interleukin-6 (IL6) and C-reactive protein (CRP). Spontaneously expectorated sputum was collected for standard microbiological culture and a subset was also assayed for IL8, a marker of neutrophilic inflammation and IL6.

Results There were 196 patients with 266 sputum samples (52% 0 PPM, 38% 1 PPM, 10% 2 PPM). Their mean age was 68.0 years (SD 8.1); 61% were male; forced expiratory volume in 1 s (FEV_1)% predicted 47.1 (18.3) and 49.8 (36.7) pack years smoking history.

Conclusions The presence of a single PPM on sputum culture at exacerbation is associated with an increase in systemic and airway neutrophilic inflammation and a lower airway IL6 (table 1). Unexpectedly, dual PPMs are associated with less systemic inflammation than single PPMs and they share the same inflammatory profile as non-bacterial exacerbations. This suggests that dual PPMs may be non-contributory to exacerbations. Inhibitory competition arising from the acquisition of a second bacterial strain might explain their relative non-pathogenicity.

Screening and treatment of tuberculosis

P108 THE NATIONAL MULTIDRUG RESISTANT TB SERVICE

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Introduction The low incidence of multidrug resistant tuberculosis (MDRTB) in the UK means that few specialists treating tuberculosis have much experience of managing patients with MDRTB and no mechanism for collecting data on the progress of such patients exists. To attempt to overcome this gap, with the support of relevant professional bodies and a grant from Genus Pharma, the MDRTB Service was established at the Liverpool Heart and Chest Hospital in January 2008.

Method The Service offers ready access to expert advice on the management of patients with MDRTB via an electronic committee of TB experts. The second function of the Service is to collect data on all MDRTB cases identified in the UK, to record outcomes and develop a consensus on the most effective methods of treatment.

Results This submission is an update to the report which was presented at the 2008 BTS winter meeting.[1] Since its founding, the MDRTB Service has been approached with 62 TB cases. Of these, 48 were confirmed as MDR and 3 XDRTB while the remainder could not be confirmed as MDR, were isoniazid mono-resistant or were more general requests for advice. Regular updates on these cases are being sought and treatment patterns and results recorded. An analysis of the initial data shows that 69% of cases had received no previous treatment for TB. Over half were likely to have been infectious, with 57% of the cases being sputum smear positive at diagnosis. The majority of the cases were of a non-white ethnic background, the highest number being Asian (40%). The split between male and female was 65% male to 35% female, while 78% of cases were aged between 24 and 44. Drug resistance patterns revealed that MDRTB is associated with high levels of resistance to other drugs: streptomycin (56%), ethambutol (42%) and pyrazinamide (36%) (fig 1). For a total of 37.5 patient-years of follow-up, only one death has been recorded.

1. **Cullen DM**, Davies PDO. The national multi-drug resistant tuberculosis service: the first six months. *Thorax* 2008;**63**(Suppl VII):A147.

P109 TREATMENT INTERRUPTIONS AND INCONSISTENT SUPPLY OF ANTI-TUBERCULOSIS DRUGS IN THE UK: A NATIONAL REVIEW

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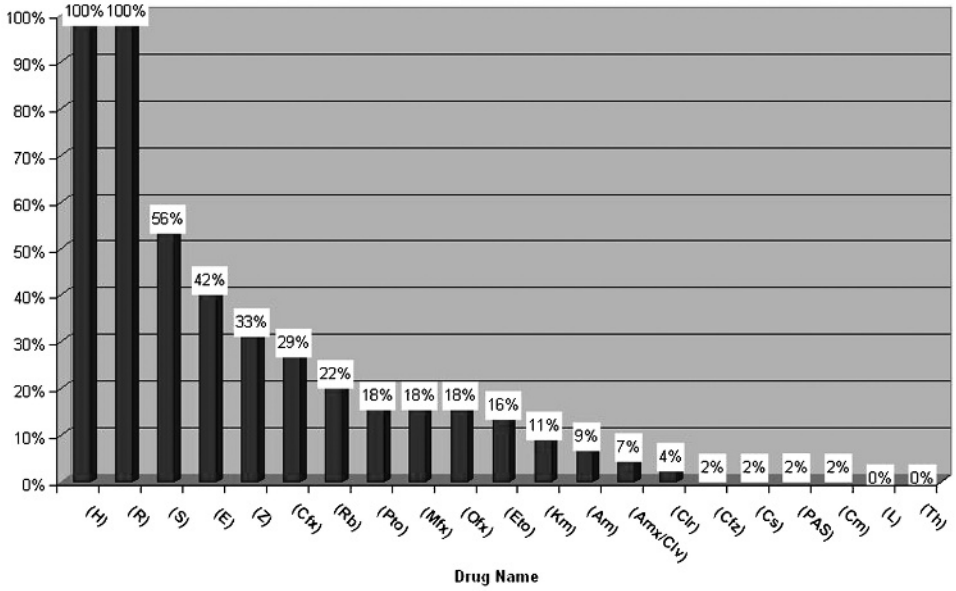
Introduction The 2004 Department of Health TB Action plan highlighted the need to provide "high quality treatment and care for all people with TB". Anecdotal evidence suggests that there are problems in obtaining anti-tuberculosis drugs in the UK for both adults and children. We report the first UK survey to evaluate anti-tuberculosis drug supply and its impact on patient care within TB treatment services.

Methods A questionnaire was sent to pharmacists with a specialist interest in respiratory medicine or infectious diseases working at UK centres providing TB treatment. This asked whether they had experienced difficulties obtaining anti-tuberculosis drugs over a 2-year period and whether this resulted in unintentional interruption or alteration of treatment.



Abstract P108 Figure 1 MDRTB drug resistance pattern.

Abstract P109 Table 1

Drug	Number of trusts with experience of using drug	Problems with drug supply encountered		
		Number (%) of trusts affected	Number (%) of trusts having to interrupt treatment	Number (%) of trusts having to alter treatment regimen
Isoniazid	66	19 (29%)	4 (6%)	4 (6%)
Rifampicin	65	3 (5%)	0 (0%)	0 (0%)
Pyrazinamide	65	13 (20%)	4 (6%)	1 (2%)
Ethambutol	65	7 (11%)	2 (3%)	1 (2%)
Amikacin	47	4 (9%)	0 (0%)	0 (0%)
Streptomycin	44	12 (27%)	2 (5%)	2 (5%)
Moxifloxacin	51	3 (6%)	0 (0%)	0 (0%)
Prothionamide	34	5 (15%)	3 (9%)	1 (3%)

Results Responses were received from 67 UK NHS hospital trusts who account for approximately 40% of all UK TB notifications. 42 (63%) trusts reported difficulties in obtaining anti-tuberculosis drugs in the previous 2 years. This was not restricted to any one group of drug or licensing status in the UK (table 1). One in 4 trusts reported problems with isoniazid drug supplies, 1 in 5 with pyrazinamide and 1 in 10 with ethambutol. At least 10% of trusts using rifabutin, capreomycin, streptomycin, ofloxacin, prothionamide, ethionamide, cycloserine, PAS or clofazimine had difficulty in obtaining these. At least 5% of trusts using isoniazid, pyrazinamide, rifabutin, capreomycin, ofloxacin, prothionamide, PAS or clofazimine reported that they had to interrupt the prescribed treatment regimen in at least one patient because of difficulties obtaining supplies. The treatment regimen had to be altered in more than 5% of trusts using isoniazid, rifabutin, capreomycin or PAS, although the numbers using some of these drugs were small.

Conclusions A large number of UK trusts have experienced difficulties obtaining a wide range of anti-tuberculosis drugs. The actual number of patients affected by interruptions or alterations in their treatment regimen is fairly low, but this may have had a significant clinical impact on the treatment of both sensitive and drug-resistant TB. Our data argue for national strategic guidance to ensure a consistent and reliable supply of anti-tuberculosis drugs through improved drug information which can promptly alert treatment centres to potential supply issues.

P110 DOES A SPECIALIST TB NURSE SERVICE IMPROVE OUTCOME?

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Introduction and Objectives Poor compliance is the pre-eminent obstacle to successful treatment of patients with tuberculosis (TB). Following national guidelines,[1 2] our primary care trust appointed two community-based TB nurses aiming to improve compliance, outcome and cost of treatment. We audited the effectiveness of our previous hospital-based system of monthly clinic visits (2006) versus a nurse-led system (2008).

Methods We retrospectively examined case notes for all patients referred to the TB nurses during 2008. We excluded those who were partially treated before referral, given chemoprophylaxis, changed diagnosis or died within the first month of treatment. Using the same exclusion criteria, we compared these results with our last audit of a clinic-based TB service (31/8/05–28/2/06; denoted ''2006a'') and information from cases notified to the Health Protection Agency (HPA) in 2006 (''2006b''). We present the data for the key standards measured. A priori exception was applied. We also present financial data for the nurse-led service from April 2008 to March 2009. Statistical analysis was carried out with STATA. The Fisher exact test and the Student *t* test were used.

Abstract P110 Table 1 Percentage of patients achieving key standards or key measurements, in 2006a, 2006b and 2008

	2006a		2006b		2008		
	n	Number achieved (%)	n	Number achieved (%)	n	Number achieved (%)	p Value
Completion of treatment	19	16 (84)	58	32 (55%)	59	56 (94)	<0.0001 (3-way Fisher exact test)
Counselling regarding HIV in first month	22	7 (32)	–	–	64	44 (69)	0.005
Assessed for requiring DOT	22	1* (5)	–	–	64	59* (92)	<0.0001
Uninterrupted medication	20	3 (15)	–	–	64	59 (92)	<0.0001
Monthly reviews (clinic or community)	21	13 (59)	–	–	61	53 (86)	0.004
		Number	–	–		Number	
Mean % of clinic or community reviews not attended (95% CI)	22	17% (4 to 30)	–	–	64	6% (2 to 10)	0.01

22 patients were included for the audit in 2006a. 117 patients were referred to the TB nurses during 2008; 64 were suitable for audit. 61 patients were notified to the HPA in 2006.
*One patient in each year required directly observed therapy (DOT).

Results The results are shown in table 1. In 2008, 62/64 (97%) of patients were given TB nurse contact details within 2 working days. Each outpatient clinic review costs £104. Over the financial year 2008–9, 268 such reviews were replaced by nurses, saving £27872. The TB nurses also undertook 771 additional face-to-face or telephone contacts, a mean of 15 contacts per patient.

Conclusions The introduction of the TB nurse service has led to a statistically significant improvement in all standards audited. In particular, during the first year of the nurse service the completion rates exceeded the Department of Health target.[2] The TB nurse service provides significantly better care than the previous hospital-based clinic and leads to reduced non-attendance rates.

1. **Department of Health**. *Stopping tuberculosis in England: an Action Plan from the Chief Medical Officer*. London: HM Stationery Office, 2004.
2. **Department of Health**. *Tuberculosis prevention and treatment: a toolkit for planning, commissioning, and delivering high-quality services in England*. London: HM Stationery Office, 2007.

P111 WHO GETS DIRECTLY OBSERVED THERAPY? USE OF A RISK MANAGEMENT TOOL TO IDENTIFY TB PATIENTS AT GREATEST NEED

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Introduction and Methods Elimination of tuberculosis (TB) in the UK requires that all patients with active TB successfully complete treatment. A national directly observed therapy (DOT) programme might achieve this although, realistically, resource constraints make this untenable. A patient risk assessment tool may assist in predicting those requiring DOT. Here we report use of a brief healthcare worker-administered risk assessment tool based on factors associated with treatment non-adherence. Originally produced by North East London TB Network, we have adopted this for all patients in our London sector with active TB starting treatment since June 2008. The completed tick-box questionnaire (12 questions) gives a total score that represents global risk of non-adherence. This is used to allocate patients to one of three groups: (1) high score = require DOT, (2) intermediate score = need for increased supervision or (3) low = self-medicate.

Results 500 patients were notified between June 2008 and June 2009. 391 (78%) had a complete assessment performed. Of these, 39 (10%) were identified as requiring DOT. In most cases significant psychological health issues were the main driver for this. 33 (8%) required increased supervision such as use of a nurse-filled weekly dossette box. 319 (82%) of subjects assessed had a low score, indicating that self-medication was a reasonable option. Six (2%) of these were placed on DOT, as the clinician had specific patient concerns not captured by their total score. To date, 182 subjects have been evaluated after 6 months of treatment. 67% have completed (2% with DOT); 18% continue on therapy, almost exclusively due to drug resistance, adverse effects or extent of disease. Outcomes were unavailable for the majority of patients transferred out of London.

Conclusions Our data suggest that the assessment tool enables allocation of limited resources in a simple, pragmatic and objective manner based on patient need. Some of the questions appear to duplicate risk factors and a simpler questionnaire should be evaluated, with scores allocating patients as either needing DOT or able to self-medicate.

P112 NO IMPACT OF HIV CO-INFECTION ON THE FREQUENCY OF ADVERSE EVENTS IN PATIENTS TREATED FOR ACTIVE TUBERCULOSIS: A PROSPECTIVE STUDY

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Background There are an increasing number of effective combination anti-retroviral therapy (CART) options that can be used together with anti-tuberculosis treatments in TB/HIV co-infected subjects. Previously, severe adverse events have been reported in up to 40% of such individuals. We hypothesised that the different adverse event profiles of current CART plus greater physician experience would result in a reduced frequency of adverse events in a contemporary population.

Methods Single-centre prospective observational cohort study of 166 consecutive individuals (44 HIV+ and 122 HIV−) being treated for active tuberculosis (TB). Adverse events occurring during anti-tuberculosis therapy were assessed using the AIDS Clinical Trials group criteria, where grade III or IV represented serious events. Symptomatic hepatitis was classified as AST or ALT greater than three times upper limit of normal with severe nausea and/or persistent vomiting.

Results Any adverse event was observed in 20/44 (45%) HIV+ and 45/122 (37%) HIV− subjects ($p = 0.31$, table 1). The commonest of these were arthralgia and rash, which occurred at a similar frequency in HIV+ and HIV− subjects. Severe events (grade III or IV) were noted in 8/44 (18%) HIV+ and 21/45 (17%) HIV− subjects ($p = 0.88$). Elevations in transaminases to more than three times normal with accompanying symptoms were the most frequent severe events, occurring in 5/44 (11%) HIV+ and 10/122 (8%) HIV− individuals. Complete interruption of anti-tuberculosis therapy occurred in 1/44 (2%) of HIV+ and 10/122 (8%) of HIV− ($p = 0.29$), while regimen alterations leading to more prolonged treatment were needed in 2/44 (5%) HIV+ and 5/122 (4%) HIV− individuals. The frequency of any adverse events in HIV+ receiving CART plus anti-tuberculosis therapy was 37% (11/30) compared with 64% (9/14) in those using anti-tuberculosis therapy alone ($p = 0.09$).

Conclusion Despite adverse events occurring at a high frequency in both HIV+ and HIV− subjects, our prospective study indicates that severe episodes are less common than previously reported. HIV co-infection does not appear to impact on interruption or prolongation of anti-tuberculosis therapy.

Abstract P112 Table 1

	HIV-infected (n = 44)			HIV-uninfected (n = 122)		
	Mild or moderate	Severe	Total	Mild or moderate	Severe	Total
Any adverse event	12 (27%)	8 (18%)	20 (45%)	24 (20%)	21 (17%)	45 (37%)
Arthralgia	7 (16%)	4 (9%)	11 (25%)	17 (14%)	6 (5%)	23 (19%)
Rash	8 (18%)	0 (0%)	8 (18%)	9 (7%)	0 (0%)	9 (7%)
Symptomatic hepatitis	NA	5 (11%)	5 (11%)	NA	10 (8%)	10 (8%)
Anti-TB treatment interruption due to adverse event	NA	NA	1 (2%)	NA	NA	10 (8%)

P113 ASSESSMENT OF RISK FACTORS FOR MILD ADVERSE DRUG REACTIONS TO STANDARD ANTI-TUBERCULOUS THERAPY AND EFFECTS ON COMPLIANCE

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doi:10.1136/thx.2009.127167i

Introduction and Objectives The incidence of moderate[1] to severe[1–4] adverse drug reactions (ADRs) to anti-tuberculous therapy, requiring modification or discontinuation of therapy, and risk factors[1–4] has previously been investigated. These studies identified increasing age,[1–4] female sex,[1–3] pyrazinamide,[1 2 4] baseline AST ⩾80 U/l,[1] hepatitis,[4] drug resistance,[1] white ethnicity,[3] Asian birth[2] and HIV positivity[2] as risk factors. Minor ADRs, not requiring modification of therapy, have not previously been investigated. A better understanding of incidence, type and risk factors for these may improve patient concordance.

Methods A retrospective review of all cases of active tuberculosis (TB) treated with the standard drug regimen over 3.5 ears in a London hospital including data for age, ethnicity, country of birth, presenting symptoms, site of infection, smear and culture positivity, weight and HIV status was performed. Patients were reviewed monthly and a standard proforma completed. Patients suffering major ADRs were excluded.

Results Of 224 cases, 79 (35%) suffered an ADR, 110 ADRs were recorded, with 26 (33%) patients suffering multiple ADRs. Mean age 37 years (range 0–84), 135 male patients (60%). ADRs reported were joint pains (30 cases), itch (29), nausea and vomiting (22), rash (21), visual disturbance (4) and peripheral neuropathy (4). 52% (11/21) patients aged ⩾65 suffered one or more ADRs compared to 34% (69/203) aged <65 (p = 0.047). 29% (5/17) of ethnically British patients suffered multiple ADRs compared with 10% (21/207) non-British patients (p = 0.009). Female sex has consistently been found to be a risk factor for severe ADRs;[1–3] this is not the case for minor ADRs. Patients suffering minor ADRs were no less compliant. In the ADR group, 11% of patients were non-compliant compared with 10% in the non-ADR group. This is better than targeted by WHO and similar to other Western studies.[5]

Conclusions We found that age ⩾65 is a risk factor for minor ADRs of standard TB therapy and that British ethnicity is a risk for multiple ADRs. The presence of minor ADRs does not affect patient compliance. This study was limited by small size and limited ethnic variation; a larger study is recommended.

1. *Int J Tuberc Lung Dis* 2007;**11**:868–75.
2. *Am J Respir Crit Care Med* 2003;**167**:1472–7.
3. *Tuberc Lung Dis* 1996;**77**:37–42.
4. *Eur Respir J* 1996;**9**:2026–30.
5. **National Collaborating Centre for Chronic Conditions**. *Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control*. London: Royal College of Physicians, 2006.

P114 CHEMOPROPHYLAXIS FOLLOWING AN OUTBREAK OF ISONIAZID-RESISTANT TUBERCULOSIS IN A COMMUNITY SCHOOL: COMPLIANCE AND TOLERANCE IN AN ADOLESCENT POPULATION TO A REGIME OF RIFAMPICIN AND ETHAMBUTOL

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Background There is sparse literature concerning the compliance to chemoprophylaxis regimes for resistant strains of tuberculosis (TB), especially in an adolescent population. Following a cluster of cases, a screening programme (n = 790 using Quantiferon assay) identified 77 individuals with positive tests. This study aims to examine the objective versus self-reported compliance rates and side effects experienced in this group over a 6-month treatment period.

Methods Electronic patient records were reviewed and data on patient reported compliance to the clinic physician, attendance rates and side effects (reported and biochemical) were collected. At every clinic visit patients were given a urine specimen pot which was sent for laboratory analysis as an objective measure of compliance. A total of 57 patients (aged 11–16) were included (exclusions: 6 active disease, 7 previous TB/latent TB, 2 non-attendees, 5 insufficient data).

Results Patient-reported missed doses were 108 giving a subjective compliance rate of 98.7%. Total clinic appointments booked for the cohort were 470 of which 366 were attended (77.8%, mean 6.4/patient) and 104 not attended (22.2%, mean 1.8/patient, range 1–11). Side effects recorded in 6 patients (10.5%) included vomiting/nausea (3), rash (1), abdominal discomfort (2), all mild, self-limiting and without treatment interruption. There was no significant biochemical abnormality in any patient. 17.1% of submitted urine specimen pots were returned unfilled. The results of urinary rifampicin detection are shown in table 1.

Abstract P114 Table 1 Results of urinary samples tested for the presence of rifampicin

	Total cohort with latent TB (n = 57)	Patients attending all clinics and 100% reported compliance (n = 23)	Patients missing clinics ± reporting non-compliance (n = 34)
% (n) of samples positive for rifampicin	67.1% (116)	77.5% (55)	59.8% (61)
% (n) of samples negative for rifampicin	32.9% (57)	22.5% (16)	40.2% (41)

Summary of results

- Significant proportion unable/unwilling to provide urine specimens.
- Urinary rifampicin detection suggests lower compliance rates than rates self-reported, especially in patients with a history of missed appointments and previous non-compliance.
- Regime appears to be well tolerated

Conclusions More work is required to develop a robust strategy for monitoring adherence within the adolescent population, which may involve multiple indices and a multidisciplinary approach to identify individuals at risk of non-compliance.

P115 SAFETY OF MOXIFLOXACIN WHEN USED TO TREAT ACTIVE TUBERCULOSIS IN PATIENTS AT RISK OF HEPATOTOXICITY

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Background Hepatotoxicity is the commonest adverse event encountered in patients receiving anti-tuberculosis (TB) therapy. Risk factors include age, abnormal baseline transaminases, malnutrition, HIV and hepatitis B and C. The fluoroquinolones, including moxifloxacin, were felt to provide an alternative agent in the face of hepatotoxicity. In 2008, however, a drug alert documented an idiosyncratic fulminant hepatitis as a result of moxifloxacin and questioned the safety of this drug in such circumstances. Here we review our experience of this new anti-TB drug.

Abstract P115 Table 1

ALT/AST	Moxifloxacin (%)	Standard treatment (%)
1.25–2.5 ULN	28.5	22.6
2.5–5.0 ULN	11.4	13.2
5–10 ULN	8.6	7.6
>10 ULN	0	2.5

Methods We performed a single-centre case-controlled study of changes in transaminases in subjects receiving moxifloxacin-containing or standard anti-TB therapy between January 2005 and March 2008. In the study group, subjects were identified through the tuberculosis database and pharmacy records and included if they had received moxifloxacin for more than 3 days. The control group was selected from all patients receiving standard therapy.
Results 35 patients received moxifloxacin and 159 controls were identified. Median duration of moxifloxacin was 63 days (IQR 26.5–136). The study group was more likely to be older (median age 54 years vs 33 years, standard arm, $p<0.0001$) and to have active hepatitis B (25.7% vs 3.8%; $p<0.0001$) or hepatitis C (14.3% vs 4.2%; $p = 0.024$). Background liver disease was more common: cirrhosis incidence 8.57% vs 0% ($p = 0.022$), other liver disease 11.4% vs 0% ($p<0.0001$) and liver transplantation 11.4% vs 0% ($p = 0.001$) (moxifloxacin vs standard therapy). Baseline transaminases were normal in both groups (median ALT 27 vs 24 IU/l, AST 28 vs 29 IU/l; $p = 0.36$ and 0.40 respectively; moxifloxacin vs standard). The frequency of hepatic adverse events is shown in table 1. There was no significant difference between the two groups at any grade. Treatment was interrupted as a result of hepatic side effects in 11.4% (moxifloxacin) vs 6.9% ($p = 0.08$).
Conclusion Moxifloxacin, when used in a group of patients at high risk of drug-induced hepatotoxicity, did not lead to an increased frequency of either mild or severe transaminitis in comparison to standard quadruple therapy anti-TB therapy.

P116 UTILITY OF EARLY MORNING URINE CULTURE IN THE DIAGNOSIS OF TUBERCULOSIS

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Early morning urine (EMU) has been widely used in the diagnostic screening of suspected tuberculosis (TB). The diagnostic yield has been variable in different studies.[1 2] We studied the diagnostic yield and its cost effectiveness in our hospital serving an inner city population with a high incidence of tuberculosis.
Method We collected data retrospectively from all the urine samples cultured for TB in 2008. The demographic profile, suspected site of infection, final diagnosis and the role of EMU in achieving the diagnosis were recorded.
Results 581 urine samples were sent for liquid mycobacterial culture from 279 suspected TB patients (150M:129F, median age 40.5 years (SD 21.64)). The patients' ethnic background was Asian (n = 186), Afro-Caribbean (n = 55) and Caucasian (n = 38). Mycobacteria were cultured from 20 (3.4%) urine specimens from 12 patients. 10 patients cultured MTB, 1 patient cultured *M gordonae* of doubtful significance and in 1 patient the culture was contaminated before speciation. Of the 279 suspected TB patients, 67 (24%) had a final diagnosis and treatment for TB. 55 out of 67 patients had smear positive/culture proven MTB; 12 were diagnosed on clinical/radiological/histological features without a microbiological isolate. 11 patients had disseminated TB. Of these, 7 had a positive urine culture with 2 patients having documented renal involvement. Urine culture alone was positive in only 2 patients, 1 with renal TB and 1 had disseminated TB with AAFB shown in the resected ileocaecal specimen (table 1).

Abstract P116 Table 1 Characteristics of the smear/culture positive 55 patients

Primary site	Number of patients	Positive urine culture	Positive smear/culture from other sites
Pulmonary	30	3	30
Disseminated	11	7	11
Lymph node	5	0	5
Pleural	3	0	3
Paraspinal/abscess	3	0	3
Scrotal/testicular	1	0	1
Renal	1	1	0
Meningeal	1	0	1

Discussion The cost of one urine culture is conservatively estimated to be £11. To obtain diagnosis, typing and sensitivities, we recommend that urine samples be sent in suspected disseminated and genitourinary TB. Urine TB culture, where there is a clear focus of infection elsewhere, does not appear to be a cost-effective method even in a high incidence population.

1. **Mortier**, *et al*. Assessment of urine analysis for the diagnosis of tuberculosis. *BMJ* 1996;**312**:27–8.
2. **Gopinath** *et al*. Urine as an adjunct specimen for the diagnosis of active pulmonary tuberculosis. *Int J Infect Dis* 2009;**13**:374–9.

P117 CLINICAL UTILITY OF ENDOBRONCHIAL ULTRASOUND-GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION (EBUS-TBNA) FOR THE DIAGNOSIS OF MEDIASTINAL TUBERCULOUS LYMPHADENITIS

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Introduction and Objectives The incidence of mediastinal tuberculous lymphadenitis (TBLA) is on the rise in developed countries and the diagnosis is often challenging due to the pauci-bacillary nature of the disease. A clinical suspicion is supported by tuberculin skin test (TST) and interferon-gamma release assay (IGRA) data, but diagnosis can only be confirmed with culture or cytology. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is now used extensively in the staging of lung cancer and may have a role in the diagnosis of isolated mediastinal TBLA. We hypothesised that using EBUS-TBNA in conjunction with supporting clinical evidence would enhance our ability to confidently diagnose mediastinal TBLA and exclude other pathologies.
Materials and Methods We retrospectively identified 70 HIV negative patients who underwent EBUS-TBNA over a 16-month period. 11 were performed as part of a staging procedure for carcinoma and were therefore excluded from our study. The remaining 59 procedures were performed in patients with isolated mediastinal lymphadenopathy, no pulmonary disease and pre-bronchoscopic negative sputum smears for AFB. Demographic data, IGRA, TST, lymph node (LN) cytology and culture were compared (table 1).
Results There were 24 men (41%) and 35 women (59%), with a male to female ratio of 1:1.4. Their average age was 45.7 years (17–83). A

Abstract P117 Table 1 Cytological grades and relationship to TST, IGRA and culture positivity

Cytological grade*	Number of cases (n)	TST or IGRA positive cases (n)	Culture positive cases (n)
Grade I	4	4	1
Grade II	14	8	2
Grade III	9	5	1
Grade IV	4	3	1
Grade V	5	4	1
Total	36	24	6

*Grades I, II and III were said to be highly suggestive of a tuberculous process. Grade I, epithelioid granulomatous reaction with caseation; Grade II, epithelioid granulomatous reaction without caseation; Grade III, non-granulomatous reaction with necrosis; Grade IV, non-specific; Grade V, inadequate sample.

diagnosis of TBLA was made in 61% (36/59) of the patients. 27% (16/59) were diagnosed with sarcoidosis, 3.5% (2/59) with lymphoma and reactive LN were found in 8.5% (5/59) patients. TBLA was diagnosed in 50% (18/36) of the cases using a combination of positive culture, cytology, IGRA or TST. Cytology alone was used to support the diagnosis in 28% (10/36) of the cases and culture confirmed one diagnosis (3%). 16% (6/36) of the patients had only a positive IGRA or TST and one patient was treated empirically (3%). The culture yield at 12 weeks was 16% (6/36) and the median time to culture was 45.6 days. There were no major complications and follow-up to date has demonstrated good response to anti-tuberculous therapy in all 36 patients.
Conclusion EBUS-TBNA is a safe and useful tool to aid the investigation and diagnosis of mediastinal TBLA.

P118 ROLE FOR 2-[FLUORINE-18]FLUORO-2-DEOXY-D-GLUCOSE (FDG) POSITRON EMISSION TOMOGRAPHY SCANNING IN ACTIVE TUBERCULOSIS

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Introduction and Objectives Enlarged hilar and mediastinal nodes due to active tuberculosis (TB) can be accessed by endobronchial ultrasound-guided transbronchial node aspiration (EBUS-TBNA). Positron emission tomography (PET) scanning can potentially guide which lymph node (LN) station to sample for best yield. 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG)-PET data for tuberculomas exist, but few data are available for LNs involved with active TB, although data for false positive FDG-PET results in cancer due to inactive TB is present. With the advent of EBUS-TBNA, PET may be a useful adjunct to direct sampling. We aimed to obtain a mean peak standardised uptake value (SUV) for patients treated for active mediastinal node TB and see how PET aided in directing sampling.
Method We obtained a list of 212 patients who had had a PET scan from April 2004 to end of 2008 and who were also listed on the TB register. The site of disease and TB cultures or histology were noted. The PET scan was reviewed by a nuclear medicine physician, and the peak SUV, location and size for any abnormal LN or lung lesion was recorded.
Results 14 patients had both a PET scan and TB notification, one person was denotified on finding an atypical mycobacteria. Four (30%) had culture confirmed TB, 6 (46%) had compatible histology on biopsy, 3 (23%) were empirical treatments. Four patients had only lung parenchymal lesions with mean ± SEM size of 1.62 ± 0.3 cm and mean ± SEM SUV 1.42 ± 0.2. The overall SUV of the mediastinal nodes was mean ± SEM 4.5 ± 0.4. In five patients (38%) the PET result guided the site for LN sampling, three of which underwent EBUS-TBNA. One case had uveitis and encephalitis and a subcentimetre but FDG-PET avid LN subsequently sampled by mediastinoscopy to give TB compatible histology. The frequency of abnormal LN station and the mean ± SEM peak SUV uptake is presented in table 1.

Abstract P118 Table 1

Lymph node station	No (%) FDG-PET avid lymph nodes (N = 28)	Peak SUV (mean ± SEM)
Subcarinal	6 (21%)	4.7 ± 0.7
Precarinal	6 (18%)	3.8 ± 0.5
Right hilum	4 (14%)	5.57 ± 2.1
Left hilum	3 (10%)	4.2 ± 0.5
Aortopulmonary window	2 (7%)	5.1
Right paratracheal	1 (0.03%)	7.7
Left paratracheal	1 (0.03%)	2.9
Other stations	5	4.6, 3.8, 5.7, 4.2, 2.7

Conclusion In the era of EBUS-TBNA, PET scan data can be useful in guiding which node to sample, even if the node is not enlarged by size criteria. Precarinal, subcarinal and right hilar stations are commonly involved.

P119 CHALLENGING CURRENT PRACTICE CAN INCREASE MICROBIOLOGICAL DIAGNOSIS OF TUBERCULOSIS FROM SURGICALLY ACQUIRED SAMPLES

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Introduction To diagnose active tuberculosis (TB), NICE (2006) recommends that surgical samples should be placed in a dry pot (not formalin) and sent to microbiology for TB culture. TB culture is essential to differentiate between *M tuberculosis* and non-tuberculous mycobacteria (BTS, 1999), and enables drug susceptibility testing (BTS, 1998). The aim of this study was to improve local practice in line with the national target of 65% of TB diagnoses confirmed by laboratory culture (Department of Health, 2003).
Methods A retrospective case note analysis of 59 patients treated for all forms of TB over a 5-year period (2001–5) demonstrated that, despite the presence of at least one major TB risk factor, a high proportion of surgical samples were not sent for TB culture. A targeted awareness letter promoting NICE TB guidance was designed and sent to key clinical teams across two acute hospital trusts and the effect of this was measured by a second case note analysis of a further 61 patients over the subsequent 3-year period (2006–9).
Results Prior to the distribution of the awareness letter, 55.3% (n = 26) of patients had samples correctly sent for TB culture. After letter distribution this significantly increased to 73.4% (n = 36, p = 0.002). Clinicians not requesting TB culture (41%, n = 34) and/or the use of formalin to fix samples (62%, n = 22) were the main reasons preventing TB culture. Clinical teams not targeted with the letter did not demonstrate any improvement (p = 1.0).
Conclusion This study demonstrates that a targeted awareness letter sent to key clinical teams could promote the uptake of new recommended practice. While it is acknowledged that other influences may contribute to the increase in requests for microbiological culture, it is encouraging that, overall in this study, national targets for TB diagnosis are now being met. A sustained awareness campaign combined with changes to local operational policy will hopefully ensure that this is continued and standards are raised across all specialities.

P120 WHAT IS "ACTIVE" IN ACTIVE TUBERCULOSIS?

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Background Tuberculosis (TB) case finding using screening and review of "high-risk" populations has intuitive appeal as a strategy to improve UK TB control. This requires the presenting clinical pattern of TB to be consistent and recognisable. However, new data suggest that this is often not the case. It is likely that individual clinical presentation reflects the interaction between host immune response and *Mycobacterium tuberculosis* (*Mtb*) strain type and burden. This relationship has, so far, been poorly characterised.

Methods Pilot study of adults with culture-confirmed TB undergoing the following assessments: markers of: systemic inflammatory response (C-reactive protein (CRP)); local immunity (bronchoalveolar lavage (BAL) differential cell counts and PPD-specific T cell responses); *Mtb* load (AFB smear and time-to-liquid culture positivity (TTP)); and infecting *Mtb* strain (using RFLP IS6110 typing). Results were related to individual clinical and radiological presenting characteristics.

Results Forty-three subjects were assessed; median age 35 years (range 19–73); HIV-infected 28%; pulmonary TB 70%; miliary/disseminated disease 30%; median CRP 99 mg/l (range 1–340); TTP, pulmonary disease 13.8 days (range 2.5–33); TTP, miliary/disseminated 20.4 days (range 8–33.7); BAL AFB smear-positive pulmonary 53%; miliary/disseminated 8%. No relationship was observed between symptoms (fever, sweats, weight loss) or CRP and either TTP or lung PPD immune response. TTP correlated moderately well with BAL lymphocytosis (Spearman test, $r = 0.42$) but less so with PPD-specific response ($r = 0.25$). BAL smear-positive pulmonary disease was associated with a less vigorous lung immune response (table 1). Five *Mtb* strain clusters (genetic similarity ⩾70%) were demonstrated, although no relationship was found with either clinical presentation or lung immune response.

Conclusions Preliminary data suggest there to be an inverse relationship between local lung immune/inflammatory response and *Mtb* load, measured by either smear status or TTP. This appears to translate into clinically distinct presentations which we believe warrant further investigation.

Abstract P120 Table 1

	Miliary	Pulmonary BAL smear-negative	Pulmonary BAL smear-positive
Median (range) BAL lymphocyte %	38.9 (5.5–61.8)	29.7 (2.4–63.9)	17.0 (0.7–46.8)*
Median (range) PPD-specific % response	18.1 (1.4–79.3)	16.7 (1.9–42.5)	7.4 (0–35.1)**

*$p = 0.03$; **$p = 0.25$.

P121 PROLONGED INFECTIVITY IN URBAN UK PATIENTS WITH TB: AN UNDERAPPRECIATED PROBLEM?

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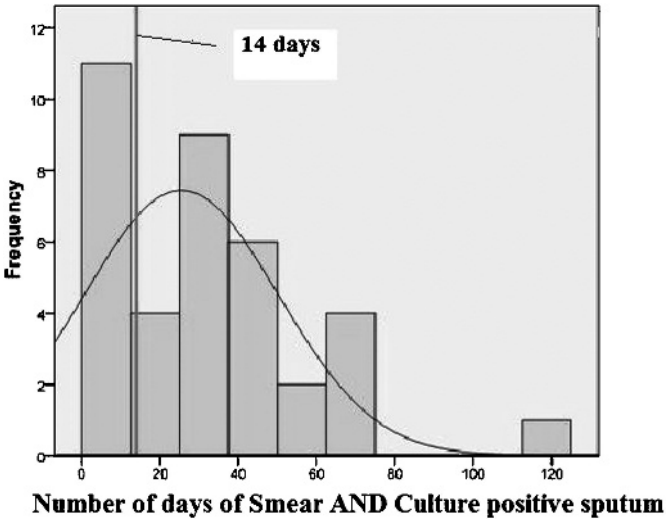
Introduction Historical data suggest that the majority of smear positive patients with pulmonary tuberculosis (TB) may be presumed to be non-infectious after 14 days of treatment. Yet in our experience, large numbers of patients in our urban UK TB clinic are smear and culture positive for considerable lengths of time despite documented compliance. We explored this observation by examining 3 years of data and undertaking an analysis for potential causal factors.

Methods All patients ($n = 51$) who had an auramine positive sputum smear for *M tuberculosis* in 2006–2008 were assessed. Of these, 14 patients with incomplete data, multidrug resistant TB or who had only one sputum smear ($n = 4$) were excluded. Data on biological, radiological and social factors were explored along with smear and culture conversion rates.

Results The mean ($\pm$SE) number of culturable smear positive days (ie, sputum positive smears that later cultured viable bacilli) on treatment was 31 ± 4.2 days (fig 1). The mean time to culture negativity was 44 ± 4.2 days. Our cohort were predominantly male (62%), with marked social dysfunction (ie, alcoholism, homelessness) in 38%. 49% of patients had a heavy (3+) bacillary load at presentation. Cavitatory disease was found in 61% of cases. 8% were HIV positive and 46% were current or ex-smokers. Factors which were significantly (Mann-Whitney U test for non-continuous variables, Spearman rank correlation for continuous variables; $p<0.05$) associated with prolonged culturable sputum smear positivity were increasing age, bacillary load, male gender and increasing C-reactive protein (CRP) levels at presentation. Male gender, increasing CRP, HIV negativity and smoking were associated with prolonged culture positivity. Cavitatory disease and extent of lobar involvement were not significantly associated with either outcome.

Conclusions This cohort of smear positive patients produced smear and culture positive bacilli for a mean period of over 30 days, suggesting that the presumptive loss of infectivity at 14 days of TB treatment may not apply to patients in this urban UK TB clinic. There were high rates of social dysfunction and advanced disease at baseline. Within this cohort, cavitation was not associated with a poorer outcome; this may be a result of the high rate of baseline cavitatory disease.



Abstract P121 Figure 1 Histogram showing distribution of culturable smear positive days on treatment.

P122 TUBERCULOSIS CONTACT TRACING AT A SCHOOL IN A LOW INCIDENCE AREA

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Background Contacts of two cases of multidrug resistant tuberculosis (MDRTB) in a school were screened. Two sisters, one aged 13 and the other aged 16, presented with respiratory tuberculosis. Relevant past history included previous treatment for tuberculosis in India which had probably been incomplete. Gene analysis and subsequent culture confirmed an extensive resistance pattern; the isolates were one drug short of being classed as extensively drug-resistant.

Contact tracing Three tranches of contact tracing took place, beginning with the closest circle of friends, followed by the tutor group and the teachers followed by the whole year group. Due to a lack of capacity among the contact tracing team, the incident team agreed to omit the Mantoux testing step and proceed to testing via a T-Spot test.

Results and actions undertaken A total of 149 contacts were screened of which 24 (16%) had positive T-Spot results. A full breakdown of groups screened and their results is given in table 1. After the third screening exercise a low level of T-Spot positives were continuing to be identified, so the incident team wrote to parents and staff across the whole school informing them of the screening exercise, explaining why everyone was not screened and the importance to be aware of any signs and symptoms of a TB infection. A letter was sent to the GPs of the whole school informing them that their patient may have been a contact of a case infected with MDRTB. Depending on the patient's age, further clinical management was carried out by the regional tertiary TB and paediatric infection centre.

Discussion This incident generated a lot of work. The low prevalence of TB locally meant that a permanent contact tracing team didn't exist, and work was carried out by the respiratory team in discussion with tertiary specialists, public health and microbiology. Other complex issues arose in the screening process, including the need for long-term follow-up of test-positive cases and anxiety amongst the non-screened group.

Recommendations For robust TB control it is important to have systems for contact tracing and managing complex cases.

P123 A SURVEY OF DOT PROVISION IN LONDON

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Background While directly observed therapy (DOT) remains the cornerstone of global tuberculosis (TB) control, recent WHO recommendations have moved beyond the initial rigid DOT concept (ie, observing patients ingesting drugs) to promote a more ''patient focused'' case management approach. Observational studies point to the effectiveness of DOT but evidence from randomised controlled trials is conflicting. Nevertheless, DOT remains an essential component of effective TB control and most countries advocate either universal or selective DOT. NICE recommends that DOT is not usually necessary in the management of most active TB cases and that all patients should have a risk assessment for non-adherence. No further guidance is provided other than to identify homeless patients and those with a history of non-adherence. Previous research in London demonstrated that one in six cases is socially complex and unlikely to complete self-supervised treatment. In March 2008 we undertook a survey in London to determine levels of use and demand for DOT and reasons for not providing DOT.

Methods Nurse case managers from all 30 TB clinics were asked to provide the number of active cases currently on treatment (3× weekly or daily), the number who require DOT (due to complex social problems or non-adherence) and the main reason for not providing DOT.

Results 22 clinics responded with a combined case load of 1803 active cases currently on treatment. 161 patients were reported as receiving DOT and a further 173 cases were identified as in need of DOT. The proportion of patients on DOT by clinic varied from 0% to 69%, and only 5 of the 22 clinics surveyed reported that all patients who need DOT get it. 75% of clinics stated that lack of staff resources was the main reason for not providing DOT to all eligible cases.

Conclusion TB services identified for themselves that they were providing DOT to only half the number of cases that needed it. Strategies to tackle this include use of outreach workers and improved liaison between specialist and community services.

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Abstract P122 table 1 Screening groups and results

Date of screening	Screening tranche	Contacts screened	Number screened	Number positive	Positives (%)
March 2009	1	Close friends of 13-year-old	9	2	18
	1	Close friends of 16-year-old	7	1	14
	1	Girls' tutor	1	0	0
March 2009	2	Year group for 13-year-old	25	3	12
	2	Tutor group of 13- and 16-year-olds	27	3	11
	2	Teachers of 13-year-old	10	5	50
	2	Other teachers for the year group 9 and 11	6	0	0
April 2009	3	Year group of 16-year-old	60	8	13
	3	Teachers who taught the two girls in last academic year	2	0	0