ABSTRACT BOOK

BIA

British Infection Association

16TH ANNUAL SCIENTIFIC MEETING

Thursday 16th May 2013

Brunei Gallery Lecture Theatre
School of Oriental & African Studies
London

Contents

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***Interim appointments; nominations to be invited*

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Programme

08-45 to 09-15 **Registration, coffee/tea & poster viewing**

09-15 to 09-20 **Welcome**

Dr Peter Moss (Hull), President of the BA

09-20 to 10-45 **Free Scientific Papers** (12 minutes each)

Chairs & discussants - Professor Shiranee Sriskandan (Imperial, London) & Professor David Dockrell (Sheffield)

1. Role of interleukin 17 in the innate immune response to pneumococcal infection is strain dependent. Neil D Ritchie et al. University of Glasgow

2. Early and non-reversible decrease of CD161++/Mucosal Associated Invariant T cells in HIV Infection. James Ussher et al. University of Oxford

3. Matrix destruction by neutrophils is exacerbated by hypoxia in Tuberculosis. Katharine Fox et al. Imperial College, London

4. Calcineurin inhibitors impair the host innate immune response to invasive aspergillosis likely due to a calcineurin-dependant defect in fungal killing in alveolar macrophages. Anand Shah et al. Imperial College, London

5. The role of CD8+ T-cell responses in the pathogenesis of HIV-2, a naturally contained human retroviral infection. Thushan de Silva et al. MRC Laboratories, The Gambia, Fajara, Gambia

6. HIV control in post-partum mothers; a turbulent time. Alexander Holroyd Burnett et al. Sheffield Medical School, University of Sheffield

7. HLA alleles in combination with innate immune genes are key determinants of viral outcome in Hepatitis C virus infection. Karen Fitzmaurice et al. University of Oxford

10-45 to 11-05 **Coffee/tea & poster viewing**

11-05 to 12-00 **International Keynote Lecture**

Professor Nelson Lee, Stanley Ho Center for Emerging Infections, Chinese University of Hong Kong

"Severe viral respiratory infections in Asia"

Chair & discussant - Professor Stephen Green (Sheffield)

12-00 to 12-40 **British Infection Association AGM**

Dr Peter Moss (Hull), Dr Stephen Barrett (Southend) Dr Albert Mifsud (London)

12-40 to 13-25 **Lunch & poster viewing**

13-25 to 14-15 **Free Scientific Papers** (12 minutes each)

Chairs & discussants - Dr Ashley Price (Newcastle upon Tyne) & Professor Tom Evans (Glasgow)

8. An Adenoviral model to unlock the secrets of Memory Inflation? Julia Colston et al. University of Oxford

9. Genotypic prediction of anti-microbial susceptibilities in *Staphylococcus aureus*. Claire Gordon et al. University of Oxford

10. The expression of TSST-1 by EMRSA-16. Hema Sharma et al. Imperial College, London

11. WWhole genome sequencing reveals C. difficile infection likely to arise from diverse sources**.** David Eyre et al. NIHR Oxford Biomedical Research Centre

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14-15 to 14-45 **UK State of the Art Lecture 1**

Professor Mark Wilcox, Consultant and Clinical Director Leeds Teaching Hospitals, Professor of Medical Microbiology, University of Leeds

"*Clostridium difficile* above and below the radar"

Chair & discussant – Dr David Partridge (Sheffield)

14-45 to 15-05 **Coffee/tea & poster viewing**

15-05 to 15-55 **Free Scientific Papers** (12 minutes each)

Chairs & discussants - Dr Andrew Ustianowski (Manchester) & Dr Martin Llewelyn (Brighton)

12. Burden, risk factors and public health implications of childhood TB in Kenya *results from the KIDS TB Study* * KIDS TB Study: Kilifi Improving Diagnosis & Surveillance of Childhood TB Study*. Andrew Brent et al. University of Oxford

13. The Imported Fever Service; a UK-wide system for improved management and diagnosis of fever in returned travellers. Alexander Aiken et al. Hospital for Tropical Diseases, London

14. Is MALDI-TOF worth it? The impact of MALDI-TOF on patients with positive blood cultures. Andree Evans et al. Royal Devon and Exeter NHS Foundation Trust

15. Investigating increasingly complex resistance in Enterobacteriaceae & Pseudomonas aeruginosa in critical care. Luke Moore et al. Imperial College, London

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15-55 to 16-25 **UK State of the Art Lecture 2**

Professor Robert Read, Southampton

"New developments in meningococcal vaccination"

Chair & discussant - Professor Christophe Tang (Oxford)

16-25 to 16-30 **Comfort break & poster viewing**

16-30 to 17-30 **Clinical Papers** (10 minutes each)

Chairs & discussants - Dr Julia Greig (Sheffield) & Dr Nick Beeching (Liverpool)

A. Is this the way to Armadillo? The wheel holds the key! Malika Mohabeer et al. Chelsea and Westminster Hospital

B. It's a bloody mystery. Charlotte Hall et al. Castle Hill Hospital

C. Fever in traveller returned from Nepal. Alison Burgess et al. Northwick Park Hospital

D. Memoirs of a complex case. Shumonta Quaderi et al. UCLH - Hospital for Tropical Diseases

E. Don't underestimate the value of microscopy! Shara Palanivel et al. St Helier hospital

F. Stroke and a fever - time to call Infectious Diseases? Sarah Logan et al. North West London Hospitals NHS Trust

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17-30 to 17-35 **Close of proceedings**

BIA Meetings Secretary

BIA Scientific Secretary

Dr Peter Moss, BIA President

Selected Poster Presentations:

Standardised microbiological investigations and syndromic algorithms: A partnership approach to high quality investigations in diagnostic microbiology
Ruhi Siddiqui et al. Public Health England, London

Audit of the management of suspected viral encephalitis in a district general hospital setting
Robert Shaw et al. Wexham Park Hospital

Linezolid for multi-drug resistant Tuberculosis: the Newcastle experience
Ewan Hunter et al. Newcastle Hospitals NHS Foundation Trust

Prospective evaluation of blood culture contamination and bacteraemia-related mortality at York Hospital.
Daniel Weiand et al. The York Hospital

TB Spine - more than a pain in the back
Shelui Collinson et al. St George's Hospital

Audit on b-lactam allergy: implications and costs
Giovanni Satta et al. Royal Free London NHS Foundation Trust

Daptomycin in the treatment of gram-positive infections and bacteraemia: Patient registry experience (2006-11)
Muhammad Raza et al. Newcastle upon Tyne NHS Foundation Trust

Infective endocarditis in the Kennemerland region (NL) 2004-2011: demography, diagnosis and prognosis
Floris van den Brink et al. St Antonius Ziekenhuis, Nieuwegein, The Netherlands

Clinical experience with daptomycin treatment of osteomyelitis: 6-year retrospective analysis from the EU-CORE^{SM} registry
R. Andrew Seaton et al. Gartnavel General Hospital

Spontaneous meticillin-sensitive *Staphylococcus aureus* discitis – short course antibiotic therapy may be adequate. Evidence from a large single centre cohort.
Thomas Locke et al. Sheffield Teaching Hospitals

The changing epidemiology of Clostridium difficile; an observational and interrupted time series study.
Thomas Moore et al. Brighton and Sussex Medical School

Causes of fever in the returning traveller
Andrew Taylor et al. UCH, London

Clostrium difficile in the emergency department: are we helping or hindering?
Timothy Shaw et al. Royal Victoria Hospital, Belfast

TB Meningitis: A wolf in wolf's clothing.
Claire Mullender et al. St Georges Hospital Healthcare NHS Trust

Deciphering Discitis: Results from a tertiary referral centre.
Richard O'Sullivan et al. Newcastle University Medical School

Invasive non-typhoidal Salmonella in patients referred to an Infectious diseases unit at Leicester Royal Infirmary.
Rosemarie FitzGerald et al. Leicester Royal Infirmary

Antifungal prescribing in patients requiring intensive (ICU) and high dependency (HDU) care at St. James's Hospital
A Talento et al. St James Hospital

Service Evaluation of the treatment of ESBL- and AmpC-producing *E.coli* bacteraemia in Sheffield: Does treatment with co-amoxiclav, piperacillin-tazobactam and cephalosporins alter clinical outcome?
Bala Subramanian et al. Sheffield Teaching Hospitals

Scratching the surface
Alison Sears et al. St George's Hospital, London

Keynote Lectures

Professor Nelson Lee
Stanley Ho Center for Emerging Infections, Chinese University of Hong Kong

Severe viral respiratory infections in Asia

In the past decade, the world has experienced continuous threats from various emerging infectious diseases caused by novel viral pathogens. Avian influenza H5N1 first emerged in 1997 in Hong Kong and re-remerged in 2003, and since then became widespread and endemic in Asia. Severe Acute Respiratory Syndrome (SARS)-associated coronavirus emerged in 2003 in Guangdong, China, which had spread via air travel to the world within just a few weeks. In 2009, a swine-origin H1N1 influenza virus had resulted in a pandemic; Asian cities were hit hard and the virus has continued to circulate. In late 2012, another coronavirus has emerged which causes lethal diseases similar to SARS. At the moment, there is an on-going epidemic caused by a novel avian influenza H7N9 virus in the east coast of China. These emerging viruses are all zoonotic in origin, have acquired ability to infect humans and escape innate host defense, and can cause rapidly fatal pneumonitis. In this lecture, the lessons learnt from the SARS outbreak in Hong Kong, and their implications for the control and management of the new coronavirus will be discussed. The impacts of severe seasonal and pandemic H1N1 influenza in Asian cities; their importance relative to other viruses such as RSV; the challenges faced in the treatment of severe influenza infections, and strategies used to prevent nosocomial transmission will be described. Clinical aspects of human H5N1 and H7N9 avian influenza infections, and the issues related to case detection and management of these emerging infections will be summarized.

Professor Robert Read
University of Southampton

New developments in meningococcal vaccination

Meningococcal vaccination has been remarkably successful -Glycoconjugate vaccines against all serogroups except meningococcal serogroup B are now available. A Meningococcal serogroup C vaccine has been used in routine vaccination campaigns in the UK since 1999 and has since been introduced in several other countries. Quadrivalent (ACYW135) conjugate vaccines have been licensed in the US and Canada and a mass vaccination campaign of 1-29 yr olds with a Men A conjugate vaccine (MenAfrivac) is currently being rolled out in the African Sub-Saharan meningitis belt. Recent data has shown that protective titres wane after glycoconjugate vaccines especially in young children despite the T-cell dependent mechanism and booster strategies are required.

Numerous strategies to protect against serogroup B have been attempted including purified outer membrane protein vaccines. These have been successful in controlling regional outbreaks with restricted clonality but the immunodominance of PorA renders them narrow in their spectrum. Another strategy resulted from annotation of the genome sequence of serogroup B *N.meningitidis*, from which multiple surface antigens were identified, a minority of which were already well described, revealing many hithero undiscovered potential surface antigens. One novel vaccine using recombinant proteins identified in this was has been licensed by the EMA which contains OMV from a single strain together with antigens NHBA, NadA, and and fHbp. The vaccine is immunogenic in infants after a 4 dose schedule (2,3,4 ad 12 months) or a single 12 month dose alone. It covers around 70% of current UK strains. A similar approach is being used in a different vaccine which combines two factor H binding protein moieties (fHbp). Whether these vaccines will be deployed in the UK may rest on whether they can elicit herd immunity by an effect on colonisation and results of carriage studies in young UK adults will be available soon.

Title	**Role of interleukin 17 in the innate immune response to pneumococcal infection is strain dependent.**
Authors	Neil D Ritchie[1], Tim J Mitchell[2], Tom J Evans[1]
Address	*University of Glasgow, Glasgow, UK[1], University of Birmingham, Birmingham, UK[2]*

Abstract

Introduction
The cytokines interleukin 17A and interleukin 22 have a role in mucosal immunity within the lung. However, their role in innate immunity to pneumococci remain poorly understood.

Aim
To assess the role of IL-17A and IL-22 in pneumococcal infection caused by two different serotypes.

Methods
Wild type (WT) , IL-17 receptor A-/- and IL-22-/- C57Bl/6 mice were infected intranasally with serotype 4 (TIGR4) and serotype 3 (SRL1) organism. Neutrophils for in vitro experiments were obtained by peritoneal lavage following injection of casein.

Results
TIGR4 was cleared from the lungs of mice within 48 hours but caused bacteraemia, empyema and clinically severe infection with marked weight loss. In contrast, SRL1 invaded into blood late in the course of infection but caused a dense pneumonia with purulent empyema. IL-17A and IL-22 were detected in alveolar lavage within 6 hours of infection. When knockout mice were infected with TIGR4, IL-17RAKO mice were more likely to reach the end-point than WT ($P < 0.05$). In contrast, when infected with SRL1 wild type mice were more likely to reach the end-point than WT ($P=0.004$). With both strains, IL-22KO mice had an intermediate response. IL17RAKO mice had decreased neutrophils in blood and lung early in the course of infection in keeping with the known biological actions of IL-17A. In vitro killing of SRL1 by mouse neutrophils was ineffective in bacterial killing whereas TIGR4 was phagocytosed and killed.

Conclusion
IL-17 is beneficial in infection caused by a highly invasive pneumococcus but harmful in localized pulmonary infection.

Title **Early and non-reversible decrease of CD161++/ Mucosal Associated Invariant T cells in HIV Infection**

Authors Cormac Cosgrove[1], James Ussher[1], Andri Rauch[2], Kathleen Gärtner[1], Ayako Kurioka[1], Michael Hühn[1], Joannah Fergusson[1], Peter Simmonds[3], Philip Goulder[1], Ted Hansen[4], Julie Fox[5], Huldrych Günthard[6], Nina Khanna[7], Fiona Powrie[1], Alan Steel[8], Brian Gazzard[8], Rodney Phillips[1], John Frater[1], Holm Uhlig[1], Paul Klenerman[1]

Addresses *University of Oxford, Oxford, UK[1], University Hospital Berne, Berne, Switzerland[2], University of Edinburgh, Edinburgh, UK[3], Washington University School of Medicine, St Louis, MO, USA[4], Guys and St Thomas' NHS Trust, London, UK[5], University Hospital Zurich, Zurich, Switzerland[6], University Hospital Basel, Basel, Switzerland[7], Chelsea and Westminster Hospital, London, UK[8]*

Abstract

Background
The risk of tuberculosis is increased early in HIV infection despite relative preservation of the $CD4^+$T-cell count. The mechanism for this is unclear. Mucosal invariant T (MAIT) cells are an abundant innate-like $CD161^+$T-cell population restricted by the non-polymorphic MHC-related 1 (MR1) protein. MAIT-cells are involved in antibacterial defense at epithelial sites. MAIT-cells are activated and secrete interferon-g upon exposure to diverse bacterial species, including *Mycobacterium tuberculosis*. The role of MAIT-cells in HIV infection remains to be defined.

Methods and Results
We analyzed MAIT-cells in the blood of patients with acute or chronic HIV infection. Significant depletion of MAIT-cells was seen in both acute and chronic HIV infection compared with healthy controls (2.4% vs 2.4% vs 10.7%, $p<0.01$). MAIT-cells were not sequestered in the colon in HIV infection compared with healthy controls (226 vs 147 cells/mm^2, $p=0.17$), and there was a significant reduction as a proportion of $CD8^+$T-cells (14.5% vs 32.3%, $p=0.0024$). No recovery was seen in the blood with prolonged antiretroviral therapy. To define the mechanism of depletion we exposed MAIT-cells in vitro to relevant stimuli including HIV and *E. coli*. While no MAIT-cell infection, activation, or death was seen with HIV, exposure to *E. coli* induced MR1-dependent activation and apoptosis.

Conclusions
We propose a model whereby MAIT-cells are lost early in HIV infection due to activation by translocated microbial products, and subsequent apoptosis. The loss of MAIT-cells in acute HIV infection may contribute to the increased susceptibility of HIV-infected patients to bacterial pathogens such as *M. tuberculosis*.

Title	**Matrix destruction by neutrophils is exacerbated by hypoxia in Tuberculosis**
Authors	Katharine Fox, Catherine Ong, Anna Ettorre, Jon Friedland
Addresses	*Imperial College of London, London, UK*

Abstract

Introduction
Hypoxic lung granulomas and tissue destruction are hallmarks of *Mycobacterium tuberculosis* (*M.tb*) infection. Neutrophils secrete proteases, such as matrix metalloproteinases (MMPs) and neutrophil elastase (NE), and mesh-works of extracellular DNA termed neutrophil extracellular traps (NETs). These are associated with tissue damage and inflammation.We hypothesise that hypoxia modulates neutrophil associated tissue destruction and inflammation in Tuberculosis (TB).

Methods
Neutrophils were stimulated with conditioned media from *M.tb*-infected monocytes (CoMTB) or UV-killed *M.tb*, and incubated in normoxia (21% oxygen) or hypoxia (1% oxygen). Protease secretion was analysed using luminex array, gelatine zymography and ELISA, and gene expression by RT-PCR. Quantitative fluorescence assays, immunofluorescence and confocal microscopy examined NETS, matrix degradation and phagocytosis. Flow cytometry and Annexin-V staining evaluated cell apoptosis.

Results
On stimulation with CoMTB hypoxia significantly increased MMP-8 secretion at 24 hours ($p<0.001$) and 30 hours ($p<0.05$); reflected in *Mmp-8* gene expression. MMP-9 secretion and gene expression was unaffected. Likewise, neutrophil elastase secretion increased 1.7 fold ($p<0.05$) in hypoxia. In hypoxia collagenase activity increased 2-fold ($p<0.01$) and elastase activity 1.6-fold ($p<0.05$).With UV-killed *M.tb* there was a significant increase in NET production; from 292 ng/ml DNA in normoxia to 590 ng/ml DNA in hypoxia ($p<0.05$). In comparison to normoxia, hypoxia decreased neutrophil apoptosis in unstimulated cells ($p < 0.01$) but not with CoMTB stimulation. Phagocytosis of *M.tb* was unaffected.

Conclusions
Hypoxia increases neutrophil-driven matrix destruction in TB which is associated with increased secretion of MMP-8, NE and NETs. Interventions targeting hypoxia-driven tissue damage may improve patient outcome.

Free Scientific Paper 4

Title	**Calcineurin inhibitors impair the host innate immune response to invasive aspergillosis likely due to a calcineurin-dependant defect in fungal killing in alveolar macrophages.**
Authors	Anand Shah[1,2], Susanne Herbst[1], Shichina Kannambath[1], Martin Carby[2], Sunil Shaunak[1], Darius Armstrong-James[1]
Addresses	*Imperial College, London, UK[1], Royal Brompton and Harefield NHS Trust, London, UK[2]*

Abstract

Invasive fungal infections are a major cause of mortality amongst solid-organ transplant recipients in whom steroids and calcineurin inhibitors form the mainstay of immunosuppression. We have developed a novel BALB/c murine model of invasive aspergillosis with transplant relevant Tacrolimus (FK506) and hydrocortisone which shows increased mortality from pulmonary aspergillosis as compared to hydrocortisone only immunosuppression. Lung histopathology showed neutrophil invasion and tracheobronchitis that was associated with reduced lung TNF-α, JE and KC at 24 hours, but increased lung TNF-α, JE and KC at 48 hours when fungal burden was high. Furthermore, FK506 directly impaired fungal killing in murine alveolar macrophages in vitro. Rag2-/- mice with pulmonary aspergillosis show significant incremental mortality with FK506 indicating a defect in the innate immune system.

To translate our work to a human clinical cohort we have shown significant reduction in TNF-α production in vitro by human alveolar macrophages stimulated with aspergillus fumigatus in the presence of FK506 alongside reduced fungal killing. We have additionally shown NFAT activation (nuclear factor of activated T cells which is the downstream transcription factor target of calcineurin) folllowing stimulation with *Aspergillus fumigatus* using nuclear translocation analysis by confocal microscopy and Imagestream analysis.

Our work to date suggests a calcineurin-dependant innate defect in fungal killing as a cause for the increased incidence of invasive fungal infections within solid organ transplantation and we present a novel relevant murine model to obtain a better mechanistic insight into the effects of calcineurin inhibitors on the innate immune response.

Title **The role of CD8+ T-cell responses in the pathogenesis of HIV-2, a naturally contained human retroviral infection**

Authors Thushan de Silva[1,3], Yanchun Peng[2], Aleksandra Leligdowicz[1,2], Irfan Zaidi[1], Lucy Li[1], Harry Griffin[2], Marie-Eve Blais[2], Tim Vincent[1], Mavinga Saraiva[1], Louis-Marie Yindom[1,2], Carla van Tienen[1], Assan Jaye[1], Hilton Whittle[1,4], Tao Dong[2], Sarah Rowland-Jones[2]

Addresses *MRC Laboratories, The Gambia, Fajara, Gambia[1], Weatherall Institute of Molecular Medicine, Oxford, UK[2], University of Sheffield, Sheffield, UK[3], London School of Tropical Medicine and Hygiene, London, UK[4]*

Abstract

Introduction
While a significant proportion of HIV-2-infected individuals are asymptomatic and maintain undetectable viral loads (controllers), 15-20% progress to AIDS and are predicted by detectable viraemia. Identifying immune correlates that distinguish these two groups should provide insights into how a potentially pathogenic retrovirus can be naturally controlled.

Methods
We performed a detailed study of HIV-2-specific cellular responses in a unique community cohort in Guinea-Bissau followed for over two decades. T-cell responses were compared between controllers (n = 33) and viraemic subjects (n = 27) using overlapping peptides, MHC class I tetramers and multi-parameter flow cytometry.

Results & discussion
HIV-2 viral control was significantly associated with a high magnitude, polyfunctional Gag-specific CD8+ T-cell response, but not with greater perforin upregulation. This potentially protective HIV-2-specific response is surprisingly narrow. HIV-2 Gag-specific CD8+ T-cells are at an earlier stage of differentiation than CMV-specific CD8+ T-cells, do not contain high levels of cytolytic markers and exhibit low levels of activation and proliferation, representing distinct properties from CD8+ T-cells associated with HIV-1 control. These data reveal the potential T-cell correlates of HIV-2 control and the detailed phenotype of virus-specific CD8+ T-cells in a naturally contained retroviral infection. Furthermore, comparison of viral capsid sequence data from HIV-1 and HIV-2 infected subjects in this cohort reveal limited T-cell driven changes in HIV-2, despite potent T-cell pressure, which may be a significant factor in the benign course of infection seen in most HIV-2 infected subjects.

Free Scientific Paper 6

Title	**HIV control in post-partum mothers; a turbulent time**
Authors	Alexander Holroyd Burnett[1], Julia M. Greig[2], Simone Naylor[2]
Addresses	*Sheffield Medical School, University of Sheffield, Sheffield, UK[1], Department of Infectious Diseases, Sheffield Teaching Hospitals, Sheffield, UK[2]*

Abstract

Background
The management of pregnant HIV positive women can be complex and much has been published on this. However less work has looked at the post-partum period. We conducted an audit of post-partum women's concordance with treatment; and investigated the reasons behind any non-concordance.

Methods
We retrospectively analysed the case notes of HIV positive pregnancies in Sheffield since January 2000. Planned ARV management and actual ARV management at 12 months post-partum was recorded, as were CD4 counts and HIV viral load (at birth, 1 month and 12 months post-partum) along with any social issues recorded in the clinic notes.

Results
47 episodes were analysed; 42 women were concordant with their management plans (89%), whilst 5 (11%) stopped treatment against advice. Of those who continued treatment 13 (40.6%) had significantly raised viral loads (>40 copies/ml) during the post-partum period. Social problems were noted for 38 (81%) women and common themes included; depression (30%), childcare problems (19%) and housing problems (13%) as well as sexual abuse, physical abuse and sex trafficking. Four of the five women who stopped treatment against advice were depressed as were 54% of the women who had a raised viral load. In contrast only 16% of women on treatment who weren't depressed had a raised viral load.

Discussion
The variety of social issues experienced emphasizes the need to continue an MDT approach into the post-partum period. Engaging with and managing psychiatric and social issues may help improve treatment outcomes in the post-partum period in HIV positive mothers.

Free Scientific Paper 7

Title	**HLA alleles in combination with innate immune genes are key determinants of viral outcome in Hepatitis C virus infection**
Author	Karen Fitzmaurice[1], Jacob Hurst[1], Megan Dring[2], Clair Gardiner[2], Paul Klenerman[1], Irish HCv Research Consortium -[2]
Address	*University of Oxford, Oxford, UK[1], Trinity College Dublin, Dublin, Ireland[2]*

Abstract

Chronic Hepatitis C virus (HCV) infection is a leading cause of liver related morbidity. Both the innate and adaptive immune response are thought to be important in determining viral outcomes. Polymorphisms associated with the IL28B gene are strongly associated with both spontaneous and treatment outcomes.

Objective
This study investigates the importance of HLA genes in the context of polymorphisms in the innate immune genes IL28B and KIR.

Design
We assess the influence of HLA Class I and II genes on viral outcomes in an Irish cohort of women who had been infected from a single source. In this cohort, a number of HLA alleles are associated with different outcomes and the impact of IL28B polymorphisms as a determinant of outcome is profound. Genotyping on 319 women was available.

Results
Logistic regression was performed and indicates that the HLA-A*03 (OR 0.36 [0.15-0.89], p=0.027) -B*27 (OR 0.12[0.03-0.45], p=<0.001), -DRB1*0101 (OR 0.2 [0.07-0.61], p=0.005), -DRB1*0401 (OR 0.31 [0.12-0.85, p=0.02) and the CC IL28B rs12979860 genotype (OR 0.1 [0.04-0.23], p<0.001) are significantly associated with viral clearance. Furthermore, DQB1*0201 (OR 4.2 (2.04-8.66], P=0.008), KIR2DS3 (OR 4.36 [1.62-11.74], p=0.004) and IL28B rs12979860 IL28B CT/TT genotype (OR 0.1[0.04-0.23], p<0.001) are associated with chronic infection. This study finds no interactive effect between IL28B and these Class I and II alleles in relation to viral clearance. There is however, a strong additive effect.

Conclusion
This data supports a critical role for the adaptive immune response in the control of HCV in concert with the innate immune response.

Title	**An Adenoviral model to unlock the secrets of Memory Inflation?**
Author	Julia Colston[1], Beatrice Bolinger[1], Alison Turner[2], Sarah Gilbert[2], Paul Klenerman[1]
Address	*Oxford University - The Peter Medawar Building for Pathogen Research, Oxford, UK[1], Oxford University - The Jenner Institute, Oxford, UK[2]*

Abstract

Introduction
"Memory Inflation" was first reported in murine cytomegalovirus (MCMV) infection. A subset of $CD8^+$ T-cell responses were noted to gradually increase over time, becoming very dominant (one response accounting for up to 30% of all $CD8^+$ T-cells). This parallels the huge expansion of $CD8^+$ T-cells seen in those infected with human CMV (HCMV), especially in the elderly, where such exaggerated responses are thought relevant to "immunosenescence". Additionally these responses are harnessed in novel vaccine design. However, the mechanisms underlying memory inflation are not well understood, particularly why only some responses inflate and not others.

Methods
We developed an *in vivo* model using a recombinant non-replicative Adenovirus expressing ßgalactosidase under a CMV promoter (Ad-LacZ). Two responses (D8V and I8V) were tracked using MHC peptide tetramers, in B6 mice and those lacking immunoproteasomes ($LMP7^{-/-}$). We then made novel vectors with the "minigenes" expressing the two epitopes (Ad-D8V and Ad-I8V).

Results
Using Ad-LacZ, inflation was observed equivalent to that of CMV. Processing of the non-inflating epitope (I8V) was completely dependent on the immunoproteasome, while that of the inflating epitope (D8V) was independent. Inflation after Ad-D8V infection was comparable to that seen in Ad-LacZ. Critically, the Ad-I8V minigene construct also induced inflation.

Discussion
Inoculation with Ad-LacZ reproduces memory inflation identical to CMV. Inflating epitopes are associated with immunoproteasome independence, suggesting presentation on non-classical antigen presenting cells. We can induce inflation to a "non-inflating" epitope by removing processing. These data have implications for the design of vaccines, as well as CMV associated "immunosenescence".

Free Scientific Paper 9

Title **Genotypic Prediction of Anti-microbial Susceptibilities in *Staphylococcus aureus***

Author Claire Gordon[1,3], Tanya Golubchik[2,3], James Price[4], Sarah Walker[3], Tim Peto[1,3], Derrick Crook[1,3]

Address *NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK[1], Department of Statistics,University of Oxford, Oxford, UK[2], Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK[3], Department of Infectios Diseases and Microbiology, Royal Sussex County Hospital, Brighton, UK[4]*

Abstract

Background
Whole genome sequencing is increasingly rapid and affordable, with costs and turnaround times likely to approach those of traditional bacterial identification and susceptibility testing methods. This study assesses the use of whole genome data for the prediction of anti-microbial susceptibilities for *Staphylococcus aureus*.

Method
Whole genome sequences of 508 non-duplicate *S. aureus* bacteraemia and nasal carriage isolates were obtained using the Illumina HiSeq 2000, and screened for 23 genes associated with resistance to 11 first line anti-microbials using BLAST. In 18 of these genes, resistance is due to gene presence (eg mecA) and in the other 5, resistance is conferred by point mutations (eg rpoB). Sequences matching the reference alleles were identified from *de novo* assembled genomes and, where relevant, screened for point mutations. Results were compared with phenotypic susceptibilities determined by disc diffusion and, where appropriate, E-test.

Results
Across all isolates, 1012 individual resistance phenotypes were found, for which genetic resistance determinants were detected in 992 (98%). Overall specificity for resistance prediction was 0.999 (95% CI 0.999-1). There were 20 false negatives for a resistance determinant (sensitivity 0.98, 95% CI: 0.96-0.99). Of these, 9 were for fucidic acid and 7 were for ciprofloxacin.

Conclusion
Whole genome sequence data reliably predicted susceptibility to 11 first line anti-microbials for *S. aureus*, supporting the use of rapid turnaround sequencing to provide fast, accurate susceptibilities. Expanding the panel of genes will improve the sensitivity at no additional cost.

Title **The Expression of TSST-1 by EMRSA-16**

Author Hema Sharma[1], Debra Smith[1], Angela Kearns[2], Shiranee Sriskandan[1]

Address *Imperial College London, London, UK[1], Health Protection Agency, London, UK[2]*

Abstract

Background
Staphylococcal toxic shock syndrome (TSS) is attributed to superantigens such as toxic shock syndrome toxin-1 (TSST-1), genetically encoded by *tst*. *Staphylococcus aureus* (SA) strains such as epidemic methicillin-resistant SA-16 (EMRSA-16) may carry *tst* but not cause TSS.

Aims
To investigate UK TSS epidemiology and TSST-1 expression by *tst*+ EMRSA-16 and methicillin-sensitive SA (MSSA).

Methods
TSS cases referred to Public Health England between January 2008 and December 2011 were analysed. EMRSA-16 and TSS-associated MSSA strains of clonal complex 30 were chosen for investigation. The *tst* gene, promoter, regulators and staphylococcal pathogenicity island (SaPI) harbouring *tst* were sequenced by whole genome sequencing. TSST-1 in supernatants was quantified by western blot. *tst* transcription was analysed by qRT-PCR. Supernatant mitogenicity was determined by human PBMC and human HLA-DQ/DR transgenic-mouse splenocyte 3[H]-thymidine incorporation assays. A mouse abscess model is being used to compare inflammation by measuring cytokines in serum and lesion fluid and TSST-1 locally.

Results
150 TSS cases were reported over four years; six (4%) due to MRSA. The *tst* gene, promoter and SaPI sequences were identical amongst strains. EMRSA-16 strain TSST-1 production and transcription peaked before MSSA and was less abundant. Excluding strains also carrying staphylococcal enterotoxin A (SEA), MSSA supernatants were more mitogenic than EMRSA-16 supernatants.

Conclusions
EMRSA-16 strains transcribe and produce less TSST-1 than MSSA strains of the same lineage. EMRSA-16 strains without SEA are less mitogenic. Differences in global gene regulators or the carriage of a large SCC*mec* element by EMRSA-16 may account for the paucity of MRSA-associated TSS.

Free Scientific Paper 11

Title	**Whole genome sequencing reveals C. difficile infection likely to arise from diverse sources**
Author	David Eyre[1], Madeleine Cule[1], Derrick Crook[1], Mark Wilcox[2], Tim Peto[1], A Sarah Walker[1]
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Abstract

Introduction
Clostridium difficile infection (CDI) has traditionally been considered predominantly transmitted within hospitals. However, endemic spread hampers identification of sources of infections and the assessment of intervention efficacy.

Methods
All symptomatic hospital/community CDI cases from Oxfordshire, UK, September2007-March2011, underwent whole-genome sequencing (WGS). Single nucleotide variants (SNVs) between cases were compared using *C. difficile* evolution rates estimated from 145 serially-sampled patients (0-2SNVs expected between transmitted isolates <124days apart, and 0-3SNVs for isolates 124-364days apart, 95% prediction intervals). Plausible epidemiological links between genetically-related cases were identified from hospital admission/community location data.

Results
1223/1253(98%) CDI were successfully sequenced. 333/957(35%) CDI from April2008-March2011 were within 2SNVs of ≥1 previous case since September2007; 428/957(45%) were >10SNVs from all previous cases. Of 333 cases ≤2SNVs from a prior case (consistent with transmission), 126/333(38%) shared ward-based contact within plausible limits on infectious/incubation periods; 120/333(36%) had no hospital/community contact. Distinct subtypes (cases >10SNVs from all previous cases) continued to be identified consistently throughout the study, suggesting cases arise from a considerable reservoir of C. difficile. Surprisingly, declines in the incidence of genetically-related CDI (≤2SNVs from a previous case) were similar to those in genetically distinct (>10SNVs) CDI suggesting interventions not just targeting symptomatic individuals, e.g. antimicrobial stewardship, have played a significant role in recent CDI declines.

Discussion
Genetically diverse sources, other than symptomatic patients, play a major part in *C. difficile* transmission. Independently of epidemiological data, 45% of Oxfordshire CDI was genetically-distinct from all previous cases. Factors other than interrupting symptomatic transmission have been important in CDI declines.

Free Scientific Paper 12

Title	**Burden, risk factors and public health implications of Childhood TB in Kenya *Results from the KIDS TB Study* * KIDS TB Study: Kilifi Improving Diagnosis & Surveillance of Childhood TB Study***
Author	Andrew Brent[1,2], Christopher Nyundo[2], Evasius Bauni[2], Michael Levin[3], Anthony Scott[4,2]
Address	*University of Oxford, Oxford, UK[1], KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya[2], Imperial College London, London, UK[3], London School of Hygiene & Tropical Medicine, London, UK[4]*

Abstract

Introduction
Children are at high risk of tuberculosis disease following infection, and may account for up to 40% of cases in high burden settings. However diagnosis is challenging and surveillance data limited. We established intensified case finding and state of the art TB diagnostics to investigate the epidemiology of childhood TB in Kenya.

Methods
The study was conducted at Kilifi District Hospital in Kenya, nested within the Kilifi Health & Demographic Surveillance Survey (KHDSS). Between 2009 and 2011 child household TB contacts and children presenting with features of TB were carefully investigated. Incidence estimates were derived using KHDSS denominator data, and adjusted for the sensitivity of hospital-based surveillance using notification, vital registration, verbal autopsy and spatial data. Epidemiological risk factors for TB were identified in a nested case control analysis.

Results
The estimated community incidence of childhood TB was 46 per 100,000/year for Kilifi. A conservative estimate suggested the disease burden in Kenya is more than double official figures. Known close TB contact, HIV infection and malnutrition were all identified as risk factors. The population attributable fraction of a known TB contact was 51.4%.

Discussion
This is one of very few prospective incidence studies from high burden countries, the first from East Africa, and the first to quantify the disease burden attributable to a known close TB contact. It suggests that most cases in Kenya are not currently diagnosed or notified, and that half of all cases are potentially preventable by implementing current recommendations for isoniazid chemoprophylaxis.

Free Scientific Paper 13

Title **The Imported Fever Service; a UK-wide system for improved management and diagnosis of fever in returned travellers**

Author Alexander Aiken[3], Jonathan Lambourne[1,2], Amanda Semper[1], Meera Chand[1,5], Jane Osborne[1], Behzad Nadjm[3], Catherine Roberts[4], Katherine Russell[5], Surabhi Taori[1], Malur Sudhanva[1,6], Peter Chiodini[3], Nick Beeching[7], Tim Brooks[1]

Address *Rare and Imported Pathogens Laboratory, Microbiology Services, PHE, Porton Down, UK[1], Clinical Microbiology & Virology, UCLH NHS Foundation Trust, London, UK[2], Hospital for Tropical Diseases, London, UK[3], Imperial College London, London, UK[4], Public Health England, London, UK[5], King's College Hospital NHS Foundation Trust, London, UK[6], Liverpool School of Tropical Medicine, Liverpool, UK[7]*

Abstract

Introduction
Poor integration of diagnostic services can delay the diagnosis of febrile illness in returning travelers, with significant clinical and public health consequences. The Imported Fever Service (IFS) was established in 2012 as a national specialist diagnostic and clinical advice service for acute imported fevers. We summarise the first 9 months' activity.

Methods
The IFS is a collaboration between the Rare and Imported Pathogens Laboratory, the Hospital for Tropical Diseases and the Liverpool School of Tropical Medicine. It combines 24-hour clinical advice and diagnostic services capable of rapidly detecting 'exotic' pathogens, including VHFs. For each referral a panel of tests, based on the patient's travel is performed and relevant clinical data are collected.

Results
Between June 2012 and February 2013, 143 cases were referred from 84 UK centres. 43 (30%) diagnoses were made following referral to the service. Patients had travelled to Africa (32%), Asia (24%) and Europe (15%). Presenting complaints included neurological (24%), undifferentiated fever (23%) and respiratory (14%). The IFS diagnosed: murine typhus (n=7), spotted fever, dengue (n=4 each), Q fever, sandfly fever, leptospirosis (n=3 each), Tick-Borne encephalitis, scrub typhus, hantavirus and CCHF (1-2 cases each). The service helped infection control and public health responses to CCHF and **autochthonous hantavirus cases.**

Discussion
Referral to the IFS resulted in rapid diagnosis of illness in 30% of returned travellers with otherwise undiagnosed fever. These diagnoses informed critical clinical, infection control and public health decisions and demonstrate the IFS model is feasible, effective and could be reproduced in other countries.

Title	**Is MALDI-TOF worth it? The impact of MALDI-TOF on patients with positive blood cultures.**
Author	Andree Evans, Michelle Hincke, Matt Allen, Cressida Auckland
Address	*Royal Devon and Exeter NHS Foundation Trust, Exeter, Devon, UK*

Abstract

MALDI-TOF (Matrix Assisted Laser Desorbtion/ Ionisation Time Of Flight) is technology with the potential to identify blood culture isolates within 5 hours of the culture becoming positive. What is unclear is if this information has any effect on clinical management of patients.

We processed 250 consecutive positive blood cultures from 210 patients by:
A - the National Standard Method

B1 - Samples positive 8 am - 1pm were processed by a rapid MALDI-TOF protocol with identification attempted on 4 hour growth from samples sub-cultured to chocolate agar

B2 - Samples positive outside these hours had colonial growth identified by MALDI-TOF from plates processed as per National Standard Method.

Patient notes were reviewed to assess impact of earlier identification on time to targeted antibiotic choice and any other clinical consequences.
This study was performed in a clinical diagnostic laboratory under normal working conditions, thus demonstrating the minimum clinical benefit that the MALDITOF protocol can deliver within these limitations.

The MALDI-TOF had demonstrable clinical benefits in 24/250 samples which led to 18 /210 patients having targeted antibiotic treatment started at least 1 day earlier than using the standard protocol. This technology improved antibiotic use, aided antimicrobial stewardship and improved patient care.

The principle benefit was seen in organisms with reliable antibiotic resistant profiles e.g. AmpC producing coliforms and Enterococci.
With further developments regarding ESBL and carbapenemase detection, this technology has the potential to revolutionise both laboratory and clinical working practices. Until these developments are available we feel that MALDI-TOF identification should be offered in our laboratory.

Free Scientific Paper 15

Title	**Investigating increasingly complex resistance in *Enterobacteriaceae* & *Pseudomonas aeruginosa* in critical care.**
Author	Luke Moore[1,2], Hugo Donaldson[2], Claire Thomas[2], Eimear Brannigan[1,2], Alison Holmes[1,2]
Address	*Centre for Infection Prevention & Management, Imperial College, London, UK[1], Imperial College Healthcare NHS Trust, London, UK[2]*

Abstract

Introduction
Time to appropriate antimicrobial therapy in critical care sepsis directly impacts outcome, with knowledge of resistance patterns being key. We investigate resistance trends in *Enterobacteriaceae* and *Pseudomonas aeruginosa* from critical care units in two UK tertiary referral hospitals to explore the utility of continued reliance on piperacillin-tazobactam and carbapenems in the empiric management of sepsis.

Method
Clinical isolates submitted to a central laboratory serving the two critical care units were retrospectively identified for a 36 month period from 2009 to 2012. Inter-unit variation and temporal trends were reviewed.

Results
Across both hospitals over the three years 3125 clinical isolates from 1081 patients were identified. Within the *Enterobacteriaceae* we find ESBL/AmpC phenotypic prevalence at 25.2- 52.2%, with carbapenem resistance at 0.7- 2.4%. Amongst *P.aeruginosa* piperacillin-tazobactam resistance was 8.4- 25.2% with carbapenem resistance at 30.7- 53.3%. We find statistically significant year by year temporal fluctuation and inter-unit variations in these resistance rates.

Discussion
Regularly updated unit specific antibiograms can assist in guiding empiric antimicrobial decisions. Continuing escalation of antimicrobials in response to resistant organisms may be further driving resistance and warrants detailed investigation. The prevalence of ESBL/AmpC producing *Enterobacteriaceae* combined with marked carbapenem resistance amongst *P.aeruginosa* gives rise to concern on reliance for either beta-lactam based therapy or carbapenems in empiric sepsis treatment. This data illustrates a key need for development of more rapid resistance determination to improve time to appropriate antimicrobial therapy in critical care sepsis. Such rapid resistance profiling may potentially be met by adoption of phenotypic or genotypic technologies.

Cryptic Clinical Case A

Title	**Is this the way to Armadillo? The wheel holds the key!**
Authors	Malika Mohabeer[1], Amita Patel[2], John Klein[2], Nicholas Price[2]
Address	*Chelsea and Westminster Hospital, London, UK[1], St Thomas Hospital, London, UK[2]*

Abstract

A 22-year-old previously fit and well, man presented to our Accident and Emergency Department with a 40-day history of malaise, fever and weight loss. He had had a recent productive cough, now resolved. He also had painful neck lumps. He had arrived in London four years previously from South America.

He was pyrexial at 38.5^0C and tachycardic. He had generalised tender lymphadenopathy including a suppurating cervical node. Examination of the mouth revealed a soft tissue mass arising from the hard palate and inflamed, swollen gums.

He had a raised white cell count with a neutrophilia of $18.9x10^9$ /L. His haemoglobin was 11.6 g/dL, C-reactive protein was 309 mg/L, alkaline phosphatase was 212 IU/L. Chest radiography was unremarkable. He was tested for HIV and multiple blood cultures were sent.

He continued to be febrile on the ward, though clinically very stable.

He was sent for lymph node resection and histological examination revealed a very typical, though unusual, appearance. Culture of pus from the cervical node revealed an organism with a similar appearance.

Computed tomography showed necrotic cervical lymph nodes and axillary and inguinal lymphadenopathy. There was no evidence of deep organ involvement.

The patient was treated with agents guided by the above findings. He remained well and, after three months, his blood tests had normalised and all physical manifestations has regressed.

Cryptic Clinical Case B

Title	**It's a bloody mystery**
Authors	Charlotte Hall[1], Kate Adams[1], Jon Lambourne[2]
Addresses	*Department of Infection and Tropical Medicine, Castle Hill Hospital, Cottingham, UK[1], Imported Fever Service, Rare and Imported Pathogens Lab, Public Health England, Salisbury, UK[2]*

Abstract

A 29-year-old Malaysian doctor presented with a four-day history of fevers, rigors, severe myalgia, and headache. Seven days previously she had returned from a fortnight's holiday in rural and urban Malaysia. On examination she was febrile (39°C), tachycardic (135bpm) and hypotensive (BP 100/60mmHg). The rest of her examination was normal.

Initial tests revealed lymphopenia (0.3 x10^9cells/L), mild thrombocytopenia (110 x10^9/L), and a CRP of 212mg/l. Renal function, coagulation profile and a CXR were normal. LFTs were normal except for bilirubin 30µmol/l. Two malaria smears were negative. Urine dip had 1+ blood. She was commenced empirically on IV amoxicillin.

Six hours after admission she developed significant haemoptysis and required intubation due to rapidly deteriorating respiratory function. CXR appearances were consistent with diffuse alveolar haemorrhage. Her antibiotic cover was broadened. By day two of admission high-frequency oscillatory ventilation was commenced and an ECMO referral was made. At this stage, negative test results included: vasculitis screen, legionella and pneumococcal urinary antigens, HIV, complement fixation tests for respiratory pathogens, leptospirosis IgM, CMV IgM and three sets of blood cultures.

Her liver enzymes, clotting screen and renal function remained stable. Bronchoscopy confirmed severe pulmonary haemorrhage.

Blood, urine and BAL fluid were sent to the Rare and Imported Pathogens Lab, HPA Porton. Urgent testing for a range of pathogens revealed the diagnosis, which was received overnight on the second day of admission. By day three, the patient began to improve and was extubated on day six. She has now fully recovered.

Cryptic Clinical Case C

Title	**Fever in traveller returned from Nepal**
Authors	Alison Burgess
Addresses	*Northwick Park Hospital, London, UK*

Abstract

Previously well 51 year old gentleman of Nepalese origin presented with fever following two weeks in Nepal. He had stayed with friends and denied insect bites or local water consumption. He presented six days after returning to the UK with a four day history of worsening fever, headache and dry cough.

On examination he was pyrexial at 39 °C but there was no other significant finding. No rash or bites. Investigations revealed Haemoglobin 14.7 WCC 6.0 (Lymph 0.77) Platelets 150, CRP 83, Na 130, K 5.1, Crea 89. Malaria screen negative. Chest radiograph normal. He was treated with ceftriaxone for typhoid.

At day 4 of admission he remained pyrexial. Additionally, he had developed a petechial rash on his trunk and splenomegally. He had worsening thrombocytopaenia (Platelets 88) and markedly raised ferritin. CT chest and abdomen demonstrated a prominent spleen only.

What should we do next? Is there a unifying diagnosis?

Cryptic Clinical Case D

Title	**Memoirs of A Complex case**
Authors	Shumonta Quaderi[1], Suranjith Seneviratne[2], Nisha Verma[2], Mike Brown[1], David Moore[1]
Address	*UCLH - Hospital for Tropical Diseases, London, UK[1], Royal Free London NHS Foundation trust, London, UK[2]*

Abstract

A 68 year old female presented with a 3 week history of dyspnoea, night sweats and right upper quadrant pain. Her symptoms started two months after an aortic valve replacement in January 2012. She had a background of rheumatic heart disease for which she had already undergone two metallic mitral valve replacements and a dual chamber pacemaker.

At presentation she was pancytopaenic {platelets 93, WCC 1.66 (neutrophils 0.94, lymphocytes 0.65, monocytes 0.05), haemoglobin 8} with evidence of haemolysis and deranged liver function tests (ALP 1117, Bilirubin 46, ALT 238).

She was initially treated empirically for prosthetic valve endocarditis although without microbiological, or echocardiographic evidence to support the diagnosis.

A liver biopsy yielded a preliminary diagnosis supported by a bone marrow aspirate and trephine.

She developed three painful ulcers of similar size in her natal cleft, PCR identifying evidence of a second opportunistic infection (OI).

She was HIV negative with normal immunoglobulins. Her CD4 T cell count was low at 248.

A clear cause for her immunosuppression could not be found and subsequent immunological tests unmasked a possible unifying cause.

Despite ongoing active treatment (she was in hospital for six months) she died of multi-organ failure.

Cryptic Clinical Case E

Title	**Clinical lessons: don't underestimate the value of microscopy!**
Authors	Shara Palanivel[1], Frances Davies[1], John Clark[1], Elizabeth Johnson[2], Philippa Youd[1], Phillip Howard[1], Stephen Sampson[1]
Address	*St Helier Hospital, Surrey, UK[1], public Health England, Bristol, UK[2]*

Abstract

A 28 year old lady was admitted from gastroenterology outpatients with an 18 month history of bloody diarrhoea, colicky abdominal pain and 20kg weight loss, with a significant deterioration in symptoms over the last 4 months. A prior diagnosis of Crohn's disease had been made following colonoscopy and biopsy four months previously and treatment with Mesalazine started with little clinical response. Ghanaian by birth, she had been resident in the UK for 10 years, and last travelled to Ghana 7 months prior to admission. She had developed chicken-pox 2 months before admission but had no other significant medical history. On physical examination she was thin, unwell and had moderate ascites. Bloods showed iron deficiency anaemia (Hb 97g/L), CRP of 16, normal electrolytes and liver function tests. Abdominal ultrasound and CT scans confirmed the presence of ascites, 14cm splenomegaly, heterogenous liver enhancement, and possible colitis. A colonoscopy showed multiple nodular lesions throughout her large bowel, and histological examination of a biopsy showed inflammation and ulceration with granulation tissue containing numerous large yeast-like fungal organisms.

Treatment was started, with rapid symptomatic improvement.

This case highlights the value of basic microbiological principles to aid in the diagnosis of unusual pathogens.

Cryptic Clinical Case F

Title	**Stroke and a fever - time to call Infectious Diseases?**
Authors	Sarah Logan, Jo Seddon, Gary Brook, Raj Bathula, Jim Buckley, Rob Davidson
Address	*North West London Hospitals NHS Trust, London, UK*

Abstract

A 57 year old diabetic presented with fever, headache and acute confusion. Neuroimaging demonstrated parietal intracerebral haemorrhage, with subarachnoid extension. Prior investigations for abdominal pain, which started 4 months after raw fish consumption on his family's fish farm in the Philippines, had revealed peripheral eosinophilia, with thickened, oedematous musculature on an abdominal CT scan.

During his admission with the intracerebral haemorrhage ivermectin and praziquantel were prescribed for positive strongyloides and toxocara serology. Four hours after taking these he dropped his conscious level. Neuroimaging demonstrated an evolving haemorrhage, with hyperintensity in the posterior pontine area and cerebral peduncles. A diagnostic procedure was performed.

Delegates

Dr	Madhumanee	Abeywardena	Leicester Royal Infirmary Hospital	Microbiology
Dr	Aula	Abbara	St Thomas' Hospital	Infectious Diseases
Dr	Joanna	Allen	Royal Free London NHS Foundation Trust	Infectious Diseases
Dr	Bridget	Atkins	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Stephen	Barrett	BIA Treasurer	
Dr	Nick	Beeching	Royal Liverpool University Hospital	Tropical Medicine
Dr	Neena	Bodasing	University Hospital of North Staffordshire	Infectious Diseases
Dr	Andrew	Brent	University of Oxford	Clinical Laboratory Sciences
Dr	Richard	Brindle	University Hospitals Bristol	Microbiology
Dr	Ruaridh	Buchanan	London School of Hygiene & Tropical Medicine	
Dr	Daniel	Burns	Birminham Heartlands Hospital / British Army	Infectious Diseases
Dr	Graeme	Calver	East Kent Hospitals Trust	Microbiology
Dr	Simon	Cathcart	Public Health England	North East Central London
Dr	Bilwanath	Chattopadhyay	The London Independent Hospital	Pathology
Dr	Amy	Chue	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Tristan	Clark	Treliske Hospital	Medcine
Dr	Katherine	Clay	Birmingham Heartlands Hospital	Infectious Diseases
Dr	Joby	Cole	University of Sheffield	Infection & Immunity
Dr	Paul	Collini	University of Sheffield	Infection & Immunity
Miss	Shelui	Collinson	St George's University	University
Dr	Julia	Colston	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Luis	Cotter	Darent Valley Hospital	Pathology
Dr	Peter	Cowling	BIA Guidelines Secretary	Microbiology
Dr	Muhammad Younis	Dahar	West Middlesex University Hospital	Microbiology
Dr	Susanna	Davis	Sheffield Teaching Hospitals NHS Foundation Trust	Medical Microbiology
Dr	Thushan	de Silva	Royal Hallamshire Hospital	ID & Tropical Medicine
Dr	Elli	Demertzi	Chelsea & Westminister Hospital	Microbiology
Dr	Kumara	Dharmasena	BIA Communications Secretary	
Dr	Helen	Dillon	University Hospitals Leicester	Infectious Diseases
Professor	David	Dockrell	University of Sheffield	Infection & Immunity
Dr	Jake	Dunning	Imperial College London	Centre for Respiratory Infection
Dr	Nicholas	Easom	UCLH	Infectious Diseases
Dr	Simon	Ellis	Royal Victoria Infirmary	Infection & Tropical Medicine
Dr	Andree	Evans	Royal Devon & Exeter Hospital	Microbiology
Professor	Tom	Evans	University of Glasgow	Molecular Microbiology
Dr	Hugo	Farne	King's College Hospital	Cardiology
Dr	Zsolt	Filetoth	Ministry of Defence	MOD
Dr	Rosemarie	FitzGerald	Leicester Royal Infirmary	Microbiology
Dr	Donall	Forde	Birmingham	Infectious Diseases
Dr	Rachel	Foster	Sheffield Teaching Hospitals NHS Foundation Trust	ID & Tropical Medicine
Ms	Katharine	Fox	Imperial College London	Medicine
Dr	Josephine	Francis	Not disclosed	
Prof	Johnathan	Friedland	Imperial College London	Infection
Dr	Arup	Ghose	The Hillingdon Hospital NHS Foundation	Microbiology

Delegates

Dr	Stephen	Glass	King's College Hospital	Microbiology
Dr	Gauri	Godbole	North Middlesex Hospital NHS Trust	Microbiology & Virology
Professor	Stephen	Green	BIA Meetings Secretary	Infectious Diseases
Dr	Julia	Greig	Sheffield Teaching Hospitals NHS Foundation Trust	ID & Tropical Medicine
Dr	Julia	Greig	Sheffield Teaching Hospitals NHS Foundation Trust	Infection
Dr	Charlotte	Hall	Castle Hill Hospital	Infectious Diseases
Dr	Mashaier	Hamad	University Hospital of North Staffordshire	Pathology
Dr	Angela	Houston	St Georges Hosptial	Clinical Infection Unit
Dr	Ewan	Hunter	Royal Victoria Infirmary	Infectious Diseases
Dr	Jasmin	Islam	Royal Sussex County Hospital	ID & Microbiology
Dr	Joe	Jarvis	London School of Hygiene & Tropical Medicine	Clinical Research
Dr	Megan	Jenkins	Southmead hospital	Infectious Diseases
Dr	Abhinav	Kumar	Kings Mill Hospital	Microbiology
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Dr	Lucy	Lamb	Imperial College London	ID & Immunity
Professor	Nelson	Lee	Chinese University of Hong Kong	Infectious Diseases
Dr	Paul	Lee	MHRA	VRMM
Dr	Joanne	Legg	Worthing Hospital	Microbiology
Dr	Patrick	Lillie	Sherwood Forest Hospitals NHS Foundation Trust	Acute Medicine
Dr	Martin	Llewelyn	Brighton & Sussex Medical School	ID & Therapeutics
Professor	Derek	Macallan	St George's University of London	Infection & Immunity
Dr	Elias	Mariolis	St James University Hospital	Infectious Diseases
Dr	Michael	Marks	University College Hospital	Hospital for Tropical Diseases
Dr	Laura	Maynard Smith	London School of Hygiene & Tropical Medicine	Infectious & Tropical Diseases
Dr	Fiona	McGilla	Brain Infections UK	Liverpool Brain Infections Group
Dr	Rolf	Meigh	Hull & East Yorkshire NHS Trust	Virology
Dr	Mark	Melzer	Barts & the London NHS Trust	Microbiology
Dr	Albert	Mifsud	BIA Secretary	
Dr	Luke	Moore	Imperial College London	Infection & Immunity
Mr	Thomas	Moore	Brighton & Sussex Medical School	Medical student
Professor	Peter	Moss	BIA President	
Dr	Claire	Mullender	St Georges Hospital	Infectious Diseases
Dr	Pavithra	Natarajan	Royal Liverpool University Hospital	Infectious Diseases
Dr	Linda	New	Epsom & St. Helier University Hospitals NHS Trust	Microbiology
Dr	Dimitrios	Nikolakopoulos	South London Healthcare NHS Trust	Microbiology
Dr	Fotinie	Ntziora	Not disclosed	
Dr	Kathryn	Nye	Health Protection Agency	Specialist Microbiology Services
Dr	Matilda	O'Donovan	Royal Cornwall Hospitals Trust	Emergency Medicine
Dr	Catherine	Ong	Imperial College London	ID & Immunity
Dr	Shara	Palanivel	St Helier Hospital	Medical Microbiology
Dr	David	Partridge	Northern General Hospital	Microbiology
Dr	Sneha	Patel	Kingston Hospital	Microbiology
Dr	Ruth	Payne	University of Oxford	The Jenner Institute

Delegates

Dr	Louise	Pealing	London School of Hygiene & Tropical Medicine	Clinical Research
Dr	Giuseppe	Pichierri	Public Health Wales/Hywel Dda Health Board	Microbiology
Dr	Gabriele	Pollara	University College Hospital	Microbiology
Dr	James	Price	Royal Sussex County Hospital	ID & Microbiology
Dr	Ashley	Price	Royal Victoria Infirmary	Infectious Diseases
Professor	Robert	Read	University of Southampton Medical School	ID & Immunity
Dr	Anna	Riddell	Hammersmith Hospital	Infectious Diseases
Dr	Michael	Riste	University Hospital of North Staffordshire	Infectious Diseases
Dr	Neil	Ritchie	University of Glasgow	Institute of Infection
Dr	Jennifer	Roe	Northwick Park Hospital	Infectious Diseases
Dr	Dunisha	Samarasinghe	Imperial College Healthcare NHS Trust	Microbiology
Dr	Giovanni	Satta	Royal Free London NHS Foundation Trust	Medical Microbiology
Dr	Noha	Seoudi	Barts Health NHS Trust	Oral Microbiology
Dr	Clare	Sepping	Royal Cornwall Hospitals Trust	Gastroenterology
Dr	Hema	Sharma	Imperial College London	Infection & Immunity
Dr	Robert	Shaw	Wexham Park Hospital	Foundation Year 1
Dr	Rob	Shorten	Royal Free London NHS Foundation Trust	Microbiology
Dr	Racheol	Sierra	St Richards Hospital	Microbiology
Dr	Karthiga	Sithamparanathan	Weston General Hospital	Microbiology
Dr	Noel	Snell	National Heart & Lung Institute	Respiratory Infections Firm
Dr	Roger	Springbett	Conquest Hospital	ID & Microbiology
Dr	Jane	Stockley	Worcestershire Royal Hospital	Medical Microbiology
Dr	Bala	Subramanian	Sheffield Teaching Hospitals NHS Foundation Trust	ID & Microbiology
Dr	Alida Fe	Talento	Trinity College Dublin	Clinical Microbiology
Dr	Si Huei	Tan	North Middlesex Hospital	Microbiology
Professor	Christophe	Tang	University of Oxford	School of Pathology
Dr	Andrew	Taylor	North Central Thames	Infectious Diseases
Dr	Simon	Tiberi	Hammersmith Hospital	Infectious Diseases
Dr	James	Ussher	University of Oxford	Medicine
Dr	Andrew	Ustianowski	North Manchester General Hospital	ID & Tropical Medicine
Dr	Floris	van den Brink	Kennemer Gasthuis Haarlem, Amsterdam	Internal Medicine/Cardiology
Dr	Alicia	Vedio	Sheffield Teaching Hospitals NHS Foundation Trust	Infection & Tropical Medicine
Dr	Simon	Warren	Royal Free London NHS Foundation Trust	Infection
Dr	Daniel	Weiand	York Hospital	Microbiology
Professor	Mark	Wilcox	Leeds Teaching Hospitals NHS Trust	Molecular Microbiology
Dr	Li-An	Wong-Taylor	West Middlesex University Hospital	Acute Medicine
Dr	Rella	Workman	Medway NHS Foundation Trust	Microbiology

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