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219. Tuberculosis: metabolism and comorbidities

P2540

Protective effect of N-acetylcysteine on anti tuberculosis drug-induced hepatotoxicity

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Introduction: Isoniazid (INH), Rifampicin (RIF) and Pyrazinamide (PZA), the first-line drugs used for tuberculosis (TB) chemotherapy, are associated with hepatotoxicity.

Aims and objectives: To study the hepatoprotective effect of N-acetylcysteine (NAC) on liver injury induced by anti-TB drugs.

Methods: A randomized clinical trial study was conducted on 65 patients with new TB and aged 60 years or over. Patients who included in the study were randomized into two groups. In Group I (n=37), drug regimens included daily doses of INH, RIF, PZA and Ethambutol. Patients in group II (n=28) were treated with the same regimen plus NAC. The patients followed up for two weeks. Liver enzymes and bilirubin were measured before treatment, after one and two weeks' treatment and whenever the patients presented with clinical features of hepatotoxicity.

Results: The Mean±SD values of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALKP) and serum bilirubin were significantly higher in the group I than in the group II after one and two weeks' treatment. Hepatotoxicity occurred in sixteen (43%) and zero patients in groups I and II respectively. The mean duration of treatment before onset of hepatotoxicity was 4.4±4.8 days.

Conclusions: NAC protects against anti-TB drug-induced hepatotoxicity.

P2541

Active tuberculosis with abnormal liver functions tests

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Background: Tuberculosis (TB) is an important problem in developing countries. Treatment have the risk of drug-induced hepatitis. The abnormal liver functions tests detected before treatment can be related to hepatic tuberculosis or to other liver disease.

Aim: Evaluate the frequency and the outcome of abnormal liver functions tests in patients treated for TB.

Materials and methods: Four hundred twenty three patients with TB (January 2006-December 2008) were reviewed.

Results: Fifty six patients (20 men and 36 women) with mean age 38,5 years (14-75 years) had an abnormal liver functions tests before treatment. There were 41 cases (80,3%) of pulmonary TB and respectively 2 cases (3,4%) of pleuro-pulmonary and lymphadenitis TB. Genital, peritoneal, cerebral, miliary TB were diagnosed in respectively 1 cases (1,7%). Elevation of γ glutamyltransferases (γ GT) and alkaline phosphatases were noted in 45 cases (80,3%), high transaminases levels were detected in 23 cases (41%), 12 patients (21,4%) have both elevation. Ultra-sonography performed in 24 cases (44,6%) showed hemangioma (1 case), dilated biliary system (1 cases) and hypodense lesion in 2 cases. Hepatitis B and C serology done in 15 cases were positif in 1 patient. Anti-tuberculous treatment (isoniazid, rifampicin, pyrazinamide and ethambutol or streptomycin) was started in all cases and outcome was favourable with normal transaminases after 3 months, elevation of γ GT and alkaline phosphatases was persisted into 3 months in 12,5% of cases.

Conclusion: Abnormal liver functions tests was mainly frequent in hepatic tuberculosis with diagnosis was still difficult. Should fine needle aspiration be necessary for diagnosis even when lesions regress after treatment?

P2542

Side-effect in the treatment of pulmonary tuberculosis by first-line drugs

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Adverse event were assessed for first-line drug in patients, who had first detected tuberculosis in 2008. 223 persons were included in our study. Side-effect were revealed in 103 (46,2%) patients. Hepatitis and gastritis were more frequent adverse events in treatment of pulmonary tuberculosis by first-line drug. The rates were 10,3% and 10,8% respectively. Renal failure were revealed in 5,8% (13 patient). Allergic reaction was occurred in 4% (8 patients). Peripheral neuropathy was determination in 4,9% (11 patients). 3,6% patients suffered from dizziness/vertigo. 1,8% patients complained about arthralgia. Hearing disturbances were established in 1,3%. Psychosis developed in 1,3%. Tuberculosis treatment was stopped in 23 patients due to side-effect. This are renal failure -11 patients, allergic reaction - 8 patients, hepatitis-12 patients. All patients had concomitant disease or pernicious

habits (alcohol consumption, drug using) in this group. There was no mortality related with side-effect in our study.

P2543

Is pyrazinamide really hepatotoxic? A study of tuberculous patients with hepatotoxicity in Bahawal Victoria hospital, Bahawalpur

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Objective: To study the hepatotoxicity of Pyrazinamide (PZA) in patients getting Anti-Tuberculous Therapy (ATT).

Study design: Observational, descriptive study.

Materials & Methods: The patients attending pulmonary unit for the treatment of Tuberculosis (TB), developing hepatotoxicity were included and the baseline data obtained about clinical symptoms and signs, and the Liver Function Tests (LFTs). In these patients hepatotoxic drugs like Rifampin (RIF) and Isoniazid (INH) were stopped but Ethambutol (ETH) and PZA were continued and Streptomycin (STP) was added. These patients were re-evaluated for hepatotoxicity weekly for next consecutive 6 weeks.

Results: Out of a total of 103 tuberculous patients, the diagnosis was pulmonary TB in most (78%) of the patients. Among Pulmonary TB patients, 52% were sputum AFB smear positive. Clinical features of ATT induced hepatotoxicity were jaundice (95%), nausea (92%), anorexia (89%), vomiting (81%) and pain right hypochondrium (32%). The mean LFTs on presentation were raised: S. Bilirubin (mean: 3.4mg/dL), S. ALT (mean: 113 IU/L), and S. Alk Phosphatase (mean: 254 IU/L). On re-scheduling the ATT regimen, RIF and INH were temporarily stopped but PZA and ETH continued, all patients recovered from hepatotoxicity in one to three weeks.

Conclusion: The study revealed that PZA looks to be non-hepatotoxic in this community (the clinical picture and deranged LFTs were settled in these patients in spite of continuation of PZA. These contradictory results may be due to:

1. Genetic and racial differences of the community
2. Data showing the hepatotoxicity of PZA alone is scarce.

P2544

Isoniazid plasma concentration monitoring in patients with pulmonary tuberculosis at a teaching referral hospital

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Therapeutic drug monitoring (TDM) is a standard clinical method used for many diseases. The use of TDM in the setting of tuberculosis (TB) will allow the clinician to make informed judgments regarding the appropriateness of drug therapy (resistance, interactions, response, ...).

The study was performed to evaluate isoniazid plasma level in patients with pulmonary tuberculosis.

The study was designed as cross-sectional, and observational. The investigation was carried out in the National Research Institute of Tuberculosis and Lung Disease. Patients with pulmonary TB were selected for the study. The excluded patients were those with diabetes, heart failure, HIV, MDR TB, and those using interacting drugs with isoniazid concentration.

Blood samples were drawn 2 hours post dose for the measurements using HPLC. Data were analyzed using SPSS (version 12.0).

Eighty-two patients (49 females and 33 males) with the age of 60.7±18.5 years met the inclusion criteria during the study period. There was no significant correlation between dose/kg of isoniazid and its plasma concentration ($p=0.94$, $r = -0.009$). Isoniazid plasma concentration were as follows: 19 (23.17%) upper than, 12 (14.63%) lower than and 51 (62.19%) within the target range. There was a direct correlation between the duration of treatment with isoniazid and its plasma concentration ($p<0.0001$, $r = 0.66$).

TDM is only part of antituberculosis monitoring. In isolation, it is of limited value. However, combined with clinical and bacteriological data, it can be a decisive tool, allowing the clinician to successfully treat even the most complicated TB patients.

P2545

Quantification of long term uptake and metabolism of isoniazid in patients treated for Mycobacterium tuberculosis infection

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Background: Resistance of Mycobacterium (M.) tuberculosis to isoniazid is the most common form of resistance to drug treatment against M. tuberculosis in-

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fection and may be the starting point for development of multiple drug resistant tuberculosis.

Objective: To develop a method for measurement of isoniazid uptake reflecting long term compliance, drug absorption and metabolism of the drug.

Subject and methods: 16 patients with M. tuberculosis infection treated with isoniazid for at least 3 months were included. Isoniazid and its metabolite acetyl isoniazid were quantified in hair by HPLC/MS. Acetyl-isoniazid/isoniazid- ratios were compared in rapid acetylators and slow acetylators by determination of N-acetyl transferase 2 (NAT-2) genotype.

Results: Isoniazid concentrations in hair varied between 0.2 to 7.2ng/mg. Acetyl-isoniazid/soniazid-ratios ranged from 39.7to 0.5%. Isoniazid was higher in the part of the hair shaft grown during treatment compared to hair grown before and after treatment. Patients with slow acetylator genotype had with a median of 5.85% a significantly lower acetyl-isoniazid/soniazid ratio compared to rapid acetylators who's ratio had a median of 22.1% (p=0.034). Isoniazid concentrations did not correlate with acetyl-isoniazid ratios indicating that factors other than NAT-2 genotype contributed to isoniazid concentrations.

Conclusion: Isoniazid/acetyl isoniazid ratio in the hair of patients on isoniazid treatment reflects NAT-2 genotype and could be used to determine acetylator phenotype and new clinically important NAT-2 polymorphisms. Determination of isoniazid concentration in hair samples could be used for monitoring of long term uptake.

P2546**Adverse reactions to antituberculosis chemotherapy: tolerance versus intolerance**

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Introduction: Adverse reactions to antituberculosis drugs can compromise treatment regimens for tuberculosis and cause a significant morbidity.

Aim: The present study investigated the types, incidence and evolution of adverse reactions to antituberculosis chemotherapy.

Material and method: A total of 827 patients with active pulmonary tuberculosis, HIV negative, were evaluated.

Results: 35 patients (4.23%) had developed adverse reactions, 25 of whom were new cases of pulmonary tuberculosis. Hepatotoxicity occurred in 85.7% of cases and was attributed to RIF (rifampin) in 40% of patients, to PZM (pyrazinamide) in 23.3%, to INH (isoniazid) in 3.33% and to combination of isoniazid and rifampin in 6.66%. In 33.3% of the cases with hepatotoxicity, the responsible drug could not be determined due to the fact that at sequential reintroduction of the drugs, was possible at the end, to get the initial regimen. 40% of patients with hepatotoxicity had presented pre-existing liver disease. Other adverse effects observed include gastrointestinal disorders, skin hypersensitivity reactions and vestibular ototoxicity.

Conclusions: Majority of the patients who developed adverse reactions were new cases of pulmonary tuberculosis. Hepatotoxicity was predominant, RIF having the highest incidence (40%). Pre-existing liver disease favors the development of hepatotoxicity. Very probably, the hepatic adaptive responses have a significant impact, explaining the gradually tolerance at complete reintroduction of the initial regimen in at least 30% of cases with hepatotoxicity.

P2547**Pulmonary TB -diabetes mellitus – an unfavorable association**

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Aim: to determine the impact of diabetes on clinical and radiological manifestations and treatment outcome of pulmonary tuberculosis (PTB) patients.

Material and method: retrospective study on 70 diabetic patients (G1) treated for TB between 2000 and 2007; this group was compared to a control group of 70 non-diabetic tuberculosis patients (G1).

Results: 67,14% percent of G1 patients had type I diabetes, 61,42% smokers. The most frequent symptom, after cough, was weight loss found in 95% of cases. Haemoptysis was noted in 30% of G1 and in 22% of G2 patients.

Radiographic abnormalities were bilateral in 40% of patients. Excavation was found in 61% of cases.

The diagnosis of PTB was made by microscopic sputum examination in 100% of G2 patients and in 61,43% of G1 patients. Sputum conversion was registered at 60 days in 50% of G1 patients and in 80% of G2 patients.

No drug resistance was noted. Insulin was required in all patients with type II diabetes.

Complications appeared in 11% cases of G1 and in 5% the patients deceased. The treatment stretched over 8 months at 71,42% of G1patients, compared to the attending batch whose period of treatment stretched over 6 months at 80% of patients in G2.

Conclusions:1. Diabetes seems to aggravate pulmonary TB course.

2. Patients with diabetes are diagnosed a lot faster because of the thorough monitorization and occasional presentation in the specialized services.

3. Despite this pulmonary TB, when associated with DM, tends to have more in-

tensive and severe clinical picture, more extensive radiological lesions and requires longer anti-TB treatment.

P2548**Diabetes, glycemic control and risk of tuberculosis: a population-based case-control study**

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Background: Diabetes has been suggested to increase the risk of active TB, but recent formal epidemiological evidence is scarce.

Aim: To examine the association between diabetes, glycemic control and TB in a population-based case-control study in North-Western Denmark (population 1.65 million).

Methods: We defined cases of active TB as all inpatients and outpatients who received a first-time principal diagnosis of TB according to the International Classification of Diseases 10th revision (ICD-10), A15-A19, in the Danish population-based National Patient Registry from January 1st 1997 to December 31st 2006. Ten controls, matched on age, sex, and length of residence within the study area, were selected for each patient with TB. We used conditional logistic regression to estimate odds ratios (ORs) for a first-time hospital diagnosis of active TB among persons with and without diabetes, controlling for potential confounding factors.

Results: We identified 1191 patients with a first-time hospital diagnosis of active TB, including 68 diabetic individuals (5.7%), and 11910 population controls, of which 480 had diabetes (4.0%). The adjusted OR for active TB was 1.29 (95% CI 0.95-1.75) among diabetic subjects compared to non-diabetic individuals. Diabetic subjects with an HbA1C level <7.0% had an adjusted OR for TB of 1.42 (95% CI 0.73-2.77), while the OR for those with an HbA1C level ≥7.0% was 1.09 (95% CI 0.59-2.00), compared to persons without diabetes.

Conclusions: The risk of TB associated with diabetes may be lower than previously suggested. We found no evidence for any association with poor glycemic control.

P2549**Estimation of the risk of tuberculosis among people with diabetes**

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Background: Treatment of latent tuberculosis (TB) infection in high risk groups such as those who are HIV positive is an important approach to TB control. Potentially, this strategy has wider applicability for other high risk groups such as people with lesser degrees of impairment of immunity. We conducted a general population historical cohort study to estimate the risk of TB among people with diabetes.

Methods: The study was conducted in New South Wales, Australia, a low incidence setting (6.5 per 100,000/year) where over 80% of all TB cases occur in overseas-born people. Cases of TB in people with diabetes were identified by record linkage using the National Diabetes Services Scheme (NDSS) database and the New South Wales TB notification database 01/2001 to 12/2006. The NDSS subsidises medical supplies used by people with diabetes. The relative risk of TB in patients with diabetes was estimated by Poisson regression with adjustment for TB incidence by country of birth, sex, age and indigenous status.

Results: There were 191 cases of TB (138, 72%, culture positive) among 306,536 people registered with NDSS. The adjusted relative risk (aRR) of TB in people with diabetes was 1.30 (95% CI 0.93 to 1.82) and the aRR for culture positive TB was 1.25 (95% CI 0.91 to 1.73). However, in people using insulin (38.6% of all people registered with NDSS) the aRRs were 2.05 (95% CI 1.28 to 3.25) and 2.24 (95% CI 1.46 to 3.44), respectively.

Conclusions: Although patients with diabetes in general did not have a significantly increased risk of developing TB, the RR was significantly increased for those on insulin. However, diabetes does not appear to be a major contributor to TB disease in this low incidence setting.

P2550**Is there any characteristics difference between pulmonary tuberculosis patients with and without diabetes mellitus type 2?**

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Study objectives: The aim of this study is to compare the clinical, radiological and bacteriological characteristics of TB patients with and without DM.

Design: A prospective case control study was performed.

Setting: National Research Institute of Tuberculosis and Lung Disease

Patients: Patients with combined pulmonary TB and DM were selected as a case group. Control subjects were selected from confirmed TB cases who met inclusion and exclusion criteria and without a history or a new diagnosis of DM type 2. Control subjects were matched to cases according to age and sex.

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Measurements and results: Forty seven type II diabetes TB patients were enrolled in study. 102 patients also met the study criteria as control. Among the clinical symptoms, there were significant differences in hemoptysis, dyspnea, and loss of appetite in the two groups, but no significant differences were found in symptoms such as cough, sputum, chest pain, night sweat, fever, and weight loss. In chest radiography results, the diabetic patients had more typical presentations (73.9%) and cavitary lesions (60%) (P value = 0.004), but the severity of the radiological presentation was not significantly different between the two groups.

Conclusions: This study demonstrates that diabetes did not affect clinical symptoms and bacteriological findings in TB patients. Moreover, the rate of MDR-TB was the same between two groups. Regarding the higher prevalence of pulmonary cavitary lesions, clinicians should be more aggressive in taking isolation precautions when treating PTB patients with DM.

P2551

The relation between radiological extent and serum lipid parameters, total protein, albumin and body mass index in patients with pulmonary tuberculosis

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It was reported that serum total cholesterol level was low in patients with pulmonary tuberculosis and cholesterol rich diet might precipitate sputum sterilization in these patients. In our study, we aimed to analyze the relation between radiological extension and serum lipid parameters, protein levels and body mass index in patients with pulmonary tuberculosis.

48 patients with tuberculosis (Group 1: 12 women, 36 men; mean age 34+13 years) and 20 healthy controls (Group 2: 11 women, 9 men; mean age 36+12 years) were included and serum total cholesterol (TC), HDL, LDL, VLDL, triglyceride, total protein, albumin, hemoglobin, leukocyte, platelet, erythrocyte sedimentation rate (ESR) and body mass index (BMI) levels were measured. Radiological extent was evaluated in three degrees as mild, moderate and severe according to chest x-ray. Besides the comparisons between Group 1 and Group 2, the groups that were graded radiologically as 1, 2, 3 were also compared.

TC, HDL, LDL, triglyceride, albumin and BMI values in patients with pulmonary tuberculosis was significantly lower ($p < 0.001$); ESR was significantly ($p < 0.001$) higher than healthy control group. Moreover mild tuberculosis (Grade 1) and moderate-severe tuberculosis (Grade 2 + Grade 3) cases were compared among each other. HDL ($p = 0.001$), albumin ($p < 0.05$) and BMI ($p < 0.001$) decreased, ESR ($p = 0.001$) increased significantly as radiological grade increased.

Our results showed that serum lipid and albumin levels were decreased in patients with pulmonary tuberculosis and this decrease was correlated with radiological extension degree.

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Elevated chitotriosidase levels in patient with pulmonary tuberculosis: correlation with radiologic extent and degree of smear positivity

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Chitotriosidase is secreted by the activated macrophages and neutrophil precursors. In recent studies, elevated chitotriosidase levels have been reported in hematologic, infectious and interstitial lung diseases and it might be accepted as an activation marker macrophages. In this study we investigated serum chitotriosidase levels in the pulmonary tuberculosis. Forty-two male patients with pulmonary tuberculosis and 21 healthy subject were enrolled into the study. The radiologic extent of the disease and degree of smear positivity were assessed. Chitotriosidase levels were measured by fluorometric method in the sera of the patients and controls. The serum chitotriosidase activities of the pulmonary tuberculosis patients were significantly higher than the control group (39.73±24.97 nmol/ml vs. 26.84±15.59 nmol/ml; $p = 0.013$). Furthermore serum chitotriosidase levels correlated significantly with radiologic extent and degree of smear positivity ($r = 0.439$, $p = 0.004$ and $r = 0.449$, $p = 0.003$ respectively).

This study has showed that serum chitotriosidase levels increase and it might be used to assess disease activity and severity.

P2553

Candidosis due to treatment pulmonary diseases

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Aim: to determinate the rate of candidosis in patients, who had course of antibiotic therapy more than 1 month.

Material and method: We examined rate of candidosis in patients from different departments of *Research Scientific Institute for Pulmonology and Phthiisology* in Minsk in 2005-2007. 945 pts were included in our study. There are 400 pts of pulmonological department, 155 patients of **intensive care unit** and thoracic surgery department, 109 patients of pulmonary tuberculosis department for adult,

155 patients of pulmonary tuberculosis department for children. *Candida albicans* was revealed in *nasal and oral swab*.

Results. The problem of candidosis is more significant in **intensive care and thoracic surgery** departments, when the index rate was 66,8% (156 pts). High level of candidosis was revealed in pulmonary tuberculosis department for adult - 45,6% (234 pts). The **majority of** fungous complication was obtained in patients with multidrug-resistance. According our data frequency developing candidosis are more than 4 time in this group. Other case of combination pulmonary tuberculosis and candidosis were occurred in patients older than 75 year or in persons had concomitant severe disease. The rate of candidosis was 40% (62 pts) among patients of pulmonary tuberculosis department for children. And the rate of fungous complication was 38% in patients suffered from infection of low air way.

Conclusion. Among the patients treated with antibiotics more than 1 month, candidosis was revealed more often in patients of **intensive care and thoracic surgery** departments, in patients with multidrug-resistance, and in patients of pulmonary tuberculosis department in age more than 75 years.

P2554

A rarely seen side effect of anti-tubercotics: lichen planus

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Side effects of antitubercotics are important subjects of mortality and morbidity during tuberculosis therapy. Major side effects causing cessation of therapy are hepatitis, gastrointestinal dysfunction and cutaneous eruptions. Lichen planus, which is a rarely seen side effect, will be presented with three cases.

Case 1: A sixty five years old female patient with tuberculosis lymphadenitis and eye tuberculosis was taking isoniazid, ethambutol, ofloxacin and streptomycin. Diffuse eritematous plaques and confluent vitelline papules were seen during the sixth month of the therapy. Punch biopsy taken from these lesions revealed the diagnosis of lichen planus.

Case 2: In an eighty six years old female patient taking first line drugs for lung tuberculosis, purple plaques with desquamation appeared on extensor surfaces of extremities during the fifth month of the therapy. These findings led to the diagnosis of lichenoid drug eruption.

Case 3: A seventy-seven years old female patient was taking second line drugs for multi-drug resistant tuberculosis. After five months, squamous plaques seen on feet, legs and back of the patient were evaluated as lichenoid drug eruption.

Lichen planus caused cessation of therapy in two cases. In third case, antituberculous therapy was completed with aid of a kerolytic agent.

Cutaneous side effects are quite often and generally seen in first two months of therapy. Risk factors mentioned for cutaneous side effects are HIV infection, multi-drug use, old age, female gender, auto-immune diseases, underlying renal and hepatic failure. Importance of cutaneous side effects was emphasized through three cases with lichen planus in two of which therapy cessation was inevitable.

P2555

Respiratory tuberculosis in lung cancer patients

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Introduction: Incidence of tuberculosis (TB) in Portugal is 30 cases/100.000 residents.

Patients with cancer, particularly those treated with chemotherapy (QT), radiotherapy (RT) and corticotherapy (CT) have increased risk of infection. Infection is a common comorbidity and a frequent cause of death in patients with cancer.

Objectives: To determine incidence of respiratory TB in lung cancer (LC) patients.

Material and methods: Microbiologic data (*Ziehl-Neelsen, culture isolation* and *Mycobacterium tuberculosis* DNA) from sputum, bronchial/bronchoalveolar lavage, pleural fluid and pleural biopsy were analysed in LC patients followed in our department between 2001 and 2007.

Results: In this group of 567 LC patients there were 6 (1.06%) with respiratory TB, all of them were males. Median age was 65 years (46-71). LC histological sub-type were: adenocarcinoma (2), small cells (2), epidermoid (1), non-small cells (1). All patients had previously been treated with QT and 5 were submitted to RT (thoracic (3), brain (1), bones (1)). One patient had previous history of TB. Immunosuppressive conditions were found in 3 patients: chronic CT (3), diabetes (1), leucopenia and lymphopenia due to recent QT (1). Symptoms and signs at presentation were: cough (5), constitutional symptoms (3) and haemoptysis (2). Five patients concluded anti-TB treatment. No side effects or complications associated to anti-TB treatment were found. Two patients died, one of them 15 days after diagnosis of TB.

Conclusion: In comparison to general population, TB was more frequent in our group of LC patients. Response and tolerance to anti-TB treatment was good. Symptoms, signs and radiological changes common to both pathologies may compromise diagnosis of TB in LC patients.

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P2556**When tuberculosis mimics lung cancer**

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Tuberculosis is a highly prevalent disease in Portugal. This pathology has capacity to mimetize other lung diseases, lung cancer being one of them.

Aim: to identify and characterize pulmonary tuberculosis cases presenting as clinical and/or radiological suspicion of primary or metastatic lung cancer.

Methods: Retrospective case review study of the last 12 years. All patients submitted to bronchoscopy due to clinical and/or radiological suspicion of lung cancer/metastasis and in whom one of the final diagnosis was pulmonary tuberculosis were included. Out of the 3211 bronchoscopic exams performed due to lung cancer suspicion, 31 patients were included.

Results: Patients included (n=31) were divided in 2 groups: the 1st group (n=13) patients with bronchoscopic findings directly associated with lung cancer (Ikeda Signs) and the 2nd group (n=18) patients without Ikeda signs. In the 1st group 6 had extrapulmonary cancer; endoscopic main findings were mucosa infiltration in 8 patients and tumoral mass in 5. Tumour suspicion was also clinical in 5 patients, radiological in 2 and clinical and radiological in 6. Two patients had simultaneous diagnose of pulmonary tuberculosis and cancer. In the 2nd group 8 patients had extrapulmonary cancer; 7 had no endoscopic findings, 7 had endobronchial inflammatory signs and 4 had other findings. Tumour suspicion was clinical in 6 patients, radiological in 8 and both clinical and radiological in 5. In latter group 2 patients had simultaneous diagnose of lung tuberculosis and cancer.

Conclusion: In tuberculosis endemic areas, mycobacteriological bronchial secretions exam should be ordered to patients submitted to bronchoscopy with lung cancer suspicion, even if Ikeda signs are present.

P2557**Comorbidities – risk factors for relapsed pulmonary TB**

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In Dolj County Romania, the value reached by pulmonary TB in 2006 was the highest among the national notified values: 169‰. The incidence of relapses continue to be higher than the national averages.

Aim: To highlight if comorbidities associated with TB could be risk factors correlated with relapses of PTB.

Material and method: observational study of 2,196 patients with PTB with chemotherapy initiated under program conditions: 778 new cases among 1995-2005 and relapsed between 2001-2006; 1,418 new cases without relapses in the follow-up interval (2001-2006). Epidemiological, clinical, bacteriological and radiological data were extracted from patients files. Kaplan-Meier survival curves were used to estimate cumulative incidence of binary events, testing the statistic significance between sub-groups by means of the Log Rank Test and Cox regression analysis to identify independent risk factors in relapsing.

Results: average age 40,07yrs, 57% of patients from rural area; 32,4% of patients had comorbidities. Relapses appear at 69,1% of patients with toxic hepatitis (estimated media 4,541yrs, IC95% 3,971-5,112), at 54,9% of patients with gastropaties (5,510yrs, IC95% 4,948-6,072), at 49% of patients with diabetes mellitus (5,218yrs, IC95% 4,606-5,828), 92,7% of cases with silicosis (4,084yrs, IC95% 3,270-4,897), 33% of cases with COPD (5,952yrs, IC95% 5,276-6,628). Silicosis, gastropaties, hepatitis, diabetes are risk factors statistical semnificatives for relapses (p<0,004).

Conclusion: Neglecting treatment of comorbidities in outpatient facilities is an element that fosters instability in the health status of former TB patients and that can contributes to the “reawakening” of bacillary lesions.

P2558**Concomitant complicated meningitis with Streptococcus pneumonia and Mycobacterium tuberculosis**

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Meningitis with mixed etiology is usually secondary to some underlying diseases such as nearby infections of sinuses, ears, post-trauma or penetration of the subarachnoid space (spinal tap, neurosurgery) and appears at youngsters and immune-depressed persons. We present the case of a 17 years old male who developed pneumococcal meningitis simultaneously with tuberculous meningitis. Diagnosis was established upon clinical and laboratory criteria. Diagnosis of pneumococcal meningitis was sustained by direct microscopic exam of smear that showed encapsulated gram-positive diplococci and the latex particle agglutination test that was positive for Streptococcus pneumoniae. Diagnosis of tuberculous meningitis was established on direct exam of smear of pellicle and positive cultures for Koch bacillus. His evolution was difficult with triventricular non aggressive

hydrocephalus, although he was treated correctly with antibiotics (meropenem, rifampin, isoniazid, pyrazinamide, ethambutol, and streptomycin), corticosteroids and cultures became negative afterwards. As the number of immunodepressed subjects increases, we mention the existence of this association (pneumococcus+Koch bacillus) as a cause of acute bacterial meningitis with incomplete resolution.

P2559**Epidemiology of neurologic disorders in patients with pulmonology tuberculosis**

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The aim: to study rate and influence of neurologic disorders on clinical course of pulmonary tuberculosis in various patients categories.

Materials: clinical records data of 258 patients with tuberculosis (new detected – 159, relapses – 99) treated in Scientific Research Institute for Pulmonology and Phthisiology during 2006-2008 were analysed. Data of 124 patients without polyneuropathy (PNP) and 134 patients with neurologic disorders has been compared.

Results: PNP spread varied from 20% in new detected to 50% in patients with relapses and chronic tuberculosis forms. Frequency has been increased with reliability with the patient age: from 32.1% in patients 18-35 years to 54.2% in patients 36-60 years, and 91.4% in persons older 60 years (p<0.001), and also in patients with accompanying pathology. All the patients with PNP had a large smoking length.

New detected patients with PNP had more complaints (38.0% and 54.2% accordingly, p<0.05), intoxicate syndrome (15.0% and 32.2%, p<0.05), anemia (0 and 11.4%, p<0.001) as compared patients without PNP. Patients with neurologic disorders had tendency to more heavy course and relapses of tuberculosis. Patients with PNP had complications with chemotherapy: side-effects of antituberculosis preparations were detected in 31.8% of this group against 17.0% in patients without PNP. Resume. PNP accompany tuberculosis frequency and make it more heavy. To risk groups with PNP we can attribute patients with relapses, chronic form of pulmonary tuberculosis, persons older 60 years, tabaco-smokers, persons with marked clinical manifestations and signs of tuberculosis intoxication, pathology (ischemia, diabetes mellitus and others).