers. qPCR-derived parasite multiplication rate (PMR) was the primary efficacy endpoint. 17 of the vaccinees and controls have since undergone a second homologous challenge to assess durability of immunity (results will be available in April 2018).

Results/Conclusions

The vaccinees had an average 20-30% reduction in the PMR compared to controls, down from 10-fold growth to \sim 7-8-fold (P=0.02). This is the first time significant in vivo efficacy has been shown for a blood-stage malaria vaccine and paves the way for future development of RH5-based vaccines.

| Title | The immunogenicity of live attenuated influenza vaccine in Gambian children: insights into reduced efficacy and effectiveness against pandemic H1N1 |
|-----------|--|
| Authors | <u>Benjamin Lindsey^{1,2}</u> , Ya Jankey Jagne ² , Edwin Armitage ² , David Jeffries ² , Nuredin Mohammed ² , Sainabou Drammeh ² , Elina Senghore ² , Hadi Sallah ² , John Tregoning ¹ , Katja Hoschler ³ , Tao Dong ⁴ , Edward Clarke ² , Beate Kampmann ^{2,1} , Thushan de Silva ^{1,2} |
| Addresses | ¹ Imperial College London, United Kingdom ² MRC Unit The Gambia at The London School of Hygiene and Tropical Medicine, Banjul, Gambia ³ Public Health England, London, United Kingdom ⁴ University of Oxford, United Kingdom |

Abstract

Introduction

Influenza-related morbidity and mortality in Africa is high. Data on influenza vaccine performance in African populations is limited, with a recent RCT in Senegal showing no efficacy of Russian-backbone live attenuated influenza vaccine (LAIV). Wider concerns exist surrounding LAIV effectiveness, particularly against pandemic H1N1 (pH1N1). We report the first LAIV immunogenicity data from African children and provide insight into the reasons behind these issues.

Methods

Gambian children aged 24-59 months (n=118) were given 2016/17 NH LAIV formulation. Vaccine shedding, haemagglutinin inhibition (HAI) titre, influenza-specific T-cell responses and mucosal-IgA were measured using RT-PCR, HAI assay, flow cytometry and ELISA respectively. Additionally, 100 children were given 2017/18 formulation LAIV, where the pH1N1 strain was updated to reflect current circulating strains.

Results

In 2016/17, significantly reduced pH1N1 shedding (13.6% children) was seen compared to H3N2 (45.8%) and B/Victoria (80.5%). Similarly, poor pH1N1-specific HAI, mucosal-IgA and T-cell responses were seen, whereas robust responses in >/1 immune compartments were seen to H3N2 and B/Victoria. Reduced pH1N1 shedding was unrelated to pre-existing immunity. Vaccination with 2017/18 LAIV showed significant improvement in pH1N1 shedding (68.3%), with 60.0% and 68.3% children shedding H3N2 and B/Victoria respectively. Immunogenicity data from the 2017/18 cohort are currently being generated and will be presented.

Discussion

Our data offer an explanation for the poor LAIV efficacy in Senegal, where pH1N1 was the predominant vaccinematched circulating strain. It also sheds light on recent poor LAIV effectiveness more globally and suggests an improvement with new pH1N1 vaccine strains.

Free Scientific Paper 10

| Title | Antimicrobial prescribing `app' fails to improve adherence to guidelines in junior doctors |
|-----------|---|
| Authors | Sheena Bhadresha ¹ , Catherine Baldwin ¹ , Reem Santos ¹ , David Enoch ¹ , Michael E Murphy ^{1,2} |
| Addresses | ¹ Cambridge University Hospitals, Cambridge, United Kingdom ² National Infection Service, Public Health England, Cambridge, United Kingdom |

Abstract

Foundation year 1(FY1) doctors are a generation familiar with mobile-phone 'apps'. We compared adherence to trust antibiotic guidelines before and after introducing an antimicrobial prescribing app.

Method

Antibiotic prescribing by FY1 doctors was extracted for Aug/Sept 2016(pre-App) and 2017(post-App) and a random 7-days (Monday-Sunday) over 7-weeks included. Adherence to trust antibiotic guidelines was assessed per documented clinical indication and drug allergy. A post-study survey of F1 antimicrobial prescribing was undertaken.

Results

Fifty-one FY1s prescribed 95 antibiotics in 76 patients in 2016 and 136 antibiotics in 112 patients in 2017. Allergies were recorded in 36(47%) and 59(53%) patients, of which 10(13%) and 26(23%) were penicillin, in the preand post-app periods respectively. There was no difference in adherence (68% vs 69%) and partial adherence (19% vs 18%) between the pre-App and post-App periods (p=0.91; p=0.92). In patients with penicillin allergy, prescriptions adhering to guidelines were higher post- app, but failed to reach statistical significance (54% vs 72%, p=0.26). Of all FY1s, 20 (39%) responded to the survey; 65% reported using the app most or all the time for antibiotic prescribing; 95% reported prescribing off guidelines at the direction of senior doctors or as per microbiology advice. Majority FY1s suggest improving prescribing by educating seniors. Three FY1s commented on app UX design and one called for paper-based guidelines.

Conclusion

Introducing a prescribing app failed to improve appropriateness of antibiotic use amongst junior doctors. Offguideline antibiotics were frequently directed by seniors who may require education on the benefits of adhering to trust antibiotic guidelines.

Free Scientific Paper 11

| Title | Evaluating the use of a 25-pathogen TaqMan Array Card for rapid diagnosis of vi bacterial, and fungal respiratory pathogens in adult intensive care patients | | | |
|-----------|--|--|--|--|
| Authors | <u>Nick K. Jones</u> ¹ , Martin D. Curran ² , Olajumoke Sule ² , David Enoch ² , Sani Aliyu ² , Hongyi Zhang ² , Hamid Jalal ² , Vilas Navapurkar ¹ , Michael E. Murphy ^{1,2} | | | |
| Addresses | ¹ Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom ² Cambridge Microbiology and Public Health Laboratories, Cambridge, United Kingdom | | | |

Abstract

Rapid diagnostics are crucial for timely implementation of pathogen-directed therapy and infection control. We compared the use of a 25-pathogen TaqMan Array Card (TAC) to conventional laboratory methods for detecting respiratory pathogens at a tertiary referral centre.

Patient demographics and conventional test data were retrospectively collected on all intensive care patients whose deep-respiratory samples had undergone TAC testing during 2016. Diagnostic performance was evaluated against that of conventional methods by comparison of result agreement (McNemar's test), cycle threshold values (Willcoxon signed-rank test), and time-to-result availability (log rank test). Significance was determined by p<0.05.

TAC results from seventy-one patients were included; 63% male, median age 59 [IQR 43.5-69], 66 (93%) collected >48 hours after admission. One or more pathogens were detected in 33 (46%) using TAC, compared to 29 (41%) by conventional methods. Overall test agreement was 93.7%. TLDA detected significantly more *Streptococcus pneumoniae* (7 vs 0; p=0.02) but failed to detect *Aspergillus* spp. in eight samples (10 vs 2;p=0.078). TAC missed one rhinovirus case and one human metapneumovirus case. There was no difference in cycle threshold values between TAC and conventional PCR. Time-to-result availability was significantly greater for bacterial culture, mycoplasma serology, BAL galactomannan, and TB culture compared to TAC (HR 2.01, 3.45, HR 1.6, 4.3, all p<0.05).

Use of TAC is associated with improved yield of *S. pneumoniae* detection and reduced time-to-result availability for a number of respiratory pathogens. Current primers for TAC *Aspergillus* detection cannot be relied upon and need to be improved to detect *Aspergillus*.

Free Scientific Paper 12

| Title | Chronic pulmonary aspergillosis (CPA) complicating tuberculosis is an unrecognised global public health issue: a cross-sectional survey |
|-----------|---|
| Authors | <u>Iain Page^{1,2}</u> , Rosemary Byanyima ³ , Sharath Hosmane ² , Nathan Onyachi ^{4,5} , Cyprian Opira ⁶ , Malcolm Richardson ^{1,7} , Anna Sharman ² , David Denning ^{1,2} |
| Addresses | ¹ The University of Manchester, United Kingdom ² Manchester University NHS Foundation Trust, Manchester, United Kingdom ³ Kampala Imaging Centre, Kampala, Uganda ⁴ Gulu Regional Referral Hospital, Gulu, Uganda ⁵ Masaka Regional Referral Hospital (current position), Masaka, Uganda ⁶ St. Mary's Hospital, Lacor, Gulu, Uganda ⁷ Manchester University NHS Foundation Trust, Manchester, United Kingdom |

Abstract

Background

Chronic pulmonary aspergillosis (CPA) complicates treated pulmonary tuberculosis. It has a five-year mortality of 38-80%. However, it responds to oral azole treatment and is amenable to surgical cure in selected cases. The global prevalence of CPA and impact of HIV co-infection on CPA prevalence are unknown.

Methods

398 treated tuberculosis patients were surveyed with CXR and *Aspergillus*-specific IgG in Gulu, Uganda between October 2012 and February 2013. 285 were resurveyed between October 2015 and January 2016. CT thorax was performed in 75 cases. Tuberculosis was excluded by GeneXpert testing. CPA was diagnosed if chronic cough or haemoptysis, raised *Aspergillus*-specific IgG, and either paracavitary fibrosis or fungal ball on CT thorax or progressive cavitation on serial chest X-rays were all present.

Findings

14 (4.9%) resurvey patients had CPA, including three with destroyed lung and one with asymptomatic simple aspergilloma. A further four (1.4%) patients had probable CPA. There was a statistically non-significant trend to less frequent CPA in the HIV positive group. The annual rate of new CPA development between surveys was 1.25% in all patients and 6.5% in those with chest X-ray cavitation (p<0.000).

Interpretation

CPA occurs in survivors of pulmonary tuberculosis frequently enough to be considered a global public health problem in both HIV positive and negative people. CPA should be considered in all patients with recurrent symptoms or new cavities after completion of tuberculosis therapy. It may be appropriate to monitor patients with residual cavities for CPA development after completion of tuberculosis therapy.

Clinical Paper A

TitleIn sight and out of mindAuthorsBlessing Essang, Hiten Thaker

Address Castle Hill Hospital, Hull, United Kingdom

Abstract without diagnosis

A previously healthy 45 year old air steward with no co-morbidities and initially presented in 2016 with haemolytic anaemia and symptoms of night sweats, unintentional weight loss of ~ a stone in 3-4 months. Examination revealed bilateral axillary lymphadenopathy and splenomegaly 4cm below the costal margin. A subsequent HIV screening test was positive. His CD4 cell count was 158 and serum viral load of 263,000 copies/ml. Due to concerning symptoms, a whole-body PET-CT and a fine needle aspiration of axillary lymph node were performed to exclude lymphoproliferative disease.

Lymph node FNA showed preserved normal lymphoid architecture, reactive germinal centres and reactive T cells – excluding lymphoma. PET-CT showed generalised low volume lymphadenopathy on both sides of the diaphragm of low to moderate intensity activity. Symptoms resolved following commencement of Emtricitabine/Tenofovir and Dolutegravir. He responded to HAART with a good response in his CD4 count (>300, last 407) but persistent low grade viraemia (range 25-73, last 64.6 copies/ml).

Two years later, with a normal CD4 count (407) and low grade HIV viraemia (<50 copies/ml), he presented with lesions he noticed appearing over 6 weeks. There are over 35 raised, well defined, purple tinted lesions found on the trunk, right shoulder, left arm and bilateral legs, ranging from 1 to 20mm in diameter. No associated pain, itch, bleeding, discharge or change in size noticed. No night sweats, no unintentional weight loss, no oral or palatal lesions and no lymphadenopathy. He had a skin biopsy which revealed the diagnosis.

Clinical Paper B

Title Scratchings beneath the surface

Authors Phillip Simpson, Ben Stone, Tom Darton

Address Sheffield Teaching Hospitals, Sheffield, United Kingdom

Abstract without diagnosis

A normally fit and well UK-born white male joiner from South Yorkshire, with no history of travel in the preceding 12 months, presented to his local emergency department with a 24-hour history of gradual onset bilateral arm pain radiating to his chest. Cardiac causes were excluded with Troponin I <17ng/L, his full blood count showed a slight lymphocytosis of 3.5 and his renal function was normal. He was treated with analgesia and discharged. His symptoms continued to worsen and he was re-admitted 4 days later. Again his Troponin was normal as was his FBC and U&E. His LFTs were abnormal, ALT 730 IU/L, AST 304 IU/L, GGT 276 IU/L, ALP 250 IU/L. He remained an inpatient for 3 days were his pain became more under control and his LFT's gradually improved. He did not complain of any abdominal pain, nausea, diarrhoea or vomiting.

He was reviewed in a neurology outpatient clinic at which he described intermittent shooting pains down both arms and had started to develop weakness in his right arm. An MRI brain and C-spine where normal and a diagnosis of brachial neuritis was made, later confirmed with NCS/EMG. An initial infection screen for HIV, hepatitis B & C, EBV and CMV all came back negative. His USS abdomen showed a normal liver.

Clinical Paper C

TitleAcute neurological presentation in an ex-Kruger National Park rangerAuthorsThomas Boland, Ruaridh Buchanan, Hector Maxwell-Scott, Saima Waseem, Nicholas Price,
Anna GoodmanAddressDepartment of Infection, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

Abstract without diagnosis

A 31 year old male presented with a nine day history of progressive headache, frontal then occipital. This was associated with vomiting, followed by increasing drowsiness, diplopia, gait impairment, incoordination and an isolated absence type seizure. Immediately prior to the onset of his symptoms he had attended a house party where he ingested large volumes of alcohol and intranasal cocaine.

Initial blood tests were unremarkable with the exception of a mild lymphopenia $0.6 \times 109/L$. HIV screen was negative. Further tests during his admission demonstrated a markedly raised IgE of 3810kU/L.

Admission CT head was unremarkable, but a subsequent MRI revealed bilateral globus pallidus necrosis and multiple non-specific T2 weight foci in the white matter and cerebellum. Chest imaging revealed a dense focus of consolidation in the right upper lobe, as well as an area of calcification in the left upper lobe; abdominal viscera appeared unremarkable.

The patient's history included recurrent skin abscesses requiring antibiotics and an undiagnosed congenital bone deformity affecting his elbows, as well as pulmonary TB ten years previously. He had not travelled outside the UK in two years, but was born and raised in South Africa and had worked as a ranger in Kruger National Park.

A diagnostic test was performed early in his admission and a targeted treatment regimen commenced.

Clinical Paper D

Title Bleeding oesophageal varices: common presentation, unusual aetiology

Authors <u>Melanie Etti</u>¹, Andrew Millar²

Addresses¹Royal Free Hospital, London, United Kingdom²North Middlesex University Hospital, London, United Kingdom

Abstract without diagnosis

A 51-year-old Zimbabwean man was admitted to hospital in hypovolaemic shock following a short history of epigastric pain and dark, offensive stools. He had been hospitalised one month prior whilst on holiday in Central America following an episode of large volume haematemesis, resulting in admission to Intensive Care.

His only other significant past medical history was that of chronic thrombocytopaenia which had been investigated by the Haematology department six years prior. He had lived in the UK for 25 years and had not returned to Zimbabwe for more than ten years. He was a non-smoker and drank only a few units of alcohol per week.

On examination, he was noted to have hepatosplenomegaly but no ascites, and digital rectal examination revealed melaena. His initial blood results showed a microcytic anaemia and an acute kidney injury. His liver enzymes were within the normal range, as were his INR and serum albumin level, suggesting preserved synthetic function of the liver.

After haemodynamic stabilisation, the patient underwent an oesophagogastroduodenoscopy, which showed multiple Grade 3 oesophageal varices, two of which were ligated. The patient subsequently underwent a Doppler abdominal ultrasound scan which identified an enlarged liver of coarse echotexture, marked splenomegaly and a "patent and prominent" portal vein.

Bloods sent for common infective, autoimmune and infiltrative causes of chronic liver disease all yielded a negative result, but could closer consideration of the patient's country of origin and his radiological findings provide a clue as to the underlying infective cause for the patient's presentation?

Clinical Paper E

| Title | A beast not from the East |
|---------|---|
| Authors | Jennifer Tomlins, Simon Tiberi |
| Address | Bart's Health NHS Trust, London, United Kingdom |

Abstract without diagnosis

We present the case of a 39 year old man originally from Lagos, Nigeria who has lived in the UK for the last 10 years. He suffered with obesity, poorly controlled diabetes, hypertension and high cholesterol. He played the trumpet professionally and lived with his aunt and uncle in East London. He had not recently travelled anywhere outside of the UK.

He presented in September 2017 following a 3 week history of right upper arm pain for which he had seen the GP and local A&E and was reassured following normal X-ray appearances of the humerus. On the day of admission he suffered a collapse and found he was no longer able to raise his right hand. Examination revealed a tender, fluctuant swelling over the mid shaft of his humerus with an associated wrist drop. An X-ray revealed multiple lytic lesions of the right humerus and his blood tests showed a grossly elevated CRP and normal white cell count.

He was admitted to ward where he began to spike temperature of greater than 39 degrees Celsius. An MRI was performed and revealed destructive changes in the proximal two thirds of the humerus with associated collections in the surrounding soft tissue and muscles. He was initiated on broad spectrum antibiotics and underwent surgical debridement of the area. Pus and tissue samples were sent to the laboratory where an unexpected gram negative bacillus was isolated 2 days later.

Clinical Paper F

| Title | From silk roads to Meltemi winds | | |
|---------|---|--|--|
| Authors | Alanah Proctor ¹ , Paschalis Vergidis ¹ , Malcolm Richardson ² , Louise Sweeney ³ | | |
| Address | ¹ National Aspergillosis Centre, Manchester, United Kingdom ² Mycology Reference Centre, Manchester, United Kingdom ³ Manchester Royal Infirmary, Manchester, United Kingdom | | |

Abstract without diagnosis

A 53yr old lady was referred to infectious diseases after presenting to hospital in Greece in August 2017 with a mild cough productive of green sputum. She was initially given oral antibiotics with no clinical improvement. She had a further course of oral antibiotics and became gradually more fatigued. She returned to the UK and was seen by her GP in October due to persistent symptoms. Her cough has worsened and she became more breathless. She also developed night sweats. CXR showed a left upper lobe lung mass.

She has a past medical history of polycystic kidney disease and renal transplant in 2006. Prior to transplant she was using peritoneal dialysis. Her current medications are tacrolimus, mycophenolate mofetil, vitamin A and calcium carbonate.

She is a retired recruitment consultant who has never smoked and drinks alcohol rarely. She enjoys spending time sailing in Crete and Greece and has also had travel to China in 2016 for a transplant fund raising event.

PET CT scanning showed a large mass over 10cm in size with peripheral high uptake and central necrosis. There was also uptake identified in mediastinal nodes.

She went onto have a diagnostic EBUS with sampling of nodes and lung mass tissue. Necrosis and focal granulomas were identified and no malignant cells seen. Organisms were identified on Grocott staining and cultures grew *Talaromyces marneffei* which was identified by microscopy in Manchester and confirmed on MALDI-TOF.

| Dr Dr Mr Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr | | Name Michael Dinesh Joti Haamed Nancy | Surname Abouyannis Aggarwal Ahir | Hospital Royal Liverpool Hospital Imperial College Healthcare NHS Trust | Department Infectious Diseases | Grade Speciality Trainee |
|--|----|--|---|---|------------------------------------|-------------------------------|
| Dr Mr Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr | | Dinesh Joti Haamed | Aggarwal | | | . , |
| Mr Mr Dr Dr Dr Dr Dr Dr Dr Dr Dr | | Joti Haamed | | | Infectious Diseases | Specialist Trainee |
| Mr Dr Dr Dr Dr Dr Dr Dr Dr Dr | | Haamed | | Newcastle University/Royal Victoria Infirmary | School of Medicine | Student |
| Dr Dr Dr Dr Dr Dr Dr Dr Dr Dr | | | Al Hassan | Cardiff University | Cardiff University | Medical Student |
| Dr Dr Dr Dr Dr Dr Dr Dr Dr | | | Allen | North Manchester General Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Dr Dr Dr Dr Dr Dr Dr Dr | | Michael | Ankcorn | NHSBT / Public Health England | Virus Reference | Clinical Research Fellow |
| Dr Dr Dr Dr Dr Dr Dr | | Vanesa | Anton Vazquez | St Georges University of London | Medical Microbiology | Clinical Research Fellowship |
| Dr Dr Dr Dr Dr Dr | | Paul | Arkell | St George's Hospital | Infection | Specialist Registrar |
| Dr Dr Dr Dr Dr | | Bridget | Atkins | Oxford University Hospitals NHS Trust | Infectious Diseases & Microbiology | |
| Dr Dr Dr Dr | | Catherine | Baldwin | Ipswich Hospital | Paediatrics | Foundation Year Doctor |
| Dr Dr Dr | | Rebecca | Bamber | University Hospital of Wales | Infectious Diseases | Specialist Registrar |
| Dr Dr | | Tristan | Banks | Pennine Acute Trust | Medicine | Specialist Registrar |
| Dr | | Katy | Baple | Worthing Hospital | General Medicine | Core Medical Trainee Doctor |
| | | Gavin | Barlow | Hull & East Yorkshire Hospitals NHS Trust | Infection | Consultant |
| | | Jessica | Barrett | Northwick Park Hospital | Infectious Diseases | Research Registrar |
| Dr | | Paul | Beckett | Sheffield Teaching Hospitals NHS FT | Medical Microbiology | Speciality Trainee |
| Dr | | Sheena | Bhadresha | North West Anglia Foundation Trust | Rotational | Foundation Year 2 Doctor |
| Dr | | Tehmina | Bharucha | Royal Free London NHS Foundation Trust | Infectious Diseases | Speciality Trainee |
| Dr | | Ranajoy | Bhattachaaya | North Manchester Gereral Hospital | Infectious Diseases | Speciality Trainee |
| Mis | | Kelly | Bicknell | Portsmouth Hospitals NHS Trust | Virology | Specialist Clinical Scientist |
| Dr | | Harriet | Billam | Nottingham University Hospitals | Microbiology/Infectious Diseases | Specialist Registrar |
| Dr | | Samkeliso | Blundell | Imperial College Healthcare NHS Trust | Microbiology | Specialist Registrar |
| Dr | | Thomas | Boland | Infectious Diseases | Infectious Diseases | Foundation Year Doctor |
| Dr | | Alec | Bonnington | North Manchester General Hospital | ID & Tropical Medicine | Consultant |
| Dr | | Michael | Boswell | Oxford University Hospitals NHS FT | Nuffield Department of Medicine | Student |
| Dr | | Alina | Botgros | Guy's & St Thomas' NHS Foundation Trust | Virology | Specialist Doctor |
| Dr | | Sara | Boyd | Imperial College London | Infectious Diseases | Specialist Registrar |
| Mr | S | Claire | Brandish | Buckinghamshire Healthcare NHS Trust | Pharmacy | Anti-Infectives Pharmacist |
| Dr | | Ruaridh | Buchanan | Guy's & St Thomas' NHS Foundation Trust | Infection | Specialist Registrar |
| Dr | | Rachael | Burke | London Deanery | Infectious Diseases | Specialist Registrar |
| Dr | | Vjeran | Cajic | Universiry Hospital Coventry | Infectious Diseases | Consultant |
| Dr | | Mark | Campbell | Oxford University Hospitals NHS FT | Infectious Diseases/Microbiology | Specialist Registrar |
| Pro | of | Barry | Campbell | University of Liverpool | Gastroenterology Research | Department Director |
| Dr | | Helen | Casey | University Hospitals Bristol | Microbiology | Speciality Trainee |
| Dr | | Arjun | Chandna | University College London Hospital | Microbiology | Speciality Trainee |
| Mr | S | Suraiya | Chandratillake | Milton Keynes University Hospital | Pharmacy | Antmicrobials Pharmacist |
| Dr | | Bilwanath | Chattopadhyay | DAMA Hospital | Medical Microbiology | Consultant |
| Dr | | Waleed | Chaudhry | Northwick Park Hospital | Accident and Emergency | Foundation Year 2 Doctor |
| Dr | | Anna | Checkley | Hospital for Tropical Diseases, London | Infectious Diseases & Microbiology | Consultant |
| Dr | | Chris | Chiu | Imperial College London | Infectious Diseases | Consultant |
| Dr | | Tristan | Clark | University of Southampton | Infectious Diseases | Honorary Consultant |
| Dr | | Joby | Cole | Sheffield Teaching Hospitals NHS FT | ID & Tropical Medicine | Specialist Registrar |
| Dr | | Julia | Colston | Oxford University Hospitals NHS FT | Infectious Diseases/Microbiology | Academic Clinical Lecturer |
| Dr | | Francesca | Conradie | Helen Joseph Hospital | Clinical HIV Research | Clinical Research Advisor |
| Dr | | Fiona | Cooke | Addenbrookes Hospital | Microbiology | Consultant |
| Dr | | Luis | Cotter | Dartford & Gravesham NHS Trust | Pathology | Associate Specialist |
| Dr | | Giovanna | Cowley | Royal Free London NHS Foundation Trust | Medicine | Doctor |
| Mr | | | | NHS Improvement | Patient Safety - AMR | AMR Project Lead |

| Title | Name | Surname | Hospital | Department | Grade |
|-------|-------------|---------------|--|----------------------------------|-----------------------------|
| Dr | Anna | Crepet | Kent, Surrey & Sussex Health Education England | Medical Microbiology/ID | Higher Specialty Trainee |
| Dr | Elizabeth | Cross | Brighton & Sussex University Hospitals | Infectious Diseases/Microbiology | Academic Clinical Fellow |
| Dr | Phoebe | Cross | Leeds Teaching Hospitals NHS Trust | Infectious Diseases | Speciality Trainee |
| Dr | Niamh | Cunningham | Barts Health NHS Trust | Medicine | Junior Clinical Fellow |
| Dr | Christopher | Darlow | North Manchester General Hospital | Infectious Diseases | Specialist Registrar |
| Dr | Thomas | Darton | University of Sheffield | IICD | Senior Lecturer |
| Dr | Mehreen | Datoo | University of Oxford | Jenner Institute | Clinical Research Fellow |
| Dr | Harriet | Davidson | St George's Hospital | Anaesthetics | Core Medical Trainee Doctor |
| Dr | John | Day | Southend University Hospital | Infectious Diseases | Consultant |
| Dr | Pete | Dayananda | Leeds Teaching Hospitals NHS trust | Microbiology | Speciality Trainee |
| Dr | Sophia | De Saram | London Training Scheme | Infectious Diseases/Microbiology | Specialist Registrar |
| Dr | Thushan | de Silva | Medical Research Council The Gambia at LSHTM | Vaccines and Immunity | Academic Clinical Fellow |
| Dr | Joseph | Delo | Imperial College Healthcare NHS Trust | Medicine | Doctor |
| Prof | David | Dockrell | University of Edinburgh | Inflammation Research | Professor |
| Dr | Selen | Dogan | Wrexham Maelor Hospital | Microbiology | Foundation Year Doctor |
| Dr | Ruth | Drury | Oxford University Hospitals NHS FT | Paediatrics | Registrar & PhD Student |
| Dr | Louise | Dunsmure | Oxford University Hospitals NHS FT | Pharmacy | Consultant Pharmacist |
| Dr | Kate | El Bouzidi | University College London | Infection & Immunity | Wellcome Trust CRF |
| Dr | Mohammed N | Elnour | West Cumberland Hospital | Medicine | Specialist Registrar |
| Dr | Celestine | Eshiwe | Hull & East Yorkshire Hospitals NHS Trust | Infectious Diseases | Specialist Registrar |
| Dr | Melanie | Etti | Royal Free London NHS Foundation Trust | Neurology | Core Medical Trainee Doctor |
| Dr | Adam | Evans | Newcastle-Upon-Tyne Hospitals | Infectious Diseases | Consultant |
| Dr | Johnny | Evans | Guy's & St Thomas' NHS Foundation Trust | Medicine | Doctor |
| Dr | Elena | Ferran | Charing Cross Hospital | Infectious Diseases | Specialist Registrar |
| Dr | Sarah Ann | Filson | King's College Hospital | Microbiology | Specialist Registrar |
| Dr | Jennifer | Fitzpatrick | Frimley Park Hospital | Infectious Diseases/Microbiology | Specialist Registrar |
| Dr | Ray | Fox | Gartnavel General Hospital | Infectious Diseases | Consultant |
| Prof | Jonathan | Friedland | Imperial College London | Infectious Diseases/Immunity | Professor |
| Dr | Susannah | Froude | Public Health Wales | Microbiology | Specialist Registrar |
| Dr | Charlie | Fry | Cheltenham General Hospital | Acute Medicine | Core Medical Trainee Doctor |
| Dr | David | Garley | Cheltenham General Hospital | Oncology | Core Medical Trainee Doctor |
| Dr | Malick | Gibani | University of Oxford | Paediatrics | Research Fellow |
| Dr | Eliza | Gil | University College London | Infection & Immunity | Research Fellow |
| Dr | Rebecca | Godfrey | Brighton & Sussex University Hospitals | Medicine | Core Medical Trainee Doctor |
| Dr | Marta | Gonzalez Sanz | University College London Hospital | Parasitology | Specialist Registrar |
| Dr | Anna | Goodman | Guy's & St Thomas' NHS Foundation Trust | Infectious Diseases | Consultant |
| Dr | Lynsey | Goodwin | North Manchester General Hospital | Infectious Diseases | Speciality Trainee |
| Dr | Deepika | Gorthy | Southend University Hospital | Diabetes & Endocrinology | Speciality Trainee |
| Ms | Shannon | Gunawardana | University of Oxford | Medical Sciences | Medical Student |
| Dr | Fergus | Hamilton | University of Bristol | Medicine | Core Medical Trainee Doctor |
| Dr | Jo | Herman | N/A | N/A | Consultant |
| Dr | Izak | Heys | North Bristol NHS Trust | Infectious Diseases | Consultant |
| Dr | Rob | Holden | Royal Lancaster Infirmary | General Medicine | Foundation Year 1 Doctor |
| Dr | Catherine | Houlihan | University College London | Infection & Immunity | Clinical Lecturer |
| Dr | Desmond | Hsu | Barts Health NHS Trust | Infection | Specialist Registrar |
| Mr | Dawid | Hubert | King's College London | GKT School of Medical Education | Medical Student |
| Dr | Alyssa | Hudson | Southmead Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Dr | Azima | Hussain | Bradford Royal Infirmary | Oncology | Doctor |
| | | | | | |

| Title | Name | Surname | Hospital | Department | Grade |
|-------|----------|---------------|---|-------------------------------------|-------------------------------|
| Dr | Anu | Jain | Epsom & St Helier Hospital | Medical Microbiology | Speciality Trainee |
| Dr | Katie | Jeffery | Oxford University Hospitals NHS Trust | Microbiology & Virology | Consultant |
| Dr | Natasha | Jesudason | Greater Glasgow & Clyde | Infectious Diseases/Virology | Speciality Trainee |
| Dr | Nick | Jones | Cambridge University Hospitals NHS FT | Clinical Virology | Academic Clinical Fellow |
| Dr | Eben | Jones | University College London Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Mr | Thomas | Jones | Newcastle Medical School | ID & Tropical Medicine | Medical Student |
| Dr | Harjit | Kaur | Perth | N/A | Medical Advisor |
| Dr | Alex | Keeley | Northwick Park Hospital | Infectious Diseases | Specialist Registrar |
| Dr | John | Kelly | Mid Essex Hospitals Trust | Medicine | Core Medical Trainee Doctor |
| Dr | Mike | Kelsey | Whittington Health | Microbiology | Consultant |
| Dr | Sarah | Kennedy | Leeds Teaching Hospitals NHS Trust | Infectious Diseases | Speciality Trainee |
| Dr | Maria | Krutikov | Barts Health NHS Trust | Infection | Specialist Registrar |
| Dr | Wasana | Kudagammana | Imperial College Healthcare NHS Trust | Microbiology | Specialist Registrar |
| Dr | Ruthiran | Kugathasan | North Middlesex Hospital | Microbiology | Specialist Registrar |
| Prof | Charles | Lacey | York Hospitals Foundation Trust | GU / HIV Medicine | Honorary Consultant |
| Dr | Rajeka | Lazarus | University Hopsital Bristol | Microbiology | Consultant |
| Dr | Marco | Lee | Leeds Teaching Hospitals NHS Trust | Microbiology | Specialist Registrar |
| Prof | Clifford | Leen | Western General Hospital | Infectious Diseases | Consultant |
| Dr | Nicolas | Lewis | Sheffield Teaching Hospitals NHS FT | Infectious Diseases | Speciality Trainee |
| Dr | Patrick | Lillie | Hull & East Yorkshire Hospitals NHS Trust | Infection | Consultant |
| Dr | Han Hua | Lim | Royal Victoria Infirmary | Infectious Diseases | International Training Fellow |
| Dr | Benjamin | Lindsey | Imperial College London | Infectious Diseases | Clinical Reseach Fellow |
| Prof | Martin | Llewelyn | Brighton & Sussex University Hospital | Microbiology | Consultant |
| Dr | Laura | Lloyd | Queen Elizabeth Hospital | Microbiology | Speciality Trainee |
| Dr | Thomas | Locke | Sheffield Teaching Hospitals NHS FT | Microbiology | Specialist Registrar |
| Dr | Olivia | Lucey | Royal Free London NHS Foundation Trust | Infectious Diseases | Specialist Registrar |
| Dr | Akish | Luintel | Whittington Hospital | Whittington Hospital | Specialist Registrar |
| Dr | William | Lynn | Ealing Hospital | Infectious Diseases | Consultant |
| Prof | Derek | Macallan | St Georges University of London | Infection & Immunity | Professor |
| Dr | Kirsten | MacGregor | North Bristol NHS Trust | Microbiology | Speciality Trainee |
| Dr | Michael | Marks | Hammersmith Hospital | Infectious Diseases | Specialist Registrar |
| Dr | Hector | Maxwell-Scott | Guy's & St Thomas' NHS Foundation Trust | Infection | Specialist Registrar |
| Dr | Angela | McBride | University College London Hospital | Infectious Diseases | Specialist Registrar |
| Dr | Naina | McCann | University College London Hospital | Infectious Diseases | Doctor |
| Dr | Ruth | McEwen | Countess of Chester Hospital | Acute Medicine | Consultant |
| Miss | Sophie | McGlen | Oxford University Hospitals NHS FT | Ambulatory Assessment | Lead Pharmacist |
| Dr | Emma | McGuire | Barts Health NHS Trust | Infection | Specialist Registrar |
| Dr | Rohan | Mehra | Portsmouth Hospital Trust | Medical Microbiology/Acute Medicine | Foundation Year 2 Doctor |
| Dr | Ellen | Mekonnen | Northwick Park Hospital | Acute Medicine | Senior House Officer |
| Dr | Mark | Melzer | WXUH Barts Health NHS Trust | Infectious Diseases & Microbiology | Consultant |
| Dr | Blair | Merrick | Newcastle upon Tyne Hospitals NHS FT | Infection & Tropical Medicine | Teaching Fellow |
| Dr | Claudia | Meyer | University Hospitals Portsmouth | Microbiology | Specialist Registrar |
| Dr | Albert | Mifsud | PHE Whitechapel | Microbiology | Consultant |
| Dr | Damien | Ming | Imperial College Healthcare NHS Trust | Microbiology | Specialist Registrar |
| Dr | Tamara | Mitchell | Sheffield Teaching Hospitals NHS FT | Microbiology | Specialist Registrar |
| Dr | Samira | Mohd Afzal | Royal Stoke University Hospital | Infectious Diseases | Specialist Registrar |
| Dr | Rachel | Moores | Royal Free London NHS Foundation Trust | Infectious Diseases | Specialist Registrar |
| Dr | Tara | Moshiri | Nottingham University Hospitals | Microbiology | Specialist Registrar |
| | | | | | |

| Title | Name | Surname | Hospital | Department | Grade |
|-------|-------------|---------------------|--|----------------------------------|-----------------------------|
| Dr | Peter | Moss | Hull & East Yorkshire Hospitals NHS Trust | Infectious Diseases | Consultant |
| Dr | Claire | Mullender | The Royal London Hospital | Virology | Specialist Registrar |
| Dr | Sara | Murthy | Royal Free London NHS Foundation Trust | Infectious Diseases | Specialist Registrar |
| Dr | Juliette | Mutuyimana | Leicester Royal Infirmary | Infectious Diseases/Microbiology | Specialist Registrar |
| Dr | Rhea | O' Regan | Queensland Health | Emergency | Doctor |
| Dr | Cavan | O'Connor | University College London Hospital | Intensive Care | Core Medical Trainee Doctor |
| Dr | Chinonye | Onyeocha | Homerton University Hospital NHS Trust | GUM/HIV | Doctor |
| Dr | Akaninyene | Otu | Manchester University Foundation Trust | National Aspergillosis Centre | Senior Clinical Fellow |
| Dr | Iain | Page | University of Manchester | National Aspergillosis Centre | Academic Clinical Lecturer |
| Miss | Aishwarya | Pai | Imperial College London | School of Medicine | Medical Student |
| Dr | Joyeeta | Palit | Sheffield Teaching Hospitals NHS FT | Microbiology | Specialist Registrar |
| Dr | Padmasayee | Papineni | Royal Free London NHS Foundation Trust | Infectious Diseases | Specialist Registrar |
| Dr | Vivak | Parkash | Sheffield Teaching Hospitals NHS FT | Infectious Diseases/Microbiology | Speciality Trainee |
| Dr | Trupti | Patel | Whittington Health | Microbiology | Consultant |
| Dr | Vinesh | Patel | LSHTM, Kent & Canterbury Hospital | Public Health | Public Health MSc Student |
| Dr | Charlotte | Patterson | Royal Free London NHS Foundation Trust | Virology | Specialist Registrar |
| Dr | Ruth | Payne | University of Sheffield | Infection & Immunity | Academic Clinical Lead |
| Dr | Giuseppe | Pichierri | Kingston Hospital NHS Foundation Trust | Microbiology | Consultant |
| Dr | Stephen | Poole | Hampshire Hospitals Foundation Trust | Microbiology | Specialist Registrar |
| Dr | Alison | Prescott | Leeds Teaching Hospitals NHS Trust | Microbiology | Doctor |
| Dr | Alanah | Proctor | Manchester University Foundation Trust | National Aspergillosis Centre | Clinical Education Fellow |
| Dr | Martha | Purcell | SASH NHS Trust | Microbiology | Specialist Registrar |
| Dr | Mustafizur | Rahman | Retired | Microbiology | Consultant |
| Dr | Natasha | Ratnaraja | Sandwell & West Birmingham Hospitals | Microbiology | Consultant |
| Prof | Rob | Read | University of Southampton | Infection & Immunity | Consultant |
| Dr | Chris | Record | St George's Hospital | Neurology | Core Medical Trainee Doctor |
| Dr | Anna | Riddell | Barts Health NHS Trust | Virology | Specialist Registrar |
| Dr | Rosalind | Rowland | University Hospitals Southampton NHS Trust | Elderly Care Medicine | Core Medical Fellow |
| Dr | Sarah | Rowland-Jones | Oxford University Hospitals NHS FT | Nuffield Department of Medicine | Professor / Hon Consultant |
| Dr | Razan | Saman | Leeds Teaching Hospitals NHS Trust | Medical Microbiology | Speciality Trainee |
| Dr | Alberto | San Francisco Ramos | Brighton & Sussex University Hospitals | Microbiology & Infection | Specialist Registrar |
| Dr | Frances | Sanderson | Imperial College Healthcare NHS Trust | Infectious Diseases | Consultant |
| Dr | Jenna | Schafers | North Manchester General Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Dr | Aisha | Shah | Bradford Royal Infirmary | Care of the Elderly | Core Medical Trainee Doctor |
| Dr | Avneet | Shahi | Southampton General Hospital | Infection | Consultant |
| Dr | Farah | Shahi | Hull & East Yorkshire Hospitals NHS Trust | Infection | LAS |
| Dr | Hamed | Sharaf | Belfast Health & Social Care Trust | Microbiology | Speciality Trainee |
| Dr | Davina | Sharma | Guy's & St Thomas' NHS Foundation Trust | Microbiology | Specialist Registrar |
| Dr | Robert | Shaw | Oxford University Hospitals NHS FT | Infectious Diseases/Microbiology | Specialist Registrar |
| Dr | Sharon | Sheehan | East Sussex Healthcare NHS Trust | Microbiology | Consultant |
| Dr | Emma | Sidebotham | Buckinghamshire Healthcare NHS Trust | Obstetrics and Gynaecology | Foundation Year Doctor |
| Dr | Phillip | Simpson | Sheffield Teaching Hospitals NHS FT | Infectious Diseases | Specialist Registrar |
| Dr | Karthiga | Sithamparanathan | NHS | Microbiology | Consultant |
| Dr | Jordan | Skittrall | Cambridge University Hospitals NHS FT | Infectious Diseases | Academic Clinical Fellow |
| Mr | Christopher | Smith | Imperial College Healthcare NHS Trust | Faculty of Medicine | PhD Student |
| Dr | Stephanie | Smith | Barts Health NHS Trust | Infection | Specialist Registrar |
| Dr | Noel | Snell | National Heart & Lung Institute | Airway section | Hon. Senior Lecturer |
| Dr | Igor | Starinskij | Salford Royal NHS Foundation Trust | Renal Medicine | Core Medical Trainee Doctor |
| | 1901 | Starmskij | Sanora Noyar milo Foundation must | Renar Preurente | |

| Title | Name | Surname | Hospital | Department | Grade |
|-------|-------------|-------------|---|----------------------------------|-------------------------------|
| Dr | Simon | Stoneham | Brighton & Sussex University Hospitals | Infectious Diseases | Academic Clinical Fellow |
| Dr | Rebecca | Stout | St George's University Hospital | Clinical Infection | Doctor |
| Dr | Findra S | Sudradjat | University of Manchester | Biology, Medicine & Health | PhD Student |
| Dr | Tadhg | Sullivan | London Northwest Healthcare NHS Trust | Infectious Diseases | Speciality Trainee |
| Dr | Freda | Sundram | Royal Free London NHS Foundation Trust | Microbiology | Consultant |
| Dr | Andrea | Szendroi | King's College Hospital | Medical Microbiology | Senior Clinical Scientist |
| Dr | Rachel | Taggart | Whiston Hospital | Microbiology | Specialist Registrar |
| Dr | Lionel | Tan | Imperial College London | Infectious Diseases | Honorary Consultant |
| Miss | Karen | Taylor | South London & Maudsley NHS FT | Infection Control | Assistant Director of Nursing |
| Mr | Joshua | Taylor | St George's Hospital | Medical Microbiology | Trainee Clinical Scientist |
| Dr | Adam | Telford | Frimley Park Hospital | General Medicine | Core Medical Trainee Doctor |
| Dr | Hiten | Thaker | Hull & East Yorkshire Hospitals NHS Trust | Infectious Diseases | Consultant |
| Dr | Clare | Thakker | Northwick Park Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Dr | Anastasia | Theodosiou | Southampton General Hospital | Infectious Diseases/Microbiology | Speciality Trainee |
| Dr | Amy | Thompson | Cheltenham General Hospital | Respiratory Medicine | Core Medical Trainee Doctor |
| Dr | Alexander | Vogt | Oxford University Hospitals NHS FT | Infectious Diseases | Specialist Registrar |
| Dr | Emma | Wall | University College London Hospital | Infection & Immunity | Academic Clinical Lecturer |
| Mr | Yang | Wang | Drexel University | Science & Health Systems | PhD Candidate |
| Dr | Victoria | Ward | University College London Hospital | Infectious Diseases | Core Medical Trainee Doctor |
| Dr | Christopher | Ward | St George's Hospital | Infection | Specialist Registrar |
| Dr | Ben | Warne | Cambridge University Hospitals NHS FT | Infectious Diseases | Specialist Registrar |
| Miss | Leila | White | Lancashire Teaching Hospitals NHS Trust | Microbiology | Clinical Scientist |
| Dr | John | Widdrington | James Cook University Hospital | Clinical Infection | Medical Student |
| Dr | Robert | Wiggins | Hospital of St John & Elizabeth | Microbiology | Consultant |
| Dr | Anna | Wild | Nottingham University Hospitals | Gartroenterology | Core Medical Trainee Doctor |
| Dr | Emma | Wiley | University College London Hospital | Microbiology | Specialist Registrar |
| Dr | Tom | Williams | Oxford University Hospitals NHS FT | Nuffield Department of Medicine | Foundation Year 2 Doctor |
| Mr | Timothy | Woodhead | Imperial College London | Faculty of Medicine | Medical Student |
| Dr | Kate | Woods | Homerton University Hospital NHS Trust | Microbiology | Consultant |
| Dr | Stephen | Wright | King Edward VII Hospital | Medicine | Physician |
| Dr | Tom | Yates | St George's Hospital | Clinical Infection | Core Trainee Doctor |

BIA Meetings Calendar

2018

FIS 2018 Event*

 $13^{\text{th}} - 15^{\text{th}}$ November 2018

Sage Gateshead

*Registration fees apply

BIA Trainees' Day

12th October 2018

Manchester

2019

3rd ID Dilemmas*

Thursday 24th January 2019

Manchester Conference Centre

*Registration fees may apply

12th HIV Dilemmas*

Friday 25th January 2019

Manchester Conference Centre

*Registration fees apply

FIS 2019 Event*

11th – 14th November 2019

Edinburgh

*Registration fees apply

BIA

Trainees' Day

Wednesday 22nd May 2019

London

BIA 21st Annual Scientific Meeting

Thursday 23rd May 2019

London

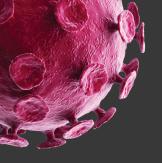
BIA Trainees' Day

October 2019

Birmingham / Manchester

More details & registration via - http://www.hartleytaylor.co.uk/confcalendar.htm

BIA Trainee Days & BIA Annual Meeting are free of charge to BIA members Call for abstracts will open in January 2019



FEDERATION OF infection societies CONFERENCE 2018

13 - 15 November 2018 Sage Gatehead





www.fis2018.co.uk

- Exciting and comprehensive programme consisting of plenary and parallel sessions delivered by an inspiring faculty of leading UK, European & International speakers
- Sessions to include:

HIV Medicine for the Microbiologist and ID Physician New Antibiotics in Immunosuppressed Patients Haematological Infections – BMT High Risk Patients The Year in Antimicrobial Stewardship BSAC Resistance Surveillance Programme Paediatric Clinical Cases and Stewardship Control of CPE

Diagnostics Travel and Tropical Medicine Bone and Joint Infection Managing Common Infections Outbreak Control Zoonosis Vaccines and much more

- Selected abstract presentations. Poster walks. Social events.
- Exhibition & Satellite Symposia opportunities

REGISTRATION NOW OPEN

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ENQUIRIES: Email: anne@hartleytaylor.co.uk / Telephone: 01565 621967



BIA Secretariat Hartley Taylor Medical Communications Ltd Suite GC, Caledonian House Tatton Street Knutsford Cheshire WA16 6AG

Administrator: Jo Wheeler

Email BIA@hartleytaylor.co.uk

Website Address http://www.britishinfection.org

Twitter @biainfection

Telephone 01565 632982