

## TB: epidemiology and diagnosis

### S1 HIGH LEVELS OF LATENT TB INFECTION, BLOOD BORNE VIRUSES AND UNMET NEED AMONG HARD TO REACH GROUPS IN LONDON: THE TB REACH STUDY

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**Background** Urban homeless people have high levels of disease and often present late for healthcare. Despite high rates of active TB in London's large homeless population, limited data are available regarding the prevalence of latent TB infection (LTBI) and blood borne viruses (BBV) - HIV, Hepatitis B & C. We have undertaken a TB/BBV screening programme to assess the prevalence of LTBI, infection with BBV and co-infection within hard to reach groups (homeless people and substance misusers) in homeless hostels and residential drug services in London.

**Method** Residents screened for TB on a mobile chest x-ray unit were approached and with consent, blood was drawn for TB IGRA (Quantiferon In-Tube) and BBV. Results were fed back to participants with onward referral as necessary.

**Results** Of 413 eligible participants, 390 (94%) reported a history of homelessness. Of these 390 participants, 89% were male, 68% were 16–49 years of age and 66% UK born. 17% were IGRA positive, 1% HIV positive (all previously known), and 10% had current and 4% past Hepatitis C. 1% of those screened had current Hepatitis B infection, 10% past infection, 18% had vaccine induced protective levels of immunity and 71% had insufficient or no Hepatitis B immunity. 29% of subjects with Hepatitis C were LTBI co-infected. Multivariate analysis identified increasing age e.g. 30–49 age group (odd ratio [OR], 2.15; 95% confidence interval [CI<sub>95%</sub>], 0.84–5.49) compared to the under 30, foreign birth (OR, 6.59; CI<sub>95%</sub>, 3.50–12.39), smoking hard drugs (OR, 2.19; CI<sub>95%</sub>, 1.02–4.64), and injecting hard drug (OR, 2.36; CI<sub>95%</sub>, 1.08–5.16) such as heroin, crack or cocaine (although 95% of injectors also smoked hard drugs) as risk factors for LTBI. Injecting drug use was the only factor associated with increased risk for Hepatitis C infection (OR, 19.62; CI<sub>95%</sub>, 8.23–46).

**Conclusion** Extremely high rates of LTBI, Hepatitis C and co-infection are present in our urban study population. Despite targeted Hepatitis B vaccination programmes, a high proportion of participants appear unvaccinated. These levels of unmet need have major implications for public and personal healthcare planning and should be recognised through appropriate targeted health and social policy.

### S2 ETHNIC VARIATION IN INFLAMMATORY PROFILE IN TUBERCULOSIS

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**Introduction and objectives** *Mycobacterium tuberculosis* (MTB) emerged as a pathogen in Africa and has co-evolved with humans following the migration to Europe and Asia some 70,000 years ago. Distinct phylogenetic lineages of MTB associate with hosts of particular genetic ancestry, both in their regions of origin and in distant

cosmopolitan urban settings where human populations of different ancestry intermingle. These different strains induce distinct patterns of cytokine and chemokine secretion ('inflammatory profiles') in human macrophages. Circulating and antigen-stimulated inflammatory profiles might therefore be expected to vary significantly between tuberculosis patients of different ethnic origin. We therefore conducted a study to determine whether such variation exists.

**Methods** We measured circulating and antigen-stimulated concentrations of 43 soluble inflammatory mediators and 14 haematological parameters in 45 patients of African ancestry and 83 patients of Eurasian ancestry receiving intensive-phase antimicrobial therapy for smear-positive pulmonary tuberculosis in London, UK. Host and bacillary genotypes were also determined. Statistical analyses were performed to compare inflammatory profiles in patients of African vs Eurasian ancestry; to investigate the influence of host and bacillary genotype on inflammatory profile; and to determine immunological correlates of speed of elimination of MTB from sputum.

**Results** Tuberculosis patients of African vs Eurasian ancestry had similar clinical characteristics, but exhibited distinct inflammatory profiles. Patients of African ancestry had lower neutrophil counts, lower serum concentrations of CCL2, CCL11 and vitamin D binding protein (DBP), and lower antigen-stimulated CCL11 secretion than those of Eurasian ancestry, but higher serum CCL5 concentrations and higher antigen-stimulated interleukin 1 receptor antagonist and IL-12 secretion. These differences did not relate to MTB strain variation between groups, but they did associate with ethnic variation in host DBP genotype. Ethnic differences in inflammatory profile became more marked following initiation of antimicrobial therapy, and immunological correlates of speed of elimination of MTB from the sputum were distinct for patients of African vs. Eurasian ancestry.

**Conclusions** Our study demonstrates a hitherto unappreciated degree of ethnic heterogeneity in inflammatory profile in tuberculosis patients. Candidate immunodiagnosics and immunological biomarkers of response to antimicrobial therapy should therefore be derived and validated in tuberculosis patients of different ethnic origin.

### S3 T CELL RESPONSES TO VITAMIN D ARE BLUNTED IN LATENT TUBERCULOSIS

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**Introduction** Low vitamin D status is associated with an increased risk of *Mycobacterium Tuberculosis*. Consistent with this, the active form of vitamin D, 1,25(OH)<sub>2</sub>D<sub>3</sub> exerts potent effects on immune cells.

T cells are thought to contribute to the control of latent tuberculosis in which patients are infected with *Mycobacterium tuberculosis* but show no signs or symptoms of the disease. How vitamin D influences T cell responses in latent patients is therefore of interest.

It has been shown that the co-suppressive protein, CTLA4, which is expressed on regulatory T cells and induced in T cells upon activation, is strongly up regulated by vitamin D and that it increases the frequency of CTLA-4+FoxP3+ cells [1]. Furthermore, vitamin D conditioned T cells are functionally suppressive. In this study we have therefore compared the effect of vitamin D upon CTLA-4 expression and the frequency of CD25+ FoxP3+ CTLA4+ cells in healthy and latent TB patients.

**Methods** Peripheral blood cells from healthy control donors (n=21) and patients with latent tuberculosis (n=12) were cultured with SEB or PPD with or without 1,25(OH)<sub>2</sub>D<sub>3</sub> or inactive 25(OH)D<sub>3</sub>. CD25+ FoxP3+ CTLA4+ frequency and the median CTLA-4