P165 TB-ST RAPID TEST FOR TUBERCULOSIS DIAGNOSIS IN A RESOURCE POOR SETTING: ARE CASES OF TUBERCULOSIS GOING UNDIAGNOSED?

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Introduction Diagnosis of tuberculosis (TB) ideally involves culture and sensitivity of the organism but in low income countries this is not practised routinely. The World Health Organisation estimates that substandard detection occurs in 40% of patients globally, with many diagnosed on clinical suspicion or response to medication. TB produces a strong antibody response suitable for simple, inexpensive and rapid serodiagnostic assays. Ongoing evaluation of a new point of care rapid serological test based on lateral flow immunochromatography (TB-ST Rapid Test, Lionex, Germany) has shown 100% specificity, with no false positive tests in normal controls and latently infected patients, but sensitivity of 36%, with false negatives in culture proven TB.
Aim Using this test in a resource poor setting to investigate whether cases of active TB may be being missed by current diagnostic methods.
Methods 498 patients in chest and HIV clinics in two rural Kenyan hospitals were investigated with the TB-ST Rapid Test and a scored questionnaire to determine symptoms and risk of TB. Results were compared with clinical diagnoses made, usually based on symptoms alone. Chest radiographs were performed in only 111 and sputum smears in 75.
Results 127/498 patients were HIV positive. Of these, only 59(46%) had a clinical diagnosis of TB, whereas 87(68.5%) had significant TB symptoms and/or risk factors, and 82(64.6%) tested TB-ST positive ($p<0.001$). Therefore clinical diagnosis accounted for significantly fewer diagnoses of active TB than suggested by either symptom and risk score or TB-ST rapid results in the HIV+ population. Of the 375 HIV− patients, 73 (19.7%) had a clinical diagnosis of TB, 46 (12.3%) scored positive for TB on the questionnaire, and 149 (40.2%) were TB-ST+ ($p<0.001$). Abstract P165 Table 1 shows positive and negative TB-ST results related to positive and negative sputum smears in 34 HIV+ and 41 HIV− patients.

Abstract P165 Table 1

	HIV +ve TB-ST +ve	HIV +ve TB-ST −ve	HIV −ve TB-ST +ve	HIV −ve TB-ST −ve
Smear negative (%)	13 (38)	8 (23.5)	9 (21.9)	11 (26.8)
Smear positive (%)	8 (23.5)	5 (15)	17 (41.5)	4 (9.8)

Conclusions Many more patients had positive TB-ST and risk and symptom scores than were being diagnosed with active TB, suggesting that TB may not always be being diagnosed or treated. Sputum smears were in greater agreement with the TB-ST in HIV− but not HIV+ patients, in whom there were considerably fewer positive smears than TB-ST results.

P166 QUANTIFERON TESTING IN CLOSE CONTACTS OF SMEAR POSITIVE PULMONARY TB IDENTIFIES PEOPLE AT LOW RISK OF SECONDARY PROGRESSION

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Introduction Interferon gamma release assays (IGRAs) are recommended for screening close contacts of patients with active tuberculosis (TB) in the UK. Compared with tuberculin skin testing, greater specificity with IGRAs reliably informs the need for chemoprophylaxis in screened contacts by identifying latent Mycobacterium tuberculosis infection (LTBI) associated with a high risk of secondary disease progression. However, the risk of secondary progression varies with the nature of disease in the primary case and is greatest for contacts of smear positive pulmonary disease. The role of IGRAs in this very high risk population is not clear.
Aim To evaluate the benefit of screening with QuantiFERON®-TB Gold (QFT) in contacts of smear positive pulmonary TB.
Methods A prospective observational study. We have offered QFT based single step screening programme for all close contacts of smear positive pulmonary TB since January 2007. We present 2-year follow-up data in tested and untested contacts that did not receive chemoprophylaxis. Secondary disease risk is estimated with Kaplan–Meier analysis and subgroups compared with the log-rank test.
Results 576 recorded contacts for 92 smear positive cases. Median follow-up 693 days (range 287–1146 days). 467 (81.1%) of contacts were QFT screened. 36% of tested contacts had a positive QFT; 83 QFT positive contacts did not receive chemoprophylaxis (group A); 101 contacts were not screened and untreated (group B); 301 were QFT negative (group C). Secondary disease occurred in 22 contacts (11 group A, 5 group B). Progression rates at 12 and 24 months are shown (Abstract P166 Table 1). Compared with the untested subgroup, a positive QFT results did not significantly increase progression risk (RR 2.1 (95% CI 0.7 to 5.9), p=0.13). A negative QFT result did significantly lower progression risk (RR 0.28 (95% CI 0.09 to 0.82) at 2 years, p=0.01). The negative predictive value of QFT compared with not testing was 93.2% (95% CI 85.8 to 97.5).

Abstract P166 Table 1

	Progression risk % (SEM)		
Observation period/days	Group A	Group B	Group C
0–365	11.7 (4.0)	5.7 (2.0)	1.0 (1.0)
365–730	15.2 (4.0)	7.4 (3.0)	2.0 (1.0)

Conclusion In contrast with other TB disease types, QFT screening in contacts of smear positive pulmonary TB does not identify contacts for chemoprophylaxis, but rather identifies contacts that we may choose not to treat.

P167 CHARACTERISATION OF TUBERCULOUS MEDIASTINAL LYMPHADENOPATHY ON CT AND CORRELATION WITH BIOMARKERS AND CHEST RADIOGRAPH FINDINGS

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Introduction The aim of this study was to characterise the anatomical pattern of mediastinal lymphadenopathy on CT in active tuberculosis (TB) and assess correlation with biomarkers and chest radiograph (CXR) findings.
Methods We conducted a retrospective analysis of patients treated for active TB with mediastinal lymphadenopathy at a tertiary centre between January 2007 and May 2009. CT scans performed prior to commencement of therapy were reviewed by two radiologists to assess for pathologically enlarged lymph nodes (LN) (short axis diameter >1.0 cm) at each of the LN stations defined by the International Association for the Study of Lung Cancer (IASLC).
Results 55 patients were included in the study. 56.3% of enlarged LNs were right sided, 32.9% were in central LN groups and 10.8% were left sided. 40.0% of patients had evidence of necrosis within LNs. The most frequently occurring enlarged LNs were in the

subcarinal (level 7; 81.8% of patients), right lower paratracheal (level 4R; 58.2%) and right hilar (level 10R; 52.7%) stations. The Abstract P167 Table 1 shows correlation of biomarkers and CXR abnormalities with extent of LN involvement on CT. Results are displayed as % group or median (IQR). There were 49.1% with a normal CXR. In this subgroup, ESR and Globulin levels also correlated with extent of LN involvement on CT. The median (IQR) LN involvement stratified by ESR levels was: 2 (1–2), 2 (1–2.8) and 5 (4–5) for ESR ≤15, ESR 16–49 and ESR >49 mm/h, respectively (p=0.039). The median (IQR) LN involvement stratified by Globulin levels was: 2 (1–3), 2 (2–4.8) and 5 (2.8–5.3) for Globulin ≤35, Globulin 36–45 and Globulin>45 g/l, respectively (p=0.048).

Abstract P167 Table 1

Number of LN stations involved	Globulin (g/l)	ESR (mm/h)	Abnormal CXR (%)
1–3 (n=26)	36.5 (32–39)	23 (9–28)	19.2
4–6 (n=24)	42 (35–50)	67 (45–96)	41.7
>6 (n=5)	45 (40–50)	84.5 (62–96.5)	80
p-Value	0.03	0.004	0.03

Conclusion Tuberculous mediastinal lymphadenopathy on CT is characterised by a specific anatomical pattern with predominance of right sided LNs and more frequent involvement of particular LN stations. A large proportion of patients with pathologically enlarged LNs on CT have normal CXRs. Biomarkers such as ESR and globulin levels correlate with extent of LN involvement on CT.

P168 RIFABUTIN IS A USEFUL ALTERNATIVE TO RIFAMPICIN IN THE TREATMENT OF ACTIVE TB/HIV CO-INFECTION

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Introduction Effectiveshort course anti-tuberculosis treatment (TB Rx) requires use of a rifamycin, typically rifampicin (RIF). However, in patients with TB/HIV co-infection it has significant drug interactions; and rifabutin (RBT) is often substituted in those taking anti-retrovirals (ARVs). Recent data suggest that the recommended dosage of RBT may be inadequate with concomitant ARVs, leading to an increased risk of subsequent rifamycin resistance after apparent successful treatment.

Aims We undertook a retrospective, single-site review of TB/HIV treatment to determine the impact of rifamycin selection on prevalence of serious (ACTG grade III or IV) adverse events (AE), TB treatment completion and TB recurrence.

Methods The characteristics and treatment outcomes, stratified by rifamycin type and ARV use for all adults with TB/HIV co-infection receiving rifamycin-based therapy as part of active TB Rx from 1997 to 2008 were examined. Rifamycin choice and dosage was in line with BHIVA guidance for TB/HIV therapy—in general RIF being used with a non-nucleoside inhibitor ARV combination and RBT with boosted protease inhibitors.

Results 143 HIV-positive individuals received rifamycin-based TB Rx during the study period (64 RIF, 56 RBT and 24 RIF/RBT in treatment switch—see Abstract P168 Table 1). 103/143 (72%) patients had culture positive disease, of whom 4 had isoniazid drug resistance. 106/143 (74%) patients used ARVs during TB Rx. Patients on ARVs who had RIF either alone, or switched from RIF to RBT during TB Rx had a higher incidence of serious AE compared to those prescribed RBT alone (p=0.002). There was no difference in the percentage of patients who completed prescribed TB Rx between the RIF and RBT groups (p=0.6). After a median follow-up of 3.2 years from start of TB Rx, 4 patients relapsed, all with a drug sensitive organism.

Abstract P168 Table 1 Rifamycin

	No ARVs during TB Rx		ARVs during TB Rx		
	RIF n=34*	RBT n=1	RIF n=28	RBT n=54	RIF + RBT n = 24
Black-African	22 (65%)	1 (100%)	21 (75%)	37 (69%)	20 (83%)
Blood CD4 count (cells/mm^3)	350 (7–831)	132	123 (13–500)	124 (2–844)	61 (11–233)
Completion of prescribed TB Rx	30 (88%)	1 (100%)	27 (96%)	52 (96%)	23 (96%)
Grade III/IV AE	14 (41%)	0	20 (71%)	17 (31%)	16 (67%)
Recurrence of TB	1 (3%)	0	2 (7%)	1 (2%)	0

Entries are number (%) or median (range).
*2 RIF pts had unknown ARV status

Conclusion Within our study population, rifabutin is a useful alternative to rifampicin in the treatment of active TB/HIV co-infection and does not appear to lead to subsequent rifamycin resistance after successful therapy. We find no evidence in this analysis to change the advice within the current national TB/HIV guidelines.

P169 SUBCLINICAL OCULAR MANIFESTATIONS OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS IN A HAMPSHIRE POPULATION

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Background Intraocular tuberculosisis capable of imitating numerous uveitis entities; the ability of TB to causeuveitis is multifactorial including virulence of the infecting organism, anindividual's immune response, and the location of the disease. The nonspecificnature of uveitis makes diagnosis difficult, and allowed to progressunchallenged, intraocular tuberculosis can be sight-threatening. We postulate that subclinical ocular signs of TB might coexist with TB activeat other sites.

Methods 14 TB latent, 14 TB active, and 3 TB-HIV co-infected patients were recruited for this pilot study, between October 2009 and April 2010, from the TB service at the Royal South Hants Hospital. At Southampton General Hospital's Eye Unit patients provided detailed ocular and tuberculosis histories; all patients then underwent a series of extensive ocular examinations, including best corrected visual acuity and colour vision, intraocular pressure, pupillary response, ocular motility, slit lamp and dilated fundus examinations; finally each patient's ocular findings were correlated against their TB and TB-HIV co-infection clinical profiles.

Results 14 patients were classified "latent TB" (IGRA positive, asymptomatic) and 14 patients were classified "active TB" (symptoms, culture positive) of whom three were "TB-HIV co-infected". Patients with active TB were identified as having significantly more symptoms associated with anterior uveitis, such as pain, photophobia, redness and blurred vision/floaters, compared to those patients with latent TB. We demonstrated objective evidence of anterior chamber inflammation inpatients with active disease, but not latent disease. The patients with HIV coinfection exhibited combined anterior and posterior segment abnormalities consistent with an active uveitis.

Conclusions The results of this pilot study suggest that patients with active TB have symptoms suggestive of uveitis, but these are unrecognised by the patient unless specifically sought. These patients have anterior chamber findings of uveitis. TB-HIV co-infected patients appear to present asymptomatically with anterior