276. Non-tuberculous and tuberculous mycobacterial infections: from epidemiology to clinical findings

P2706

The burden of tuberculosis drug resistance in Eastern Europe: The

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Aims: Surveillance the TB drug resistance on the national level and its impact upon public health in the Republic of Moldova;

The objective: to characterize the evolution of tuberculosis drug resistance in Moldova (2001-2011).

Methods: The study was retrospective, being based on the assessment results of M.tuberculosis complex drugs resistance obtained in the reference laboratories from the country.

Results: Prevalence of MDRTB among New TB cases increase from 6.3% in 2001 up to 26.4% in 2011. Trough previously treated patients (relapses, re-treatment after default, re-treatment after failure, chronic) prevalence of MDR TB was detected in 37.7% cases in 2001 and 64.3% cases in 2011. Extensively drug-resistant tuberculosis (XDR-TB) is present in some territories. The rate of XDR TB among the patients with MDR TB is 6.1% (2010). The prevalence of TB-HIV co-infection in country is 5.4%. The prevalence of MDRTB among all TB-HIV is higher such from HIV negative patients (67.8%). Reasons of high level of TB resistance in Moldova: poor in infection control in TB hospitals -exogenous re-infection of TB patients; low compliance of treatment; the lack of a rigid control of TB patients, TB/HIV co-infection.

Conclusions: At the current stage MDR TB is a serious problem for National TB Program, bringing serious public health and economic consequences. It is a very alarming phenomenon, because the success of treatment (with first-line drugs) for this form of TB is less effective than for the susceptible tuberculosis and the accumulation of a greater number of resistant strains in society can lead to the infection of population and to an increase in the number of patients with MDR&XDR TB.

P2707

The significance of a mycobacterial isolate in a low tuberculosis prevalence setting

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Introduction: The incidence of tuberculosis in semi-rural Staffordshire is very low, around 2.8/100,000/year (1). We reviewed the significance of identifying mycobacteria in this population.

Methods: Retrospective analysis of patients from our institution with mycobacterium isolated from 1st Jan 2007 to 31st July 2011, with follow up until 1st Nov 2011. For patients with multiple isolates, the first species isolated was recorded. Results: 67 patients were identified. Demographics of the M. tuberculosis(MTB) and non-tuberculous mycobacteria(NTM) patient groups are in Table 1. 22/43 (51%) of the NTM samples were considered significant and treated. Patients with NTM were older and more likely to die (p<0.001). Chronic lung disease was present in 11 (50%) of the treated NTM patients, and none of the MTB patients. 3 skin biopsies and 1 urine sample were +ve for NTM. Mycobacterial species isolated included 22 M. avium intracellularae, 6 gordonae, 4 chelonae, 3 kansassii, 3 malmoense, 2 xenopi and 1 each of shimoidei, marinum and interjectum.

Table	1
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	MTB	NTM
Patient numbers	24 (36%)	43 (64%)
Males	13 (54%)	24 (56%)
Ages (mean ± SD)	42 ± 21	66±10*
Death at end of follow up	1 (0.04%)	10 (23%)*
Pulmonary samples	16 (66%)	40 (93%)*
Smear +ve pulmonary samples	8 (33%)	6 (14%)

*p<0.001.

Conclusions: Isolates of NTM were nearly twice as common as MTB. The diagnosis should particularly be considered in older patients with underlying lung disease. Isolation of a NTM requires careful assessment of its significance and pathogenicity. The incidence of NTM infection seems to be increasing (2). References:

[1] www.hpa.org.uk, accessed Dec 2012.

[2] Martin-Casabona N et al, Int J Tuberc Lung Dis 8(10):1186-1193 (2004).

P2708

Clinical analysis of pulmonary Mycobacterium avium complex disease in Japan

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Objective: To analyze the clinical characterisitcs of patients who diagnosed pulmonary Mycobacterium complex (MAC) disease recently in the affiliated several hospitals.

Patients and methods: The subjects consisted of 150 patients who satisfied the diagnostic criteris of ATS between 2003 and 2010. We evaluated the backgrounds, diagnostic methods, microbiological findings, radiological findings, treatments, and prognosis.

Results: The average age of 150 patients with pulmonary MAC disease was 65.0 years old. The detection method was most frequently recognized by bronchoscopy (50%). The microbiological findings was smear positive for acid-fast bacilli in 98 patients (65%) and the sensitivity of isolated MAC for antituberculous drugs and otherantibiotics was comparatively good for clarithromycin (CAM) and ri-fampicin (RFP). The clinical disease type of pulmonary MAC disease consisted of nodular/bronchiectatic type in 101 patients (67%), fibrocavitary type in 43 (29%) and solitary nodular type in 6 (4%), respectively. Concerning the treatment for pulmonary MAC disease, the combined chemotherapy including CAM was performed for 76 patients (51%). Sputum conversion rate was 76%, the sputum relapse rate was 31% and the clinical improvement including radiological findings and/or clinical symptoms was ontained in 49%.

Conclusions: We positively perform the bronchoscopic examination to obtain the diagnosis of pulmonary MAC disease. The diagnosticrate of pulmonary MAC disease has recently increased with the revise of diagnostic criteria reported in 2007 and we could obtain comparatively good clinical effect by the positive performence of combination chemotherapy including the increase dose of CAM.

P2709

Pharmacokinetics of drugs for non tuberculous mycobacterial lung infections <u>Cecile Magis-Escurra</u>¹, Jakko van Ingen², Rob Aarnoutse³. ¹*Pulmonary*

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Successful treatment for Non-Tuberculous Mycobacterial (NTM) infections is easily frustrated. Little is known about the pharmacokinetics (PK) and dynamics of treatment regimens in relation to treatment outcome. Drug concentrations may be an intermedian link. In NTM disease very few PK studies have been performed. We performed a prospective, descriptive pharmacokinetic (PK) study of the plasma pharmacokinetics (full PK-curve) of rifampicin (RIF), ethambutol, clarithromycin, azithromycin, isoniazid and moxifloxacin and their active metabolites in a Dutch series of patients with clinically relevant NTM lungdisease and we compared the results with two other series from the literature. The baseline characteristics are shown in table 1.

Table 1. Baseline characteristics

Patients	14	
Male, n (%)	10 (71%)	
Mean age (range)	64.3 (43-85)	
Ethnicity	Caucasian (100%)	
Mean Weight (kg)	71,01	
BMI (range)	23.4 (19.0-30.3)	
Species	n=	

Table 2 shows the main PK results.

Table 2. Main pharmacokinetic parameters

Drugs used	n	Mean dose/kg	Mean Cmax	Mean AUC0-24
Rifampicin	14	8,51±0.74	12.813±4.28	47.833±14.84
Claritromycin	5	7.10 ± 0.81	0.426 ± 0.25	2.744 ± 0.76
Azitromycin	2	4.73±1.92	0.183 ± 0.24	2.034 ± 0.85
Ethambutol	13	$15.96{\pm}1.92$	3.275 ± 1.21	26.339±11.36

Results were generally consistent with the data published in the past by Wallace and Peloquin. Our data showed that rifampicin causes a reduction in clarithromycin and azithromycin serum concentrations. The current study has confirmed the significant PK interactions between rifampicin and clarithromycin and we feel this calls for a reevaluation of the dosing strategies in NTM lung disease as an inadequate response to treatment might be attributed to suboptimal drug exposure.

P2710

Neutrophil-dominant inflammation is associated with severity in high-resolution computed tomography (HRCT) findings in patients with nontuberculous mycobacterium (NTM) infection

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Rationale: Pulmonary NTM infections are being recognized worldwide with increasing frequency in immunocompetent patients. The clinical course of this disease varies among patients. However, the mechanism and factors associated with deterioration is not completely understood. The aim of this study was to evaluate the association between cell differentiation status in bronchoalveolar lavage (BAL) fluids and the severity of HRCT findings in patients with NTM infection.

Methods: Twenty immunocompetent patients who were diagnosed with a lung NTM infection by positive cultures and 20 healthy controls were enrolled. Based on the preferential percentage of neutrophils and lymphocytes in BAL fluids, patients were divided into two groups; a neutrophil-dominant and a lymphocyte-dominant group. The HRCT scores indicating the extent and severity of airway disease (modified method of Fowler et al. Eur Respir J 2007) was compared between the groups.

Results: The numbers of neutrophils and lymphocytes were significantly higher in patients with NTM (17.4±6.7 and 6.9±2.1 x10⁴/ml) than those in healthy controls (0.1±0.1 and 0.8±0.2 x10⁴/ml) (p<0.01, respectively). Among the NTM group, HRCT scores of the lobe in which BAL was performed in the neutrophil-dominant group (8.0±0.7) were significantly higher than the lymphocyte-dominant group (1.7±0.4) (p<0.01).

Conclusion: Neutrophil-dominant inflammation due to pulmonary NTM infection was related to severity of HRCT findings in patients with NTM infection. These results will help in understanding the biological defense mechanism against NTM.

P2711

Recovery rate of nontuberculous mycobacteria over a 10-year period at a tertiary referral hospital in Korea

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The incidence of nontuberculous mycobacteria (NTM) infection is increasing in Korea. The aim of this study was to evaluate the recovery rate of NTM from respiratory specimens over a 10-year period in a tertiary referral hospital in Korea with a intermediate tuberculosis burden.

We identified all mycobacterial isolates from respiratory specimens at the Samsung Medical Center (Seoul, Korea) obtained from January 2000 to December 2009. During the study period, 25,374 mycobacterial isolates were recovered from 8,115 patients. The proportion of NTM isolates was continuously increasing from 31.8% (167/525) in 2000 to 68.2% (3,514/5,152) in 2009 (p<0.001, test for trend). Among the acid-fast bacilli (AFB) smear-positive specimens, recovery rate of NTM isolates was also increasing from 9.2% (18/196) in 2000 to 55.1% (1,027/1,865) in 2009 (p<0.001, test for trend). The most frequently isolated NTM organisms were *Mycobacterium avium* complex (n= 4,734, 52%) and *Mycobacterium abscessus* complex (n=2.660, 29%).

This study found a rapidly increasing trend in the isolation of NTM from respiratory specimens at a referral hospital in Korea. The high proportion of NTM even among AFB-positive respiratory specimens would represent serious challenge for the diagnosis of pulmonary tuberculosis.

P2712

Risk factors for pulmonary *Mycobacterium avium-intracellulare* complex disease deterioration in immunocompetent patients

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Backgrounds and objectives: Pulmonary *Mycobacterium avium-intracellulare* complex (MAC) disease has become increasingly observed in immunocompetent patients without any underlying lung diseases. Disease progression is variable and its natural history is not well understood. We investigated possible risk factors for deterioration of pulmonary MAC disease.

Methods: A case-control study was done for 61 patients with pulmonary MAC disease who had no underlying lung diseases and were not immunosuppressed. Patients were divided into two groups: disease deterioration (Cases; N=32) and no disease deterioration (Controls; N=29). At their first visit, we examined patient characteristics, symptoms, chest CT findings, bacteriological and hematological test results, and respiratory function test results.

Results: At their first visit, Cases were more often symptomatic than Controls (90.6% vs. 37.9%; p<0.001). Cases had advanced radiological changes (CT scores 8.2 vs. 4.3; p<0.001), and more Cases than Controls had cavitation (28.1% vs. 3.4%; p=0.009), and enlarged mediastinal lymph nodes (71.9% vs. 24.1%,

p<0.001). Erythrocyte sedimentation rates (ESR) and fibrinogen levels were significantly increased in Cases. No significant differences were found between these groups for age, BMI, environmental exposure, nutritional status, immune status, or respiratory function.

Conclusions: Increased symptoms incidence, advanced radiological changes, increased ESR and high fibrinogen levels are risk factors for pulmonary MAC disease deterioration. These factors might be useful not only to predict disease deterioration but for decisions regarding the timing of introducing treatment.

P2713

Detection of volatile organic compounds in cattle caturally infected with *Mycobacterium bovis*

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We report a novel method in detecting *Mycobacterium bovis* infection in cattle based on identifying unique VOC (volatile organic compounds) profiles in the breath of cattle. The study was conducted on breath samples collected from cattle on an *M. bovis*-infected dairy in southern Colorado, USA. All animals were skin test



Figure 1. (a) Predominant VOCs in animals' breath samples. (b) Exclusive VOCs for bTB positive and bTB negative cattle.

Peak Area



Figure 2. DFA (Discriminant factor analysis) plot showing the discrimination between bTBnegative (circles, n=14) and bTB-positive (rhombs, n=8) exemplars. An insight of the bTBnegative animals from the different dairies shows the complete mixing of the exemplars from *M. bovis*-infected (green filled circles, n=4) and tuberculosis free (red open circles, n=10) dairies. positives; the presence of disease was either confirmed or infirmed after necropsy. Negative controls included breath samples from animals on two tuberculosisfree dairies in northern Colorado. Gas-chromatography/mass-spectometry analysis revealed significant differences between *M. bovis*-infected and non-infected animals in the concentrations of 15 VOC's, allowing for distinctly different VOC patterns.

Based on these results, a nanotechnology-based array of sensors was tailored for detection of of *M. bovis*-infected cattle via breath. The tailored system successfully identified all *M. bovis*-infected animals (8/8) while 21% (3/14) of non-infected animals were misclassified as *M. bovis*-infected.

The method shows promise in identifying unique VOC patterns in cattle with bovine tuberculosis. Applicability in humans warrants further study.

P2714

Clinical evaluation of GPL core IgA antibodies for serodiagnosis of MAC pulmonary disease

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Objective: To evaluate the clinical usefulness of GPL core antibodies for diagnosing MAC-PD and distinguishing MAC-PD from other lung diseases.

Methods: GPL core antibody levels were measured in 57 patients with MAC-PD, 18 with clinically suspected MAC-PD but who did not satisfy the diagnostic criteria of MAC-PD proposed by ATS, 10 with MAC contamination, 18 with pulmonary tuberculosis (TB), 9 with other nontuberculous mycobacterial (NTM) disease, 18 with other lung diseases.

Results: The positive response rate for MAC-PD was 77%, that for suspected MAC-PD was 39%, and that for MAC contamination was 10%, and that for pulmonary TB, other NTM diseases, and other lung diseases was 0%, respectively. GPL core antibody levels were significantly higher in patients with MAC-PD, including patients with clinically suspected MAC-PD, than in those in the other groups (p<0.01). The sensitivity and specificity of the antibody for diagnosing MAC-PD were 77% and 100%, respectively. Although thirteen patients with MAC-PD showed false negative responses for the GPL core antibody, five patients had immunosuppressive conditions due to underlying diseases. No significant correlations between the antibody level and species of MAC, clinical disease types, and extent of the disease on chest computed tomography were found in patients with MAC-PD.

Conclusions: The EIA kit is a useful supportive method for the rapid and convenient diagnosis of MAC-PD using a small dose of serum, and for the differentiation od MAC-PD from other lung diseases.

P2715

Clinical evaluation of interferon-gamma release assay (IGRA) in patients with nontuberculous mycobacterial disease

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Objective: To evaluate the clinical usefulness of two IGRA (QuantiFERON-TB and T-SPOT.TB) in patients with nontuberculous mycoobacrerial (NTM) disease. **Materials and methods:** The study consisted of 180 patients with NTM disease who satisfied the diagnostic criteria proposed by American Thoracic Society (ATS). Tuberculin skin test (TST) was also performed for these patients as much as possible.

Results: The causative microorganism was Mycobacterium avium in 76 patients, M. intracellulare in 60, M. kansasii in 22, M. abscessus in 7, M. marinum in 7, others in 7, respectively. While the positive response rate for M. kansasii, M. marinum, and M. szulgai (30 patients) which possess the ESAT-6 and CFP-10 (Mycobacterium tuberculosis (MTB)-specific antigens) was 60% for TST, 33% for QFT, and 40% for T-SPOT.TB, the indeterminate response rate was 7% for QFT and 0% for T-SPOT.TB, respectively. On the other hand, while the positive response rate for M.avium and M.intracellulare etc. (150 patients) was 58% for TST, 7% for QFT and 11% for T-SPOT.TB, the indeterminate response rate was 7% for QFT and 2% for T-SPOT.TB, respectively.

Conclusions: Although IGRA may be a useful diagnostic method to differentiate TB disease and MAC disease, there are several problems to be resolved before it can be used as a diagnostic method for M. kansasii disease etc. We also would like to describe the results of QFT for M. kansasii disease in other hospitals in Japan.

P2716

Pharmacokinetics and drug susceptibility testing imply limited activity of current regimens for Mycobacterium avium complex disease Jakko van Ingen, Martin Boeree, Charles Peloquin, Charles Daley. Medical Microbiology, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands Pulmonary Diseases, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands Emerging Pathogens Institute, University of Florida, Gainesville, FL, United States Mycobacterial and Respiratory Infections, National Jewish Health, Denver, CO, United States

Background: Treatment outcome in Mycobacterium avium complex (MAC) lung

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Abstract P2716 - Table 1. Average serum concentrations and pharmacokinetic calculations

Drug	Mean Cmax	Mean AUC	PD target	Median MIC	% above PD target
Rifampicin (n=299)	18.55±6.75	68.42±24.26	AUC/MIC >271; Free AUC/MIC >24.14	2	6%; 18%
Ethambutol (n=421)	$2.24{\pm}1.02$	10.18 ± 4.35	Free Cmax/MIC >1.23	1	57%
Azithromycin (n=367)	0.32 ± 0.23	1.47 ± 1.00	n.a.	n.a.	n.a.
Clarithromycin (n=59)	2.26±1.87	10.67±9.53	T50% >MIC	≤ 4	n.a.
Moxifloxacin (n=96)	4.25±1.51	18.81±6.46	Cmax/MIC >10; AUC/MIC >100	2	11%;0%

disease is poor, with cure rates of 50-70%. To understand this, we retrospectively assessed the pharmacokinetics and MICs of key drugs in MAC disease treatment. **Methods:** Pharmacokinetic and drug susceptibility data of all patients admitted at National Jewish Health, Denver, USA, in the January 2006-June 2010 period was retrieved from databases. Pharmacokinetic measurements were done by high performance liquid chromatography and gas chromatography. Isolates were identified as MAC by AccuProbe assays. MICs were determined by the BacTec460 macrodilution method; synergy between rifampicin and ethambutol was assessed. **Results:** Pharmacokinetic data, median MICs and pharmacodynamic calculations are given in Table 1. Simultaneous use of rifampicin significantly lowered serum concentrations of macrolides (30-60%) and moxifloxacin (10-15%).

Conclusions: Serum rifampicin, ethambutol and moxifloxacin concentrations attain effective levels in a minority of patients; rifampicin use exerts detrimental effects on pharmacokinetics of macrolides and moxifloxacin. This may partly explain the poor outcomes of MAC disease treatment.

P2717

PCR based method for accurate diagnosis of mycobacterial disease and description of clinical profile of disease caused by non tuberculous mycobacteria

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Introduction: Sri Lanka uses direct microscopy to diagnose tuberculosis. This method has relatively low sensitivity of 70% and cannot differentiate My-cobacterium Tuberculosis Complex (MtbC) and Non Tuberculous Mycobacteria (NTM).An accurate and rapid diagnosis of NTM could be made by Polymerase chain reaction.

Objective: To evaluate the use of PCR for accurate diagnosis and speciation of pulmonary disease caused by Mycobacteria and to describe clinical profile of disease caused by NTM.

Method: All patients diagnosed as pulmonary TB on the basis of positive sputum direct smear to acid fast bacilli during the 90 day period between 17-02-2009 to 19-05-2009 and placed on standard chemotherapy at a District TB clinic were included. Sputum of each patient was tested with 541-bp sequence of insertion element IS986 amplification. Samples which failed to amplify IS986 were analyzed by using 16S rRNA and six more gene loci, which are used as markers for identification of MtbC from NTM species. (Huard, et al. (2003) journal of clinical Microbiology; 41:1637-1650). Clinical profile and chest radiography of patients with NTM was recorded.

Results: Out of total study population of 44 patients 8 (18.18%) were confirmed to have disease due to NTM. Thirty six patients had disease due to mycobacterium tuberculosis. Out of 8 NTM patients one died. The other seven patients remained chronically ill.

Conclusion: PCR can rapidly and accurately differentiate NTM which causes a significant proportion of smear positive disease, who will remain chronically ill despite standard regime.

P2718

High incidence of the Beijing strains among multi drug resistance isolates of Mycobacterium tuberculosis from extra pulmonary tuberculosis cases in northern India

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Background: The emergence and spread of drug resistance tuberculosis has worsened the global resurgence of tuberculosis. Beijing strains are responsible for massive spread and outbreaks of Multidrug resistance Mycobacterium tuberculosis (MDR-TB) in worldwide as well as in India.

Objectives: The aim of study presented here was to investigate incidence of Beijing genotypic among MDR-TB isolates from extra pulmonary tuberculosis cases (EPTB) in Northern India.

Methods: A total of 756 specimens from patients of EPTB cases with varied presentation were studied. A total of 164 M. tuberculosis complex (MTBC) isolates recovered during the period Sept 2007-Dec 2010 were tested for drug susceptibility against SHRE by radiometric BACTEC method. MDR-TB isolates were sequenced in rpoB and katG gene for mutation analysis. All MDR-TB strains were processed by new multiplex polymerase chain reaction (PCR) for identification of Beijing strains and non Beijing strains.

Results: Of these 164 MTBC, 100(60.9%) strains were fully susceptible and 64(39.1%) strains were resistance. 21 (12.8%) strains were confirmed MDR-TB by genotypic method. The proportional of Beijing strains was significantly higher among MDR-TB strains (72.7%, p < 0.05). Genotypic analysis of rpoB gene revealed significantly higher rate of Ser531Leu mutation rate among Beijing vs. non Beijing strains (50% vs. 33.4%, p < 0.05). While mutation for Ser315Thr in katG gene was common among Beijing vs. non Beijing strains (68.2% vs. 50%, p < 0.05).

Conclusion: We found high incidence of Beijing strains among MDR-TB strains from EPTB cases in Northern India.

P2719

Identification of new immigrants to the UK for latent tuberculosis screening: A comparison of employment and primary care registries

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Introduction: Comprehensive screening for latent M.tuberculosis infection (LTBI) in immigrants relies on effective strategies for identifying at-risk groups. The utility of national registries has been suggested but not formally evaluated for this purpose.

Objectives: To compare and characterise profiles of immigrant registration on the UK National Insurance Number (NINo) and Flag-4 GP registries.

Methods: Retrospective analysis was conducted of both registries for Leicester between 2002-2009. Comparison between registries was performed on immigrants stratified by age at UK entry (<18yrs, 18-34yrs and \geq 35yrs).

Results: The total number of immigrants registering was similar for NINo (47,000) and Flag-4 (46,653). Differences existed between the registries stratified by age. Flag-4 identified immigrants across all age ranges including children. In contrast, NINo was comprised of a greater proportion of younger adults. The total number of younger adults identified with NINo was greater with a trend to significance (p=0.08). This suggests a proportion of immigrants to the UK for employment do not immediately register with a GP.

NINo overseas & Flag-4 registrations: Leicester 2002-2009

	<18	<18 years		18-34 years		>35 years	
	NINo	Flag-4	NINo	Flag-4	NINo	Flag-4	
Number	564	10674	37130	27719	9306	8260	
Proportion of total	0.012	0.229	0.79	0.594	0.198	0.177	
Difference in proportion	15						
(95% CI)	0.217 (0.2	13-0.221)	0.196 (0.1	90-0.202)	0.021 (0.0	16-0.026)	
p-value	<0	.001	<0	.001	<0	.001	

Conclusion: The UK NINo and Flag-4 registries provide complementary immigrant data in children and young adults that is relevant for TB services planning new immigrant screening.

P2720

Misdiagnosed pulmonary TB: Influencing factors and diagnostic chances in TB hospital

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Differential diagnosis of pulmonary TB is still difficult. We found the tendency to overdiagnosis of pulmonary TB in TB hospital.

Purpose: Purpose of the study was to analyze causes of diagnostic errors and improve the quality of in-hospital management of patients supposed to having of pulmonary TB.

Methods: Noncomparative retrospective study, subject of interest were medical records of 136 most difficult cases, in which previously established diagnosis of pulmonary TB was rejected. The chances for establishment of true diagnosis and influencing factors were estimated.

Results: I. Diseases, most often initially misdiagnosed as tuberculosis, were pneumonia (52%), lung cancer (20%). 2. The period from the disease manifestation up to establishment of final diagnosis was 84±72.8 (mean±SD) days. 3. Clinicoradiological signs in these cases were more characteristic for TB, than for other pulmonary diseases. 4. Factors found to be associated with false-positive diagnosis is: "limited pulmonary opacity" (OR 1.75, p=0.003), pulmonary dissemination

(OR 1.75, p=0.05), detection of low level acid-fast bacilli in sputum (OR 2.0, p=0.04), nonspecific inflammatory findings detected by flexible bronchoscopy (OR 2.2, p=0.000), age more than 40 years (OR 1.75, p=0.01), inconspicuous disease onset (OR 1.9, p=0.01), COPD (OR 1.8, p=0.04), inadequate antibacterial therapy before hospitalization.

Conclusion: Application of contemporary methodologies of diagnostic tests interpretation, use of rapid TB diagnostic is highly needed.

P2721

Follow-up of TB cases failing or defaulting the first TB treatment, in Romania Nicoleta Cioran, Horia Cocei, Elmira Ibraim. Central Coordination Unit of Romanian National Tuberculosis Program, "Marius Nasta" Institute of Pulmonology, Bucharest, Romania

Introduction: New pulmonary smear positive TB patients who fail or abandon the first treatment have a high potential to develop drug resistance, to become difficult to cure and to spread resistant mycobacterium strains for a long time.

Aim: To follow-up the new pulmonary smear positive TB cases registered in Romania in 2009, failing or abandoning the first treatment.

Methods: Retrospective, descriptive, observational study of the new pulmonary smear positive TB cases registered in Romania in 2009, who failed or defaulted the first treatment, followed-up for a 3 years period. Information has been extracted from the electronic National TB Register.

Results: Out of 9,111 new pulmonary smear positive TB cases notified in Romania in 2009, 4.4% failed and 6% abandoned the first treatment. Of these, 62% have been retreated (92.3% of failures and 39.7% of defaulters). Most were males (82.5%), in 40-44 years age group (16.3%), living in rural area (55.6%). More than half (52.4%) had no occupation, 27.9% have been tested for HIV and of them 3.65% found positive. Out of 97.4% culture positive cases, 9.7% were MDR-TB (57 cases). The outcome rates of the first retreatment were: 48% success, 8.3% decease, 11.9% failure and 23% default; 8.8% are still continuing treatment. Of 205 cases failing or abandoning first retreatment, 129 (63%) restarted a second retreatment regimen, with 17.8% success rate and 34% still continuing treatment. Conclusions: The patients failing or abandoning TB treatment should be closely followed-up in order to retreat and cure as much as we can.

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Comparative performance of interferon gamma release assays in detection of latent tuberculosis infection among health-care professionals

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Latent tuberculosis infection (LTBI) presents as the immersed part of the iceberg. Since health-care professionals (HCPs) are a group at increased risk of LTBI, the aim of this study was to clarify the role of IFN- γ response based on QuantiFERON-TB GOLD In Tube (QFT-GIT) and T-SPOT.TB assays in HCPs screening, comparing with the tuberculin skin test (TST).

In this cross-sectional comparative study, HCPs were interviewed according to a risk factor questionnaire from July 2011 to January 2012. Subjects who had a history of household contact with a pulmonary tuberculosis (PTB) case or had an underlying immunosuppressive disorder were excluded from the study. A total of 95 eligible HCPs working in a university hospital in northeast of Iran and in hospital wards with the highest number of admissions for patients with PTB were evaluated. The mean age of participants was 33±7 years with a female/male ratio of 57/38. 84 HCPs (88.4%) were bacille Calmette-Guérin (BCG) vaccinated at birth. Of the 95 HCPs, 43.2% were positive by TST, and about 29% by each of the IGRAs. Of 53 (55.8%) individuals with a positive test, 15 (28.3%) were positive to all three tests and 26 (49.1%) were simultaneously positive to at least two tests. The global agreements (k) between QFT-GIT and T-SPOT.TB with TST, and between the two IGRAs were 0.737, 0.684, and 0.779 respectively.

BCG vaccination and prevalence of nontuberculous mycobacteria associated with reactivity to TST reagent could explain a part of discordance observed between the tests. To lessen concerns about interpretation of the results, we would recommend concomitant application of at least two tests for LTBL

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Risk factors for extrapulmonar tuberculosis Inês Sanches¹, Aurora Carvalho^{2,3}, Raquel Duarte^{2,3,4}. ¹Pulmonology Department, Centro Hospitalar e Universitário de Coimbra- Hospital Geral, Coimbra, Portugal; ²Pulmonology Department, Chest Disease Centre of Vila Nova de Gaia, Vila Nova de Gaia, Portugal; ³Pulmonology Department, Centro Hospitalar de Vila Nova de Gaia/Espinho EPE, Vila Nova de Gaia, Portugal; ⁴Department of Clinical Epidemiology, Predictive Medicine and Public Health University of Porto Medical School, Porto, Portugal

Introduction: Tuberculosis (TB) remains a major global public health problem and 20% of all cases are extrapulmonar. The purpose of this study was to identify risk factors associated with extrapulmonar tuberculosis.

Methods: We performed a transversal study involving all patients with extrapulmonar tuberculosis registered in a TB reference centre in northern Portugal, between January 2008 and January 2012. We evaluated demographic data, comorbidities, BCG vaccination and anterior tuberculosis treatments. Multivariable logistic regression was used to identify independent risk factors (p<0.05).

Results: Among the 386 patients studied, 260 (67.4%) had pulmonary tuberculosis (PT) and 126 (32.6%) had extrapulmonary TB (EPTB). Being older than 40 years old (OR=2.09; 95%CI: 1.29-3.38), female (OR=1.63; 95%CI=1.02-2.6) and HIV positive (OR=2.72, 95%CI=1.25-5.93) were independent risk factors for EPTB. Alcoholism (OR=0.30; 95%IC: 0.12-0.75) is associated with higher risk for TB. Previous liver disease (OR=22.30; 95%IC: 1.89-263.57) was an independent risk factor for peritoneal TB. HIV co-infection (OR=12.97; 95%IC: 1.71-48.42) and the presence of previous TB treatment (OR= 7.62; 95%IC: 1.00-57.9) increase the risk of disseminated disease

Conclusion: We identified independent risk factors for EPTB compared with TB. Recognizing risk factors associated with EPTB is essencial to suspect of disease and may help to get an accurate diagnosis.

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Clinical characteristics and treatment outcomes of tuberculosis in the elderly <u>Yong Soo Kwon</u>¹, Su Young Chi¹, Yu Il Kim¹, Sung Chul Lim¹, Yoo Duk Choi² Internal Medicine, Chonnam National University Hospital, Gwangju, Korea; ²Pathology, Chonnam National University Hospital, Gwangju, Korea

Background: The purpose of this study was to describe the differences clinical characteristics and treatment outcomes between elderly TB patients and young TB patients

Methods: The medical records of 271 young(aged 20 to 64 at diagnosis) and 199 elderly(aged 65 and older) TB patients, who were newly diagnosed with and treated for TB from May 2008 to August 2010, were analyzed retrospectively. Results: Respiratory symptoms such as cough, sputum, and dyspnea and comorbid medical conditions such as cardiovascular disease, diabetes mellitus and chronic obstructive pulmonary disease were more frequent in elderly TB patients. In chest CT scan of pulmonary TB patients, findings of active TB such as nodules (< 30 mm in diameter), masses (> 30 mm in diameter), and cavities were less frequently found in elderly TB patients except consolidations. However in microbiological diagnosis, positive TB culture rates were higher in elderly TB patients. Of those with known results of drug sensitive test, resistance to any drugs were more frequently found in younger TB patients. In adverse drug reactions, the incidences were not different between two groups except severe GI troubles which were more frequently developed in elderly TB patients. There were no significant differences in the rates of treatment success (97% vs. 93.7%, p=0.161), failure (0% vs. 0.7%, p=0.619), and deaths due to TB (0.5% vs. 1.1%, p=0.844) between two groups.

Conclusions: Elderly TB patients presented more frequent respiratory symptoms and showed less frequent active TB findings on chest CT scan. Treatment success rates of elderly TB patients were not inferior to those of younger TB patients without development of more frequent adverse drug reactions.

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The ratio of non-tuberculosis mycobacteria and co-morbidities in our hospital in the last five years

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Non tuberculosis mycobacterial infections (NTM) with chronic pulmonary diseases have increased in recent years. HIV infections and other co-morbid pulmonary diseases seem to be responsible for this relation as well as improvement in diagnostic techniques. Prolonged life time in COPD and cystic fibrosis generates special risk. NTM colonisation may cause clinical infection and progression in destructive pulmonary diseases. The objective of this study is to evaluate the NTM growth ratio and clinical features of these patients.

In our laboratory, approximately 25.000 specimens are cultured yearly with classic method (Lowenstein-Jensen). In this retrospective analyse, 185 NTM (1.58%) were identified in 11.681 tuberculosis culture positive specimens between 2004 and 2009.

Results: 33 patient files were examined out of 55 patients with NTM infection. Seven patients were female, 26 were male. Fifteen patients were \geq 65 years old and the others were < 65 years old. COPD, bronchiectasis. diabetes mellitus, malignancy, HCV infection were diagnosed in 10, 10, 6, 8 and 1 patients, respectively. Nodules, cavitary lesions and fibrosis were seen in computerised tomographies of 31 patients and in x- rays of two patients. In only 7 of 55 patient's cultures were identified as *M. abscessus (2), M. szulgai(3), M. intracellulare(1), M. xenopi(1)*. Thirty-one patients with NTM (93.39%) had chronic systemic or pulmonary diseases. **Conclusion:** In future, the ratio of diagnosing and treatment of NTM infections in older immun- competent patients with chronic diseases are going to be increased with developing laboratory tests, CT and the awareness of togetherness of NTM infections and chronic diseases.