limited by its serious adverse reactions. Aim of this study was to evaluate the efficacy and tolerability of a daily dose of 600 mgr of L in combination with other drugs against mycobacteria, in patients with culture proven MDR-TB and NTM disease.
Method: Between Sept 2008 and Jan 2011 in our TB Unit/Outpatient Clinic we followed 34 MDR-TB + XDR-TB and 18 NTM pts. Of them, 19 pts (2 XDR, 4 NTM), all HIV (–), had been treated with L which was added to regimens for 4-24 months (median 17). Sputum cultures, blood count/chemistry, ophalmologic and neurologic examination were undertaken on a regular basis.
Results: 16 pts completed treatment and were cured. Cultures became negative in all pts in an average of 14–32 weeks. One died after 5 months of treatment due to chronic respiratory failure and progressive M. avium disease, 2 discontinued (no adherence) after 5 and 7 months. 3 of 16 pts experienced adverse events, which led to withdrawal of L in all 3. 2 pts developed bone marrow depression and one optic neuropathy. Blood transfusions were given to both pts and bone marrow function normalized after cessation of L.
Conclusion: Linezolid seems highly effective in combination treatment of MDR-TB, XDR-TB and NTM disease. The majority of patients on L had positive treatment outcomes. All pts under L treatment should be monitored closely for presence of serious adverse reactions.

P4399
Safety, tolerability and efficacy of linezolid for the treatment of M/XDR-TB: A systematic review and meta-analysis
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Background: ≥40% of M/XDR-TB cases treated off-label with a linezolid-containing anti-TB regimen experienced adverse events (AE).
Aim: We performed a systematic review/meta-analysis according to PRISMA guidelines on safety, tolerability and efficacy of linezolid in M/XDR-TB patients.
Methods: 2 reviewers independently analyzed 9 articles using an electronic form. Original data were provided by the senior Authors of 5/9 studies.
Results: Out of 130 cases 92 (70.8%) and 38 (29.2%) were affected by MDR- and XDR-TB, respectively. 51/75 (68%) were born in Europe (35/51, 68.6%, in FSU countries), 14/75 (18.7%) in Asia and 7/75 (9.3%) in Africa; 78/130 (60%) were males, 14/116 (12.1%) HIV+ and 59/82 (72%) migrants. 83/127 (65.4%) have been previously treated, 94/118 (79.7%) were smear-positive and 22/116 (19%) underwent surgery. Median (IQR) hospital stay was 144.5 (66-194) days. Overall, 94/127 (74%) achieved treatment success, 16/127 (12.6%) died, 1/127 (0.8%) failed, 4/127 (3.2%) defaulted, 1/127 (0.8%) was transferred-out, 11/127 (8.7%) being still on treatment. 62/121 (51.2) experienced AE, 41/130 (31.5%) requiring linezolid interruption (36/120, 30%, episodes of anaemia, 26/120, 21.7%, peripheral neuropathy, 15/120, 12.5%, thrombocytopenia, 16/120, 13.3%, gastro-intestinal disorders, 8/120, 6.7%, leucopoenia). 41/62 (66.1%) cases had reversible AE. Patients treated with 1,200 mg/day (78/130, 60%) suffered significantly more AE than those treated with 600 mg/day (50/130, 38.5%): 44/78, 56.4%, vs. 16/50, 32%, respectively (P=0.008).
Conclusion: The toxicity of linezolid is dose-dependent and the drug should be used only for the most severe, otherwise untreatable cases.

436. Treatment of tuberculosis and adverse drug reactions

P4398
Efficacy and safety of linezolid for the treatment of multidrug resistant tuberculosis (MDR-TB) and disease by non tuberculous mycobacteria (NTM)
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Linezolid's (L) long-term use in the treatment of MDR-TB and NTM may be

P4400
Linezolid in the treatment of multi- and extensively drug-resistance tuberculosis
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Background: Some known antibacterial drugs can be used as anti-tuberculosis agents. But all of them must initially be tested as a component of long-therm poly-chemotherapy. The most promising one, linezolid (Lz), is now in the spot-light of TB-experts [G.B. Migliori et al., Eur Respir J 2009; 34:387-393].
Aims: To obtain data on efficacy and safety of Lz in the treatment of multi- (MDR) and extensively (XDR) drug-resistance tuberculosis (TB).
Methods: The prospective unblinded non-randomized one-centered study, includes 35 pulmonary TB pts (18-71 y.o., 21 m and 14 f); MDR in 19 pts (7 new and 12 re-treated), XDR in 16 (3 and 13). Lz (600 mg q.d.) was included in treatment

regimen, tailored by drug susceptibility tests, as 4th, 5th or 6th drug for 4-20 weeks. XDR was the strict indication for Lz, MDR - only if found impossible to create the adequate chemotherapy regimen (min 4 drugs) due to intolerance and/or resistance to second-line drugs.
Results: After 4 weeks of treatment in all cases the evident resolution of clinical and X-ray symptoms was obtained. The sputum smear negativation totally score 85,7% (30 pts): 73,3% after 8 week, additional 6,7% after 12 weeks and 3,3% else after 16 week. The severe side-effects, attributed to Lz, occurred in 2 pts (5,7%): peroneal neuropathy and obstinate vomiting. Anemia, thrombocytopenia were not registered.
Conclusion: The regimens included L (min 8 week) are high-effective in MDR and XDR TB in spite of long-term ineffective previously treatment. The Lz safety is quit well over a period of 8-16 weeks. Lz must be considered as a drug of choice after obtaining more accurate information on optimal length of administration, taking into account its high price.

P4401
Linezolide in complex treatment of XDR-TB patients
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Objective: To assess efficiency of treatment of XDR TB patients with linezolide.
Materials and methods: Treatment of 78 XDR TB patients, enrolled in this study, consisted besides chemotherapy of collapse therapy, additional albuminous nutrition, and also supporting therapy, aimed at prevention of possible side effects. All TB patients were treated with Cm, Mfx, Cs, PAS, Pto, Z, Amx/Clv and Clr. Patients were divided into two groups: main group included 44 patients who received complex treatment and linezolide in the dose of 600 mg per day during 6 months and the other group (controls) consisted of 34 patients receiving the same complex treatment without linezolide. Therapy results were assessed in 12 months by frequency of negativation of M. tuberculosis with a culture method and by clinical and X-ray dynamics of a treatment process.
Results: Culture method confirmed that 77,3% of patients became cultures negative in 12 months in the main group and only 35,3% of patients in the group of controls ($p<0,05$). In the main group in 12 months 18 (40,9%) patients showed healing of cavities and resolution of infiltrations, 16 (36,4%) patients had closing of cavities from one side with expressed resolution of infiltration, 8 (18,2%) patients had positive clinical and X-ray dynamics with reduction of the size of a destruction. In the group of controls there were observed healing of cavities and resolution of infiltrations at 8 (23,5%) patients; positive X-ray dynamics and healing of destructions from one side- at 2 (5,9%) patients, $p<0,05$.
Conclusion: Inclusion of linezolide into regimen of chemotherapy for XDR TB patients signifcantly increases efficiency of their treatment.

P4402
Adverse events in the treatment of multidrug-resistant tuberculosis
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Objective: To study the frequency and nature of side effect in patients receiving second line anti TB drugs
Introduction: Ojha Institute of Chest Diseases (DUHS) Karachi Pakistan is managing drug resistant TB patients since 1996. AAdverse events associated with second line drugs have a severe impact on adherence. Frequency of adverse events is not studied in resource-limited settings. Since 2009 patients are being managed according to WHO guideline. Treatment regimen is tailored t and data management i and account of side effect is maintained
Method: Patients registered from 1st -01- 2009 to 30-09-10 were included Data from DR TB 01 was recorded in Microsoft excel and o SPSS 16 and analyzed
Results: 440 patients were registered.Age range from 9 -76 year (mean 32.9,). ratio of male to female was 54.7: 45.3. 99.3% had pulmonary tuberculosis
Abdominal symptom were present in 51.4%, heart burn 48 (11.3%), abdominal pain/discomfort in 71 16.7%, epigastric pain in 29.3%, nausea and vomiting in 28.2%.
Vertigo observed in 140 (31.7%), hearing loss in 3.5% Depression in 5%, anxiety in 22 (5%), headache in 56 (12.7%) and 0.7%. had uneasiness.Psychosis in 12 (2.8%).y one had seizure, 43 joint pain. Hypothyroidism in 15 patients. Mild itching present in 7,5% cases one had exfoliated dermatitis. The onset of symptom was from seven days to 120 day. Most patients responded to symptomatic treatment, Drug were transiently stopped in patients with psychosis, completely in patient with exfoliative dermatitis and changed in 02 patients with gasteritis and one with psychosis
Conclusion: Gastrointestinal event were most frequent.Treatment can be continued with treatment of adverse event in most of the cases.

P4403

WITHDRAWN

P4404
Adverse events during treatment for latent tuberculosis infection
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Aim: To determine adverse events in patients taking treatment for latent tuberculosis infection (LTBI).
Methods: Records of all patients who received treatment for LTBI at the Chest Clinic of a large tertiary hospital between 01/2000 and 04/2008 were reviewed. An adverse event was defined as any change in health status that led to treatment interruption or cessation. Liver function tests were not performed routinely during follow-up, except when the patient was considered to be at an increased risk of developing hepatitis.
Results: Of 201 patients in whom treatment for LTBI was initiated 143 (71%) received isoniazid for 6 months, 32 (15%) received a combination of isoniazid and rifampicin for 6 months, and the remainder were treated with different regimens. Their mean (SD) age was 21 (17) years and 44% were male. Nineteen patients (9.5%) experienced an adverse event. Seven patients developed a rash, four had lethargy and/or mood disorders, three had subclinical hepatitis, four experienced severe nausea, vomiting and/or other gastrointestinal symptoms and three had features of peripheral neuropathy. In eight patients who experienced an adverse event medication was temporarily ceased and then re-started without change; in four the treatment regimen was changed; and in seven the treatment was ceased completely. The risk of adverse events was not significantly related to age, sex, drug regimen (single drug versus combination therapy) or baseline transaminase levels.
Conclusions: In this cohort almost 1 in 10 patients on treatment for LTBI experienced an adverse event. Although the adverse events were generally mild to moderate, this risk has to be taken into account when deciding whether to advise treatment for LTBI.

P4405
Severe adverse effects of antitubercular drugs and patient management
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Introduction: Tuberculosis is an infectious disease which can be totally cured by combining antitubercular drugs. Current therapeutic regimens with isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin have proved successful in treating tuberculosis. However, they are associated to a high rate of adverse effects that can lead to therapeutic failure.
Patients and methods: We retrospectively reviewed records of patients who present severe adverse effects of antitubercular drugs. We also examined the frequency of and reasons for changing drug regimens.
Results: Thirty two patients (20 men) mean age 47 years (18-80 years) were enrolled.
Predominant locations of tuberculosis are pulmonary (40%).
Cutaneous manifestations were the most frequent (40% of cases), predominantly

urticarial associated with fever in 6 cases. Anemia was noted in two cases and thrombocytopenia was noted in one case, anaphylactic shock in two cases, a systemic toxidermia in two cases and renal failure in one patien. Interrupting either one drug or the whole treatment was necessary to define the cause of the reaction. The clinical evolution of hypersensitivity signs was favorable in all cases following definitive withdrawal of the responsible drug. Complete recovery from tuberculosis occurred in all cases.
Rifampicin was incriminated in 15 cases, pyrazinamide in 9 cases, isoniazid in 4 cases, streptomycin in 4 cases and Ethambutol in 1 case.
Interrupting either one drug or the whole treatment was necessary to define the cause of the reaction. The clinical evolution of hypersensitivity signs was favorable in all cases following definitive withdrawal of the responsible drug. Complete recovery from tuberculosis occurred in all cases

P4406
Individualized treatment regimens with second line anti-TB drugs (SLD) compared to first line anti-TB drug (FLD) only in new pulmonary TB patients, culture confirmed with full sensibility at drug sensibility test (DST)
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Background: SLD are known as less efficient than FLD. However in clinical practice some of new pulmonary confirmed, fully sensible at DST TB cases are treated with individualized anti-TB regimens containing SLD.
Material and method: In Romania, 3845 new, pulmonary culture-confirmed TB cases, with full sensibility at DST registered between 01.01.2006-31.01.2007 were analyzed for anti-TB treatment regimen, treatment outcome, duration of treatment.
Results: Out of 3845 cases, 79 (2.1%) cases were treated with regimens containing at least one SLD for at least one month and 3766 (97,9%) were treated with FLD only.
Out of 79 cases treated with mixed FLD-SLD, 61 (77.1%) were successfully treated. Out of 3766 cases treated with FLD only, 3309 (87.7%) were successfully treated. The difference between the success rates was statistically significant ($p<0.001$). The medium duration of treatment among the 79 cases treated with mixed FLD-SLD was 27 weeks (3 weeks more than a standard category I anti-TB regiment hat last 24 weeks).
Conclusions: Individualized treatment regimens with SLD should be kept only for very few cases with severe adverse reaction against FLD.
NTP-s must assure uninterrupted supply with at least FLD

P4407
Monitoring of antituberculous drugs adverse events during the treatment of multidrug-resistant pulmonary tuberculosis
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Setting: The known determinants of drug-resistance development are non-compliance with prescribed treatment. Clinical management of multidrug-resistant tuberculosis (MDR-TB) requires lengthy multidrug regimens that often cause adverse events. Interruptions in treatment may result from the adverse events.
Design: We retrospectively reviewed medical records of 220 patients with MDR-TB who received individualized treatment in accordance with the recommendations of the WHO. A multiple logistic regression model was performed to determine whether the occurrence of adverse reactions was associated with poor treatment outcome.
Results: One or more adverse events were observed in all patients in the study. With an average of one patient receiving treatment, noted 10.4 episodes of adverse events. The most commonly reported events were nausea and vomiting (61%), dizziness (56%), abdominal pain (39%), arthralgia (31%), ototoxicity (19%) and dermatological effects (19%), psychiatric disorders (8%), hepatitis (4%) and renal failure (3%). These events led the clinicians to change in drug dose or withdraw one or more drugs from the treatment regimen temporarily or permanently.
Conclusion: Antituberculous drugs adverse events and connected with them treatment interruptions are observed more often in treatment of MDR-TB. MDR-TB patients who are female, older or have severe TB disease should be closely monitored for treatment-related adverse events. Obtained data allow to predict possible adverse events of MDR-TB chemotherapy, to provide the availability of medications necessary for adverse events reduction, including emergency cases.

P4408
Incidence and timing of hepatotoxicity due to anti-tuberculous treatment
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Hepatotoxicity is a life threatening complication of anti-tuberculous treatment. It is unclear how closely to monitor liver enzymes during treatment. In the absence of liver risk factors, the American Thoracic Society advises checking them if symptoms develop. The aim of this study was to assess the timing and causative factors associated with hepatotoxicity.
We reviewed patients treated for TB in Leeds between 2006 and 2010. Elevations of aminotransferase (ALT) greater than two times the upper limit of normal (ULN) were considered abnormal. Our local policy recommends that patients should have ALT checked at weeks 0, 2, 4 and 8.
634 patents underwent treatment for TB during this period. 46 (7.3%) patients had ALT rises two times ULN and 14 (2.2%) five times ULN. Interestingly, hepatotoxicity was more common in Caucasians ($p=0.02$) and increasing age ($p=0.07$). Gender, HIV status, pregnancy, and organs affected by TB did not predict hepatotoxicity. The average time for the hepatotoxicity to develop was 28 days (range 3-306); however, this time was increased to 42 days (4-306) in patients with ALT rises greater than five times ULN. Only one patient presented with clinical symptoms of hepatitis, this patient subsequently died from liver failure. In the 14 patients with rises five times ULN, the cause was felt to be pyrazinamide in 8, isoniazid in 3, rifampicin in 1, and not established in 2.
It is unknown whether identifying an elevated ALT and stopping treatment prior to symptoms reduces the severity of liver injury. We feel that careful biochemical monitoring and prompt cessation of treatment is appropriate. Only 2 patients developed hepatitis with ALT five times ULN at a time point beyond our 8 week protocol.

P4409
Antituberculosis fixed multi-dose combination and single drug therapy in active tuberculosis: What is the benefit?
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Background: Fixed dose combinations (FDCs) in tuberculosis (TB) therapy reduce the number of tablets to be consumed, simplify the medication regimen and potentially improve compliance.
Aim of study: Compare the efficacy and acceptability of anti-TB FDCs as single tablets (ST) in patients with active TB.
Patients and methods: A total of consecutive 94 patients (57 men and 37 women; mean age 38,1±3,3 years) were randomly distributed into 2 groups: trial group (n= 41) patients treated daily with anti-TB FDCs and control group (n= 53) treated with standardized regimen (single tablets).
Results: Stratified analyses showed a similar pattern for all the group dermographic, clinical and radiologic finding. The dosage of isoniazid, pyrazinamid and ethambutol was adequate in all patients. For rifampicin, dosage was statistically too low in trial group (p= 0,04). Serious adverse events were noted in 39% cases of trial group vs 11,5% cases in control group. According of cutaneous reactions (7,3% vs 5,7%) and toxic hepatitis (7,3% vs 3,7%) there was no statistically difference in 2 groups. Hematologic effects (21% vs 0%) were stastically higher in trial group (p= 0,018). All patients had a successful outcome. At 2 months of treatment, 50% of patients in trial group achieved sputum conversion vs 43% patients in control group without statistically significant difference. Radiologic sequellae was noted in 51% in trial group vs 36% in control group.
Conclusion: The efficacy of the anti-TB FDCs regimen was non-inferior to that of the standardized regimens. But, hematologic effects were significantly higher in the group of patients treated with anti-TB FDCs.

P4410
Allergic reactions to rifampicin in tuberculosis treatment
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Introduction: Immuno-allergic reactions to antituberculous treatment occur in 4 to 5% of cases and cause serious problem in the management of tuberculosis especially when due to major drug such as rifampicin.
Aim of the study: To describe different allergic reactions to rifampicin, the means of their confirmation and their management.
Methods: Retrospective study including all patients treated for tuberculosis (TB) and who developed allergic reactions to rifampicin between January 2000 and December 2009.
Results: Twelve (12) patients were included with mean age of 42 years. Mean delay of symptoms was 30 days after antituberculous treatment onset. Cutaneous reactions were noted in 11 patients, fever in 5 patients and anaphylactic reactions in 2 patients. Two patients had thrombocytopenia with hemorrhagic syndrome and 4 had hepatic cytolysis. Rifampicin responsibility was admitted after interruption of all the treatment and reintroduction one by one in 10 patients. In 2 cases the occurrence of thrombocytopenia after interrupted use of rifampicin and normalization of platelet level when rifampicin was stopped, allowed diagnosis. In 6 cases allergic reactions to rifampicin was associated to other antituberculous drug allergy. Rapid oral desensitization to rifampicin was successfully conducted in 4 patients. In 8 patients, rifampicin was definitively stopped, substituted by other antituberculous drug in two patients.
Conclusion: Severe allergic reactions to rifampicin are rare but can cause serious problem in tuberculosis management. In these cases rapid oral desensitization represent an interesting alternative.

P4411

Incidence of peripheral neuropathy during daily TB chemotherapy: Indian experience

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It is a routine practice to prescribe prophylactic pyridoxine to patients on TB chemotherapy to prevent Isoniazide induced neuropathy. However this adverse effect seems to be uncommon in our experience. We did a prospective study to determine the incidence of peripheral neuropathy in patients on daily TB chemotherapy. A total of 559 patients on standard daily TB chemotherapy as per WHO categorization were followed throughout the course of treatment. No patient received prophylactic pyridoxine. Patients with proven or suspected drug resistance were excluded from the study. Patients with existing peripheral neuropathy or those suffering from a condition predisposing to neuropathy such as diabetes, were also excluded. Patients reporting with symptoms of peripheral neuropathy such as tingling, numbness and other paraesthesias during the TB chemotherapy were followed. Other causes of neuropathy were ruled out. They were given daily vitamin B-complex (containing Pyridoxine 3 mg) one tablet thrice a day for one week. They were given 100 mg Pyridoxine daily only if there was no response. A total of 26/559 patients (4.65%) developed neuropathy symptoms. 19/26 (73.07%) patients responded to one week course of B-complex and never had recurrence of symptoms. 7/559 (1.25%) patients needed 100 mg of pyridoxine to relieve their symptoms. This indicates very low incidence of peripheral neuropathy in patients on daily TB chemotherapy without use of prophylactic pyridoxine, in Indian scenario.

P4412

Ethambutol induced bullous and lichenoid skin eruptions

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Introduction: Ethambutol is an essential drug for tuberculosis treatment. It has been in use since 1961. Its major side effect is on visual system, cutaneous side effects are rarely descripted in the literature including purpura, pruritic erythematous papules and exfoliative dermatitis.
Materials and methods: We report one case of ethambutol induced bullous and lichenoïd skin rashes confirmed by provocation test.
Results: It's about 73 years old woman, diabetic,treated of lung tuberculosis with Isoniazid, Rifampicin, pyrazinamid and ethambutol. After 25 days for treatment she reported generalised itching. Cutaneous examination revealed vesiculo-bullous eruptions on chest and abdominal wall, hyperpigmented face and diffuse desquamation on the limbs. All anti tuberculosis drugs were stopped and patient was put on local corticosteroïd therapy for two weeks. The lesions cleared completely. Because of its low risk of entraining skin side effect, ethambutol was introduced the first drug in a dose of 20 mg/kg. 24 hours later this provocation test, generalised itching and erythematovisicular skin eruptions more marked on the extremities were appeared, further administration of ethambutol was stopped. Patch tests will be programmed when lesions disappeared.
Clinician should be alerted to consider ethambutol also as one of possible drug causing cutaneous eruptions.

P4413

Research on in vitro release kinetics of isoniazid (IZN) and omeprazole from oral tablets

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Introduction: The study aimed to follow the in vitro release kinetics of IZN and omeprazole, the influence of applied methods and release evaluation when associated with other antituberculous drugs.
Materials and method: As reasearch method on the in vitro release of IZN and omeprazole it has been used the method of resistance in acid enviroment and dissolution method in neutral media. In order to evaluate the resistance in acidic conditions, 6 samples were taken in the time interval 5–110 minutes, while for dissolution in neutral media evaluation 11 samples were collected in the time interval from 10 to 320 minutes.
Results: Solubilization in acidic media: For IZN it was found a release degree of 85.9% at 5 minute and of 88.7% at 110 minutes. When associated with omeprazole, the maximum release degree it was identified at 30 minutes of 95.1%; when associated with other antituberculous drugs, the maximum release degree was found at 15 minutes of 99.6%. We found a very loz release degree for omeprazole; the first concentrations being detected after 75 minutes and after 110 minutes we found a releae degree of only 8.1%. Solubilization in neutral conditions: the lack of any IZN traces reveals that complete dissolution took place in acidic media, while for omeprazole it was found a 5.8% release degree at 10 minutes and of 40.2% after 320 minutes.
Conclusions: IZN shows a sensitive release pattern in the presence of antotuberculous drugs and a slightly sensitive release pattern in the presence of omeprazole. Instead, omeprazole shows a very low release pattern when associated with IZN or other anituberculous drugs, which could cause modifications of the plasma concentrations.

P4414

Influence of inhaled bronchodilator therapy on bacterioexcretion and LQ in patients with pulmonary TB infection with concomitant broncho-obstructive syndrome

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Aims: To evaluate the influence of bronchodilator therapy on bacterioexcretion and LQ in patients with lung TB with concomitant broncho-obstructive syndrome.
We examined 123 patients with pulmonary TB, 47 of which had infiltrative form (IFTB), 42 patients had fibrotico-cavernous form of TB (FCTB), in 33 cases residual post-TB pulmonary sclerosis (PPS) was diagnosed. In 65 cases we used bronchodilator therapy with inhaled M-cholinolytics and LABA (study group), rest of patients received teophylline per os (control group). All TB patients were treated with chemotherapy according WHO recommendations, excluding patients with PPS, in these cases no any chemotherapy was prescribed. Bacterioexcretion was assessed at the study start point, and after that it was controlled monthly till the 3rd month of therapy, this parameter was shown as a percentage of positive cases among the whole cohort of patients.
LQ evaluated at start and finish the study process using SGRQ questionnaire.
We determined that bronchodilator usage accelerated rates of sputum clearance in IFTB patients on 16,8%, in FCTB patients – on 14,8%. The most dynamic data were obtained in IFTB patients. LQ in study group for IFTB patients improved on 26,9%, in control group – on 8,7%. "Symptoms" scale diminished up to 32%, "daily activity" improved for 35%, and "impact" scale of SGRQ for study group fell down up to 19,7%.
Conclusion: Modern bronchodilator therapy can accelerate the rate of sputum clearance due to drainage bronchial function and due to diminishing the ability for concomitant infection to arise, in the same time improving LQ of such patients greatly.

P4415

In vitro susceptibility of M. avium against protionamide

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Introduction: M. avium is a potentially pathogenic mycobacterial species to humans, which is classified as difficult to cure. By the American Thoracic Society resistance testing in vitro in the case of newly diagnosed mycobacteriosis is recommended only for clarithromycin, but with treatment failure is shown the option for further testing. No data were so far reported for the the susceptibility of M. avium to protionamide in vitro in the literature.
Methods: All M. avium strains that could be isolated from clinical materials in our laboratory from Jan 1st 2008 to May 31st 2010, were subjected to susceptibility testing on solid media according to DIN 58943rd.
Results: Out of 67 strains only one turned out to be resistant at an inhibitory concentration of 5 micrograms/ml protionamide. While only one further strain showed resistance to clarithromycin (32 mcg/ml), 18 strains showed resistance to moxifloxacin (4 mcg/ml).
Conclusions: Despite the absence of clinical treatment studies protionamide should be considered as a treatment option for mycobacteriosis by M. avium in the case of treatment failure or intolerance of a drug of first-line therapy.

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Susceptibility of *mycobacterium avium complex* and *mycobacterium xenopi* to rifampin, rifapentine, clarithromycin and moxifloxacin, alone or in combination with ethambutol

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Background: Pulmonary disease due to *M. avium* complex [MAC], and *M. xenopi* [Mx]) is a growing health problem in industrialized countries and the optimal antibiotic treatment is still debated. We conducted a in vitro study to evaluate the activity of the main antibiotics on MAC and Mx.
Methods: For MAC strain 101 and Mx ATCC strain 700898, minimal inhibitory concentrations (MICs), of clarithromycin (CLA), moxifloxacin (MXF), rifampin (RIF), rifapentine (RPT), ethambutol (EMB) were determined on 7H11 media. Inoculum was 2.7 log10 CFU of Mx and 4.5 log10 CFU of MAC. Plates were read after 28 days of incubation at 37°C (MAC) or 42°C (Mx). MIC was defined as the lowest drug concentration that inhibits ≥99% of colonies compared to control. Combinations of EMB-RIF, EMB-RPT, MXF-CLA and EMB-MXF for Mx and MAC were tested using the checkerboard method.
Results: For MAC, MIC was >4 for CLA, 2 for MXF, >16 for RIF, >4 for RPT, 16 for EMB. For Mx, MIC was >4 for CLA, 2 for MXF, >16 for RIF, 4 for RPT, 16 for EMB. For both Mx and MAC, MIC was 1 for CLA when we

used Mueller Hinton media (pH=7.3 for Mueller Hinton media vs pH=6.6 for 7H11). Synergy was observed for EMB-RIF, EMB-MXF, MXF-CLA against Mx, and for EMB-RPT against both Mx and MAC. An additive effect was found for CLA-MXF, EMB-RIF, EMB-MXF against MAC.
Conclusion: The addition of EMB decreased the MIC of RPT against both MAC and Mx and decreased MIC of MXF and RIF against Mx. So, EMB could increase the in vivo activity of these antibiotics against these mycobacterial opportunistic pathogens. No antagonism between MXF and CLA was found.

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In vitro susceptibility of mycobacterium bovis against moxifloxacin
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Introduction: Mycobacterium bovis, the causative agent of bovine tuberculosis is also responsible for diseases in humans. To date there are no data available on the in vitro susceptibility of M. bovis strains to moxifloxacin, an established second line drug in the treatment of disease caused by M. tuberculosis.
Methods: From M. bovis-positive cultures from BAL, sputum, pleural effusion or cerebrospinal fluid of 34 pts from the years 1993-2010, we retrospectively evaluated the sensitivity in vitro and the minimum inhibitory concentrations of moxifloxacin. Culturing and resistance testing was performed on solid Middlebrook agar plates.
Results: Out of 34 tested M. bovis-positive cultures 33 showed a sensitivity to moxifloxacin at 2 or 4 mcg/ml. Only one strain showed resistance.
Conclusion: Our study of a small group of patients shows a high sensitivity rate of moxifloxacin against M. bovis strains. Despite the absence of clinical treatment studies, we see a potential use of moxifloxacin as a second line drug, with regular ineffectiveness of the first-line drug pyrazinamide in M. bovis.