time interval was too short for them to be screened for TB. Abstract S41 table 1 illustrates the differences between NICE and BHIVA strategies over the 10-year period. Neither screening method had optimal sensitivity and specificity. Both guidelines' eligible groups were only twice as likely to develop active TB compared to those ineligible for screening. NICE guidelines were poorly specific while the BHIVA strategy missed 42% of cases (largely as they were either UK born or on ART). Using data from our UK HIV population, we find that new TB screening guidance does not appear to discriminate those at risk of active TB.

S42 EARLY IDENTIFICATION OF *MYCOBACTERIUM TUBERCULOSIS* (*M.tb*) AND *MYCOBACTERIUM* OTHER THAN *TUBERCULOSIS* (MOTT) BY "CORD FORMATION" EVALUATION IN LIQUID CULTURE

doi:10.1136/thoraxjnl-2011-201054b.42

A Elshaghir, S Abdullah, F Sundram, D D Creer. *Barnet and Chase Farm Hospitals NHS Trust, London, UK*

The identification of *M.tb* in smear negative samples has the inherent TB culture delays. These delays potentially affect treatment choices and contact tracing decisions particularly where TB prevalence is low and isolation of MOTT common. Faster molecular techniques are expensive and not universally available. The identification of cord formation¹ in positive cultures gives an early indication of the likely TB culture result before the final reference laboratory identification (local audit data: *M.tb* 12.3±5.9 d, MOTT 13.7±11.6 d). We evaluated the presence of cord formation in AFB smears prepared from MGIT tubes and stained by auramine-phenol staining from positive liquid culture (BACTEC MGIT growth supplement medium) for the presumptive identification of *M.tb*. We prospectively evaluated 612 positive mycobacterial culture specimens from 316 patients over 3 years. All specimens were sent to our local reference laboratory for species identification. The identification of *M.tb* by the presence of cord formation was compared with the subsequent reference laboratory report. 420/426 samples showing cording by smear microscopy were confirmed by the reference laboratory as *M.tb* (PPV: 98.6%). 182/186 non-cording culture positive specimens were confirmed as MOTT (NPV: 97.9%). The 6/612 (0.9%) MOTT misidentified as *M.tb* by cording were *M.kansasii* as previously described.¹ The 4/612 (0.7%) *M.tb* misidentified as MOTT by the absence of cording were all 3+ sputum smear positive samples as previously described.² The presumptive identification of *M.tb* and MOTT by the presence or absence of cording in liquid culture is both sensitive and specific. This technique has a potentially significant impact on treatment timing and contact tracing decisions.

REFERENCES

1. McCarter YS, et al. Cord formation in BACTEC medium is a reliable, rapid method for presumptive identification of *Mycobacterium tuberculosis* complex. *J Clin Microbiol* 1998;**36**:2769–71.
2. Koksalan OK, et al. Reliability of cord formation in BACTEC 12B/13A media for presumptive identification of *Mycobacterium tuberculosis* complex in laboratories with a high prevalence of *Mycobacterium tuberculosis*. *Eur J Clin Microbiol Infect Dis* 2002;**21**:314–17.

S43 POLYFUNCTIONAL T CELLS REVEAL THE SPECTRUM OF TUBERCULOSIS IN HIV CO-INFECTION THROUGH THE IDENTIFICATION OF IMMUNOLOGICAL CORRELATES OF LATENT AND ACTIVE DISEASE

doi:10.1136/thoraxjnl-2011-201054b.43

¹K M Pollock, ¹D Montamat-Sicotte, ²G Cooke, ¹M Kapembwa, ³O M Kon, ²G P Taylor, ¹A Lavani. ¹Department of Respiratory Medicine, Tuberculosis Research Unit, National

Heart and Lung Institute, Imperial College London, London, UK; ²Department of Medicine, Division of Infectious Diseases, Imperial College London, London, UK; ³Tuberculosis Service, St Mary's Hospital, Imperial College Healthcare Trust, London, UK

Background Approximately one-third of the world's population is infected with *Mycobacterium tuberculosis* (MTB), mostly as latent tuberculosis infection (LTBI). HIV co-infection confers the single greatest risk of progression to active tuberculosis (TB) and thus provides an opportunity to study the host–pathogen interaction in LTBI. The stage of TB disease and effect of advancing HIV infection should be reflected in the phenotype and function of MTB-specific T cells.

Aims To compare MTB-specific CD4+ and CD8+ T cell responses in donors from four clinical phenotypes (TB/HIV, TB, LTBI/HIV and LTBI) and test whether TB in the context of HIV is a spectrum of disease dependent on mycobacterial load consequent upon advancing immunosuppression and viraemia.

Methods Donors (n=84) with or without HIV co-infection were carefully selected for active TB or LTBI. Peripheral blood mononuclear cells (PBMCs) were stimulated overnight with purified protein derivative (PPD) or a combination of MTB-specific antigens. An 11-colour intracellular cytokine secretion assay was used to assess CD3, CD4, CD8, IFN- γ , IL-2 and TNF- α expression.

Results The proportion of participants with a CD8+ PPD-specific IFN- γ (p=0.001) or TNF- α (p=0.006) response closely mirrored stage of TB disease, whereas the equivalent CD4 response was unaffected. The proportion of CD4+ and CD8+ PPD-specific cells increased with TB stage for IFN- γ and TNF- α , but did not increase in HIV/TB co-infection compared with TB (Abstract S43 figure 1). When individual cytokine subsets were examined, the percentage of

Abstract S43 Figure 1 The proportion of CD3+ CD4+ and CD8+ cells with a total cytokine response to PPD or MTB antigens following 16 h of stimulation. PBMCs were stained with an 11-colour panel including a dead cell marker and fluorochrome-conjugated antibodies for CD3, CD4, CD8, IFN- γ , IL-2 and TNF- α and acquired on an LSR-II flow cytometer.

CD4+ and CD8+ cells producing IFN- γ , TNF- α or dual responses was higher in all participants with TB compared with LTBI. CD4+IL-2+ cells were reduced by HIV co-infection, especially IFN- γ +IL-2+ cells ($p=0.008$) and this was apparent as a proportion of total cytokine response ($p=0.016$).

Conclusions The proportion of CD8+ IFN- γ or TNF- α responders was a more sensitive indicator of TB stage than CD4 responses. CD4 + IL-2 responses were vulnerable to HIV co-infection, possibly affecting CD8+ IFN- γ and TNF- α responses at high viral loads, increasing susceptibility to active TB. These immune correlates of the TB spectrum and the MTB-specific T-cell deficiencies caused by HIV co-infection are important in rationalising treatment of co-infection as well as testing new vaccines and therapeutics.

Cystic fibrosis: bench to bedside

S44 LUNG CLEARANCE INDEX (LCI) AND FEV₁ CORRELATE EQUALLY WITH TREATMENT BURDEN AS MEASURED BY CYSTIC FIBROSIS QUESTIONNAIRE-REVISED (CFQ-R)

doi:10.1136/thoraxjnl-2011-201054b.44

¹K O'Neill, ²J M Bradley, ³M Tunney, ¹J S Elborn. ¹Centre for Infection and Immunity, Queen's University Belfast, Belfast, UK; ²Health and Rehabilitation Sciences Research Institute, University of Ulster, UK; ³School of Pharmacy, Queen's University Belfast, Belfast, UK

Introduction LCI derived from multiple breath washout (MBW), measures the elimination of an inert marker gas during tidal breathing and is a sensitive measure of ventilation inhomogeneity in CF. LCI is more sensitive than FEV₁ and FEF₂₅₋₇₅ in detecting airways abnormalities and does not require a forced manoeuvre. The CFQ-R is a validated patient reported outcome used to assess health related quality of life (HRQoL) and patient perception of symptoms. There is a need to better understand the relationship between LCI, HRQoL and symptoms.

Objective To investigate the relationship between LCI, FEV₁ % pred, HRQoL and symptoms as measured by the CFQ-R.

Methods These data are part of a larger study investigating the role of LCI as a tool to monitor lung function longitudinally. Patients were recruited from the adult and paediatric CF centres in Belfast Health and Social Care Trust. Inclusion criteria: clinical diagnosis of CF; clinically stable (exacerbation free=4 weeks); informed consent. Age appropriate versions of the CFQ-R were used (patients >14 years, children aged 12 and 13, children aged 6–11). A parent questionnaire was completed in addition where appropriate (for children aged 6–13). The instrument yielded a score of 0–100 for each domain, with higher numbers indicating better function on various domains. Participants completed three MBW tests, using 0.2% sulphur hexafluoride and a modified Innocor device. LCI was reported as the mean of at least 2 acceptable tests. Spirometry was performed to ATS/ERS standards.

Results Data were collected for 21 patients (15M:6F), age range 6–51 yrs, mean (SD) 26.4 (13.7). Mean (SD) FEV₁ % pred was 77.1 (16.3). Mean (SD) LCI was 9.4 (2.5) (normal <7.5). LCI correlated negatively with FEV₁% pred ($r=-0.62$ $p=0.003$). The domain of treatment burden was significantly correlated with LCI ($r=-0.67$ $p=0.001$) and FEV₁% pred ($r=0.69$ $p=0.001$). However no correlation was observed with respiratory symptoms or any other domain of the CFQ-R.

Conclusion Patients with a greater treatment burden are more likely to have more severe lung disease. The severity of CF lung disease as determined by FEV₁% pred and LCI correlate equally with treatment burden. This further validates LCI as a useful measure of lung function.

S45 CLINICAL EFFICACY OF SEASONAL INFLUENZA VACCINATION IN ADULTS WITH CYSTIC FIBROSIS

doi:10.1136/thoraxjnl-2011-201054b.45

¹W G Flight, ²K J Mutton, ¹A K Webb, ¹R J Bright-Thomas, ¹A M Jones. ¹Manchester Adult Cystic Fibrosis Centre, Manchester, UK; ²Department of Virology, Manchester Royal Infirmary, Manchester, UK

Introduction Influenza vaccination produces an adequate serological response in adults with cystic fibrosis (CF)¹ and is a recommended part of routine CF care. There is little evidence to date, however, of a clinical benefit from influenza vaccination in this patient group. We compared prospectively the rate of influenza infection with vaccination status among 100 adults with CF over the 2010/2011 UK influenza season.

Methods 100 adults with CF were enrolled in a prospective observational study of respiratory viruses between December 2010 and March 2011. Sputum, nose- and throat-swabs for PCR-based virological analysis were sent every 2 months and additionally at onset of acute respiratory illness through to June 2011. Prior to enrolment, sputum was sent for virology at onset of pulmonary exacerbations as part of routine care. Details of influenza vaccination status were obtained from the CF centre's database and GP records. Previous infection with influenza A/H1N1 was determined from clinical records.

Results Patients had a median age of 28 years (range 18–62). 88% had received the 2010/2011 seasonal influenza vaccine (A/California/7/2009/H1N1, A/Perth/16/2009/H3N2 & B/Brisbane/60/2008). 44% of the cohort had received the 2009 monovalent swine-origin influenza A/H1N1 vaccine and 8 patients had previously had PCR-confirmed swine-origin influenza. Over the study period there were 10 cases of influenza: 5 influenza A/H1N1, 4 influenza B and 1 dual influenza A/B infection. Among patients who received the 2010/2011 seasonal vaccine, 9/88 (10.2%) suffered influenza compared with 1/12 (8.3%) of those who had not been vaccinated (OR 1.25; 95% CI 0.14 to 10.9). All 9/9 patients who developed influenza despite being vaccinated were homozygous for the F508del mutation compared with 43/79 (55.7%) of vaccinated patients who did not develop influenza ($p=0.009$). No significant difference was seen between these groups with regard to age, gender, BMI, lung function, diabetes mellitus or use of oral corticosteroids.

Conclusions Influenza vaccination may have limited clinical efficacy in adults with CF. The influence of CF genotype on susceptibility to influenza infection and response to vaccination requires further investigation.

REFERENCE

1. Ong ELC, et al. Influenza vaccination in adults with cystic fibrosis. *BMJ* 1991;**303**:557.

S46 A COMPARISON OF THREE DIFFERENT SPECIMEN TYPES FOR THE DIAGNOSIS OF VIRAL RESPIRATORY INFECTIONS IN ADULTS WITH CYSTIC FIBROSIS

doi:10.1136/thoraxjnl-2011-201054b.46

¹W G Flight, ²K J Mutton, ³B Isalska, ¹R J Bright-Thomas, ¹A M Jones. ¹Manchester Adult Cystic Fibrosis Centre, Manchester, UK; ²Department of Virology, Manchester Royal Infirmary, Manchester, UK; ³Department of Microbiology, University Hospital of South Manchester, Manchester, UK

Introduction Respiratory viruses have been associated with increased symptoms and a decline in lung function in patients with cystic fibrosis (CF). The optimal means of diagnosis of respiratory viruses in CF is unclear. We compared the suitability of sputum,