British Infection Association

Free Scientific Paper 1

Title **A scalable Multiplex Serology platform applied to UK Biobank helps define host-pathogen relationships**

Authors Alexander J Mentzer[1,2], Nicole Brenner[3,4], Naomi Allen[5,6], Thomas J Littlejohns[6], Amanda Y Chong[1], Adrian Cortes[2], Rachael Almond[5], Michael Hill[6,7], Simon Sheard[5], Gil McVean[2], Adrian VS Hill[1,8], Tim Waterboer[3]

Addresses *[1]The Wellcome Centre for Human Genetics, University of Oxford, Oxford, United Kingdom.*
[2]Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, University of Oxford, Oxford, United Kingdom.
[3]Infections and Cancer Epidemiology, German Cancer Research Center (DKFZ), Heidelberg, Germany.
[4]Faculty of Biosciences, Heidelberg University, Heidelberg, Germany.
[5]UK Biobank, Stockport, United Kingdom.
[6]Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom.
[7]MRC-Population Health Research Unit, University of Oxford, Oxford, United Kingdom.
[8]The Jenner Institute, University of Oxford, Oxford, United Kingdom

---

Abstract

Introduction
Some infectious agents are recognised causes of cancer, although their aetiological role in other chronic disease outcomes is less well defined. Confirming associations and understanding mechanisms involving infectious agents and subsequent chronic disease risk may be possible through measuring exposure to multiple infectious agents in large-scale prospective cohorts such as UK Biobank (UKB).

Methods
Following expert consensus we designed a Multiplex Serology platform capable of simultaneously measuring quantitative antibody responses against 45 antigens from 20 infectious agents implicated in chronic disease pathogenesis, including human herpes, hepatitis, polyoma, papilloma, and immunodeficiency viruses, *Chlamydia trachomatis*, *Helicobacter pylori* and *Toxoplasma gondii*. After applying this panel to a subset of UKB participants (n=9,695) we tested associations between infectious agents and demographic and genetic risk modifiers and cancer disease outcomes.

Results
The Multiplex Serology panel confirmed well-known epidemiological associations between antibody responses against infectious agents and sociodemographic characteristics (e.g. ethnicity and lifetime sexual partners), genetic variants (e.g. rs6927022 with Epstein-Barr virus (EBV) EBNA-1 antibody; $P=9.5\times10^{-91}$) and disease outcomes including HPV-16 sero-positivity and cervical neoplasia (OR 2.28 (1.38-3.63); $P=8.8\times10^{-4}$), and EBV responses and multiple sclerosis through genetic correlation (genome-wide $r_G=0.31$, $P=0.02$).

Discussion
This dataset is one of the largest sero-prevalence studies including a diverse range of infectious agents in a prospective UK cohort. Our results demonstrate the validity and reproducibility of our Multiplex Serology approach in large-scale epidemiological studies. Measuring serological markers of infectious agents in UKB will improve our understanding of host-pathogen relationships that potentially have important implications for human health.

British Infection Association

Free Scientific Paper 2

Title **Host genetic variation in the complement factor H locus protective against meningococcal disease is strongly associated with susceptibility to rheumatic heart disease**

Authors Tom Parks[1,2], Kathryn Auckland[2], Balraj Mittal[3], Benjamin J Cairns[2], Joseph Kado[4], Mai Ling Perman[4], Mariana M Mirabel[5], John S K Kauwe[6], Kathryn J Robson[2], Shiranee Sriskandan[7], Andrew C Steer[8], Adrian V S Hill[2]

Addresses *[1]London School of Hygiene & Tropical Medicine, London, United Kingdom. [2]University of Oxford, Oxford, United Kingdom.*
[3]Babasahen Bhimrao Ambedkar University, Lucknow, India.
[4]Fiji National University, Suva, Fiji.
[5]Institut National de la Santé et de la Recherche Médicale, Paris, France.
[6]Brigham Young University, Provo, USA.
[7]Imperial College London, London, United Kingdom.
[8]Murdoch Children's Research Institute, Melbourne, Australia

---

Abstract

Introduction
Triggered by the bacterial pathogen *Streptococcus pyogenes*, rheumatic heart disease (RHD) is a leading infectious cause of death and disability in children and young adults in developing countries. Owing to the limitations of current disease control strategies, we sought to identify common host genetic variants associated with susceptibility to this neglected disease, which in the long-term could facilitate development of vaccines and therapeutics.

Methods
We undertook a genome-wide association study of susceptibility to RHD in 1707 cases and 4060 controls predominantly of Pacific Islander, South Asian and European ancestry. This included cases of RHD and healthy controls recruited in the Pacific and India, as well as cases of mitral stenosis and controls from the UK Biobank study. After analyses compensating for confounding in seven ancestral groups, we performed a fixed-effects meta-analysis at each of the 4.2 million variants present in all seven groups with minor allele frequency of 5% or more.

Results
We identified a novel RHD susceptibility locus overlapping the complement factor H (CFH) locus on chromosome 1. The most associated variant (rs200749956) conferred a 1.5-fold increase risk of RHD (odds ratio, OR, 1.49, 95% confidence intervals, CI, 1.32-1.70, $P=3.2x10^{-10}$) and was previously found to be a strong inverse correlate of serum CFH, which plays a key role in regulating the alternative complement pathway. Strikingly, the signal also included several common variants previously associated with a 1.6-fold reduced risk of meningococcal disease that conferred a 1.3-fold increased risk of RHD (e.g. rs72482675, OR 1.34, 95% CI 1.22-1.47, $P=1.1x10^{-9}$).

Discussion
Despite conferring protection against meningococcal disease, CFH variants were associated with the major post-infective consequence of *S. pyogenes* infection, perhaps reflecting balancing selection. Moreover, the discovery that CFH variants contribute to RHD pathogenesis raises the possibility of repurposing existing complement inhibitors as a therapy to prevent or stall the auto-inflammatory process.

British Infection Association

Free Scientific Paper 3

Title **Cerebral Pericytes: A Novel Therapeutic Target in Pneumococcal Meningitis?**

Authors Eliza Gil, Cristina Venturini, Mahdad Noursadeghi

Address *UCL, London, United Kingdom*

Abstract

The high rates of mortality and neurodisability in bacterial meningitis are associated with the tissue damage mediated by the influx of neutrophils into the brain. The development of host-directed therapies that reduce neutrophil accumulation may offer novel therapeutic opportunities as an adjunct to antimicrobial therapy.

The interaction of pericytes and endothelial cells has been described to play an important role in neutrophil recruitment in mouse models of skin and soft tissue infection. The cerebral vasculature has the highest density of pericytes in the body and pericyte dysfunction is thought to play a role in several neuroinflammatory processes, however, the role of pericytes in the response to cerebral infection has not been described.

Here human brain pericytes are shown to drive neutrophil recruitment across the blood-brain barrier in an in vitro model of pneumococcal meningitis. Neutrophil recruitment is enhanced by the presence of pericytes, most potently by the pericyte response to pneumococcal-stimulated macrophages. This effect is mediated by pericyte-secreted chemokines, which are actively transported across the endothelial barrier.

We propose a model whereby cerebrovascular tissue resident innate immune cells act as sentinels of neuroinfection, activating the endothelial and pericyte layer of the blood-brain barrier, with the pericytes markedly amplifying neutrophil recruitment to the site of infection via secretion of neutrophil chemokines. Together this suggests two novel targets in neuroinfection, the pericyte inflammatory response and chemokine translocation across the blood-brain barrier, which could be targeted to inhibit neutrophil recruitment into the brain.

British Infection Association

Free Scientific Paper 4

Title **Exaggerated in vivo IL-17 responses discriminate recall responses in active TB**

Authors Gabriele Pollara[1], Carolin Turner[1], Gillian Tomlinson[1], Lucy Bell[1], Ayesha Khan[1], Luis Felipe Peralta[2], Anna Folino[3], Ayse Akarca[1], Cristina Venturini[1], Tina Baker[1], Fabio Ricciardolo[3], Teresa Marafioti[1], Cesar Ugarte-Gil[4], David Moore[5,6], Benjamin Chain[1], Mahdad Noursadeghi[1]

Addresses [1]University College London, London, United Kingdom.
[2]Universidad Peruana Cayetano HerediaUniversidad Peruana Cayetano HerediaUniversidad Peruana Cayetano HerediaUniversidad Peruana Cayetano Heredia, Lima, Peru.
[3]University of Turin, Turin, Italy.
[4]Universidad Peruana Cayetano Heredia Peruana Cayetano HerediaUniversidad Peruana Cayetano Heredia, Lima, Peru.
[5]London School of Hygiene & Tropical Medicine, London, United Kingdom.
[6]Universidad Peruana Cayetano Heredia, Lima, Peru

Abstract

Introduction
Host immune responses at the site of *Mycobacterium tuberculosis* (Mtb) infection serve to contain the pathogen, but also mediate the pathogenesis of tuberculosis (TB) and onward transmission of infection. Based on the premise that active TB disease is predominantly a manifestation of immunopathology, we tested the hypothesis that immune responses at the site of host-pathogen interactions would reveal enrichment of immunopathologic responses in patients with active TB that were absent in individuals with equivalent immune memory for Mtb but without disease.

Methods
In cohorts of patients with active TB and cured or latent infection, we undertook molecular profiling at the site of a tuberculin skin test to model in vivo host-pathogen interactions in Mtb infection. Genome-wide transcriptional differences were identified by differential gene expression analyses. Enrichment of immune cells and cytokine activity was derived using specific transcriptional modules. Findings were validated in independent cohorts of patients with active TB, as well as Mtb infected tissues.

Results
Active TB in humans is associated with exaggerated IL-17A/F expression, accumulation of Th17 cells and IL-17A bioactivity, including increased neutrophil recruitment and matrix metalloproteinase-1 expression directly implicated in TB pathogenesis. These features discriminate recall responses in patients with active TB from those with cured or latent infection, and are also evident at the site of TB disease.

Discussion
Our data are consistent with a model in which elevated Th17 responses within tissues drive immunopathology and transmission in active TB, and support targeting of the IL-17A/F pathway in host-directed therapy for active TB.

British Infection Association

Free Scientific Paper 5

Title **Long-term survivors following autologous haematopoetic stem cell transplantation have significant defects in the immune repertoire to vaccine preventable diseases**

Authors Hayley Colton, Diana Greenfield, Thushan DeSilva, John Snowden, Nick Morley, Cariad Evans, Josh Wright

Address *Sheffield Teaching Hospitals, Sheffield, United Kingdom*

Abstract

Introduction
Infection-related mortality can reach 8% following autologous haematopoetic stem cell transplantation (aHSCT). Current guidelines recommend a routine vaccination programme post-HSCT to reduce the risk of vaccine preventable diseases (VPD), yet this is often not completed.

Methods
A 1-year prospective, single-centre observational study was conducted in a HSCT late-effects clinic to explore whether patients post-aHSCT who were not routinely revaccinated had reconstituted their immunity to a range of VPD. Antibody titres to diphtheria, tetanus, measles, mumps, rubella, varicella zoster virus (VZV), pneumococcal serotypes included in the 13-valent vaccine (PCV13) and *Haemophilus influenzae type B* (Hib) were measured as part of routine clinical care.

Results
56 sequential clinic attendees ≥2 years post-aHSCT were included. Median age (range) was 48 years (22-72) and median time from aHSCT 7 years (2-29). Immunity to diphtheria and PCV13 serotypes was poor, with 98.2% and 100% considered non-immune. There was heterogeneity in immunity to measles, mumps and rubella, with 34.5%, 50.9% and 29.1% considered non-immune. In the measles-seropositive group (who under current guidelines would not receive MMR vaccine), 47.2% were non-immune to mumps, and 25% to rubella. 10.9% and 20% were considered non-immune to VZV and tetanus respectively. Immunity to Hib was good, with only 5.5% of patients considered non-immune.

Conclusion
Significant deficiencies in humoral immunity to VPD were observed. A strategy involving screening and subsequent selected vaccination should be considered in long term survivors post-aHSCT who did not undergo a routine revaccination programme. Late Effects Clinics provide a good opportunity to facilitate this pragmatic approach.

British Infection Association

Free Scientific Paper 6

Title **Plasma matrix metalloproteinase-8 (MMP-8) and procollagen III N-terminal propeptide (PIIINP) associate with mortality in advanced HIV-tuberculosis disease**

Authors Naomi Walker[1], Charlotte Schutz[2], Amy Ward[2], David Barr[2], Graeme Meintjes[2]

Addresses *[1]London School of Hygiene and Tropical Medicine, London, United Kingdom.*
[2]University of Cape Town, Cape Town, South Africa

Abstract

Introduction
Novel tuberculosis (TB) diagnostic and treatment strategies are essential to reduce high mortality and morbidity in HIV-1-infected patients with active TB. We investigated the diagnostic and prognostic potential of plasma MMP-8 (neutrophil collagenase) and PIIINP, a matrix degradation product released during collagen turnover, in hospitalised HIV-infected patients.

Methods
Patients with TB symptoms were investigated with mycobacterial culture, Xpert and urine LAM prior to TB treatment initiation. Vital status was determined at 12 weeks. Enrolment plasma MMP-8 and PIIINP concentrations were measured (Luminex/ELISA). Analysis was by Mann-Whitney U, receiver operating characteristics curve and logistic regression.

Results
437 patients were included. Median CD4 count was 62 cells/mm^3 (IQR 22.5-133). TB was microbiologically confirmed in 313 (71.6%). Death occurred in 83/437 (19.0%). Plasma MMP-8 was elevated in confirmed TB compared to non-TB, median 23712 pg/ml (IQR 7688-47571) vs 10602 (2019-32205), p=0.002. In confirmed TB, both MMP-8 and PIIINP were elevated in patients with mycobacteraemia (blood stream infection) compared to non-mycobacteraemic patients and MMP-8 predicted mycobacteraemia (AUC 0.759, 95% CI 0.712-0.806, p<0.001). In confirmed TB patients who died compared to survivors, PIIINP was elevated (median 44544, IQR 26728-99228 vs 19908, IQR 12368-33316, p<0.001), as was MMP-8 (median 32811, IQR 12060-66934 vs 20201, IQR 6050-40561, p=0.002). PIIINP predicted mortality in TB (AUC 0.752, 95% CI 0.683-0.821, p<0.001) and was associated with increased unadjusted and adjusted odds of death.

Conclusion
Amongst high risk patients, elevated plasma MMP-8 and PIIINP indicate *Mycobacterium tuberculosis* dissemination and predict death, identifying the most at risk patients for targeted interventions.

British Infection Association

Free Scientific Paper 7

Title **Using genetic diversity to evaluate undetected *Staphylococcus aureus* carriage**

Authors James Price[1], Leanne Barker[2], Kevin Cole[3], Derrick Crook[2], John Paul[3], Martin Llewelyn[1]

Addresses *[1]Brighton and Sussex Medical School, Brighton, United Kingdom.*
[2]John Radcliffe Hospital, Oxford, United Kingdom.
[3]PHE, Brighton, United Kingdom

Abstract

Background
Nosocomial *Staphylococcus aureus* acquisition is often attributed to staff transmission but in non-outbreak settings whole-genome sequencing (WGS) rarely reveals donors for apparent acquisitions. We hypothesize that such 'acquisitions' may be explained by cryptic carriage. To address this we assess genetic diversity in different carriage profiles to investigate undetected persisting carriage.

Methods
Over seven years 521 community patients were screened two-monthly for nasal *S. aureus* carriage. All isolates were spa-typed. Multiple colonies of isolates from four carriage profiles (continuous [+++++] and discountinuous [++-++] detection, transient [- - + - -] and persisting [- - + + +] acquisition) underwent WGS to assess genomic relatedness using single nucleotide variants (SNV).

Results
Within patients exhibiting discontinuous detection (n=6) the maximum average cross-sectional diversity at sampling-points was lower (2 SNV, standard deviation (SD) 3-4) than diversity observed in continuous (n=12) detection (11 SNV (SD 13-19), p=0.6). Cross-sectional diversity observed at single sample-points in transient (n=11) and persistent (n=5) acquisition was low (0.4 SNV (SD 1) and 2 SNV (SD 1) respectively). Between profile-groups the maximum average cross-sectional diversity in discontinuous detection was lower than continuous detection (p=0.01), but comparable to transient and persisting acquisition. Over time the maximum average longitudinal-diversity observed in discontinuous detection was higher (17 SNV (SD 14) over 6-26 months, equating to 18 SNV per year) than continuous detection (37 SNV (SD 26) over 26-48 months, equating to 10 SNV per year, p=0.055).

Conclusions
Low cross-sectional diversity associated with discontinuous detection suggests persisting, yet intermittently detected, carriage of the same strain. Surprisingly, accumulated diversity is greater for discontinuously detected than for continuously detected *S. aureus*, possibly reflecting differing selective pressures related to antibiotic exposure or host immunity. Further work is required to investigate factors associated with discontinuous carriage and its clinical and diagnostic significance.

British Infection Association

Free Scientific Paper 8

Title **Latent Tuberculosis Infection Outcomes in a UK population**

Authors David Smith, Benjamin Patterson, Laurence John, Robert Davidson

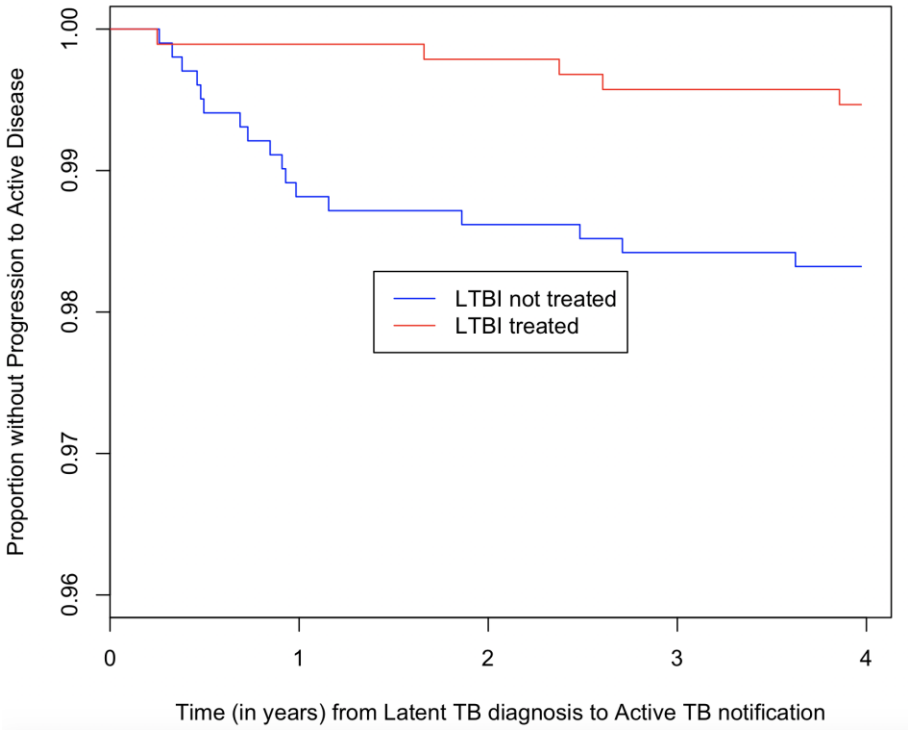
Address *Northwick Park Hospital, London, United Kingdom*

Abstract

Background
The National Institute of Clinical Excellence (NICE) recommendation for latent tuberculosis infection (LTBI) treatment is based on studies with non-UK participants. We investigated the outcome of LTBI in a representative UK population, comparing treatment and non-treatment strategies.

Methods
A retrospective cohort of cases with positive mantoux (>5mm regardless of prior BCG status) or positive IGRA (Quantiferon) at Northwick Park Hospital were identified from a purpose-built electronic medical record. This database was linked with the London TB Register to estimate the incidence of active tuberculosis in this cohort

Figure 1. shows a Kaplan-Meier survival curve comparing the two groups.



Results
Between April 2010 and January 2019, 1950 patients were diagnosed with LTBI comprising 937 (48.1%) who received a latent treatment regimen and 1013 (51.9%) who were not clinically appropriate, declined treatment or were lost to follow-up. This represents 6793 patient-years of follow-up. The median follow-up from LTBI diagnosis was 3.7 years (IQR: 2.0 to 5.0). We identified 22 cases of active TB disease in those with prior LTBI from the London TB register. 17 (1.7%) in untreated LTBI and 5 (0.5%) in treated. The number needed to treat (NNT) to prevent a case of active TB is 87.

Conclusion
Our data suggest that the NNT for an ethnically diverse London population is higher than previously reported in other low prevalence settings. This may be because of higher rates of re-exposure. We feel these data should prompt a cost-benefit and risk benefit analysis of treatment for LTBI in such a population.

British Infection Association

Free Scientific Paper 9

Title	**Early monitoring of liver tests predicts drug-induced liver injury from anti-tuberculous medications**
Authors	Benjamin Patterson[1], Aula Abbara[2], Merle Hendersen[3], Simon Collin[4], William Lynn[5], Laurence John[1]
Addresses	*[1]Department of Infection, Northwick Park Hospital, London, United Kingdom.* *[2]Department of Infection, Imperial College, London, United Kingdom.* *[3]Royal Brompton Hospital, London, United Kingdom.* *[4]School of Social and Community Medicine, Bristol University, Bristol, United Kingdom.* *[5]Department of Infection, Ealing Hospital, London, United Kingdom*

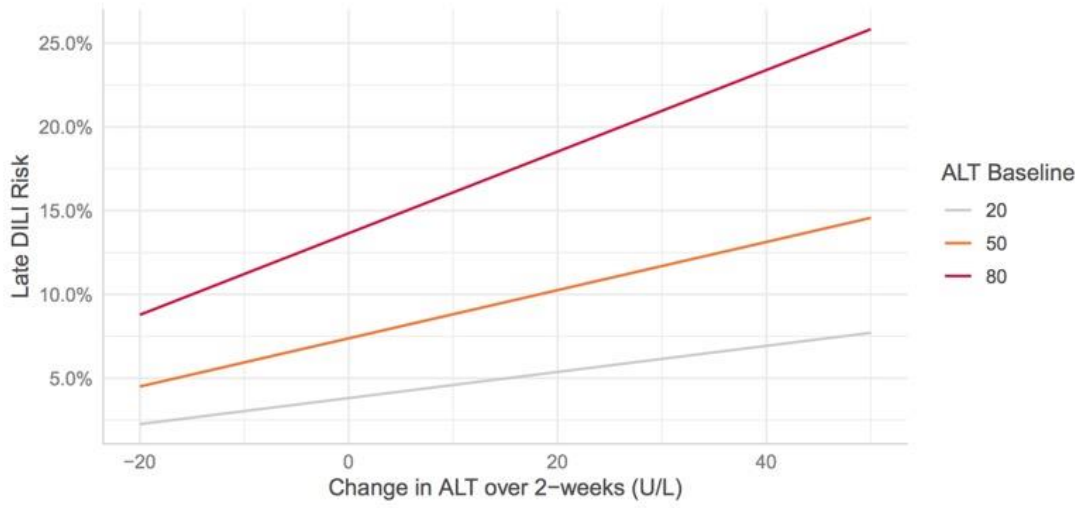
Abstract

Background
We describe the predictive value of liver tests (LTs) at baseline and at 2-weeks after initiation of anti-tuberculous treatment (ATT) for the detection of DILI.

Methods
Patients initiating ATT were monitored with routine LTs at baseline (up to 8 weeks before and 1 week after initiation) and after 2-weeks (1 to 3 weeks after initiation) of therapy. A logistical regression model was constructed to determine the predictive utility of alanine aminotransferase (ALT) level in conjunction with the gradient of the ALT change over two-weeks for subsequent development of DILI (defined by the British Thoracic Society criteria) occurring later in treatment (late DILI).

Results
683 patients with active tuberculosis managed at Northwick Park Hospital between January 2015 and December 2018 were monitored with routine LTs. 70 cases (10.2%) of ATT-associated DILI were diagnosed. 37 cases (52.9%) of DILI occurred later than the 2-week LT sample. ALT values at baseline and 2-weeks significantly predicted the occurrence of late DILI and the predictive effect was additive. Risk of late DILI was 2-fold greater for every 30 U/L increment in ALT at baseline (OR 2.04, 95% CI 1.24 to 3.28 p=0.003) and 1.7-fold greater for every 30 U/L increment in ALT at 2-weeks (OR 1.74, 95% CI 1.24 to 2.37 p<0.001).

Figure 1. Risk of late DILI predicted by ALT at baseline and ALT change at 2-weeks



Conclusion: Routine 2-week LTs capture early DILI and predict late DILI in patients on ATT.

British Infection Association

Free Scientific Paper 10

Title: Translating the OVIVA study criteria to a UK OPAT cohort: clinical and financial impacts

Authors Lucy Bell[1], Imogen Clarke[1], Tommy Rampling[1], Stephen Morris-Jones[1], Surjo De[1], Katharina Kranzer[1,2], Sarah Logan[1], Gabriele Pollara[1,3], Michael Marks[1,2]

Addresses *[1]University College London Hospitals NHS Foundation Trust, London, United Kingdom.*
[2]London School of Hygiene and Tropical Medicine, London, United Kingdom.
[3]University College London, London, United Kingdom

Abstract

Introduction
Intravenous antibiotic therapy delivered by OPAT carries an appreciable risk of adverse events (Underwood et al 2018). The OVIVA study (Li et al. 2019) demonstrated the non-inferiority of oral antibiotics in treating bone & joint infections that are routinely managed by extended intravenous antibiotic therapy. The applicability of this protocol in a non-trial setting is currently unknown. We aimed to assess the impact of the OVIVA protocols on use of intravenous antibiotics in UK OPAT services.

Methods and results
We studied a cohort of 157 patients with bone or joint infections cared for by the UCLH OPAT service between 01/01/2015–30/06/2017.

The most common diagnoses were prosthetic joint infections (40.7%), vertebral osteomyelitis (22.9%) and extra-axial osteomyelitis (19.7%). Orthopaedic fixation device infections and native joint infections accounted for the remainder. Median duration of IV therapy delivered was 21 days (IQR 11–41). Cephalosporins were the most frequently used antibiotic class (41.5%), followed by glycopeptides (32.6%), lipopeptides (12.7%) and carbapenems (11.6%).The majority (86%) of patients had ≥1 surgical or interventional procedure prior to OPAT referral (range 0–7).

A blinded clinician reviewed clinical and microbiological data for each case and determined if it fulfilled inclusion criteria for oral treatment as described in OVIVA. We determined the number of avoidable days of intravenous therapy, and financial savings.

Discussion
We demonstrate that a large proportion of UK patients receiving OPAT care could be treated with oral antibiotics akin to the criteria used in OVIVA, minimising duration of intravenous therapy and offering economic benefits.

British Infection Association

Free Scientific Paper 11

Title **Heterogeneity of antibiotic recommendations for common inpatient infections in the United Kingdom**

Authors Daniel Pan[1], Tamsin Nash[1], Thomas Hine[1], Sarah Whitehorn[1], Gavin Barlow[1,2]

Addresses *[1]Hull and East Yorkshire Hospital NHS Trust, Hull, United Kingdom.*
[2]Hull York Medical School, Hull, United Kingdom

Abstract

Background
Increasing heterogeneity of antimicrobial recommendations has been hypothesised to slow down antimicrobial resistance. We aimed to investigate hospital antibiotic recommendations, both within and across hospitals, for seven common inpatient indications.

Methods
We collected data on antimicrobial recommendations from 51 hospital trusts between December 2016 to February 2017. Only first-line empiric recommendations were included for seven common inpatient infections: severe (CURB65≥3) community acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), infective exacerbation of COPD (iCOPD), cellulitis, uncomplicated urinary tract infection (uUTI), intraabdominal infection (IAI) and sepsis of unknown source.

Results
Across the seven indications, 357 antibiotic recommendations were identified in 51 hospital trusts. A large proportion of trusts offered beta-lactams (60% to 100%) as part of first-line therapy for all indications apart from uUTI. Few trusts offered prescribers a choice between antibiotic classes, except in uUTI for which 41% offered a choice, mostly between nitrofurantoin or trimethoprim (33% of trusts) and in iCOPD (22% of trusts; most commonly between amoxicillin and doxycycline [10% of trusts]). No trusts offered prescribers a choice between classes of antibiotic for HAP, cellulitis, IAI or sepsis of unknown origin. A piperacillin-tazobactam based regimen was recommended for HAP in 59%, for sepsis of unknown source in 39% and for IAI in 30% of trusts.

Conclusion
Heterogenous antimicrobial prescribing is not encouraged by hospital guidelines in the UK, although there is notable variation of antimicrobial recommendations between hospitals for some indications. Piperacillin-tazobactam was still relatively commonly recommended for some infections despite ongoing national incentives at the time of the study.

British Infection Association

Free Scientific Paper 12

Title **A Retrospective 10-year review of infectious and non-infectious diagnoses in patients with haematology malignancy presenting with potential central nervous system infection**

Authors Roshina Gnanadurai, Emma Lim, Harpreet Hyare, Robert Miller

Address *University College London Hospitals, London, United Kingdom*

Abstract

Introduction
Central nervous system (CNS) infection in patients with haematologic malignancy is common because of iatrogenic immunosuppression. Symptoms can mimic other diagnoses such as malignant CNS infiltration or treatment related side effects, which often poses diagnostic challenges. We conducted a 10-year retrospective review of cases of potential CNS infection in this cohort in a tertiary referral centre describing infectious and non-infectious diagnoses with correlation of magnetic resonance imaging of the head (MRH).

Methods
To capture patients with potential CNS infection, all MRH scans in patients with haematological malignancy in a tertiary referral centre (10/2007 through 10/2017) were identified from electronic records (n=1855). Of these, MRH for investigation of suspected CNS infection were identified using keyword searches of radiology reports. Each patient's MRH scan was independently re-reported by two radiologists. Diagnosis of CNS infection was confirmed by review of clinical and laboratory data by two clinicians.

Results
One hundred and ten patients had MRH for investigation of CNS infection; 31 with presumed or confirmed CNS infection. Commonest aetiology included cytomegalovirus (CMV) retinitis, encephalitis or disseminated infection (n=7), intracerebral toxoplasmosis (n=5) and disseminated fungal infection (n=5). Non-infectious diagnoses (n=26) were mainly due to malignant CNS infiltration (n=14). MRH was found to be 90% sensitive and > 96% specific in diagnoses of CNS infection.

Discussion
Cases of potential CNS infection in haematologic malignancy cohort can be diagnostically challenging, confirmed in our study where comparable numbers were found to have infectious (28%) and non-infectious (24%) diagnoses. MRH is shown to be a valuable tool.

British Infection Association

Clinical Paper A

Title **A Spanish Query**

Authors Ankush Dhariwal[1], Sarah Jawad[2], Tihana Bicanic[3]

Addresses *[1]Barts Health, London, United Kingdom.*
[2]St Georges University Hospitals, London, United Kingdom.
[3]St Georges University of London, London, United Kingdom

Abstract without diagnosis

We present a case of a 21-year old man with unexplained fevers, pancytopenia, and hepatosplenomegaly. He initially presented in Barcelona in August 2018 with fever, weight loss, and night sweats, and had hepatosplenomegaly and pancytopenia. He was born in the UK, and had lived his life between the UK and Spain, including Barcelona and Valencia. He worked in a pastry factory, and had a pet dog that was well. He had never worked with animals, or consumed unpasteurised dairy or raw meat. Amongst numerous investigations, Coxiella burnetii serology was positive (Phase 1, 1:180; Phase 2 1:640), and he was treated for Q fever with 2 weeks of doxycycline. His fever resolved and his blood count normalised. Subsequently he re-presented in January 2019 with recurrence of his symptoms, with a spleen of 28cm demonstrated on CT, with no other remarkable imaging findings. He was HIV negative. Two bone marrow biopsies demonstrated only reactive changes, and no parasites were seen. He continued to spike temperatures over 38°C, with no response to piperacillin-tazobactam.

British Infection Association

Clinical Paper B

Title **You have goat to be kidding me!**

Authors Joseph Yates, Patrick Lillie, Emma Helbren, Anda Samson

Address *Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom*

Abstract without diagnosis

An 80-year-old female presented with a two-year history of fatigue, decreased appetite, weight loss, and night sweats. She had an established diagnosis of paroxysmal nocturnal haemoglobinuria and aplastic anaemia which had been managed with regular eculizumab infusions, an anti-complement C5 monoclonal antibody, for the past 7-years.CT showed multiple thromboemboli, a pancreatic mass, splenic lesions, and upper abdominal/retroperitoneal lymphadenopathy. Pancreatic biopsies revealed granulomatous tissue only. Special stains found no evidence of acid-fast bacilli or fungal elements. PCR for DNA of mycobacterium tuberculosis complex was negative, as were mycobacterial and standard bacterial cultures. She was referred to oncology for ongoing management as malignancy remained the most likely diagnosis. The patient presented 6-months later with a new ulcerated lesion on her right ankle. MRI revealed an extensive tumour around the peroneal tendon sheath together with a localised circumscribed lesion in the fibula. Histology showed an inflammatory process with suppurative granulomas. She denied recent and past exposure to tuberculosis contacts. However, on further enquiry, she mentioned living on a farm during the Second World War, where she drank unpasteurised goats' milk on a regular basis. The biopsy of the lesion subsequently grew an organism that was consistent with her presentation.

British Infection Association

Clinical Paper C

Title **He moves in mysterious ways.**

Authors Harry J Carr[1,2], Ulrich Schwab[2], Matthias L Schmid[2], D Ashley Price[2]

Addresses *[1]Newcastle University School of Medical Sciences, Newcastle Upon Tyne, United Kingdom.*
[2]Department of Infection & Tropical Medicine, Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom

---

Abstract without diagnosis

Two previously documented cases exist of this unusual presentation of an acute movement disorder syndrome. A 22-year-old male was admitted with non-segmental subcortical myoclonus (N-SSM), fevers and fluctuant GCS. Little history was obtained with a monosyllabic expressive dysphasia. Collateral histories were sought. His flat mates found him seated, disorientated, with a bilateral fine tremor, developing abnormal jerking movements, increasing confusion and headache over 6hrs. His father had contacted him 12hrs previously, no suspicion of problems, save mild lumbar spinal pain, radiating bilaterally to the popliteal fossae for 1 week, no longer present. On examination; tachycardia (106bpm), GCS 10-15, N-SSM (brisk startle reflex and myoclonus), increased tone bilaterally. MRI brain, not possible (agitation). An EEG, suggestive of a moderate encephalitis. LP protein *1.33g/l, WCC *50cells/ul (lymphocytosis), glucose 3.2mmol/l.IV aciclovir, ceftriaxone and amoxicillin were initiated empirically. The intermittent fever continued. Deranged LFTs developed over the subsequent 48hrs (*ALT 500, *ALP 230). CSF PCR –ve. Toxicology screen –ve. Day 3. MRI showed enlarged jugulodigastric nodes, brain normal. Propofol sedation (agitation) mediated improved myoclonus and speech over 24hrs.The patient was discharged without sequelae. NB: References and video of myoclonus available for presentation.

British Infection Association

Clinical Paper D

Title **Two of a Kind: 3 PET scans, 2 PCRs and finally 1 diagnosis!**

Authors Fay Dickson[1], Phillipa Bunrns[2], Kirstine Eastick[2], Matthew Edey[1], Patrick Lillie[2]

Addresses *[1]Dept of Renal Medicine, Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom.*
[2]Dept of Infection, Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom

---

Abstract without diagnosis

We present the case of 31-year-old identical twins who are significantly immunocompromised due to an unidentified genetic syndrome causing hypogammaglobulinaemia and progressive renal dysfunction leading to renal transplantation and fortnightly intravenous immunoglobulin replacement.In November 2017, Twin One presented with right supraclavicular lymphadenopathy, fevers and weight loss. Excision biopsy of the lymph node showed granulomatous inflammation. Standard microbiology, TB and fungal cultures were negative as were viral, fungal and bacterial PCRs.Between January 2018 and February 2019, Twin Two had two hospital admissions and three outpatient consultations relating to unexplained fevers. Several diagnoses were considered during this timeframe, including post-transplant lymphoproliferative disorder and Pneumocystis jirovecii pneumonia. Multiple investigations were undertaken including a bone marrow biopsy and three CT PET scans.At the time, the case presented a diagnostic challenge due to the unreliability of serology testing in patients receiving intravenous immunoglobulin and the unavailability of a confirmatory test. This test has since been made available and biopsy samples have now confirmed the suspected diagnosis.

British Infection Association

Clinical Paper E

Title **A fatal misidentification**

Authors Umang Agrawal, Krutarth Kanjiya, Rasika Sirsat, Rajeev Soman, Camilla Rodrigues, Ayesha Sunavala

Address *PD Hinduja Hospital and MRC, Mumbai, India*

Abstract without diagnosis

A 67-year Indian businessman, hailing from a coastal region of Western India, was admitted with high grade fever and productive cough for 15 days and weight loss (14 pounds) for 3 months. He had poorly controlled diabetes and was on maintenance hemodialysis via arteriovenous fistula for diabetic kidney disease. He was admitted with similar complaints elsewhere 2 months ago. His blood culture then had grown acinetobacter species (selective resistance to aminoglycosides and polymyxins, but susceptibility to the 3rd and 4th generation cephalosporins, cotrimoxazole and carbapenems) He showed partial response to 10 days of meropenem. On examination, he was febrile, tachycardic and had multiple tender nodules over joints and muscles. Blood cultures were requested. Chest imaging showed pneumonia. PET scan showed multifocal osteomyelitis. Blood cultures grew the offending pathogen.

British Infection Association

Clinical Paper F

Title **The unusual case of the swollen finger**

Authors Vino Srirathan, Jemma Montelle, Manjusha Narayanan, Sahan Rannan-Eliya, Uli Schwab

Address *The Newcastle upon Tyne Hospitals, Newcastle-Upon-Tyne, United Kingdom*

Abstract without diagnosis

A 20-year-old male presented with 4 weeks of pain and swelling of the left fifth digit. Five months previously, he travelled outside of the UK for a summer camp. Serial x-rays 6 days apart showed interval medullary lucency of the proximal phalynx. Oral flucloxacillin was commenced and urgent referral to the sarcoma service was planned. MRI scan showed prominent lysis and abnormal marrow of the entire proximal phalynx with soft tissue swelling. Progressive finger swelling and erythema over one week required surgical debridement of pus on five occasions over three weeks. Consecutive antibiotic courses of flucloxacillin, co-amoxiclav and clindamycin were given. Samples from initial washouts grew mixed skin flora on enrichment. Histology showed mixed inflammatory infiltrate in keeping with acute osteomyelitis, with negative stains for bacteria, mycobacteria and fungi. Histology of tissue from the fifth washout showed granulation containing fungal elements. These were single celled capsulated organisms, occasionally in pairs. Intravenous amphotericin was commenced. 18s PCR of tissue was positive, and 16s PCR was positive for Staphylococcus aureus. Culture confirmed the diagnosis after nine days. The patient later disclosed a history of left apical thoracic pain, however CXR and CT scan showed only focal scarring in the left apex. Two weeks of amphotericin was followed by oral itraconazole, planned duration 6-12 months. There was sustained improvement of swelling and movement. The finger was preserved as per patient wishes, but function lost. This case was diagnostically challenging, and travel history was essential in making the diagnosis early, prior to laboratory confirmation.