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## 271. Tuberculosis: clinical findings III

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**P2612****The situation of extrapulmonary tuberculosis in Japan: Affected organ and rate of bacteriologically detection**

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**Introduction:** To bacteriologically confirm diagnosis of tuberculosis (TB) is preferable. However, extrapulmonary TB (EPTB) is difficult because collecting samples are not simple like sputum samples, and burden for patients and doctors. In addition, smear examination tend to be negative. In Japan, patients access to examination easily because of health system. That is why, EPTB may be more bacteriologically confirmed in Japan.

**Objectives:** It is interesting to look into % of EPTBs bacteriologically confirmed by organs, because it would be a good guide for national TB programmes in high-burden countries which type of EPTBs are more likely to be confirmed.

**Methods:** EPTB data were collected from public health centre from 2008 to 2010 in the whole country. Study variables were affected organ of by age group, gender, nationality, month of diagnosis, prefectural, occupational and treatment history.

**Results:** The total number of EPTBs in Japan from 2008 to 2010 was 14,711. The most affected organ was pleura (7,043 cases) followed by lymph node excluded hilar lymph node and miliary TB (2,882 and 1,433 cases, respectively). Overall % of bacteriologically confirmed EPTB was 30.6%. The organ which was highest % of all EPTBs was renal/urinary tract (75.9%) followed by auris and joint/bone excluded vertebral bones (75.0% and 65.8%, respectively). Whilst the organ which was lowest % of all EPTBs was oculus (4.1%) followed by pleura and hilar lymph node (16.3% and 21.8%, respectively).

**Conclusions:** Our study demonstrated that 14,711 cases of EPTB were found in Japan from 2008 to 2010. The most affected organ was pleura, however, the % of bacteriologically confirmed pleural TB was only 16.3%.

**P2613****Culture-positive pulmonary tuberculosis with a normal chest x-ray in the absence of HIV co-infection**

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**Aims:** Normal chest x-rays (CXRs) have been found in those with culture-positive pulmonary tuberculosis, even without HIV co-infection. We wished to know how frequently this occurs, how frequently such patients are smear-positive and therefore infectious, whether contacts of these patients had evidence of tuberculosis and whether the site of disease can be identified by CT scan.

**Methods:** Records from the tuberculosis clinic at the Homerton Hospital, London, were reviewed for the period 2003-January 2012. All cases of culture positive pulmonary tuberculosis were reviewed and for those with a reported normal CXR the case notes were reviewed.

**Results:** 13 of 364 cases of culture positive pulmonary tuberculosis had a normal CXR. This included 6 of 34 (18%) with HIV co-infection. The frequency of a normal CXR was 3 of 233 (1.3%) with a negative HIV test. Data from one case without an HIV test and another with ++ smear but no culture are included:

**Conclusions:** Although 3 sputum samples were usually sent, often only one proved culture-positive. CT scans may not reveal active disease. Two with a positive smear had contacts who had forms of TB suggesting recent infection.

Abstract P2613 – Table 1

Code	Reason for investigation	CT	Sputum smear	Days to culture	HIV test	Contacts	Outcome
4.090	cough; weight loss	nd	3 –	13	negative	5	Mother MLN
6.047	Haemoptysis	Normal	3 –	7	nd	4	All DNA
6.073	Cough, haemoptysis, weight loss	nd	++ , 2 –	no culture	nd	1	mother: miliary TB
6.064	Refugee; QFT 2.6 IU/L	nd	3 –	24	negative	2	Case worker QFT +
12.009	Contact; PPD 23mm, QFT 0.38 IU/L cough 2m after 1st seen	normal	1 –	25	negative	refused	

nd = not done; MLN = mediastinal lymphadenopathy; QFN = Quantiferon Gold in tube.

**P2614****The factors associated to pulmonary impairment in patients with treated tuberculosis**

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Tuberculosis is associated with frequent pulmonary impairment. Low lung function is an independent predictor of all-cause or respiratory disease mortality. The aim of the study was to ascertain the factors affecting lung function in patients treated for pulmonary tuberculosis.

**Methods:** In 302 patients who were treated for pulmonary tuberculosis (188 men and 114 women between the ages of 20 and 82 years) and observed at local dispensaries pulmonary function tests were performed.

**Results:** Out of 302 patients, 114 (37.8%) had low lung function (FEV1 < 80% predicted). According to ATS/ERS criteria we classified 8.3% of subjects as having mild impairment; 18.2% of subjects as having moderate impairment; and 11.3% of subjects as having severe impairment. Risk factors for low lung function were positive culture in the past (odds ratio [OR] 4.3; 95% confidential interval [CI] 2.43 to 7.71; p<0.001), age 40 or older (OR 2.73; 95% CI 1.46 to 5.11; p=0.002); recurrence of tuberculosis (OR 2.61; 95% CI 1.38 to 4.91; p=0.004); education less than 15 yrs (OR 1.79; 95% CI 1.05 to 3.05; p<0.05). We did not find influence of gender (males vs females, OR 1.36; 95% CI 0.84 to 2.21; p>0.05); smoking ever vs never (OR 1.21; 95% CI 0.74 to 1.97; p>0.05).

**Conclusion:** Risk factors for low lung function were culture-positive pulmonary tuberculosis in the past, age more than 40 years, recurrence of tuberculosis which may increase the prevalence of low lung function in the patients treated for pulmonary tuberculosis.

**P2615****Sensitivity and specificity of St. George's Respiratory Questionnaire in predicting low lung function in patients treated for pulmonary tuberculosis**

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Tuberculosis is associated with frequent pulmonary impairment. This supports performance of pulmonary function tests in the course of treatment and after a cure but until now pulmonary function testing had not been included in tuberculosis treatment guidelines. The aim of the study was to assess the usefulness St. George's Respiratory Questionnaire (SGRQ) for predicting low lung function in patients after treatment of pulmonary tuberculosis.

**Methods:** We investigated 226 patients older than 40 years who were cured for pulmonary tuberculosis (145 males and 81 females). Quality of Life was studied by SGRQ. Pulmonary function was studied by spirometry. Receiver Operating Characteristic (ROC) curve analysis was used for assessment of sensitivity and specificity.

**Results:** Out of 226 patients, 97 (42.9%) had low lung function (FEV1 < 80% predicted). According to ATS/ERS criteria we classified 8.8% of subjects as having mild impairment; 20.8% of subjects as having moderate impairment; and 13.3% of subjects as having severe impairment. According ROC curve analysis for low lung function, when 29% of Total SGRQ score was chosen as the cut-off, the sensitivity, specificity, positive value and negative value were 57.7%, 83%, 72%, and 72%, respectively. Area under the ROC curve (AUC) was 0.75 (95% confidential interval [CI] 0.69 to 0.81; p<0.001). AUC was a bit bigger in male than in female (0.79 vs 0.69).

**Conclusion:** Total SGRQ of 29% may be the best cut-off in low pulmonary function detection. Higher Total SGRQ score was associated with higher probability of low pulmonary function.

**P2616****Reasons for late diagnostics of lung cancer in pulmonary tuberculosis patients**

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The aim of this study was to find out reasons for late diagnostics of lung cancer (LC) in pulmonary tuberculosis (TB) pts have been admitted and treated in the RRPC for pulmonology and tuberculosis in 2006-2011.

**Methods:** Data of 6 pts with TB and peripheral LC (grA) (3m,3w, age 66±4), 11 pts with TB and central LC (grB) (8m,3w, age 64±3) were examined. X-ray, HRCT, sputum microscopy, cytology had been performed in all pts. Bronchoscopy had been performed in 4 pts of grA, 9 pts of grB, lobectomy-in 1 pts of grA.

**Results:** LC has been diagnosed during bronchoscopy by morphological investigation of tissue sampling in 2 (50%) pts of grA, 9 (100%) pts of grB, during lobectomy by morphological investigation of tissue sampling in 1 pts of grA, by sputum cytology in 1 pts of grA, in 1 pts of grB. In 1 (17%) pts of grA, 4 (36.4%) pts of grB have been found IB stage of LC, in 3 (27.2%) pts of grB-IIIa stage of LC, in 5 (83%) pts of grA, in 4 (36.4%) pts of grB-IV stage of LC. LC in TB pts have been diagnosed in 1 week-16 months (1 week-1 month-in 8 (47%), in 2 months-in 2 (12%), in 3 months-in 2 (12%), in 4 months-in 3 (17%), in 6 months-in 1 (6%), in 16 months-in 1 (6%) pts). The reasons for late diagnosis of LC since detection of X-ray changes in TB pts were incorrect interpretation of X-ray data, delaying using of invasive methods of investigation-in 6 (50%), late health-care seeking-in 1 (8%), pts severity, delaying using of invasive methods of investigation-in 2 (17%), did not carrying out invasive methods of investigation-in 3 (25%) pts.

**Conclusions:** LC in TB pts has been diagnosed late in 12 (71%) pts. The main reason for late diagnostics of LC in TB pts is delaying using of invasive methods of investigation.

**P2617****Clinical features of pulmonary tuberculosis in patients with diabetes mellitus**

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**Background:** Prevalence of pulmonary tuberculosis (PTB) is rather high in diabetic patients.

**Objectives:** To find out whether there is a difference in clinical presentation of PTB in diabetic patients comparing to non-diabetic patients affected by PTB.

**Methods:** The study comprised 194 TB patients divided in two groups, i.e. diabetic patients with established diagnosis of PTB, and the patients affected only by PTB. Clinical symptoms of both groups were reviewed and compared in the time of establishing PTB diagnosis. The frequency of new and relapse pulmonary TB, cavitary and ulcerous PTB were observed.

**Results:** Women are more commonly affected by PTB than men in the diabetic group (p<0.05). Cough was more common in diabetic patients (95.9%) affected by PTB than non-diabetic patients (77.3%), hemoptysis in 29.9% diabetic patients and 13.4% without diabetes. Fever (p<0.001), shortness of breath (p<0.001), chest pain (p<0.0001) and night sweat (p<0.001) were more common in diabetic patients than non-diabetics. The cavitary (p<0.05) and ulcerous PTB (p<0.05) were also more common in diabetic patients. There was no significant difference in new and relapse PTB between two groups.

**Conclusions:** PTB in diabetic patients is more likely to present with more severe clinical presentation, i. e. significantly more symptoms, as well as more cavitary and ulcerous TB lesions.

**P2618****Pleural fluid AFB culture predicts the development of residual pleural thickening in tuberculosis**

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Radiographic residual pleural thickening (RPT) develops up to half of patients with pleural tuberculosis. We sought to find whether results from AFB culture of pleural fluid predicted the development of RPT.

Forty patients (25 males and 15 females; mean age 44 yrs) with tuberculosis pleurisy were included. These patients were diagnosed as pleural effusion on the basis of lymphodominant exudate and high ADA levels. Patients who were suspicious of empyema were excluded. RPT and microbiological and biochemical

parameters of both pleural fluid and sputum were measured. Twenty patients showed positive pleural fluid AFB culture results while the other 20 patients were AFB culture negative. Four patients among 38 patients had positive PCR results for tuberculosis and all of them had positive pleural fluid AFB culture results. Thirty five patients (88%) were accompanied with pulmonary tuberculosis in chest radiography. Both sputum and bronchial washing AFB culture showed higher positive results in patients with positive pleural fluid AFB culture results ( $p=0.001$ ) compared to the group with negative culture results. The patients with positive AFB culture in pleural fluid had greater RPT one year after initiation of antituberculous treatment compared with those with negative AFB culture. The mean RPT of pleural fluid AFB culture positive group and culture negative group were  $1.5 \pm 22.7$  and  $0.63 \pm 2.75$  ( $p=0.046$ ), respectively. There were no differences in pleural adenosine deaminase levels, initial amount of pleural effusion, need for percutaneous drainage, and RPT at the termination period of treatment. This study demonstrated that AFB culture results predicted the development of RPT.

#### P2619

##### Granulomatous mastitis treated as tuberculosis: Preliminary results of surveillance programme

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**Introduction:** Breast involvement of tuberculosis is an uncommon, but not a rare disorder especially among developing countries and accurate diagnosis of disease is not always possible.

**Aim:** To analyze the demographic, clinical, radiological, histopathological data of patients with granulomatous mastitis those who were highly suspected as tuberculosis and to observe the preemptive tuberculosis treatment outcomes.

**Method:** Between 2009-2011 surveillance programme data is retrospectively investigated.

**Results:** Among 48 patients reported as granulomatous disease postoperatively, only 17 were highly suspected as tuberculosis mastitis according to clinical, radiological and postoperative pathological evaluation. The median age was 34 years (range, 21-52, female). The major complaints were breast mass, pain and nipple discharge. Breast ultrasonography revealed common findings indicating the lesions as abscess, mastitis, ductal inflammatory disease and even breast carcinoma. 7 of the 22 patients were suspected as breast carcinoma. Wide local excision was the mainstay of both accurate diagnosis and surgical treatment. None of the patients had active pulmonary or sequelae radiological tuberculosis findings. All the patients were started HRZE treatment with duration of 9 months. 6 of 17 patients have complete response to standard treatment without recurrence. The remaining patients are still under therapy without any complication.

**Conclusion:** We think that additional to clinical features, ultra sonographic findings with pathologically proven granulomatous mastitis can be highly suspicious point and preemptive treatment can be started in this group of patients especially in developing countries.

#### P2620

##### Frequency, severity and risk factors of drug-induced liver injury during treatment of new tuberculosis patients

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**Background:** Drug-induced liver injury (DILI) is one of the most serious problems complicating anti-tuberculosis (anti-TB) treatment. The aim of the study was to assess the incidence, severity and risk factors for DILI among new TB patients.

**Methods:** 200 HIV-uninfected new pulmonary TB patients admitted to Research and Clinical Center for TB control 2009 to 2011 were monitored for clinical and laboratory signs of DILI during the intensive phase of treatment. The median age was 28.0 (IQR 22-44) yrs, 93 were female, 108 were smear-positive, 172 received only first-line anti-TB drugs. The relationship between independent covariates (demographic and clinical data of patients) with frequency of DILI was analysed using multivariate logistic regression.

**Results:** The frequency of DILI (serum alanine aminotransferase (ALT) > 3 x the upper limit of normal [ULN]) was 32.5% (65/200 patients). Severe hepatotoxicity (ALT > 10 x ULN) occurred in 10.5% (21/200). 42 patients (21%) experienced hepatic adaptation (asymptomatic, transient elevation of ALT < 3 x ULN). The type of DILI was hepatocellular in 90.8%, cholestatic in 6.2% and mixed in 3.1%. The relationship between drug and DILI was definitive in 60% (39/65) cases. Female sex (OR = 2.11, 95%CI: 1.08-4.12) and a history of drug/food allergy (OR = 2.94, 95%CI: 1.33-6.49) were identified as risk factors for developing a DILI.

**Conclusion:** Drug-induced liver injury is frequent complication of anti-TB treatment among new TB cases associated with female sex and a history of drug/food allergy, but not with alcohol abuse and concomitant diseases.

#### P2621

##### Pulmonary tuberculosis presentation – Late diagnosis, advanced disease

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Pulmonary TB is the disseminating form of the disease. Rates are particularly high in urban areas associated with poverty, crowded living, social instability and HIV infection.

**Objective:** To describe clinical and radiological manifestations of pulmonary TB in a big Brazilian city and to evaluate the time between beginning of symptoms and diagnosis.

**Methods:** Prospective descriptive study; patients with positive smear proceeding from the public laboratories of the city of Belo Horizonte were prospectively included between May 2006 and April 2008. Demographic data were investigated. Blood samples were drawn for HIV. Chest radiographs (CXR) – were examined. Sputa were cultured whenever possible.

**Results:** 224 cases were included, 150 (67.0%) of the male sex. Age was 39.3 ( $\pm 13.0$ ). Pulmonary manifestations occurred in almost all cases and systemic manifestations in 90%.

##### Respiratory manifestations of pulmonary TB (n = 224)

Manifestation	Frequency	%
Cough/production	221	98.7
Wheezing	111	49.8
Hemoptysis	71	31.7
Thoracic pain	165	73.7
Dispnoea	146	65.2

Time from beginning of symptoms and diagnosis was 16.26 ( $\pm 18.75$ ) weeks. Cavitations were seen in 67.1% of cases.

##### Radiologic extension of pulmonary TB (n = 218)

Radiological presentation	n	%
Bilateral cavitary	96	42.8
Unilateral cavitary	50	22.3
Bilateral not cavitary	49	21.9
Unilateral not cavitary	26	10.3

MRTB occurred in 3/158 with culture (1.9%). HIV was positive in 5/222 (2.3%).

**Conclusion:** Pulmonary positive TB had a late diagnosis in this big Brazilian city. Clinical presentation was of advanced disease with frequent cavitary lesions though multi resistance and HIV were not prevalent. Faster diagnosis should become available for high burden countries cities.

#### P2622

##### Bacteriological confirmation in a series of patients with exudative pleural collections, presumed of tuberculous origin

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We analysed a series of 23 cases of pleuritis diagnosed in 2011 in our pneumology department. There were 23 patients, 14 males and 9 females, aged between 21 and 80.

Pleural fluid analysis: exudate, 100% lymphocytes in 22 cases and with 90% neutrophils one case, with proteins 3,8 – 6,2 g/dl, LDH 274 – 1743 u/l and ADA 47,5 – 196 u/l. Ziehl – Neelsen smears for BAAR from the pleural fluid were negative in all cases.

We obtained bacteriological confirmation in 4 cases from 23 (17,4%) – cultures typical for *Mycobacterium tuberculosis*.

Bacteriological confirmation coming too late, the criteria for choosing an antituberculous treatment were – epidemiologic, the analysis of pleural fluid (lymphocytic exudate with high ADA) and exclusion of other etiologies after performing CT scans and bronchoscopy.

We administered a standard regimen with Isoniazide, Rifampicin, Pyrazinamide and Ethambutol 7/7 in the first two months continued with HR 3/7. At the end of the hospital stay we obtained important resolution of the pleuritis in all cases and at the end of the treatment - normal chest X-rays at 20 patients, 3 having residual pachypleuritis.

We obtained bacteriological confirmation at one patient with liver cirrhosis of viral (HCV) origin, one patient with 4 month pregnancy, one student with no other comorbidity and one patient with the contact.

In conclusion - bacteriological confirmation after cca 45 days of delay did not influence the therapeutic decision and the absence of confirmation didn't change the type of treatment at that patients with favourable outcome. We must also consider a relative high prevalence of tuberculous pleurisy in a high endemicity country as Romania.

**P2623****Antituberculosis chemotherapy toxicity reduction**

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Increasing number of TB patients with co-morbidities (including hepatitis) affects the tolerance to treatment and - as a consequence - the efficiency of the treatment.

**Purpose:** To reduce the toxicity of TB treatment.

**Method:** A prospective study of 92 patients with pulmonary tuberculosis with drug-sensitive MBT. Study Design: "Case control". TB Patients were treated by standard chemotherapy regimens, including those in the study group (46 patients) - anti-TB medications lecithin-based ultra-emulsion.

**Results:** The application of anti-TB drugs in form of lecithin-based ultra-emulsion does not reduce the effectiveness of treatment in comparison with the conventional method, while significantly improves patient tolerance to chemotherapy. The analysis of tolerance demonstrated that adverse events were occurring with standard chemotherapy in 19 (41.3%), the application of the proposed method - only in 3 patients (6.5%,  $p < 0.001$ ,  $\chi^2$ ). We found that of development hepatotoxic reactions is 9.4 ( $p = 0.008$ ,  $\chi^2$ ) in patients with the standard chemotherapy of pulmonary tuberculosis with chronic viral hepatitis. Hepatotoxic reactions were not registered in group with application of anti-TB medications lecithin-based ultra-emulsion.

**Conclusion:** The proposed method for the treatment of pulmonary tuberculosis prevents development of hepatotoxic complications. The patent of the Russian Federation has been obtained.

**P2624****Tuberculosis in immunocompromised hosts: Pathogenetic and pathologic peculiarities**

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Fast spreading of HIV-infection is one of the leading reasons of TB incidence increase. HIV-associated immunodeficiency leads to transition TB from infection to disease. Active TB strengthens HIV replication due to rapid synthesis of proinflammatory cytokines. In Belarus, the annual tendency to HIV-associated TB increase is observed. In 2002, a total of 35 HIV/TB patients was registered, whereas 265 in 2009.

The purpose of study: to investigate pathogenetic and pathologic peculiarities of pulmonary TB in patients with HIV/AIDS.

**Methods:** Morphological study of HIV/AIDS-associated TB was carried out on autopsy material of 11 patients died in center clinic in 2006-2010. The control group was 10 not HIV-infected TB patients.

The causes of death in HIV-infected patients were generalized TB with extrapulmonary manifestations in 6 cases, caseous pneumonia in 2 cases, acute progressing disseminated TB in 3 patients. We distinguished following pathogenetic variants of associated HIV/TB pathology: HIV was primary, duration of observation before TB revealing 5-7 years; TB was primary, duration of observation before HIV revealing 1-3 years; HIV/TB were revealed simultaneously. Peculiarities of TB coursing in AIDS patients compared with non HIV-associated TB were: loss of wavy TB coursing signs and specific inflammation features; monomorphy of TB inflammation foci; prevalence of necrotic suppurative foci; absence of productive inflammation elements on foci periphery; absence of localization and organizations signs of TB foci.

Morphological peculiarities of HIV/TB determine diagnostics complexity and require histobacteriological study with Ziehl-Nielsen staining.

**P2625****Spinal tuberculosis**

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**Introduction:** Spinal tuberculosis is rare, but represents the most common form of osteo-articular tuberculosis in endemic countries.

**Methods:** From January 2000 to December 2010, we collected 16 cases of spinal tuberculosis. We analyzed clinical and radiological profile, means of confirmation and treatment.

**Results:** Spinal and chest pain were the most frequent signs. Four patients had neurological signs. The diagnosis was made by the detection of bacillus in the pus of paravertebral abscess in 6 cases, by histological study of vertebral biopsy in 5 cases, biopsy of another associated lesion in 1 case and in front of clinical and radiological (mainly CT and MRN) arguments with good clinical evolution under antibiacy treatment in 4 cases. The antibiacy treatment associating at least 4 drugs was indicated and correctly followed by all patients. Surgical drainage was associated in 5 cases. The evolution was good in all cases.

**Discussion:** Diagnosis of spinal tuberculosis is late when there is no neurological sign. Imaging can make early diagnosis with MRN. Prognosis is good when treatment is begun early.

**P2626****Hepatotoxicity of antituberculosis chemotherapy in patients with liver cirrhosis**

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**Background:** We compared liver cirrhosis (LC) and control patients who were received standard short-course antituberculous (TB) therapy to evaluate the risk of drug induced hepatotoxicity (DIH) in LC patients.

**Methods:** Forty two LC patients with newly diagnosed active TB who were received isoniazid, rifampin, ethambutol, and/or pyrazinamide were included in the study. One hundred forty eight patients were selected as control subjects. DIH was defined as a liver transaminase level  $\geq 120$  IU/L.

**Results:** Of all LC patients, the etiology of LC consisted of alcoholic in 31 (74%), hepatitis B in 8 (19%), and hepatitis C in 3 (7%). Mean Child-Pugh score of all LC patients was  $7.1 \pm 1.2$  and Child's A and B were 16 (38%) and 26 (62%), respectively. Pyrazinamide containing regimens were more commonly used in control patients (24 of 42 LC patients [57%] vs. 138 of 148 control patients [93%],  $p=0.001$ ). Elevated liver enzyme including transient elevation of transaminase was more frequently found in LC patients (31 of 42 LC patients [74%] vs. 69 of 148 control patients [47%],  $p=0.002$ ). DIH was also more frequently found in LC patients (6 of 42 LC patients [14%] vs. 6 of 148 control patients [4%],  $p=0.016$ ). In 5 out of 6 LC patients showed DIH, isoniazid and rifampin were successfully rechallenged and maintained until the end of treatment.

**Conclusion:** Our data suggested that LC patients with active TB should be closely monitored liver function tests due to more frequent hepatotoxicity during anti-TB treatment including isoniazid and rifampin.

**P2627****Features of TB/HIV co-infection and treatment outcome**

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In Moldova prevalence of HIV-infection is 0,42%, there are 6404 cumulative cases with HIV. The prevalence of HIV among TB new cases is 5,2%. The most frequent AIDS-related condition is TB, which determines fatal outcome. Aim of this retrospective study on 135 patients is evaluation of clinical, X-ray features and treatment outcome in TB/HIV co-infection.

**Results:** Men predominated 67%, young aged (20-40 yrs) 80%, unmarried 78%, unemployed 76%, with bad living conditions 82% and known TB contact 70%. Most of patients, 74% were new TB cases, 19% relapse cases, 67% had infiltrative TB, 42% of which caseous pneumonia, 22% had disseminated and generalized TB. Most of them, 70%, were passively detected, with acute onset in 47% cases and insidious onset in 48% cases, all had signs of broncho-pulmonary and intoxication syndrome. TB developed on the background of HIV-infection in 53% cases. TB and HIV were detected simultaneously in 26% cases. Co-morbidities had 62% cases, most frequently drug-iv using 28%, chronic hepatitis 31% and alcoholism in 21% cases. At the detection, sputum smears and culture were positive for acid-fast bacilli in 46% cases, showing primary resistance in 40%. Radiological was revealed bilateral extensive TB in 69%, disseminated TB in 22% cases. All cases received DOTS, 35% had associated antiretroviral (ARV) treatment. Outcome: anti-TB treatment completed 22%, deaths in 1 year after TB detection 62% cases, default 7% and continue anti-TB treatment 7%.

**Conclusions:** TB/HIV co-infection is most frequent in high-risk population for TB, predominates extensive and generalized forms of TB with high rate of mortality without ARV-treatment.

**P2628****Etiological diagnostics of tuberculous pleurisy (PTB) in HIV-positive and HIV-negative patients**

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**Purpose:** Verification of PTB by molecular-genetic methods (MG) in patients with and without HIV co-infection.

**Methods:** Pleural fluid (PF) of the patients was analyzed using MG. Isolation of DNA and amplification of nucleotide sequence IS6110 which is a marker of Mycobacterium TB (MTB) was carried out using real time PCR method (RT-PCR). Express evaluation of MBT drug resistance (DR) was performed using "TB-BIOCHIP" (TBCh) system. This method helps to identify IS6110 sequence in the sample and simultaneously identify mutations in rpoB gene associated with DR in rifampicin (R)-resistant strains, and in genes katG, inhA and ahpC-oxyR in isoniazid (H)-resistant strains.

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**Results:** Group 1 included 72 HIV-infected patients with PTB. DNA of MBT was isolated in PF of 63.8% (n=46) cases. TBCh was made in 40 specimens. Mutations in rpoB gene were found in 29 (72.5%) samples, among them 20 (68.9%) were due to codon 531 (Ser-Leu) replacement. Other common replacements were in codons 511 (n=4), 512 (n=4). DR to H was found in 30 (75.0%) samples. KatG mutations were found in 26 (86.6%) samples, mostly in the katG315-80.7% (n=21) and inhA mutations - in 26.9% (n=7) cases. Mutations confirming HR resistance were present in 24 (60.0%) samples. 95 HIV-negative patients with PTB were group 2 among them DNA MBT was found in 21 tests (22.1%). DR to H was presented by gene katG mutations in codon 315 (66.7%). DR to R was determined by gene rpoB mutations in codons 531 (57.1%), 526 (n=4), 516 (n=2).

**Conclusion:** Sensitivity of MG methods in detection of PTB was more promising in HIV(+) than in HIV(-) patients (p=0.001). Though total DR prevalence was high, the DR rates were similar in both groups.

#### P2629

##### Smear negative pulmonary tuberculosis in HIV: Over diagnosed or under investigated

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**Introduction:** A significant proportion of HIV infected individuals with respiratory complaints and abnormal chest radiograph are labelled as tuberculosis and started empirical treatment without detailed investigations.

**Aims:** The aim of the study was to verify the empirical diagnosis of smear negative pulmonary tuberculosis in HIV infected individuals using diagnostic modalities available at a tertiary medical center in resource limited settings.

**Methods:** 50 HIV infected individuals with respiratory complaints, an abnormal chest radiograph, and negative sputum for AFB and labelled smear negative pulmonary tuberculosis underwent detailed history, physical examination, and a series of microbiological investigations. HRCT scans of the chest were performed to verify the chest x-ray findings. In the absence of definitive diagnosis on the initial smears, the patients underwent bronchoscopy and sampling of respiratory secretions from the affected areas.

**Results:** Out of the fifty patients enrolled in the study, definitive diagnosis was reached in 47 patients of which 14 patients (28%) had bronchiectasis, 13 patients (26%) had Pneumocystis jiroveci pneumonia, 5 patients (10%) bacterial pneumonia, and 8 patients (16%) had fungal pneumonia. 6 patients (12%) had non infective conditions like cardiomyopathy (3 patients), bronchial asthma (1 patient), non small cell carcinoma (1 patient), and interstitial lung disease (1 patient). Only 1 patient was confirmed to have tuberculosis on sputum AFB culture and also on bronchial washings AFB smears.

**Conclusion:** A wide variety of respiratory conditions other than tuberculosis can be definitively diagnosed in HIV infected individuals if investigated in detail.

#### P2630

##### Therapeutic drug monitoring of isoniazid, rifampin, and pyrazinamide in HIV-infected patients with tuberculosis

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**Introduction:** Therapeutic drug monitoring (TDM) is the process of adjusting drug dosages based on serum concentration data. Several reports have shown altered pharmacokinetic profiles for the anti-tuberculosis (TB) drugs in HIV patients. Such patients may benefit from TDM and early interventions may prevent the development of further drug resistance.

**Aims:** This study aimed to determine serum isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) concentrations in a cohort of patients with HIV-related TB who were treated in a referral TB center.

**Methods:** Twenty HIV-infected patients who received 4 first-line anti-TB drugs for active TB were eligible for the study. Venous blood was obtained 2 h after daily dose of INH (5mg/kg), RIF (10 mg/kg), and PZA (25 mg/kg). Serum levels of anti-TB drugs were analyzed using high-pressure liquid chromatography (HPLC) and compared with published normal ranges.

**Results:** Of the 20 patients (mean age 36.25 years, range 30-57 years), 18 (90%) had a very low maximum concentration of INH (<1 µg/mL), and 2 (10%) had a low maximum concentration of INH (<2 µg/mL). All patients had a very low maximum concentration of RIF (<7 µg/mL) and 7 (35%) had a low maximum concentration of PZA (<20 µg/mL).

**Conclusions:** Low serum concentrations of INH, RIF, and PZA, which may be related to malabsorption, are common in HIV-infected TB patients. TDM of anti-TB drugs may help clinicians to optimize drug therapy and improve TB cure rates.

#### P2631

##### HIV/TB co-morbidity epidemiology in Siberian Federal District 2008-2010

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The epidemiological situation with HIV infection is diverse for each region in Siberian Federal District (SFO). An increase in HIV prevalence was registered in these areas in different years and currently it varies considerably. Since 2001, the Irkutsk region, which has reached rate of 1196.8 per 100 000 population in 2010, occupies the "leading" position among other SFO territories. The lowest prevalence of HIV infection in 2010 was registered in the Republic of Tyva (15.1 per 100 000 people, respectively).

**Purpose:** The assessment of TB-HIV co-morbidity epidemiological situation in 2008-2010 in the SFO.

**Methods:** A retrospective analysis of annual report forms from territories of SFO and the analysis of personified registration cards of coinfecting patients.

**Results:** The incidence of tuberculosis varies slightly in the SFO in 2008-2010: 132.9, 129.2 and 121.5 per 100 thousand population, respectively, without difference in tendencies of situations. Noticeable increase by 1.5 times in new TB-HIV cases registration pertains to period of 2008 to 2010 (2008 - 1573 patients, 2010 - 2318), with growth of the reservoir of infection in 2.3 times. Proportion of patients with TB/HIV in the penitentiary system is in the range of 6.3% to 52.6% for the different region. The proportion of patients with co-infection among TB patients exceeds 5% threshold in five territories and it continues to grow (data 2008-2010): Irkutsk region - 15.9%, Kemerovo region - 10.0-15.3%, Republic of Buryatia - 9.6-14.9%, Altai Krai - 5.5-10.8%, Zabaikalski Krai - 5.9-8.3%.

**Conclusions:** Further deterioration of epidemiological indicators of TB-HIV co-morbidity demonstrates the demand to improve TB-HIV Control programs, including prevention.