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# Tropical Diseases Bulletin

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**1-** 20153441565 KERKHOFF, A. D.; MEINTJES, G.; BURTON, R.; VOGT, M.; WOOD, R.; LAWN, S. D. **Relationship between blood concentrations of hepcidin and anemia severity, mycobacterial burden, and mortality among patients with HIV-associated tuberculosis.** *Journal of Infectious Diseases* (2016) **213** (1) 61-70 Oxford University Press, Oxford, UK [En, 45 Ref.] Department of Medicine, University of California San Francisco School of Medicine, 505 Parnassus Ave, Box 0119, San Francisco, CA 94143, USA. Email: andrew-kerkhoff@gmail.com

BACKGROUND: Anemia is very common in patients with human immunodeficiency virus (HIV)-associated tuberculosis, and hepcidin may be key in mediating this. We explored the relationship between blood hepcidin concentrations and anemia severity, mycobacterial burden and mortality in patients with HIV-associated tuberculosis. METHODS: Consecutive unselected HIV-infected adults in South Africa were systematically investigated for tuberculosis. Three groups were studied: 116 hospitalized inpatients with HIV infection and tuberculosis (hereafter, "hospitalized patients"), 58 ambulatory outpatients with HIV infection and newly diagnosed tuberculosis (hereafter, "ambulatory patients with tuberculosis"), and 58 ambulatory outpatients with HIV infection and without tuberculosis (hereafter, "ambulatory patients without tuberculosis"). Blood hepcidin concentrations were determined for all patients. Vital status at 3 months was determined, and independent predictors of mortality were identified. RESULTS: Median hepcidin concentrations were 38.8 ng/mL among hospitalized patients, 19.1 ng/mL among ambulatory patients with tuberculosis, and 5.9 ng/mL among ambulatory patients without tuberculosis (P<.001). In both groups with HIV-associated tuberculosis, hepcidin concentrations were strongly associated with greater anemia severity. Additionally, strong, graded associations were observed between hepcidin and composite indices of mycobacterial burden and dissemination. Patients dying within 3 months had significantly higher hepcidin concentrations, which independently predicted mortality. Conclusions: High hepcidin concentrations were strongly associated with disseminated disease, anemia, and poor prognosis in patients with HIV-associated tuberculosis. Hepcidin may be a mechanistically important mediator underlying the high prevalence of severe anemia in these patients.

**2-** 20163009000 YUAN, LI.; LIGU M.; XIANG, L. Y.; ZHANG, H.; ZHENG, F.; LI, Z. **Genotypic characteristics of *Mycobacterium tuberculosis* circulating in Xinjiang, China.** *Infectious Diseases* (2016) **48** (2) 108-115 Taylor and Francis Online, Abingdon, UK [En, 32 Ref.] Department of Immunology, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China. Email: Zhuoyali@mails.tjmu.edu.cn

BACKGROUND: Tuberculosis (TB), a chronic infectious disease caused by *Mycobacterium tuberculosis* (MTB), poses a serious threat to human health. We investigated the genotypes of MTB in the high prevalence province Xinjiang, China. METHODS: From March 2010 to May 2013, 381 MTB isolates from patients with pulmonary TB were analyzed by molecular typing of 24 mycobacterial interspersed repetitive unit-variable number tandem repeat loci and PCR detection of the deleted regions of difference of the Beijing/W lineage and its sublineages. RESULTS: These isolates were shown to be highly polymorphic and to be composed of 345 unique genotypes, including 30 genotype clusters consisting of 2 or 3 strains and 315 individual genotypes. The genotype clustering rate was 17.32% and recent transmission index was low (9.45%). The Beijing/W lineage strains accounted for 57.48% of the isolates, and this predominant family strain was further subdivided into four sublineages: 181 (69.86%), 207 (14.61%), 105 (10.96%), and 150 (4.56%). CONCLUSIONS: The Beijing/W lineage (especially sublineage 181) strains were predominant and were associated with the transmissibility of TB in Xinjiang. Based on our data, we hypothesize that the circulating MTB strains in Xinjiang have significant genetic diversity and that the majority of the TB in Xinjiang may be explained by non-recent transmission emerging by endogenous reactivation. The possibility of outbreak is low, and current measures to control TB should first focus on standardized treatment of TB patients to prevent reactivation of latent infections.

**3-** 20163010062 ZELNER, J. L.; MURRAY, M. B.; BECERRA, M. C.; GALEA, J.; LECCA, L.; CALDERON, R.; YATACO, R.; CONTRERAS, C.; ZHANG ZIBIAO; MANJOURIDES, J.; GRENFELL, B. T.; COHEN, T. **Identifying hotspots of multidrug-resistant tuberculosis transmission using spatial and molecular genetic data.** *Journal of Infectious Diseases* (2016) **213** (2) 287-294 Oxford Journals, Oxford, UK [En, 24 Ref.] Robert Wood Johnson Foundation Health and Society Scholars Program, Interdisciplinary Center for Innovative Theory and Empirics (INCITE) & Mailman School of Public Health, Columbia University, 701A Knox Hall, Mail Code 9649, New York, NY 10027, USA. Email: jlz2115@columbia.edu

BACKGROUND: We aimed to identify and determine the etiology of "hotspots" of concentrated multidrug-resistant tuberculosis (MDR-tuberculosis) risk in Lima, Peru. METHODS: From 2009 to 2012, we conducted a prospective cohort study among households of tuberculosis cases from 106 health center (HC) areas in Lima, Peru. All notified tuberculosis cases and their household contacts were followed for 1 year. Symptomatic individuals were screened by microscopy and culture; positive cultures were tested for drug susceptibility (DST) and genotyped by 24-loci mycobacterial interspersed repetitive units-variable-number tandem repeats (MIRU-VNTR). RESULTS: 3286 individuals with culture-confirmed disease, DST, and 24-loci MIRU-VNTR were included in our analysis. Our analysis reveals: (1) heterogeneity in annual per-capita incidence of tuberculosis and MDR-tuberculosis by HC, with a rate of MDR-tuberculosis 89 times greater (95% confidence interval [CI], 54,185) in the most-affected versus the least-affected HC; (2) high risk for MDR-tuberculosis in a region spanning several HCs (odds ratio=3.19, 95% CI, 2.33, 4.36); and (3) spatial aggregation of MDR-tuberculosis genotypes, suggesting localized transmission. CONCLUSIONS: These findings reveal that localized transmission is an important driver of the epidemic of MDR-tuberculosis in Lima. Efforts to interrupt transmission may be most effective if targeted to this area of the city.

**4-** 20163038653 NANSUMBA, M.; KUMBAKUMBA, E.; ORIKIRIZA, P.; MULLER, Y.; NACKERS, F.; DEBEAUDRAP, P.; BOUM, Y., II; BONNET, M. **Detection yield and tolerability of string test for diagnosis of childhood intrathoracic tuberculosis.** *Pediatric Infectious Disease Journal* (2016) **35** (2) 146-151 Wolters Kluwer, Hagerstown, USA [En 27 Res.] Epicentre Mbarara Research Centre, P.O. Box 1956, Mbarara, Uganda. maryline.bonnet@epicentre.msf.org

BACKGROUND: Difficulty to obtain sputum in children complicates diagnosis of intrathoracic tuberculosis (TB). The intragastric string test (ST) used for retrieval of enteric pathogens might be an alternative specimen collection method but requires further evaluation of its utility in TB diagnosis. We conducted a cross-sectional study comparing the TB detection yield and the tolerability of ST and sputum induction (SI) in children. METHODS: Two ST and SI procedures were performed in children (3-14 years of age) who were clinically suspected of having TB. The string was removed after a 2-hour gastric downtime, and SI was done after a maximum of 20 minutes nebulization with 5% saline solution. LED-fluorescence microscopy and mycobacterial cultures were performed on all specimens, and XpertMTB/RIF assay was performed on stored specimen sediments. Tolerability questionnaires were administered to parents of children. RESULTS: Of 137 included children (median age: 8.1 years; 33.3% with HIV infection), 14 (10.2%) were diagnosed with TB, 10 (71.4%) by ST and 12 (85.7%) by SI. Among 105 children with both ST and SI performed, 5 (4.8%) versus 4 (3.8%) were smear positive using ST and SI, respectively (McNemar P =1.00). Nine (8.6%) in each group had positive cultures (P=1.00). Of 64 children tested with XpertMTB/RIF, 3 (4.7%) of the ST group versus 4 (6.3%) of the SI group were TB positive (P=1.00). No adverse serious events were reported. ST could not be performed in 22 of 137 (16.1%) children because they were unable to swallow the capsule. CONCLUSIONS: TB detection yield was comparable between ST and SI. The tolerability of ST in young children might be improved by the reduction of the size of the capsule.

**5-** 20163045440 SHULDINER, J.; LEVENTHAL, A.; CHEMTOB, D.; MOR, Z. **Mortality after anti-tuberculosis treatment completion: results of long-term follow-up.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 43-48 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 27 Ref.] Hadassah School of Public Health and Community Medicine, Braun Hebrew University, Jerusalem, Israel. Email: Zohar.Mor@rml.health.gov.il

BACKGROUND: *Mycobacterium tuberculosis* affects the lung parenchyma even after successful treatment. OBJECTIVE: To assess long-term mortality in a cohort of individuals who had recovered from tuberculosis (TB), and to compare their mortality rate and causes of death with those of the general population. METHODS: This retrospective cohort study of all Israeli citizens who recovered from tuberculosis between 2000 and 2010 included all patient files and death certificates and/or hospitalisation records of deceased individuals. Death rates were computed using standard mortality rates (SMR). Cox proportional hazard regression was conducted to identify risk factors for death, and causes of death were compared with those in the general Israeli population. RESULTS: Over 11 years of follow-up, comprising 18246 person-years, 389 (12.0%) Israeli citizens died after completion of anti-tuberculosis treatment, giving an SMR of 3.7. The SMR was strongly correlated with age, and was highest in males and individuals aged 25-44 years. Compared to the general population, among

individuals who recovered from TB there were more deaths due to septicaemia and pneumonia, and fewer deaths due to cerebrovascular diseases, stroke and diabetes (P<0.05). CONCLUSIONS: Individuals who recover from TB are at higher risk of long-term mortality than the general population, and their causes of death are different. Periodical follow-up might be beneficial for individuals to facilitate early diagnosis.

**6-** 20163045442 CHEN, K. S.; LIU, T.; LIN, R. R.; PENG, Y. P.; XIONG, G. C. **Tuberculosis transmission and risk factors in a Chinese antimony mining community.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 57-62 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 26 Ref.] Key Laboratory of Medical Molecular Virology, Fudan University, Shanghai, China. Email: Chenks100@126.com

SETTING: An antimony mine in Jiangxi Province, China. OBJECTIVE: To investigate the incidence of tuberculosis (TB) transmission and associated risk factors in a Chinese antimony mining community. DESIGN: Retrospective cohort study METHODS: The 15-locus mycobacterial interspersed repetitive unit-variable number of tandem repeats (MIRU-VNTR15-China) method was used to determine clustering of patients. A region of difference (RD105) deletion-targeted multiplex polymerase chain reaction was adopted to identify Beijing strains. Risk factors for clustering were assessed. RESULTS: Of 263 TB patients, 175 were distributed into 35 clusters. Estimated recent transmission of TB was 53.2% within the community. Patients who failed treatment were more likely to be in clusters (adjusted odds ratio [aOR] 0.03, 95%CI 2.12-6.89). Patients with multiresistant isolates were more likely to have failed treatment and to be in a cluster than those carrying a susceptible strain (aOR 0.001, 95%CI 4.89-29.7). CONCLUSIONS: Individuals who fail treatment are an important source of infection in TB transmission, and multiresistant isolates are mostly responsible for this. TB control plans need to focus on treatment failure cases in the community.

**7-** 20163045443 AGUILERA, X. P.; GONZÃ¡LEZ, C.; NÃ¡JERA-DE FERRARI, M.; HIRMAS, M.; DELGADO, I.; OLEA, A.; LEZAETA, L.; MONTAÃ±A, A.; GONZÃ¡LEZ, P.; HORMAZÃ¡BAL, J. C.; FERNÃ¡NDEZ, J.; GARCÃA, C.; HERRERA, T. **Tuberculosis in prisoners and their contacts in Chile: estimating incidence and latent infection.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 63-70 Ingenta Connect Ltd, Paris, France [En, 35 Ref.] Centro de Epidemiologãa y PolÃticas de Salud, Facultad de Medicina, ClÃnica Alemana de Santiago-Universidad del Desarrollo, 12438 Avenida Las Condes, Lo Barnechea, Santiago 771-0162, Chile. Email: xaguilera@udd.cl

SETTING: Contact investigation of tuberculosis (TB) patients in Chilean prisons. OBJECTIVE: (1) To estimate TB incidence and the prevalence of latent tuberculous infection (LTBI) among prisoners and their contacts; and (2) to determine factors associated with disease transmission. DESIGN: Cross-sectional study conducted in 46 prisons (51% of the total prison population) to assess the prevalence of and risk factors for LTBI among contacts of prisoners newly diagnosed with pulmonary TB. We used in vitro interferon-gamma release assays to establish LTBI and a questionnaire to address risk factors. RESULTS: During the 1-year follow-up, we studied 418 contacts of 33 active TB cases. We found high TB incidence (123.9 per 100000 prisoners) and high LTBI prevalence (29.4%) among contacts. LTBI rates are significantly higher in prison inmates than in non-prisoners (33.2% vs. 15.6%). Male sex, illicit drugs, malnutrition, corticosteroid use, low educational level and sharing a cell with a

case increase the risk of LTBI. Multivariate analyses showed that corticosteroid use, duration of incarceration and overcrowding are the most relevant determinants for LTBI among all contacts. CONCLUSIONS: Our results confirm that incarceration increases the risk of tuberculous infection and TB disease, and that it was associated not only with origin from vulnerable groups, but also with the prison environment. Reinforcing TB control is essential to prevent TB transmission in prisons.

**8-** 20163045445 BURMEN, B.; MODI, S.; CAVANAUGH, J. S.; MUTTAI, H.; MCCARTHY, K. D.; ALEXANDER, H.; CAIN, K. **Tuberculosis screening outcomes for newly diagnosed persons living with HIV, Nyanza province, Kenya, 2009.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 79-84 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 29 Ref.] Kenya Medical Research Institute (KEMRI), Center for Global Health Research, Busia Road, Kisumu, Kenya. Email: bburmen@kemricdc.org

SETTING: Fifteen human immunodeficiency virus (HIV) clinics in Nyanza Region, Western Kenya. OBJECTIVE: To describe routine tuberculosis (TB) screening and diagnostic practices among newly enrolled people living with HIV (PLHIV) prior to the implementation of World Health Organization recommended TB intensified case finding. DESIGN: Retrospective chart abstraction of PLHIV aged ≥ 7 years who were newly enrolled in HIV care in July and August 2009, and who had not received antiretroviral treatment in the preceding 2 years or been diagnosed with TB in the previous year. Factors associated with evidence of TB diagnostic evaluation among symptomatic PLHIV were assessed. RESULTS: Of 1020 patients included in the analysis, 995 (98%) were screened for TB at enrolment and 613 (62%) reported TB symptoms. Ninety-six (16%) patients with symptoms had evidence of referral for TB diagnostic evaluation, including patients at large clinics, those with advanced HIV disease and those reporting multiple TB symptoms. Among the 43 (45%) with documented evaluation results, 26 (60%) were diagnosed with TB. CONCLUSION: Although most PLHIV were screened for TB, very few underwent an evaluation, and the proportion diagnosed with TB was very low. Efforts to improve TB screening should focus on standardizing the intensified case finding algorithm and linkage to, and adequate infrastructure for, TB diagnostic evaluation.

**9-** 20163045446 KAPOOR, S.; GUPTA, A.; SHAH, M. **Cost-effectiveness of isoniazid preventive therapy for HIV-infected pregnant women in India.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 85-92 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 29 Ref.] Johns Hopkins University School of Medicine, PCTB Building-224, 725 N Wolfe St., Baltimore, MD 21205, USA. Email: skapoor@jhmi.com

BACKGROUND: India has a high burden of active tuberculosis (TB) and human immunodeficiency virus (HIV) infection. Pregnancy increases the risks of developing TB in HIV-infected women. Isoniazid preventive therapy (IPT) reduces progression to TB, but may increase costs and hepatotoxicity. The cost-effectiveness of IPT for HIV-infected pregnant women in India is unknown. DESIGN: We evaluated the cost-effectiveness of antepartum IPT among HIV-infected women in India using a decision-analytic model. We compared current practice (no IPT) with: Intervention 1 (IPT regardless of CD4 count) and Intervention 2 (IPT for those with CD4 count ≤ 200 cells/μl). We modeled IPT irrespective of tuberculin skin test (TST) status and TST-driven strategies. Primary outcomes were anticipated costs, disability-adjusted life-years (DALYs) and TB

cases. RESULTS: Both IPT interventions are highly cost-effective compared to no IPT at current willingness-to-pay thresholds (respectively US$178.00 and US$201.00 per DALY averted for Interventions 1 and 2). However, providing IPT irrespective of CD4 count results in the greatest health benefits (21 TB cases averted/1000 patients) compared to current practice. IPT irrespective of TST status was also highly cost-effective compared to TST-driven IPT (respectively US$1027.00 and US$1154.00/DALY averted for Interventions 1 and 2). CONCLUSION: Antepartum IPT for HIV-infected women is highly cost-effective for TB prevention compared to current practices in India.

**10-** 20163045449 KIM, J.; SUNG, H.; PARK, J. S.; CHOI, S. H.; SHIM, T. S.; KIM, M. N. **Subspecies distribution and macrolide and fluoroquinolone resistance genetics of *Mycobacterium abscessus* in Korea.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 109-114 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 32 Ref.] Depart-ment of Asan Medical Center and University of Ulsan College of Medicine, 88 Olympic-ro-43-gil, Songpa-gu, Seoul 138-736, Korea Republic. Email: sung@amc.seoul.kr

BACKGROUND: Treating *Mycobacterium abscessus* infections with antimicrobials remains difficult, possibly due to drug resistance. OBJECTIVE: To investigate the subspecies distribution of *M. abscessus* and its correlation with antibiotic susceptibility and the genetics of antibiotic resistance, focusing on macrolides and fluoroquinolones, in the Republic of Korea. DESIGN: A total of 53 M. abscessus isolates were identified to the subspecies level by sequencing of hsp65 and erm(41). The minimal inhibitory concentrations (MICs) of clarithromycin (CLM) and ciprofloxacin (CFX) were determined using SensititreTM RAPMYCO plates. The rrl, gyrA and gyrB genes were sequenced to elucidate the molecular mechanisms of macrolide and fluoroquinolone resistance. RESULTS: Isolates included 22 *M. abscessus* subsp. abscessus and 31 *M. abscessus* subsp. bolletii. erm(41) sequences showing subspecies-specific deletions and sequence variations in the 28th nucleotide were concordant with inducible CLM resistance; however, mutations in rrl were not detected. Low- and high-level CFX resistance was observed in respectively 19 (35.8%) and 10 (18.9%) of the 53 clinical isolates, regardless of subspecies. However, no non-synonymous mutations were detected in gyrA or gyrB. CONCLUSION: Sequencing of the erm gene and subspeciation of *M. abscessus* may be used to predict inducible macrolide susceptibility. Further studies of the relationship between specific mutations in gyrA or gyrB to MIC change are required.

**11-** 20163045450 KO, Y.; LEE, H. K.; LEE, Y. S.; KIM, M. Y.; SHIN, J. H.; SHIM, E. J.; PARK, S. Y.; MO, E. K.; PARK, Y. B. **Accuracy of Xpert® MTB/RIF assay compared with AdvanSureTM TB/NTM real-time PCR using bronchoscopy specimens.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (1) 115-120 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 25 Ref.] Department of Pulmonary and Critical Care Medicine, Kangdong Sacred Heart Hospital, Hallym University College of Medicine, 150 Seongan-ro Gangdong-gu, Seoul 134-701, Korea Republic. Email: koyus@naver.com

BACKGROUND: The performance of Xpert® MTB/RIF assay, an automated nucleic acid amplification test (NAAT) that was developed for the detection of tuberculosis (TB), has been evaluated in various clinical settings. However, few studies have compared Xpert with other NAATs, especially its performance using lower respiratory tract specimens (LRTS). OBJECTIVE: To

compare the practical diagnostic performance of the Xpert assay with that of the AdvanSureTM TB/NTM RT-PCR kit in the detection of pulmonary TB (PTB), using LRTS obtained through bronchoscopy. RESULTS: Of 249 patients included, 105 had culture-confirmed PTB. Using culture as reference, the overall sensitivity of Xpert and AdvanSure was respectively 92.4% and 83.8%. When acid-fast bacilli smear results were taken into consideration, the sensitivity of Xpert for smear-positive and smear-negative LRTS was respectively 100% and 88.9%, while that of the AdvanSure was 100% and 76.4%. Xpert showed better results than AdvanSure in terms of sensitivity in smear-negative LRTS (P=0.012), but no difference in smear-positive LRTS. CONCLUSIONS: Xpert may be advantageous in the detection of PTB using LRTS, particularly in low microbiological burden settings.

**12-** 20163045455 BELARD, S.; TAMAROZZI, F.; BUSTINDUY, A. L.; WALLRAUCH, C.; GROBUSCH, M. P.; KUHN, W.; BRUNETTI, E.; JOEKES, E.; HELLER, T. **Point-of-care ultrasound assessment of tropical infectious diseases - a review of applications and perspectives.** *American Journal of Tropical Medicine and Hygiene* (2016) **94** (1) 8-21 American Society of Tropical Medicine and Hygiene, Deerfield, USA [En, 130 Ref.] Center of Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Division of Internal Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands. sabine.belard@charite.de; f_tamarozzi@yahoo.com; bustinji06@gmail.com; claudia-wallrauch@web.de; m.p.grobusch@amc.uva.nl; echnatom@web.de; tkuhn@gru.edu; enrico.brunetti@unipv.it

The development of good quality and affordable ultrasound machines has led to the establishment and implementation of numerous point-of-care ultrasound (POCUS) protocols in various medical disciplines. POCUS for major infectious diseases endemic in tropical regions has received less attention, despite its likely even more pronounced benefit for populations with limited access to imaging infrastructure. Focused assessment with sonography for HIV-associated TB (FASH) and echinococcosis (FASE) are the only two POCUS protocols for tropical infectious diseases, which have been formally investigated and which have been implemented in routine patient care today. This review collates the available evidence for FASH and FASE, and discusses sonographic experiences reported for urinary and intestinal schistosomiasis, lymphatic filariasis, viral hemorrhagic fevers, amebic liver abscess, and visceral leishmaniasis. Potential POCUS protocols are suggested and technical as well as training aspects in the context of resource-limited settings are reviewed. Using the focused approach for tropical infectious diseases will make ultrasound diagnosis available to patients who would otherwise have very limited or no access to medical imaging.

**13-** 20163046624 WANG, Y.; WANG, R.; MING, J.; LIU, G.; CHEN, T.; LIU, X.; LIU, H.; ZHEN, Y.; CHENG, G. **Effects of dust storm events on weekly clinic visits related to pulmonary tuberculosis disease in Minqin, China.** *Atmospheric Environment* (2016) **127** 205-212 Elsevier Ltd, Philadelphia, USA [En, 54 Ref.] Cold and Arid Regions Environmental and Engineering Research Institute, Chinese Academy of Science, Donggang West Road 320, Lanzhou City, China.

Pulmonary tuberculosis (PTB) is a major public health problem in China. Minqin, a Northwest county of China, has a very high number of annual PTB clinic visits and it is also known for its severe dust storms. The epidemic usually begins in February and ends in July, while the dust storms mainly occur throughout spring and early summer, thereby suggesting that there might be a

close link between the causative agent of PTB and dust storms. We investigated the general impact of dust storms on PTB over time by analyzing the variation in weekly clinic visits in Minqin during 2005-2012. We used the Mann-Whitney-Pettitt test and a regression model to determine the seasonal periodicity of PTB and dust storms in a time series, as well as assessing the relationships between meteorological variables and weekly PTB clinic visits. After comparing the number of weekly PTB cases in Gansu province with dust storm events, we detected a clear link between the population dynamics of PTB and climate events, i.e., the onset of epidemics and dust storms (defined by an atmospheric index) occurred in almost the same mean week. Thus, particulate matter might be the cause of PTB outbreaks on dust storm days. It is highly likely that the significant decline in annual clinic visits was closely associated with improvements in the local environment, which prevented desertification and decreased the frequency of dust storm events. To the best of our knowledge, this is the first population-based study to provide clear evidence that a PTB epidemic was affected by dust storms in China, which may give insights into the association between this environmental problem and the evolution of epidemic disease.

**14-** 20163048149 LEE, S. W.; WU, S. H. L.; HUANG, G. M.; HUANG, K. Y.; LEE, T. Y.; WENG, WENG, T. Y. J. **Gene expression profiling identifies candidate biomarkers for active and latent tuberculosis.** *BMC Bioinformatics* (2016) **17** (1) 3 BioMed Central, London, UK [En, 66 Ref.] Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan District, Taoyuan City, Taiwan. Email: julweng@saturn.yzu.edu.tw

BACKGROUND: Tuberculosis (TB) is a serious infectious disease in that 90% of those latently infected with *Mycobacterium tuberculosis* present no symptoms, but possess a 10% lifetime chance of developing active TB. To prevent the spread of the disease, early diagnosis is crucial. However, current methods of detection require improvement in sensitivity, efficiency or specificity. In the present study, we conducted a microarray experiment, comparing the gene expression profiles in the peripheral blood mononuclear cells among individuals with active TB, latent infection, and healthy conditions in a Taiwanese population. RESULTS: Bioinformatics analysis revealed that most of the differentially expressed genes belonged to immune responses, inflammation pathways, and cell cycle control. Subsequent RT-PCR validation identified four differentially expressed genes, NEMF, ASUN, DHX29 and PTPRC, as potential biomarkers for the detection of active and latent TB infections. Receiver operating characteristic analysis showed that the expression level of PTPRC may discriminate active TB patients from healthy individuals, while ASUN could differentiate between the latent state of TB infection and healthy condition. In contrast, DHX29 may be used to identify latently infected individuals among active TB patients or healthy individuals. To test the concept of using these biomarkers as diagnostic support, we constructed classification models using these candidate biomarkers and found the NaÃ¯ve Bayes-based model built with ASUN, DHX29, and PTPRC to yield the best performance. CONCLUSIONS: Our study demonstrated that gene expression profiles in the blood can be used to identify not only active TB patients, but also to differentiate latently infected patients from their healthy counterparts. Validation of the constructed computational model in a larger sample size would confirm the reliability of the biomarkers and facilitate the development of a cost-effective and sensitive molecular diagnostic platform for TB.

**15-** 20163051568 TRIPATHI, R.; SINHA, P.; KUMARI, R.; CHAUBEY, P.; PANDEY, A.; ANUPURBA, S. **Detection of rifampicin resistance in tuberculosis by molecular methods: a report from Eastern Uttar Pradesh, India.** *Indian Journal of Medical Microbiology* (2016) **34** (1) 92-94 Medknow Publications, Mumbai, India [En, 13 Ref.] Department of Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

Diagnosis of drug resistance tuberculosis (TB) by the gold standard method is labour intensive and time consuming. Hence, there is an urgent need for introduction of rapid diagnostic techniques. Line probe assay (LPA) and cartridge-based nucleic acid amplification test (CBNAAT) have been introduced in India under Revised National Tuberculosis Control Program. Spot and morning sputum samples of previously treated patients by anti-TB drugs were subjected to LPA or CBNAAT. Total 682/1253 (54.4%) were diagnosed as rifampicin-resistant. The patients could be diagnosed early by molecular methods and put on second line treatment.

**16-** 20163051569 MITRA, S.; GUNASEKARAN, K.; CHACKO, G.; HANSDAK, S. G. **Leprous neuromyositis: a rare clinical entity and review of the literature.** *Indian Journal of Medical Microbiology* (2016) **34** (1) 95-97 Medknow Publications, Mumbai, India [En, 7 Ref.] Department of Medicine, Christian Medical College, Vellore, Tamil Nadu, India.

*Mycobacterium leprae*, the causative agent of leprosy (Hansen's disease), is a slow growing intracellular acid-fast bacillus that affects the skin, peripheral nerves and respiratory tract. In patients with suppressed cell-mediated immunity, the infiltration of the Bacilli can produce disseminated illness such as leprous neuromyositis. We reported a case of 56-year-old gentleman presenting with pyrexia of unknown origin, asymmetric sensory motor axonal polyneuropathy and was on chronic exogenous steroid therapy. On evaluation, his skin, muscle, nerve and bone marrow biopsy showed numerous globi of acid-fast Bacilli suggestive of leprous neuromyositis, a rare form of disseminated Hansen's disease. We reported this case in view of its rarity, atypical manifestation of a relatively rare disease and literature review on poor electrophysiological correlation in the diagnosis of leprous neuromyositis as compared to the histopathological examination.

**17-** 20163057543 ELLENDER, C. M.; LAW, D. B.; THOMSON, R. M.; EATHER, G. W. **Safety of IV amikacin in the treatment of pulmonary non-tuberculous mycobacterial disease.** *Respirology* (2016) **21** (2) 357-362 Wiley-Blackwell, Melbourne, Australia [En, 14 Ref.] Department of Respiratory and Sleep Medicine, Princess Alexandra Hospital, Ipswich Road, Woolloongabba Brisbane, Qld. 4102, Australia. Email: geoffrey.eather@health.qld.gov.au

BACKGROUND AND OBJECTIVE: Pulmonary non-tuberculous mycobacterial (NTM) disease has a high mortality rate and often requires treatment with intravenous amikacin. We report on safety data in patients treated with intravenous amikacin for pulmonary. METHODS: A retrospective observational study (2002-2012) was performed including 45 patients that met American Thoracic Society criteria for pulmonary NTM disease and were treated with intravenous amikacin at three hospitals in Brisbane, Australia. The aim was to define the rates of common adverse effects, the patient and regimen factors associated with these adverse effects and describe the rates of treatment success and associated factors. RESULTS: Forty-five patients (34 women; median age 63 years) were treated for *Mycobacterium intracellulare* (25),

*Mycobacterium abscessus* (13), *Mycobacterium avium* (6) and *Mycobacterium fortuitum* (1) using multi-drug therapy that included IV amikacin. Transient ototoxicity was seen in eight (18%) but long-term ototoxicity was seen in only three (7%). There were no cases of nephrotoxicity and no long-term vestibulotoxicity. Sustained culture conversion at 6 months was only found in 17 (38%), however, the majority (34 patients, 76%) had a clinical response to treatment determined by an improvement in symptoms. CONCLUSION: Carefully selected and closely monitored patients with pulmonary NTM can be treated using IV amikacin safely with low rates of toxicity. No pretreatment patient or regimen factors were predictive of toxicity or treatment success in this small cohort. Lower treatment success rates were found than previous trials suggest there is a difficult balance in this patient group between treatment success and toxicities.

**18-** 20163057607 XIONG, J. H.; CHONG, M.; SHA, X. W.; ZHENG, J.; HAO, W.; YANG, Y. L.; YONG, N. **Association between genetic variants in NOD2, C13orf31, and CCDC122 genes and leprosy among the Chinese Yi population.** *International Journal of Dermatology* (2016) **55** (1) 65-69 Wiley-Blackwell, Oxford, UK [En, 21 Ref.] Southwest Jiaotong University, Chengdu, Sichuan, China. Email: syypfk@163.com

BACKGROUND: A significant association between single nucleotide polymorphisms in NOD2, C13orf31, and CCDC122 genes and leprosy has been reported in a previous genome-wide association study of leprosy in the Chinese Han population. However, it remains unknown whether this association exists among the Chinese Yi population. The aim of this study was to investigate whether single nucleotide polymorphisms in NOD2, C13orf31, and CCDC122 genes are associated with leprosy among the Chinese Yi population in China. METHODS: We genotyped rs9302752, rs7194886, rs8057341, and rs3135499 in the NOD2 gene; rs3764147 and rs10507522 in the C13orf31 gene; and rs3088362 and rs9533634 in the CCDC122 gene in a Chinese Yi cohort comprised of 319 patients with leprosy and 355 ethnic-matched controls. The differences between the patients and healthy controls were analyzed using chi-squared analysis. RESULTS: Significant differences of rs3135499 in NOD2, rs3764147 and rs10507522 in C13orf31, and rs3088362 and rs9533634 in CCDC122 were observed between the patients and the healthy control groups in the cohort. The allelic P values and odd ratios were as follows: rs3135499, 1.0×10-8 and 2.55; rs3764147, 1.7×10-7 and 1.88; rs10507522, 1.16×10-5 and 1.95; rs3088362, 8.2×10-4 and 1.51; rs9533634, 5.34×10-5 and 1.73. No significant differences were found in the distributions of rs9302752, rs7194886, and rs8057341 between the patients and healthy controls. CONCLUSIONS: We demonstrated that genetic variants in the NOD2, C13orf31, and CCDC122 genes are closely associated with leprosy among the Chinese Yi population, which implicates the pathogenic role of NOD2, C13orf31, and CCDC122 genes in a different ethnicity.

**19-** 20163062773 MOUNGUENGUI, D.; KOMBILA, U. D.; ONDOUNDA, M.; IBINGA, L. D.; MBETHE, L. G.; MAGNE, C.; NZENZE, J. R.; BOGUIKOUMA, J. B. **Tuberculosis of the breast: four cases report at the Armies Instruction's Hospital Omar Bongo Ondimba (HIAOBO) in Libreville (Gabon).** *Bulletin de la Société de Pathologie Exotique* (2016) **109** (1) 5-7 Lavoisier, Cachan, France [Fr, 11 Ref.] Hcircumflex˜pital d'instruction des armées Omar Bongo Ondimba (HIA-OBO), 5e Arrondissement, Quartier PK 9 route Melen, BP, Libreville, Gabon. Email: dios-dado2002@yahoo.fr

*Mammary tuberculosis* is a rare localization of extra pulmonary tuberculosis. Its frequency increases proportionally with the HIV pandemic. We report four cases of breast tuberculosis diagnosed in the general medicine department of HIAOBO including two with positive HIV serology. It is necessary to know this extra pulmonary form/feature as the differential diagnosis with breast tumors is sometimes difficult.

**20-** 20163065839 DIA, M. L.; GUEYE, P.; BA, F.; CISSE, N. N.; BALDE, O.; DIOUF, B.; SARR, M.; SOW, A. I.; CISSE, M. F. **Molecular detection of resistance to rifampicin and isoniazid in tuberculosis patients in Senegal.** *African Journal of Microbiology Research* (2016) **10** (1) 41-44 Academic Journals, Lagos, Nigeria [En, 13 Ref.] Bacteriology-Virology Laboratory, Fann University Hospital Center, Dakar, Senegal. Email: laminedia2004@yahoo.fr

The aim of this study was to use molecular methods to determine the profile of resistance to rifampicin (RMP or RIF) and isoniazid (INH) in mycobacteria from tuberculosis patients in Senegal. Sputum samples (48) received by the mycobacterial laboratory of the National Antituberculosis Program (NATP) in Senegal between 2012 and 2014 were studied. Most of these samples came from patients in treatment failure or relapse (58.33%). They were tested with the Xpert MTB/RIF or line-probe assays (LPAs) or both. 17 (35.41%) isolates resistant to INH, 16 (33.33%) resistant to RMP, and 16 that were multidrug-resistant (MDR) (33.33%) were identified. Two isolates (4.16%) were susceptible to INH, but resistant to RMP (INH-S/RIF-R). The molecular tests facilitated the rapid detection of MDR isolates. However, INH resistance should be assessed in all cases in which RIF resistance is detected, given the demonstrated existence of INH-S/RIF-R strains.

**21-** 20163067167 MOHANTY, P. S.; FARAH NAAZ; DHEERAJ KATARA; LAMA MISBA; DILIP KUMAR; DWIVEDI, D. K.; TIWARI, A. K.; CHAUHAN, D. S.; BANSAL, A. K.; TRIPATHY, S. P.; KATOCH K. **Viability of *Mycobacterium leprae* in the environment and its role in leprosy dissemination.** *Indian Journal of Dermatology, Venereology & Leprology* (2016) **83** (1) 23-27 Medknow Ltd, Mumbai, India [En, 24 Ref.] Department of Microbiology and Molecular Biology, National JALMA Institute for Leprosy and Other Mycobacterial Diseases, Dr. M Miyazaki Marg, Tajganj, Agra-282 004, Uttar Pradesh, India. Email: m.sarathipartha @gmail.com

BACKGROUND: Leprosy, a chronic disease caused by *Mycobacterium leprae*, is a public health concern in certain countries, including India. Although the prevalence of the disease has fallen drastically over time, new cases continue to occur at nearly the same rate in many regions. Several endemic pockets have been observed in India and elsewhere. The precise dynamics of leprosy transmission are still not clearly understood. Both live bacilli as well as *M. leprae* DNA have been detected in the soil and water of endemic areas; they possibly play an important role in disease transmission. AIMS: To study the occurrence of viable *M. leprae* in environmental samples collected from areas of residence of patients with active leprosy. METHODS: The study was conducted on 169 newly diagnosed leprosy patients in Ghatampur, Uttar Pradesh, India. Soil and water samples were collected from their areas of residence using a standardized protocol. An equal number of soil and water samples were also collected from non-patient areas of the same or adjoining villages. The environmental samples collected from the patients surroundings were subjected to 16S ribosomal RNA gene analysis after obtaining informed consent. RESULTS: About a quarter of the environmental samples

collected from patient areas, (25.4% of soil samples and 24.2% of water samples) were found to be positive for specific 16S ribosomal RNA genes of *M. leprae*. Environmental samples collected from non-patient areas were all found negative for *M. leprae* 16S ribosomal RNA genes. Limitations: The major limitation of the study was that the sample size was small. CONCLUSION: The study demonstrated the presence of viable strains of *M. leprae* in skin smear samples of paucibacillary patients and multibacillary patients, as well as in the environmental samples obtained from around their houses. This could play an important role in the continued transmission of leprosy.

**22-** 20163067174 SHIVASWAMY, U.; NEELAMBIKE, S. M. **Drug resistance pattern of mycobacterial isolates in HIV and non-HIV population in South India.** *Lung India* (2016) **33** (1) 27-31 Medknow Publications, Mumbai, India [En, 27 Ref.] Department of Microbiology, University of Mysore, Mysore, Karnataka, India. Email: mnsumana12@gmail.com

BACKGROUND: Emergence of drug resistance has complicated the treatment of tuberculosis (TB). WHO reports India to be one among 27 "high burden" multidrug-resistant (MDR) TB countries. OBJECTIVE: To diagnose TB and detect drug resistance of mycobacterial isolates in acid-fast bacilli (AFB) smear negative HIV reactive patients (Group A) and compare them with HIV seropositive AFB smear positive (Group B) and HIV-seronegative AFB positive cases (Group C). MATERIALS AND METHODS: Clinical specimens collected in all groups were processed as per the standard protocol except blood, which was processed by lysis centrifugation technique. They were then inoculated with Lowenstein-Jensen media and the isolates obtained were subjected to drug susceptibility test (DST) by proportion method and genotype MTBDR plus assay. RESULTS: In Group A, 162 patients were included. Of the 443 clinical samples collected, 76 mycobacterial strains were obtained from 67 (41%) patients. Of these, 50 (65.8%) were sensitive to all drugs and 26 (34.2%) resistant to one or more anti-tubercular drugs. Antibiogram of Group A when compared with Group B and C showed that the MDR rate 6.6%, 6.7% and 8% respectively did not differ much; but resistance to at least single drug was (26 [34.2%], 3 [10%], and 8 [16%]), respectively. CONCLUSION: Our study suggests that HIV has no influence on the anti-tubercular resistance pattern, but increased MDR rate along with HIV in high TB burden setting stresses the need for early diagnosis and DST in providing proper regimens and improve prognosis.

**23-** 20163067226 ZHANG, T.; DU, J.; YIN, X. Y.; XUE, F. Z.; LIU, Y. X.; LI, R. Z.; LUO, C.; LI, L.; LI, X. J. **Adverse events in treating smear-positive tuberculosis patients in China.** *International Journal of Environmental Research and Public Health* (2016) **13** (1) 86-96 MDPI AG, Basel, Switzerland [En, 42 Ref.] Department of Biostatistics, School of Public Health, Shandong University, Jinan 250012, China. Email: tao_zhang@live.com

This study aimed to estimate the adverse events (AE) rate during anti-tuberculosis treatment and to explore AE-related risk factors. New and previously treated smear-positive tuberculosis (TB) cases were enrolled from eight regions in China between April 2009 and October 2010. The AE rate was estimated, and AE risk factors during anti-TB treatment were assessed using Cox proportional models. Among 2091 Chinese subjects with anti-TB treatment, 462 (22.1%, 95% confidence interval (CI), 20.3-23.9) patients developed AE, with liver injury and gastrointestinal reactions constituting the most common AE. Specifically, 9.8% (95% CI, 8.5-11.1)

and 6.3% (95% CI, 5.3-7.4) developed liver injuries and gastrointestinal reactions, respectively. We found that AE rate differed by regions, TB knowledge score, symptoms score and smoking status. Liver injuries were associated with age, sex and smoking status; gastrointestinal reactions were associated with education level and symptom score. Improving patients' knowledge on TB could reduce AE rate.

**24-** 20163069986 MILLÁN-LOU, M. I.; OLLÉ-GOIG, J. E.; TORTOLA, M. T.; MARTIN, C.; SAMPER, S. **Mycobacterial diversity causing multi- and extensively drug-resistant tuberculosis in Djibouti, Horn of Africa.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (2) 150-153 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 17 Ref.] Instituto de Investigación Sanitaria Aragón, Instituto Aragonés de Ciencias de la Salud, Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Hospital Universitario Miguel Servet, University of Zaragoza, P. Email: ssamper.iacs@aragon.es

On detecting a high prevalence of multidrug-resistant tuberculosis (TB) in Djibouti, 32 *Mycobacterium tuberculosis* isolates of patients hospitalised in the TB referral centre of the capital were genotyped. A high variety of *M. tuberculosis* lineages, including lineage 1, Indo-Oceanic, lineage 2, East-Asian, lineage 3, East-African Indian and lineage 4, Euro-American, were detected.

**25-** 20163069989 MAJUMDAR, T.; BHATTACHARYA, S.; BARMAN, D.; BHOUMIK, P.; BIR, R. **Detection of multidrug-resistant tuberculosis using MGITTM and MAS-PCR in Tripura, India.** *International Journal of Tuberculosis and Lung Disease* (2016) **20** (2) 166-169 International Union Against Tuberculosis and Lung Disease, Paris, France [En, 17 Ref.] Department of Microbiology, Agartala Government Medical College, Agartala - 799 006, India. Email: drtapan1@rediffmail.com; drtapan1960@gmail.com

BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) poses a global threat that is further compounded by the human immunodeficiency virus (HIV) epidemic. OBJECTIVE: To detect MDR-TB among pulmonary TB (PTB) patients with or without HIV coinfection by isolating and identifying *Mycobacterium tuberculosis* from clinical samples and performing drug susceptibility testing (DST). METHODS: Sputum was collected from presumed PTB cases. Microscopic examination was performed following Ziehl-Neelsen (ZN) staining and cultured in Löwenstein-Jensen (LJ) medium. First-line anti-tuberculosis DST of the isolates was performed using MGIT™ (Mycobacterial Growth Indicator Tube) and multiplex allele-specific polymerase chain reaction (MAS-PCR). RESULTS: Of 172 study subjects, 59.3% (102/172) were smear-positive and 40.7% (70/172) were smear-negative. In the smear-positive and -negative groups, respectively 62.7% (64/102) and 8.6% (6/70) were culture-positive. DST on MGIT showed a cumulative resistance of 7.1% (5/70) to isoniazid (INH) and rifampicin. More ethambutol (EMB) and combined INH+EMB resistance was detected using MAS-PCR. CONCLUSION: MDR-TB is a problem in Tripura, and culture and phenotypic DST are required for diagnosis. MAS-PCR may provide an alternative rapid screening tool.

**26-** 20163073440 LEROLLE, N.; LAANANI, M.; RIVIÃ¨RE, S.; GALICIER, L.; COPPO, P.; MEYNARD, J. L.; MOLINA, J. M.; AZOULAY, E.; AUMONT, C.; MARZAC, C.; FARDET, L.; LAMBOTTE, O. **Diversity and combinations of infectious agents in 38 adults with an infection-triggered reactive haemophagocytic syndrome: a multicenter study.** *Clinical Microbiology and Infection* (2016)

**22** (3) 268.e1-268.e8 Elsevier Ltd, Oxford, UK [En, 28 Ref.] Nathalie Lerolle, Moussa Laanani, Sébastien Rivière, Lionel Galicier, Paul Coppo, Jean-Luc Meynard, Jean-Michel Molina, Elie Azoulay, Cedric Aumont, Christophe Marzac, Laurence Fardet, Olivier Lambotte.

Reactive haemophagocytic syndrome (HS) is a rare condition that occurs in patients with infections, haematological malignancies or autoimmune diseases. Although various micro-organisms are thought to trigger HS, most of the literature data on this topic have been gathered in single-centre case series. Here, we sought to characterize infectious triggers in a large, multicentre cohort of patients with HS. Patients were included in the present study if HS was solely due to one or more infections. Detailed microbiological data were recorded. Of the 162 patients with HS in the cohort, 40 (25%) had at least one infection and 38 of the latter (including 14 women, 36.8%) were included. The median age was 46 years. Seven patients were presumed to be immunocompetent (18.4%), whereas 19 patients (50%) were infected with human immunodeficiency virus and 12 patients (31.6%) were immunocompromised for other reasons. Twenty-seven patients (71.1%) had a single infection, whereas six (15.8%) and five (13.1%) patients had, respectively, two and three concomitant infections. We observed pyogenic bacterial infections ( n =7), tuberculosis (n=10), non-tuberculous mycobacteriosis (n=3), viral infections (n=17: 11 cytomegalovirus, three Epstein-Barr virus, two human herpesvirus 8, one herpes simplex virus 2), parasitic infections (n=8: four disseminated toxoplasmosis, one leishmaniasis, three malaria), fungal infections (n=5: four pulmonary pneumocystosis and one candidaemia). Eighteen patients (47.4%) received corticosteroids and / or etoposide. Twelve patients died (31.6%). All multiple infections and all deaths occurred in immunocompromised patients. When compared with patients suffering from malignancy-associated HS, patients with infection-triggered HS were younger and more likely to be immunocompromised, and had a better outcome.

**27-** 20163073950 HONG, J. Y.; JANG, S. H.; KIM, S. Y.; CHUNG, K. S.; SONG, J. H.; PARK, M. S.; KIM, Y. S.; KIM, S. K.; CHANG, J.; KANG, Y. A. **Elevated serum CA 19-9 levels in patients with pulmonary nontuberculous mycobacterial disease.** *Brazilian Journal of Infectious Diseases* (2016) **20** (1) 26-32 Elsevier Editora Ltda, SÃ£o Paulo, Brazil [En, 29 Ref.] Division of Pulmonary and Critical Care Medicine, Department of Medicine, Chuncheon Sacred Heart Hospital, Hallym University Medical Center, Chuncheon, Gangwon-do, Korea Republic. Email: mdkang@yuhs.ac

Increased serum CA 19-9 levels in patients with nonmalignant diseases have been investigated in previous reports. This study evaluates the clinical significance of serum CA 19-9 elevation in pulmonary nontuberculous mycobacterial disease and pulmonary tuberculosis. The median CA 19-9 level was higher in patients with pulmonary nontuberculous mycobacterial disease than in patients with pulmonary tuberculosis (pulmonary nontuberculous mycobacterial disease: 13.80, tuberculosis: 5.85, p<0.001). A multivariate logistic regression analysis performed in this study showed that Mycobacterium abscessus (OR 9.97, 95% CI: 1.58, 62.80; p=0.014) and active phase of pulmonary nontuberculous mycobacterial disease (OR 12.18, 95% CI: 1.07, 138.36, p=0.044) were found to be risk factors for serum CA 19-9 elevation in pulmonary nontuberculous mycobacterial disease. The serum CA 19-9 levels showed a tendency to decrease during successful treatment of pulmonary nontuberculous myco-

bacterial disease but not in pulmonary tuberculosis. These findings suggest that CA 19-9 may be a useful marker for monitoring therapeutic responses in pulmonary nontuberculous mycobacterial disease, although it is not pulmonary nontuberculous mycobacterial disease-specific marker.

**28-** 20163073951 SHINU, P.; SINGH, V.; NAIR, A. **Isoniazid and rifampin drug susceptibility testing: application of 2,3,5-triphenyl tetrazolium chloride assay and microscopic-observation drug-susceptibility assay directly on Ziehl-Neelsen smear positive sputum specimens.** *Brazilian Journal of Infectious Diseases* (2016) **20** (1) 33-40 Elsevier Editora Ltda, SÃ£o Paulo, Brazil [En, 28 Ref.] Department of Microbiology, M.M.I.M.S.R., MM University, Mullana, Ambala 133 207, India. Email: shinup 1983@gmail.com

The current study was aimed to evaluate the performance of direct 2,3,5-triphenyl tetrazolium chloride assay and direct microscopic observation drug susceptibility assay with indirect Löwenstein-Jensen proportion method directly on Ziehl-Neelsen smear positive sputum specimens. METHODS: Direct acid fast bacilli smear positive sputum specimens (n=264) were subjected to isoniazid and rifampicin drug susceptibility testing by direct 2,3,5-triphenyl tetrazolium chloride assay, direct microscopic observation drug susceptibility assay, and the performances were compared with indirect Löwenstein-Jensen proportion method. RESULTS: The direct 2,3,5-triphenyl tetrazolium chloride assay demonstrated an overall sensitivity, specificity, positive predictive value, and negative predictive value of 99.2%, 82.4%, 99.2%, and 88.5%, respectively, for the detection of isoniazid and rifampicin resistant *Mycobacterium tuberculosis* isolates when compared to indirect Löwenstein-Jensen proportion method. Likewise, the overall sensitivity, specificity, positive predictive value and negative predictive value of direct microscopic observation drug susceptibility assay were 98.8%, 82.4%, 99.2%, and 78.2%, respectively. CONCLUSION: The direct 2,3,5-triphenyl tetrazolium chloride assay was found to be an economical alternative method for the rapid and accurate detection of isoniazid and rifampicin resistance from direct acid fast bacilli smear positive sputum specimens.

**29-** 20163073952 AHMAD, N.; JAVAID, A.; SYED AZHAR, S. S.; MING, L. C. AHMAD, I.; KHAN, A. H. **Resistance patterns, prevalence, and predictors of fluoroquinolones resistance in multidrug resistant tuberculosis patients.** *Brazilian Journal of Infectious Diseases* (2016) **20** (1) 41-47 Elsevier Editora Ltda, SÃ£o Paulo, Brazil [En, 32 Ref.] Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia. Email: nafeesuob@gmail.com

BACKGROUND: Fluoroquinolones are the backbone of multidrug resistant tuberculosis treatment regimens. Despite the high burden of multidrug resistant tuberculosis in the country, little is known about drug resistance patterns, prevalence, and predictors of fluoroquinolones resistance among multidrug resistant tuberculosis patients from Pakistan. OBJECTIVE: To evaluate drug resistance patterns, prevalence, and predictors of fluoroquinolones resistance in multidrug resistant tuberculosis patients. METHODS: This was a cross-sectional study conducted at a programmatic management unit of drug resistant tuberculosis, Lady Reading Hospital Peshawar, Pakistan. Two hundred and forty-three newly diagnosed multidrug resistant tuberculosis patients consecutively enrolled for treatment at study site from January 1, 2012 to July 28, 2013 were included in the study.

A standardized data collection form was used to collect patients' socio-demographic, microbiological, and clinical data. SPSS 16 was used for data analysis. Results High degree of drug resistance (median 5 drugs, range 2-8) was observed. High proportion of patients was resistant to all five first-line anti-tuberculosis drugs (62.6%), and more than half were resistant to second line drugs (55.1%). The majority of the patients were ofloxacin resistant (52.7%). Upon multivariate analysis previous tuberculosis treatment at private (OR=1.953, p=0.034) and public private mix (OR=2.824, p=0.046) sectors were predictors of ofloxacin resistance. CONCLUSION: The high degree of drug resistance observed, particularly to fluoroquinolones, is alarming. We recommend the adoption of more restrictive policies to control non-prescription sale of fluoroquinolones, its rational use by physicians, and training doctors in both private and public-private mix sectors to prevent further increase in fluoroquinolones resistant *Mycobacterium tuberculosis* strains.

**30-** 20163074239 WINGLEE, K.; MCGUIRE, A. M.; MAIGA, M.; ABEEL, T.; SHEA, T.; DESJARDINS, C. A.; DIARRA, B.; BAYA, B.; SANOGO, M.; DIALLO, S.; EARL, A. M.; BISHAI, W. R. **Whole genome sequencing of *Mycobacterium africanum* strains from Mali provides insights into the mechanisms of geographic restriction.** *PLoS Neglected Tropical Diseases* (2016) **10** (1) e0004332 Plos.org, San Francisco, USA [En, 115 Ref.] Center for Tuberculosis Research, Department of Medicine, Johns Hopkins University, Baltimore, Maryland, USA. Email: aearl@broadinstitute.org; wbishai1@jhmi.edu

BACKGROUND: *Mycobacterium africanum*, made up of lineages 5 and 6 within the *Mycobacterium tuberculosis* complex (MTC), causes up to half of all tuberculosis cases in West Africa, but is rarely found outside of this region. The reasons for this geographical restriction remain unknown. Possible reasons include a geographically restricted animal reservoir, a unique preference for hosts of West African ethnicity, and an inability to compete with other lineages outside of West Africa. These latter two hypotheses could be caused by loss of fitness or altered interactions with the host immune system. METHODOLOGY/ PRINCIPAL FINDINGS: We sequenced 92 MTC clinical isolates from Mali, including two lineage 5 and 24 lineage 6 strains. Our genome sequencing assembly, alignment, phylogeny and average nucleotide identity analyses enabled us to identify features that typify lineages 5 and 6 and made clear that these lineages do not constitute a distinct species within the MTC. We found that in Mali, lineage 6 and lineage 4 strains have similar levels of diversity and evolve drug resistance through similar mechanisms. In the process, we identified a putative novel streptomycin resistance mutation. In addition, we found evidence of person-to-person transmission of lineage 6 isolates and showed that lineage 6 is not enriched for mutations in virulence-associated genes. CONCLUSIONS: This is the largest collection of lineage 5 and 6 whole genome sequences to date, and our assembly and alignment data provide valuable insights into what distinguishes these lineages from other MTC lineages. Lineages 5 and 6 do not appear to be geographically restricted due to an inability to transmit between West African hosts or to an elevated number of mutations in virulence-associated genes. However, lineage-specific mutations, such as mutations in cell wall structure, secretion systems and cofactor biosynthesis, provide alternative mechanisms that may lead to host specificity.

**31-** 20163093678 SHARMA, A.; BLOSS, E.; HEILIG, C. M.; CLICK, E. S. **Tuberculosis caused by *Mycobacterium africanum*, United States,**

**2004-2013.** *Emerging Infectious Diseases* (2016) **22** (3) 396-403 National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, USA [En, 39 Res.] Centers for Disease Control and Prevention, Atlanta, Georgia, USA. Email: asharma4@cdc.gov

*Mycobacterium africanum* is endemic to West Africa and causes tuberculosis (TB). We reviewed reported cases of TB in the United States during 2004-2013 that had lineage assigned by genotype (spoligotype and mycobacterial interspersed repetitive unit variable number tandem repeats). *M. africanum* caused 315 (0.4%) of 73,290 TB cases with lineage assigned by genotype. TB caused by *M. africanum* was associated more with persons from West Africa (adjusted odds ratio [aOR] 253.8, 95% CI 59.9-1,076.1) and USborn black persons (aOR 5.7, 95% CI 1.2-25.9) than with US-born white persons. TB caused by *M. africanum* did not show differences in clinical characteristics when compared with TB caused by *M. tuberculosis.* Clustered cases defined as > 2 cases in a county with identical 24-locus mycobacterial interspersed repetitive unit genotypes, were less likely for *M. africanum* (aOR 0.1, 95% CI 0.1-0.4), which suggests that *M. africanum* is not commonly transmitted in the United States.

**32-** 20163094123 LAMBERT, S. M.; NIGUSSE, S. D.; ALEMBO, D. T.; WALKER, S. L.; NICHOLLS, P. G.; IDRISS, M. H.; YAMUAH, L. K.; LOCKWOOD, D. N. J. **Comparison of efficacy and safety of ciclosporin to prednisolone in the treatment of Erythema Nodosum Leprosum: two randomised, double blind, controlled pilot studies in Ethiopia.** *PLoS Neglected Tropical Diseases* (2016) **10** (2) e0004149 Public Library of Sciences (PLoS), San Francisco, USA [En, 29 Ref.] Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK. Email: saba.lambert@ lshtm.ac.uk

BACKGROUND: Erythema Nodosum Leprosum (ENL) is a serious complication of leprosy. It is normally treated with high dose steroids, but its recurrent nature leads to prolonged steroid usage and associated side effects. There is little evidence on the efficacy of alternative treatments for ENL, especially for patients who have become steroid resistant or have steroid side effects. These two pilot studies compare the efficacy and side effect profile of ciclosporin plus prednisolone against prednisolone alone in the treatment of patients with either new ENL or chronic and recurrent ENL. METHODS AND RESULTS: Thirteen patients with new ENL and twenty patients with chronic ENL were recruited into two double-blinded randomised controlled trials. Patients were randomised to receive ciclosporin and prednisolone or prednisolone treatment only. Patients with acute ENL had a delay of 16 weeks in the occurrence of ENL flare-up episode, with less severe flare-ups and decreased requirements for additional prednisolone. Patients with chronic ENL on ciclosporin had the first episode of ENL flare-up 4 weeks earlier than those on prednisolone, as well as more severe ENL flare-ups requiring 2.5 times more additional prednisolone. Adverse events attributable to prednisolone were more common that those attributable to ciclosporin. CONCLUSIONS: This is the first clinical trial on ENL management set in the African context, and also the first trial in leprosy to use patients' assessment of outcomes. Patients on ciclosporin showed promising results in the management of acute ENL in this small pilot study. But ciclosporin, did not appear to have a significant steroid-sparing effects in patients with chronic ENL, which may have been due to the prolonged use of steroids in these patients in combination with a too rapid decrease of steroids in patients given ciclosporin. Further research is needed to determine whether the promising

results of ciclosporin in acute ENL can be reproduced on a larger scale.

**33-** 20163094149 FAVA, V. M.; MANRY, J.; COBAT, A.; ORLOVA, M.; NGUYEN VAN THUC; NGUYEN NGOC BA; VU HONG THAI; ABEL, L.; ALCAÃ¯S, A.; SCHURR, E. A missense LRRK2 variant is a risk factor for excessive inflammatory responses in leprosy. *PLoS Neglected Tropical Diseases* (2016) **10** (2) e0004412 Public Library of Sciences (PLoS), San Francisco, USA [En, 41 Ref.] Program in Infectious Diseases and Immunity in Global Health, Research Institute of the McGill University Health Centre, Montreal, Canada. Email: erwin.schurr@mcgill.ca

BACKGROUND: Depending on the epidemiological setting, a variable proportion of leprosy patients will suffer from excessive pro-inflammatory responses, termed type-1 reactions (T1R). The LRRK2 gene encodes a multi-functional protein that has been shown to modulate pro-inflammatory responses. Variants near the LRRK2 gene have been associated with leprosy in some but not in other studies. We hypothesized that LRRK2 was a T1R susceptibility gene and that inconsistent association results might reflect different proportions of patients with T1R in the different sample settings. Hence, we evaluated the association of LRRK2 variants with T1R susceptibility. METHODOLOGY: An association scan of the LRRK2 locus was performed using 156 single-nucleotide polymorphisms (SNPs). Evidence of association was evaluated in two family-based samples: A set of T1R-affected and a second set of T1R-free families. Only SNPs significant for T1R-affected families with significant evidence of heterogeneity relative to T1R-free families were considered T1R-specific. An expression quantitative trait locus (eQTL) analysis was applied to evaluate the impact of T1R-specific SNPs on LRRK2 gene transcriptional levels. PRINCIPAL FINDINGS: A total of 18 T1R-specific variants organized in four bins were detected. The core SNP capturing the T1R association was the LRRK2 missense variant M2397T (rs3761863) that affects LRRK2 protein turnover. Additionally, a bin of nine SNPs associated with T1R were eQTLs for LRRK2 in unstimulated whole blood cells but not after exposure to *Mycobacterium leprae* antigen. SIGNIFICANCE: The results support a preferential association of LRRK2 variants with T1R. LRRK2 involvement in T1R is likely due to a pathological pro-inflammatory loop modulated by LRRK2 availability. Interestingly, the M2397T variant was reported in association with Crohn's disease with the same risk allele as in T1R suggesting common inflammatory mechanism in these two distinct diseases.

**34-** 20163094263 SARRAFZADEH, S. A.; MAHLOOJIRAD, M.; NOURIZADEH, M.; CASANOVA, J. L.; POURPAK, Z.; BUSTAMANTE, J.; MOIN, M. **Mendelian susceptibility to mycobacterial disease due to IL-12Rβ1 deficiency in three Iranian children.** *Iranian Journal of Public Health* (2016) **45** (2) 249-254 School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences, Tehran, Iran [En, 13 Ref.] Immunology, Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Email: mmoin@sina.tums.ac.ir

Mendelian susceptibility to mycobacterial diseases (MSMD) is a rare inheritance syndrome, characterized by a disseminated infection with mycobacterium in children following BCG vaccination at birth. Regarding the vaccination program in Iran, it may consider as a public health problem. The pathogenesis of MSMD is dependent on either insufficient production of IFN-gamma (γ) or inadequate response to it. Here, we want to introduce three cases including two siblings and one girl from two unrelated families

with severe mycobacterial infections referred to Immunology, Asthma and Allergy Research Institute (IAARI), from 2013 to 2015; their MSMD was confirmed by both cytokine assessment and genetic analysis. Regarding the clinical features of the patients, cell proliferation against a mitogen and BCG antigen was ordered in a lymphocyte transformation test (LTT) setting. ELISA was performed for the measurement of IL-12p70 and IFN-γ in whole blood samples activated by BCG+recombinant human IFN-γ and BCG+ recombinant human IL-12, respectively. In contrast to mitogen, the antigen-dependent proliferation activity of the patients' leukocytes was significantly lower than that in normal range. We identified a homozygous mutation in IL12RB1 gene for two kindred who had a homozygous mutation affecting an essential splice site. For the third patient, a novel frameshift deletion in IL12RB1 gene was found. The genetic study results confirmed the impaired function of stimulated lymphocytes to release IFN-γ following stimulation with BCG+IL-12 while the response to rhIFN-γ for IL-12p70 production was relatively intact. Our findings show that cellular and molecular assessments are needed for precise identification of immunodeficiency disorders especially those without clear-cut diagnostic criteria.

**35-** 20163100826 PRABHAVATHI ,M; AHAMED KABEER, B.S; DEENADAYALAN A; RAJA, A. **In vitro QuantiFERON-TB gold antigen specific interleukin-1beta to diagnose TB among HIV-positive subjects.** *Tuberculosis* (2016) **96** 27-30 Elsevier Ltd, Oxford, UK [En, 12 Ref.] Department of Immunology, National Institute for Research in Tuberculosis (ICMR), No. 1, Mayor Sathyamoorthy Road, Chetpet, Chennai, 600 031, Tamil Nadu, India. prabha.biochem1@gmail.com; bkabeer@sidra.org; harianbu1@gmail.com; alameluraja@gmail.com

BACKGROUND: The recently introduced IFN-γ release assay (IGRA) has been reported to improve the diagnosis of TB. However, IGRA has suboptimal sensitivity to diagnose TB among HIV co-infected subjects. Apart from IFN-γ, the pro inflammatory cytokines such as Interleukin-1beta (IL-1β), Tumor necrosis factor-alpha (TNF-α), IL-2, IL-6, IL-8 and IL-12 are also play a major role in mycobacterial infections. This study aimed to analyze these cytokines for detecting active TB among HIV sero positive subjects.

MATERIALS AND METHODS: We had prospectively enrolled 53 HIV positive subjects and 55 HIV-TB co-infected patients from India. IGRA was performed by using QuantiFERON TB-Gold In tube (QFT-GIT) method. TB antigen specific IL-1β, TNF-α, IL-2, IL-6, IL-8 and IL-12 levels were evaluated by ELISA in plasma harvested from QFT-GIT tubes. RESULTS AND CONCLUSION: The TB antigen specific IL-1β levels were significantly elevated in HIV-TB co-infected patients compared to HIV positive subjects (p=0.0004). The specificity of both IL-1β (50.94%) and QFT-GIT (52.83%) remained similar in HIV positive subjects (p=0.24). However, IL-1β had shown higher sensitivity (72.73%) than QFT-GIT (54.55%) to diagnose TB among HIV co-infected patients. Moreover, in culture test positive HIV-TB patients, antigen specific IL-1β exhibited sensitivity of 84.21%; whereas QFT-GIT exhibited only 57.89% sensitivity. Unlike IFN-γ (the read out marker of QFT-GIT), antigen specific IL-1β levels were not influenced by low CD4 counts. The other cytokine levels were not significantly differ between the 2 groups. From this study we concluded that TB antigen specific IL-1β may be an additional biomarker for active TB diagnosis among HIV positive subjects.

**36-** 20163100834 NUNES-COSTA, D.; ALARICO, S.; DALCOLMO, M. P.; CORREIA-NEVES, M.; EMPADINHAS, N. **The looming tide of**

**nontuberculous mycobacterial infections in Portugal and Brazil.** *Tuberculosis* (2016) **96** (1) 107-119 Elsevier Ltd, Oxford, UK [En, 129 Ref.] CNC - Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal. Email: numenius@cnc.uc.pt

Nontuberculous mycobacteria (NTM) are widely disseminated in the environment and an emerging cause of infectious diseases worldwide. Their remarkable natural resistance to disinfectants and antibiotics and an ability to survive under low-nutrient conditions allows NTM to colonize and persist in man-made environments such as household and hospital water distribution systems. This overlap between human and NTM environments afforded new opportunities for human exposure, and for expression of their often neglected and underestimated pathogenic potential. Some risk factors predisposing to NTM disease have been identified and are mainly associated with immune fragilities of the human host. However, infections in apparently immunocompetent persons are also increasingly reported. The purpose of this review is to bring attention to this emerging health problem in Portugal and Brazil and to emphasize the urgent need for increased surveillance and more comprehensive epidemiological data in both countries, where such information is scarce and seriously thwarts the adoption of proper preventive strategies and therapeutic options.

**37-** 20163106577 YUN, M. R.; HAN, S. J.; YOO, W. G.; KWON, T. S.; LEE, S. H.; LEE, J. S.; KIM, D. W. **Draft genome sequence of *Mycobacterium tuberculosis* KT-0204, isolated in South Korea.** *Genome Announcement* (2016) **4** (1) e01519-15 American Society for Microbiology, Washington, USA [En, 11 Ref.] Division of Biosafety Evaluation and Control, Korea National Institute of Health, Korea Centers for Disease Control and Prevention, Chungbuk, Korea Republic. Email: cosmosljs@gmail.com

Here, we describe the draft genome sequence of *Mycobacterium tuberculosis* KT-0204, non-Beijing family. This sequence will reveal genes related to the evolution and adaptation of *M. tuberculosis* KT-0204 in human hosts.

**38-** 20163106625 KWON, T.; HAN, S. J.; YOO, W. G.; YUN, M. R.; LEE, S. H.; LEE, J. S.; KIM, D. W. **Draft Genome Sequence of *Mycobacterium tuberculosis* KT-0133, Isolated in South Korea.** *Genome Announcement* (2016) **4** (1) e01731-15 American Society for Microbiology, Washington, USA [En, 9 Ref.] School of Biological Sciences, Seoul National University, Seoul, Korea Republic. Email: cosmosljs@gmail.com

Here, we present the draft genome sequence of *Mycobacterium tuberculosis* KT-0133, which belongs to the Korean-Beijing family. This sequence will provide a new perspective on the evolution and accommodation of *M. tuberculosis* KT-0133 in human hosts.

**39-** 20163106630 KWON, T.; HAN, S. J.; YOO, W. G.; YUN, M. R.; LEE, S. H.; LEE, J. S.; KIM, D. W. **Draft genome sequence of *Mycobacterium tuberculosis* KT-0184, isolated in South Korea.** *Genome Announcement* (2016) **4** (1) e01755-15 American Society for Microbiology, Washington, USA [En, 9 Ref.] School of Biological Sciences, Seoul National University, Seoul, Korea Republic. Email: cosmosljs@gmail.com

Here, we describe the draft genome sequence of *Mycobacterium tuberculosis* KT-0184, from the Beijing family. This genome will provide insight into the evolution and adaptation of *M. tuberculosis* KT-0184 in human hosts.

**40-** 20163109199 SALT, E.; WIGGINS, A. T.; RAYENS, M. K.; HUAMAN, M. A.; MANNINO, D.; SCHWIETERMAN, P.; MERKLEY, S. A.; JONES, A. R.; CROFFORD, L. J. **Risk factors for targeted fungal and mycobacterial infections in patients taking tumor necrosis factor inhibitors.** *Arthritis &*

*Rheumatology* (2016) **68** (3) 597-603 Wiley-Blackwell, Hoboken, USA [En, 15 Ref.] College of Nursing, University of Kentucky, 315 College of Nursing Building, 751 Rose Street, Lexington, KY 40536-0232, USA. Email: egsalt0@uky.edu

OBJECTIVE: To identify predictors of the receipt of medical care, including the receipt of pre-drug screening, for diagnostically targeted fungal or mycobacterial infections among patients prescribed a tumor necrosis factor inhibitor (TNFi). METHODS: We conducted a case-control study using deidentified patient health claims information from a data set representing a commercially insured US population of 15 million patients annually from January 1, 2007 to December 31, 2009. Descriptive statistics as well as a 2-sample t-test, chi-square test of association, Fisher's exact test, and multivariate logistic regression were used for data analysis. RESULTS: A total of 30,772 patients received a TNFi during the study period. Of these, 158 patients (0.51%) developed targeted fungal and/or mycobacterial infections (cases). The median number of infections per case was 1.0 (interquartile range 1.0-2.0). Tuberculosis was diagnosed in 61% of cases, followed by histoplasmosis in 60%, non-tuberculous mycobacterial infections in 11%, coccidioidomycosis in 10%, unspecified fungal infection in 8%, blastomycosis in 4%, cryptococcal infection in 3%, and pneumocystosis in 2%. Compared to controls (n=474), a higher proportion of cases were prescribed prednisone (55% versus 37%; P<0.001). Patients who were prescribed prednisone during the study period were twice as likely as those not taking prednisone to seek medical care attributable to a targeted fungal or mycobacterial infection (odds ratio 2.03; P<0.001). CONCLUSION: Development of a targeted fungal or mycobacterial infection among patients taking a TNFi is rare. Concomitant use of prednisone predicted development of such infections.

**41-** 20163112509 BOJANG, A. L.; MENDY, F. S.; TIENTCHEU, L. D.; OTU, J.; ANTONIO, M.; KAMPMANN, B.; AGBLA, S.; SUTHERLAND, J. S. **Comparison of TB-LAMP, GeneXpert MTB/RIF and culture for diagnosis of pulmonary tuberculosis in The Gambia.** *Journal of Infection* (2016) **72** (3) 332-337 Elsevier Ltd, Oxford, UK [En, 17 Res.] Vaccines and Immunity Theme, Medical Research Council (MRC) Unit, Fajara, Gambia. jsutherland@mrc.gm

BACKGROUND: Diagnosis of tuberculosis (TB) remains difficult, particularly in resource-limited settings. The development of nucleic acid-based tests for detection of *Mycobacterium tuberculosis* complex (MTBC) has significantly increased sensitivity compared to conventional smear microscopy and provides results within a matter of hours compared to weeks for the current gold-standard, liquid culture. METHODS: In this study we performed side-by-side comparison of mycobacterial detection assays on sputum samples from 285 subjects presenting with symptoms suggestive of TB in The Gambia and a cross-sectional cohort of 156 confirmed TB patients with a median of 2 months of treatment. A novel assay, Loop-Mediated Amplification test for TB (TB-LAMP), was compared to smear microscopy, MGIT culture and GeneXpert MTB/RIF for all samples. RESULTS: When culture was used as the reference standard, we found an overall sensitivity for TB-LAMP of 99% (95% CI: 94.5-99.8) and specificity of 94% (95% CI: 89.3-96.7). When latent class analysis was performed, TB-LAMP had 98.6% (95% CI: 95.9-100) sensitivity and 99% (95% CI: 98.2-100) specificity compared to 91.1% (95% CI: 86.1-96) sensitivity and 100% (95% CI: 98.2-100) specificity for MGIT culture. GeneXpert had the highest sensitivity 99.1% (95% CI: 97.1-100) but the lowest specificity 96% (95% CI: 92.6-98.3). Both TB-LAMP and GeneXpert showed high sensitivity and specificity regardless

of age or strain of infection. CONCLUSION: Our findings show the diagnostic utility of both GeneXpert and TB-LAMP in The Gambia. Whilst TB-LAMP requires less infrastructure, it is unable to detect drug-resistant patterns and therefore would be most suitable as a screening test for new TB cases in peripheral health clinics.

**42-** 20163118287 HEIDARIEH, P.; MIRSAEIDI, M.; HASHEMZADEH, M.; FEIZABADI, M. M.; BOSTANABAD, S. Z.; NOBAR, M. G.; SHAHRAKI, A. H. **In vitro antimicrobial susceptibility of nontuberculous mycobacteria in Iran.** *Microbial Drug Resistance* (2016) **22** (2) 172-178 Mary Ann Liebert Publishers, New Rochelle, USA [En, 41 Ref.] Department of Microbiology, School of Medicine, Alborz University of Medical Sciences, Alborz, Iran. abdolrazaghh@gmail.com

Many species of nontuberculous mycobacteria (NTM) have long been identified as important causes of human disease, the incidence of which is rising. Several reports have suggested increasing trend of both in vitro and in vivo resistance to available treatment regimes. The aim of this study was to evaluate antibiotic susceptibility of clinically relevant NTM isolates using standard microbroth dilution test. Antimicrobial susceptibility testing was performed following National Committee for Clinical Laboratory Standards methods for NTM isolates, including 85 *Mycobacterium fortuitum*, 39 *Mycobacterium chelonae*, and 30 *Mycobacterium abscessus* subsp. abscessus as rapidly growing mycobacteria and 48 *Mycobacterium simiae* and 40 *Mycobacterium kansasii* as slowly growing mycobacteria. All isolates were recovered from various types of clinical samples and identified by multilocus sequence analysis. Trimethoprim sulfamethoxazole (TMP-SMZ), amikacin, tobramycin, clarithromycin, moxifloxacin, linezolid, and imipenem showed better activity against *M. fortuitum* rather than meropenem, ciprofloxacin, cefoxitin, and doxycycline. Amikacin was active against 93% of *M. abscessus* subsp. abscessus. Linezolid, clarithromycin, cefoxitin, ciprofloxacin, imipenem, moxifloxacin, tobramycin, TMP-SMZ, doxycycline and meropenem showed some activities on *M. abscessus* subsp. abscessus as well. The majority of *M. abscessus* subsp. abscessus and *M. chelonae* strains were multidrug resistant. Among the 40 isolates of *M. kansasii*, all were susceptible to ethambutol, isoniazid, clarithromycin, moxifloxacin, and linezolid. These isolates were also resistant to doxycycline and 50% were resistant to rifampicin and ciprofloxacin. *M. simiae* was resistant to clarithromycin, doxycycline, isoniazid, and TMP-SMZ, and the majority of isolates showed high levels of resistance to linezolid, ethambutol, ciprofloxacin, streptomycin, and rifampicin. The majority of *M. simiae* isolates were multidrug resistant. Our data confirm the need for performing of standard susceptibility testing of any clinically important NTM isolate.

**43-** 20163121722 CHARTIER, C.; ALBARIC, O.; CESBRON, N.; DESPRES, J.; HOOGVELD, C.; MICHELET, L.; BOSCHIROLI, M. L. **Tuberculoid nodular thelitis in a dairy goat flock.** *Veterinary Journal* (2016) **209** 199-200 Elsevier Ltd, Oxford, UK [En, 10 Ref.] LUNAM Université, Oniris, Nantes-Atlantic College of Veterinary Medicine and Food Sciences and Engineering, F-44307 Nantes, France. Email: christophe.chartier@oniris-nantes.fr

An unusual outbreak of teat/udder skin lesions occurred in a dairy goat flock in France. Lesions.

**44-** 20163134863 ARYA, S.; KUSHWAHA, R.; JAIN, S.; BUNKAR, M. **Concomitant infection with *Mycobacterium leprae* and *Mycobacterium tuberculosis* in an immunocompetent patient: a rare association.** *International Journal of Medicine and Public Health* (2016) **6** (1) 50-52

SciBiolMed.Org, Bangalore, India [En, 10 Ref.] Department of Dermatology, Venereology and Leprology, Government Medical College, Kota - 324 010, Rajasthan, India. Email: savita2009arya @gmail.com

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, a microorganism that usually affects skin and nerves. Although it is well-controlled by multidrug therapy but the disease may be aggravated by acute inflammatory reaction that causes permanent tissue damage, particularly to peripheral nerves. Cutaneous tuberculosis (CT) is a variant of extrapulmonary tuberculosis. Both mycobacterial infections are endemic in developing countries like India, but the simultaneous occurrence of CT and leprosy is very rarely reported. Here, we are reporting a case of borderline lepromatous leprosy and CT (lupus vulgaris) co-infection in an immuno-competent patient, diagnosed simultaneously and managed accordingly. First appeared as circular, indurated, erythematous areas of skin and progressed to form dark raised haemorrhagic crusts and ulcerative plaques. Histopathological examination revealed marked granulomatous dermatitis with multifocal ulceration. The granulomatous inflammation, with frequent Langhans type multinucleated cells and central caseous necrosis, was indicative of mycobacterial infection. The presence of non-cultivable mycobacteria was confirmed by sequencing PCR products from DNA extracted directly from the lesions and sequences matched a novel mycobacterial pathogen closely related to *M. leprae* and *M. lepromatosis* and previously identified in cattle thelitis. The association of nodular gross lesions and tuberculoid granulomas on the teat and lower udder, and the presence of mycobacteria DNA support a diagnosis of tuberculoid nodular thelitis in goats due to mycobacterial infection.

**45-** 20163134985 GEHRE, F.; SAMRAT KUMAR; KENDALL, L.; MEBRAT EJO; SECKA, O.; OFORI-ANYINAM, B.; ABATIH, E.; ANTONIO, M.; BERKVENS, D.; JONG, B. C. DE. **A mycobacterial perspective on tuberculosis in West Africa: significant geographical variation of *M. africanum* and other *M. tuberculosis* complex lineages.** *PLoS Neglected Tropical Diseases* (2016) **10** (3) e0004408 Public Library of Sciences (PLoS), San Francisco, USA [En, 28 Ref.] Mycobacterial Unit, Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium. fgehre@mrc.gm; fgehre@itg.be

BACKGROUND: Phylogenetically distinct *Mycobacterium tuberculosis* lineages differ in their phenotypes and pathogenicity. Consequently, understanding mycobacterial population structures phylogeographically is essential for design, interpretation and generalizability of clinical trials. Comprehensive efforts are lacking to date to establish the West African mycobacterial population structure on a sub-continental scale, which has diagnostic implications and can inform the design of clinical TB trials. METHODOLOGY / PRINCIPAL FINDINGS: We collated novel and published genotyping (spoligotyping) data and classified spoligotypes into mycobacterial lineages/families using TBLineage and Spotclust, followed by phylogeographic analyses using statistics (logistic regression) and lineage axis plot analysis in GenGIS, in which a phylogenetic tree constructed in MIRU-VNTRplus was analysed. Combining spoligotyping data from 16 previously published studies with novel data from the Gambia, we obtained a total of 3580 isolates from 12 countries and identified 6 lineages comprising 32 families. By using stringent analytical tools we demonstrate for the first time a significant phylogeographic separation between western and eastern West Africa not only of the two *M. africanum* (West Africa 1 and 2) but also of several

major *M. tuberculosis* sensu stricto families, such as LAM10 and Haarlem 3. Moreover, in a longitudinal logistic regression analysis for grouped data we showed that *M. africanum* West Africa 2 remains a persistent health concern. CONCLUSIONS/SIGNIFICANCE: Because of the geographical divide of the mycobacterial populations in West Africa, individual research findings from one country cannot be generalized across the whole region. The unequal geographical family distribution should be considered in placement and design of future clinical trials in West Africa.

**46-** 20163135259 OLIVEIRA, L. N. C.; MUNIZ SOBRINHO, J. DA S.; VIANA-MAGNO, L. A.; MELO, S. C. O.; MACHO, A.; RIOS-SANTOS, F. **Detection of multidrug-resistant *Mycobacterium tuberculosis* strains isolated in Brazil using a multimarker genetic assay for katG and rpoB genes.** *Brazilian Journal of Infectious Diseases* (2016) **20** (2) 166-172 Elsevier Ltd, Oxford, UK [En, 49 Ref.] Laboratório de Farmacogenômica e Epidemiologia Molecular (LAFEM), Universidade Estadual de Santa Cruz (UESC), Ilhéus, BA, Brazil. Email: fabriciorios@yahoo.com

Multidrug-resistant tuberculosis (MDRTB) is a serious world health problem that limits public actions to control tuberculosis, because the most used anti-tuberculosis first-line drugs fail to stop mycobacterium spread. Consequently, a quick detection through molecular diagnosis is essential to reduce morbidity and medical costs. Despite the availability of several molecular-based commercial-kits to diagnose multidrug-resistant tuberculosis, their diagnostic value might diverge worldwide since *Mycobacterium tuberculosis* genetic variability differs according to geographic location. Here, we studied the predictive value of four common mycobacterial mutations in strains isolated from endemic areas of Brazil. Mutations were found at the frequency of 41.9% for katG, 25.6% for inhA, and 69.8% for rpoB genes in multidrug-resistant strains. Multimarker analysis revealed that combination of only two mutations ("katG /S315T+ rpoB /S531 L") was a better surrogate of multidrug-resistant tuberculosis than single-marker analysis (86% sensitivity vs. 62.8%). Prediction of multidrug-resistant tuberculosis was not improved by adding a third or fourth mutation in the model. Therefore, rather than using diagnostic kits detecting several mutations, we propose a simple dual-marker panel to detect multidrug-resistant tuberculosis, with 86% sensitivity and 100% specificity. In conclusion, this approach (previous genetic study + analysis of only prevalent markers) would considerably decrease the processing costs while retaining diagnostic accuracy.

**47-** 20163139436 BRUM, C. B.; RAMOS, D. F.; ABILLEIRA, F. DE S.; SILVA, A. B. S.; GROLL, A. VON; SILVA, P. E. A. DA. **The BACTEC MGIT(tm) 320 system as a laboratory tool to diagnose tuberculosis in a Brazilian hospital with a high prevalence of HIV infection.** *Revista da Sociedade Brasileira de Medicina Tropical* (2016) **49** (1) 112-114 SciELO Brasil, Washington, USA [En, 14 Ref.] Faculdade de Medicina, Núcleo de Pesquisa em Microbiologia Médica, Universidade Federal do Rio Grande, Rio Grande, Rio Grande do Sul, Brazil. pedrefurg@gmail.com

INTRODUCTION: The World Health Organization endorses the BACTEC Mycobacterial Growth Indicator Tube (MGIT)<sup xmlns="http://www.w3.org/1999/xhtml">TM</sup> system as a rapid, sensitive, and specific method to diagnostic of tuberculosis. Here, we compared the performance of this system against Ogawa-Kudoh cultures and microscopy. METHODS: A total of 927 samples were obtained between December 2011 and December 2013 from 652 cases of suspected tuberculosis at the School Hospital of the Federal University of Rio Grande in Brazil.

RESULTS: The MGIT system confirmed tuberculosis in more cases in less time. CONCLUSIONS: The MGIT system is an effective tool for early diagnosis of tuberculosis, especially in patients with HIV/AIDS.

**48-** 20163141097 LONG, L. C.; FOX, M. P.; SAULS, C.; EVANS, D.; SANNE, I.; ROSEN, S. B. **The high cost of HIV-positive inpatient care at an urban hospital in Johannesburg, South Africa.** *PLoS ONE* (2016) **11** (2) e0148546 Public Library of Sciences (PLoS), San Francisco, USA [En, 31 Ref.] Department of Internal Medical, School of Clinical Medicine, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa. Email: llong@heroza.org

BACKGROUND: While most HIV care is provided on an outpatient basis, hospitals continue to treat serious HIV-related admissions, which is relatively resource-intensive and expensive. This study reports the primary reasons for HIV-related admission at a regional, urban hospital in Johannesburg, South Africa and estimates the associated lengths of stay and costs. METHODS AND FINDINGS: A retrospective cohort study of adult, medical admissions was conducted. Each admission was assigned a reason for admission and an outcome. The length of stay was calculated for all patients (N=1,041) and for HIV-positive patients (n=469), actual utilization and associated costs were also estimated. Just under half were known to be HIV-positive admissions. Deaths and transfers were proportionately higher amongst HIV-positive admissions compared to HIV-negative and unknown. The three most common reasons for admission were tuberculosis and other mycobacterial infections (18%, n=187), cardiovascular disorders (12%, n=127) and bacterial infections (12%, n=121). The study sample utilized a total of 7,733 bed days of those, 55% (4,259/7,733) were for HIV-positive patients. The average cost per admission amongst confirmed HIV-positive patients, which was an average of 9.3 days in length, was $1,783 (United States Dollars). CONCLUSIONS: Even in the era of large-scale antiretroviral treatment, inpatient facilities in South Africa shoulder a significant HIV burden. The majority of this burden is related to patients not on ART (298/469, 64%), and accounts for more than half of all inpatient resources. Reducing the costs of inpatient care is thus another important benefit of expanding access to ART, promoting earlier ART initiation, and achieving rates of ART retention and adherence.

**49-** 20163144091 SHAMSI, M.; ZOLFAGHARI, M. R.; FARNIA, P. **Association of IFN-γ and P2X7 receptor gene polymorphisms in susceptibility to tuberculosis among Iranian patients.** *Acta Microbiologica et Immunologica Hungarica* (2016) **63** (1) 93-101 Akadémiai Kiadó, Budapest, Hungary [En, 25 Ref.] Mycobacteriology Research Centre, National Research Institute of Tuberculosis and Lung Disease, Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mreza.zolfaghary@gmail.com

Interferon-gamma (IFN- γ) and P2X7 receptor are crucial for host defence against mycobacterial infections. Recent studies have indicated that IFN- γ, IFN-V receptor 1 (IFN- γ R1) and P2X7 gene polymorphisms are associated with susceptibility to pulmonary tuberculosis (TB). However, the relationship between IFN-γ and P2X7 polymorphism and TB susceptibility remains inconclusive in Iranian population. For this reason, single nucleotide polymorphisms (SNPs) in IFN-γ (G+2109A), IFN-Î³R1 (G-611A) and P2X7 genes (at -762, 1513 position) in patients (n=100) were assessed using PCR-RFLP. Data were analysed with SPSS version 18. For the 2109 loci of IFN-γ gene, the frequency of mutant alleles between patients and controls were not statistically significant. However, there was a significant

difference between the TB patient and controls for -611 alleles of IFN- γ R1 (P=0.01). Additionally, the frequency of P2X7 gene polymorphisms (SNP-762 and 1513) between patients and controls was statistically significant. In conclusions, our study revealed a significant association of IFN-γ R1 and P2X7 genes polymorphisms with risk of developing TB in Iranian population.

**50-** 20163145013 CARVALHO, I. A.; SCHWARZ, D. G. G.; PIETRALONGA, P. A. G.; FARIA, A. C. S.; BRAGA, I. F. E.; CARVALHO, G. D.; VALENTE, F. L.; MACHADO, J. P.; GUIMARÃ£ES, L. M. P.; FERRARI, M. DE L. A.; SILVA JÃºNIOR, A.; MOREIRA, M. A. S. **Presence of *Mycobacterium avium* subsp. paratuberculosis (MAP) in Brazilian patients with inflammatory bowel diseases and in controls.** *Sao Paulo Medical Journal* (2016) **134** (1) 13-19 SciElo Brasil, Sao Paulo, Brazil [En, Br, 27 Ref.] Veterinary Department, Universidade Federal de ViÃ§osa (UFV), Minas Gerais, Brazil. Email: masm@ufv.br

CONTEXT AND OBJECTIVE: *Mycobacterium avium* subsp. paratuberculosis (MAP) has attracted the interest of researchers because of similarities between paratuberculosis and Crohn's disease (CD). The aim of this study was to evaluate the frequency of MAP through cultures, histology and polymerase chain reaction (PCR) on intestinal biopsies from Brazilian CD patients. Quantitative real time PCR (qRT-PCR) was performed on positive samples. DESIGN AND SETTING: Analytical cross-sectional study with control group at two federal universities. METHODS: Fresh samples were collected from 25 patients; five with CD, eight with ulcerative colitis (UC) and 12 controls with non-inflammatory bowel disease (nIBD). Formalin-fixed paraffin-embedded (FFPE) samples from 143 patients were also collected: 44 CD, 49 UC and 56 nIBD. RESULTS: None of the fresh samples was positive for MAP. Five FFPE samples (one CD, two UC and two nIBD) and three fresh samples (one in each group) were positive through IS 900 -PCR. qRT-PCR was performed on these eight samples. Among the FFPE samples, there were 192.12 copies/Âµl in the CD group, 72.28 copies/Âµl in UC and 81.43 copies/Âµl in nIBD. Among the fresh samples, there were 432.99 copies/Âµl, 167.92 copies/Âµl and 249.73 copies/Âµl in the CD, UC and nIBD groups, respectively. The highest bacterial load was in the CD group. CONCLUSION: This study does not provide evidence for a role of MAP in the etiology of CD, although MAP DNA was detected in all three patient groups. This is the first report of MAP presence in human intestinal biopsies in Brazil.

**51-** 20163152467 BELL, L. C. K.; POLLARA, G.; PASCOE, M.; TOMLINSON, G. S.; LEHLOENYA, R. J.; ROE, J.; MELDAU, R.; MILLER, R. F.; RAMSAY, A.; CHAIN, B. M.; DHEDA, K.; NOURSADEGHI, M. **In vivo molecular dissection of the effects of HIV-1 in active tuberculosis.** *PLoS Pathogens* (2016) **12** (3) e1005469 Public Library of Sciences (PLoS), San Francisco, USA [En, 64 Ref.] Division of Infection and Immunity, University College London, London, UK. Email: m.noursadeghi@ucl.ac.uk

Increased risk of tuberculosis (TB) associated with HIV-1 infection is primarily attributed to deficient T helper (Th)1 immune responses, but most people with active TB have robust Th1 responses, indicating that these are not sufficient to protect against disease. Recent findings suggest that favourable outcomes following *Mycobacterium tuberculosis* infection arise from finely balanced inflammatory and regulatory pathways, achieving pathogen control without immunopathology. We hypothesised that HIV-1 and antiretroviral therapy (ART) exert widespread changes to cell mediated immunity, which may compromise the optimal host protective response to TB and provide novel insights into the correlates of

immune protection and pathogenesis. We sought to define these effects in patients with active TB by transcriptional profiling of tuberculin skin tests (TST) to make comprehensive molecular level assessments of in vivo human immune responses at the site of a standardised mycobacterial challenge. We showed that the TST transcriptome accurately reflects the molecular pathology at the site of human pulmonary TB, and used this approach to investigate immune dysregulation in HIV-1/TB co-infected patients with distinct clinical phenotypes associated with TST reactivity or anergy and unmasking TB immune reconstitution inflammatory syndrome (IRIS) after initiation of ART. HIV-1 infected patients with positive TSTs exhibited preserved Th1 responses but deficient immunoregulatory IL10-inducible responses. Those with clinically negative TSTs revealed profound energy of innate as well as adaptive immune responses, except for preservation of type 1 interferon activity, implicated in impaired anti-mycobacterial immunity. Patients with unmasking TB IRIS showed recovery of Th1 immunity to normal levels, but exaggerated Th2-associated responses specifically. These mechanisms of immune dysregulation were localised to the tissue microenvironment and not evident in peripheral blood. TST molecular profiling categorised different mechanisms of immunological dysfunction in HIV-1 infection beyond the effects on CD4 T cells, each associated with increased risk of TB disease and amenable to host-directed therapies.

**52-** 20163164350 TIWARI, A.; RICHARDUS, J. H. **Investment case concepts in leprosy elimination: a systematic review.** *Leprosy Review* (2016) **87** (1) 2-22 LEPRA, Colchester, UK [En, 112 Ref.] Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Room Na-2219; P.O. Box 2040, 3000 CA Rotterdam, Netherlands. Email: a.tiwari@erasmusmc.nl

INTRODUCTION: Leprosy continues to be a global public health problem, but draws less attention because 'prevalence based elimination' has been misinterpreted as eradication. The ongoing transmission of *M. leprae* has renewed interest in complete elimination. The aim of our study is to review systematically the literature regarding the elimination of leprosy, and to assess this information on its applicability for defining a Leprosy Elimination Investment Case (LEIC) based on Eradication Investment Case guidelines. METHODOLOGY: A literature search was conducted using the MeSH subheadings and synonyms of leprosy. A total of 1007 articles were considered and 112 were included in the final selection. The search focused on the literature covering leprosy elimination and its public health aspects. The LEIC framework was adapted from an existing "Guide to Preparing an Eradication Investment Case". RESULTS: The LEIC framework provided 11 topics under which information was synthesized from the literature. The fields were categorised under sections: (1) Proposed investment; (2) Rationale for investing; (3) Issues to consider when moving from control to eradication; (4) Management and governance. Scanty quantitative data are available for developing a LEIC, particularly regarding disease burden, and new interventions that could contribute to elimination are not yet applied routinely. DISCUSSION: For monitoring global elimination, it is necessary to measure disease burden comprehensively and contact centered preventive interventions should be part of a global elimination strategy. The biological and technical feasibility of elimination is not certain and advanced microbiological and operational research is necessary to understand transmission better. The current WHO road map for leprosy elimination is too vague and needs further structuring through a thoroughly prepared LEIC.

**53-** 20163164351 LI, J. L.; YANG, L. L.; WANG, Y.; LIU, H.; LIU, J.; CROSS, H. **How to improve early case detection in low endemic areas with pockets of leprosy: a study of newly detected leprosy patients in Guizhou province, People's Republic of China.** *Leprosy Review* (2016) **87** (1) 23-31 LEPRA, Colchester, UK [En, 18 Ref.] Guizhou Provincial Center for Disease Control and Prevention, 100# Bageyan Road, Guiyang 550004, China. Email: 740820442@qq.com

Although leprosy in China is controlled at a low endemic level, the number of new cases in Guizhou province has shown no significant decrease over the past 20 years. Guizhou remains the province with the second highest prevalence in China. The authors conducted a study in which the characteristics of newly detected leprosy cases, found between 2008 and 2012 in Guizhou, were analysed. These cases represented people from pocket areas of leprosy in a generally low endemic environment. The purpose of the study was to understand characters of newly detected cases, strong points and weakness of routine detection approaches for improving the effectiveness of early case detection in the future. The analysis considered data that was collected from a 'Leprosy Management Information' report system and also from annual statistical reports of leprosy that reflect the situation throughout the province. 1274 new patients were detected in Guizhou from 2008 to 2012. That number included 58 (4.6%) children (0-14 years old). The average age of patients at diagnosis was 42.6Â±16.5 years. The proportion of people with WHO Grade 2 disability (WHO DG2) among new patients was 35.7% and the proportion of people with Grade 1 disability (DG1) constituted 10.1%. The average delay before diagnosis after the onset of symptoms of leprosy was 41.7Â±49.8 months. Suspect survey was a major method by which most cases were detected. Trough this method 790 (62.0%) new patients were detected. It was also in this group that the highest proportion of people with WHO DG2 359 of 790 (45.4%) was reported. Self-reporting, diagnosis at a general skin clinic, household contact examination, and spot surveys accounted for 13.0%, 11.8%, 11.5% and 1.7% of other cases detected respectively. It was generally found that cases detected through household contact examinations were earlier cases (delay to diagnosis <24 months=70.7%). It was also recorded that fewer of these had WHO DG2 (12.9%). The proportion of men with WHO DG2 was higher than that of females (38.2% compared with 28.8%). The proportion of Han Chinese new cases with WHO DG2 was significantly higher than that of the main minority group (41.5% compared with 29.2%). The proportion of new cases among the main minority group who self-reported (50%) was significantly higher than those detected through other detection approaches. Detecting leprosy early in low endemic situations where pockets persist was difficult to achieve. The authors suggest that if more early patients are to be detected earlier, the quality of suspect surveys and household contact examination should be improved. Professional training and supervision might affect that result. Greater emphasis should be given to the role of general skin clinics as surveillance sites and advocacy for new health policy that will enhance the detection leprosy should be sustained.

**54-** 20163164352 AJALLA, M. E. A.; ANDRADE, S. M. O. DE.; TAMAKI, E. M.; WAISSMANN, W.; DEITTRICH, S. H. C.; NASCIMENTO, V. A. DO. **Leprosy in Brazilian counties bordering Para-guay: Mato Grosso do Sul State, 2001-2011.** *Leprosy Review* (2016) **87** (1) 32-41 LEPRA, Colchester, UK [En, 31 Ref.] Universidade Federal de Mato Grosso do Sul, Campo Grande, Mato Grosso do Sul, Brazil. Email: mabeajalla@gmail. com

BACKGROUND: In Mato Grosso do Sul state, Brazil, the dry border shared with Paraguay is a territory marked by facilities in the flow of goods, services and people, bringing difficulties for surveillance of communicable diseases. PURPOSE: The purpose of this study is to characterise leprosy epidemiologically in dry border municipalities of Mato Grosso do Sul in Brazil with contiguous urban areas with neighbouring Paraguayan counties, in the period 2001-2011. METHODS: This is an exploratory descriptive investigation that includes the four dry border municipalities of Mato Grosso do Sul (Coronel Sapucaia, Paranhos, Ponta Porã, and Sete Quedas) in Brazil whose urban areas are contiguous with Paraguay. Data comprised the period 2001-2011. RESULTS: The rates of leprosy detection and prevalence oscillated along the study period, increasing in the last 2 years investigated. The detection rate was 3.3/10 000 in 2011, up from 1.7/10000 in 2009. Prevalence was 5.3/10000 in 2011, up from 2.5/10000 in 2009. The Virchowian disease form was predominant in 8 of the 11 years investigated. Most patients were male, with limited formal education (44.2% with less than 4 years of study). CONCLUSION: In the border of Brazil, most (greater than 70%) of the cases detected were classified as multibacillary. The higher coefficient found in Brazilian municipalities was the Virchowian clinical form, which can influence the operational classification in multibacillary. The predominance of the Virchowian clinical form, larger number of patients in rural areas and children under 15 years of age provides new information on the manifestations of the disease in the border territories. The study revealed that municipalities with contiguous cross-border urban areas with Paraguay have unique epidemiological features that need to be addressed by policies focusing leprosy as a public health priority.

**55-** 20163164354 DEL'ARCO, R.; OLIVEIRA, A. B. DE.; NARDI, S. M. T.; PASCHOAL, V. D. **The association between neuropathic pain and disability grades in leprosy.** *Leprosy Review* (2016) **87** (1) 53-59 LEPRA, Colchester, UK [En, 31 Ref.] Santa Casa de Misericórdia de São José do Rio Preto, São Paulo, Brazil. Email: susilenenardi @gmail.com

OBJECTIVE: To detect neuropathic pain in people who have had leprosy and correlate this association with the WHO Degree of Physical Disability classification (DPD-WHO). PATIENTS AND METHODS: Data were collected from medical records, interviews and physical examinations of patients treated in 2013 in a regional referral service that attends 102 municipals. Clinical and general data, the DPD-WHO classification and the Douleur Neuropathique 4 Questionnaire (DN4) were utilised to determine the profile and to diagnose neuropathic pain. RESULTS: Of 84 treated patients, 37 (44.1%) had leprosy-related pain at the time of the interview. The mean age was 53 years, 51.4% were women; 75.7% had multibacillary disease and 72.9% had some kind of reactional episode. Of the 37 patients with pain, 22 (59.5%) had neuropathic pain and 15 (40.5%) had nociceptive pain. The most frequently reported symptoms related to neuropathic pain, apart from numbness (64.9%), were tingling and touch hypoesthesia (56.8%). Of 22 patients with neuropathic pain, 20 had some physical disability; 14 (63.6%) had Grade I disability, six (27.2%) Grade II, and two (9.3%) Grade zero disability. An association was found between neuropathic pain and degree of disability (P-value & lt; 005). CONCLUSION: Of the patients who reported pain related to leprosy, 59-5% had neuropathic pain. The DN4 seems to be suitable for determining the presence of neuropathic pain in leprosy. There is an association between the degree of disability and

neuropathic pain, i.e. patients with neuropathic pain tend to have a physical disability too.

**56-** 20163164355 LIMA, P. O. DE P.; CUNHA, F. M. B.; GONCEDILLA˜ALVES, H. DE S.; AIRES, M. A. P.; ALMEIDA, R. L. F. DE.; KERR, L. R. F. S. **Correlation between clinical tests and electroneuromyography for the diagnosis of leprosy neuropathy.** *Leprosy Review* (2016) **87** (1) 60-69 LEPRA, Colchester, UK [En, 34 Ref.] Department of Physical Therapy, Federal University of Ceara, Rua Alexandre Baraúna, 949, Fortaleza, CE, 60430-110, Brazil. Email: pedrolima@ufc.br

BACKGROUND: In leprosy, sensory function of nerves is evaluated with monofilaments test and the motor function with voluntary muscle test, however electroneuromyography is considered as the gold-standard tool. OBJECTIVES: This study aimed: (i) to evaluate the correlation between clinical tests and electroneuromyography for the diagnosis of leprosy neuropathy; and (ii) to identify the prevalence of leprosy neuropathy and the most compromised peripheral nerves in leprosy. METHODS: We analysed the data from a nested case-control study that identified 166 patients diagnosed with leprosy neuropathy confirmed by electromyography. This study was designed for an analysis of correlation between the diagnostic tests. RESULTS: The most prevalent type of the neural damage was the sensory and motor multiple mononeuropathy, observed in 62 (37.3%) cases. The highest prevalence was the ulnar nerve in 67 (40.3%) cases. Agreement specified by nerves was moderate, (ranging from k=0.58 in the deep peroneal nerve to k=0.41 in the posterior tibial nerve). Overall agreement between the clinical tests and electroneuromyography was very poor. Monofilaments test with k=0.02 (95% CI 0.00-0.12) and voluntary muscle test with 0.16 (95% CI 0.04 to 0.28, P=0.01). CONCLUSIONS: There is a low to moderate correlation between clinical tests (monofilaments and voluntary muscle tests) and the electroneuromyography examination. The most prevalent type of neural impairment was the sensory and motor multiple mononeuropathy, and the most affected nerve was the ulnar.

**57-** 20163164357 SAVE, M. P.; DIGHE, A. R.; MOHAN NATRAJAN; SHETTY, V. P. **Association of viable *Mycobacterium leprae* with type 1 reaction in leprosy.** *Leprosy Review* (2016) **87** (1) 78-92 LEPRA, Colchester, UK [En, 28 Ref.] The Foundation for Medical Research, Worli, Mumbai -400 018, India. Email: mohannatrajan13@gmail.com

The working hypothesis is that, viable *Mycobacterium leprae* (*M. leprae*) play a crucial role in the precipitation of Type 1 reaction (T1R) in leprosy. MATERIAL AND METHODS: A total of 165 new multibacillary patients were studied. To demonstrate presence of viable *M. leprae* in reactional lesion (T1R+), three tests were used concurrently viz. growth in the mouse foot pad (MFP), immunohistochemical detection of *M. leprae* secretory protein Ag85, and 16s rRNA - using *in situ* RT-PCR. Mirror biopsies and non reactional lesions served as controls (T1R-). FINDINGS: A significantly higher proportion of lesion biopsy homogenates obtained at onset, from T1R(+) cases have shown unequivocal growth in MFP, proving the presence of viable bacteria, as compared to T1R(-) ( P <0.005). In contrast, few Mirror biopsies were positive in both T1R(+) and T1R(-). With respect to Ag85, while the overall positivity was higher in T1R(+) (74%), however the intensity of staining (Grade â‰¥2+) was disproportionately higher in T1R(+) BT-BB lesions 11/20 (55%). In the rebiopsies obtained during a repeat episode of T1R, Ag 85 as well as 16s rRNA, positivity (62% & 100%) was higher in T1R(+). It is inferred therefore

'viable' bacteria are an essential component in T1R and difference in the quality of bacilli, not the quantity or the ratio of dead to viable play a role in the precipitation of T1R. In conclusion, the findings show that 'metabolically active' *M. leprae* is a component/prerequisite and the secretory protein Ag 85, might be the trigger for precipitation of T1R.

**58-** 20163164359 VILLADA, G.; ZAREI, M.; ROMAGOSA, R.; FORGIONE, P.; FABBROCINI, G.; ROMANELLI, P. **Autochthonous borderline tuberculoid leprosy in a man from Florida.** *Leprosy Review* (2016) **87** (1) 101-103 LEPRA, Colchester, UK [En, 8 Ref.] Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, 1600 N.W. 10th Avenue, RMSB #2023C, Miami, FL 33136, USA. Email: promanelli@med.miami.edu

Leprosy (Hansen's disease) is a chronic contagious granulomatous disease principally affecting the skin and peripheral nervous system, caused by *Mycobacterium leprae*. In this report, we present a case of autochthonous leprosy in a man from Florida as the first human case reported from this region. Authors believe dermatologists need to be aware of the possibility of autochthonous transmission of leprosy in the Eastern-Southern United States, and should consider leprosy in any patient with atypical skin lesions, even when a history of contact with armadillo is missing.

**59-** 20163164360 ROHATGI, S.; NAVEEN, S.; SALUNKE, P.; SOMESHWAR, S.; JERAJANI, H. R.; JOSHI, R. **The story of a deformed leprous foot.** *Leprosy Review* (2016) **87** (1) 104-108 LEPRA, Colchester, UK [En, 12 Ref.] Department of Dermatology, Venereology and Leprosy, MGM Medical College and Hospital, 502/A, Sai Prasad Residency, Kharghar Sector 10, Navi Mumbai - 410210, Maharashtra, India. Email: shaurya023@gmail.com

Eccrine syringofibroadenoma (ESFA) is a rare adnexal tumour of eccrine ductal proliferation. A 50 year old treated case of leprosy presented with a chronic non healing ulcer of 5 years duration on the deformity laden right foot. Multiple verrucous papules and plaques were seen surrounding the ulcer which showed histopathological findings consistent with ESFA. Although ESFA constitutes a rare association with leprosy, considering the load of treated cases in our country and elsewhere, it may represent an under-reported entity which requires more attention in the post elimination era.

**60-** 20163170398 RANJBAR, R.; HAFEZI-MOGHADAM, M. S. **Design and construction of a DNA origami drug delivery system based on MPT64 antibody aptamer for tuberculosis treatment.** *Electronic Physician* (2016) **8** (2) 1857-1864 Electronic Physician, Mashhad, Iran [En, 28 Ref.] Molecular Biology Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran. Email: sa.hafezi@gmail.com

INTRODUCTION: With all of the developments on infectious diseases, tuberculosis (TB) remains a cause of death among people. One of the most promising assembly techniques in nano-technology is "scaffolded DNA origami" to design and construct a nano-scale drug delivery system. Because of the global health problems of tuberculosis, the development of potent new anti-tuberculosis drug delivery system without cross-resistance with known anti-mycobacterial agents is urgently needed. The aim of this study was to design a nano-scale drug delivery system for TB treatment using the DNA origami method METHODS: In this study, we presented an experimental research on a DNA drug delivery system for treating Tuberculosis. TEM images were visualized with an FEI Tecnai T12 BioTWIN at 120 kV. The model was designed by caDNAno software and computational prediction of the 3D

solution shape and its flexibility was calculated with a CanDo server. RESULTS: Synthesizing the product was imaged using transmission electron microscopy after negative-staining by uranyl formate. CONCLUSION: We constructed a multi-layer 3D DNA nanostructure system by designing square lattice geometry with the scaffolded-DNA-origami method. With changes in the lock and key sequences, we recommend that this system be used for other infectious diseases to target the pathogenic bacteria.

**61-** 20163194234 PUYÉN, Z. M.; ACOSTA, J.; OBREGON, G.; PACHECO, E.; RAMIREZ, H.; MENDOZA, A.; MARÍN, D.; HARRIES, A. D. **Use and evaluation of a line probe assay in patients with tuberculosis in Peru: 2011-2013.** *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* (2016) **39** (1) 19-25 Pan American Health Organization, Washington, USA [En, 30 Ref.] Centro Nacional de Salud Pública, Instituto Nacional de Salud, Lima, Peru. Email: zpuyeng@gmail.com

OBJECTIVE: To determine the use and performance of a line probe assay (LPA) compared with conventional culture and drug sensitivity testing (CDST) in patients registered with tuberculosis (TB) under routine program conditions in Peru in 2011-2013. METHODS: This was a descriptive, operational research, cross-sectional study of sputum specimens from patients with smear-positive pulmonary TB and mycobacterial cultures from patients with smear-negative or positive TB. Drug resistance to rifampicin and/or isoniazid detected by LPA was compared to CDST. Sensitivity, specificity, and predictive values were calculated and reliability for detecting drug resistance was assessed through kappa coefficient, with values 0.61-0.80 showing substantial correlation, and 0.81 or above showing almost-perfect correlation. RESULTS: In 2011-2013, there were 16 169 LPA tests performed, with the proportion of TB patients receiving the test increasing from 3.2% to 30.2%. In all, 2 905 LPA test results were compared to CDST. For LPA in sputum specimens, sensitivity for rifampicin was 92%; isoniazid, 94%; and MDR-TB, 88%; while specificity for rifampicin was 92%; isoniazid, 92%; and MDR-TB, 95%. For LPA in mycobacterial cultures, sensitivity for rifampicin was 95%; isoniazid, 96%; and MDR-TB, 90%; while specificity for rifampicin was 85%; isoniazid, 91%; and MDR-TB, 94%. Kappa coefficients were at 0.81 or above for all comparisons of LPA with CDST using sputum specimens and cultures, except for isoniazid in cultures, which was at 0.79. CONCLUSIONS: This study suggests that LPA is a reliable and rapid screening test for drug-resistant TB and should be considered suitable for routine use and scale up in Peru.

**62-** 20163194241 OREJEL, I.; CASTELLANOS, M.; MARÍN, D.; MENDOZA, A.; HARRIES, A. D. **Culture and drug sensitivity testing among patients with pulmonary tuberculosis in Mexico: national data for 2009-2013.** *Revista Pana mericana de Salud Pública/Pan American Journal of Public Health* (2016) **39** (1) 65-68 SciELO Brasil, Washington, USA [En, 11 Ref.] National Tuberculosis Control Program, Mexico City, Mexico. Email: ivonneorejel@yahoo.com.mx

This study documented the number and results of mycobacterial culture and drug sensitivity testing (CDST) in Mexico from 2009-2013 and assessed whether states with a higher risk of multidrug-resistant tuberculosis (MDR-TB) performed more CDST and had more cultures showing MDR-TB. Data for this longitudinal, descriptive, operational research study came from the electronic records of 31 state public health laboratories in Mexico. The total number of CDSTs was 6 470, increasing from 2 143 in the first 2 years to 4 327 in the latter 3 years. There was a significant increase in the proportion of cultures showing sensitivity to

all drugs, from 53.1% to 60.9% in 2011-2013 (P <0.001) and a significant decrease in the proportion showing MDR-TB, from 28.2% in 2009 to 19.8% in 2013 (P <0.001). Cases of extensively drug resistant tuberculosis were <1% per year. In the 12 states with higher risk for MDR-TB, significantly more CDSTs (2 382 test) were done in 2011-2013 than in the other 19 states (1 945 tests). Also, for each year the proportion of cultures showing MDR-TB was significantly higher in high risk MDR-TB states than in lower risk ones (P <0.001). During the 5-year study period, CDST was scaled up in Mexico, particularly in high-risk MDR-TB states where a higher proportion of cultures showed MDR-TB. Scale up and wider coverage of CDST should continue.

**63-** 20163210741 SINGHAL, P.; DIXIT, P.; SINGH, P.; JAISWAL, I.; SINGH, M.; JAIN A. **A study on pre-XDR & amp; XDR tuberculosis & amp; their prevalent genotypes in clinical isolates of *Mycobacterium tuberculosis* in north India.** *Indian Journal of Medical Research* (2016) **143** (3) 341-347 Wolter Kluwer, New Delhi, India [En, 37 Ref.] Department of Microbiology, King George's Medical University, Lucknow 226 003, Uttar Pradesh, India. amita602002@yahoo.com

BACKGROUND & AMP; OBJECTIVES: Pre-extensively drug resistant (pre-XDR) and extensively drug resistant tuberculosis (XDR-TB) have been areas of growing concern, and are posing threat to global efforts of TB control. The present study was planned to study the presence of pre-XDR and XDR *Mycobacterium tuberculosis* and their genotypes in clinical isolates obtained from previously treated cases of pulmonary TB. METHODS: A total of 219 isolates obtained from previously treated cases of pulmonary TB were subjected to first-line (streptomycin, isoniazid, rifampicin and ethambutol) and second-line (ofloxacin, kanamycin, capreomycin and amikacin) drug susceptibility testing on solid Lowenstein-Jensen medium by proportion method. Genotyping was done for pre-XDR and XDR-TB isolates using 12 loci Mycobacterial Interspersed Repetitive Units-Variable Number Tandem Repeats (MIRU-VNTR). RESULTS: Multi-drug resistance was observed in 39.7 per cent (87/219) isolates. pre-XDR and XDR *M. tuberculosis* isolates amongst 87 multi-drug resistant (MDR) TB isolates were 43 (49.4%) and 10 (11.4%), respectively. Two most dominant genotypes among pre-XDR and XDR *M. tuberculosis* isolates were Beijing and Delhi/CAS types. Interpretation & CONCLUSIONS: Resistance to second-line anti-tubercular drugs should be routinely assessed in areas endemic for TB. Similar genotype patterns were seen in pre-XDR and XDR-TB isolates. Beijing and Delhi/CAS were predominant genotypes.

**64-** 20163213525 JONES-LÓPEZ, E. C.; ACUÑA-VILLAORDUÑA, C.; SSEBIDANDI, M.; GAEDDERT, M.; KUBIAK, R. W.; AYAKAKA, I.; WHITE, L. F.; JOLOBA, M.; OKWERA, A.; FENNELLYA, K. P. **Cough aerosols of *Mycobacterium tuberculosis* in the prediction of incident tuberculosis disease in household contacts.** *Clinical Infectious Diseases* (2016) **63** (1) 10-20 Oxford Journals, Oxford, UK [En, 40 Ref.] Section of Infectious Diseases, Department of Medicine, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, USA. Email: edward.jones@bmc.org

BACKGROUND: Tuberculosis disease develops in only 5%-10% of humans infected with *Mycobacterium tuberculosis*. The mechanisms underlying this variability remain poorly understood. We recently demonstrated that colony-forming units of *M. tuberculosis* in cough-generated aerosols are a better predictor of infection than the standard sputum acid-fast bacilli smear. We hypothesized that cough

aerosol cultures may also predict progression to tuberculosis disease in contacts. METHODS*:* We conducted a retrospective cohort study of 85 patients with smear-positive tuberculosis and their 369 household contacts in Kampala, Uganda. Index case patients underwent a standard evaluation, and we cultured *M. tuberculosis* from cough aerosols. Contacts underwent a standard evaluation at enrollment, and they were later traced to determine their tuberculosis status. RESULTS*:* During a median follow-up of 3.9 years, 8 (2%) of the contacts developed tuberculosis disease. In unadjusted and adjusted analyses, incident tuberculosis disease in contacts was associated with sputum Mycobacterial Growth Indicator Tube culture (odds ratio, 8.2; 95% confidence interval, 1.1-59.2; P=.04), exposure to a high-aerosol tuberculosis case patient (6.0, 1.4-25.2; P=.01), and marginally, human immunodeficiency virus in the contact (6.11; 0.89-41.7; P=.07). We present data demonstrating that sputum and aerosol specimens measure 2 related but different phenomena. CONCLUSIONS*:* We found an increased risk of tuberculosis progression among contacts of high-aerosol case patients. The hypothesis that a larger infectious inoculum, represented by high aerosol production, determines the risk of disease progression deserves evaluation in future prospective studies.

**65-** 20163215834 DHAR, K.; SHENOY, V. P.; VISHWANATH S.; PRABHU M. **Disseminated *Mycobacterium avium* intracellulare complex (MAC) disease in a retropositive patient caused by noncompliance of HAART.** *Annals of Tropical Medicine and Public Health* (2016) **9** (3) 194-196 Medknow Publications, Mumbai, India [En, 11 Res.] Department of Microbiology, Kasturba Medical College, Manipal University, Manipal, Karnataka, India.

*Mycobacterium avium* intracellulare complex (MAC) is the most common mycobacterial cause [after *Mycobacterium tuberculosis* (MTB)] of an opportunistic disease in human immunodeficiency virus / acquired immune deficiency syndrome (HIV/AIDS) patients with low CD4+ cell count. We report a case of disseminated MAC disease in a 46-year-old retropositive patient, noncompliant to highly active antiretroviral therapy (HAART), with CD4+ T-lymphocyte count of 10 cells/mm3. MAC was isolated in culture from multiple specimens including bone marrow aspirate, blood culture, and bronchoalveolar lavage (BAL) fluid. The patient was successfully treated with the following second-line antitubercular therapies: clarithromycin, rifabutin, and ethambutol.

**66-** 20163297426 DAVIES, H. D.; **Committee on Infectious Diseases. Infectious complications with the use of biologic response modifiers in infants and children.** *Pediatrics* (2016) **138** (2) 2016-1209 American Academy of Pediatrics, Elk Grove Village, USA [En, 174 Ref.]

Biologic response modifiers (BRMs) are substances that interact with and modify the host immune system. BRMs that dampen the immune system are used to treat conditions such as juvenile idiopathic arthritis, psoriatic arthritis, or inflammatory bowel disease and often in combination with other immunosuppressive agents, such as methotrexate and corticosteroids. Cytokines that are targeted include tumor necrosis factor α; interleukins (ILs) 6, 12, and 23; and the receptors for IL-1α (IL-1A) and IL-1β (IL-1B) as well as other molecules. Although the risk varies with the class of BRM, patients receiving immune-dampening BRMs generally are at increased risk of infection or reactivation with mycobacterial infections (*Mycobacterium tuberculosis* and nontuberculous mycobacteria), some viral (herpes simplex virus, varicella-zoster

virus, Epstein-Barr virus, hepatitis B) and fungal (histoplasmosis, coccidioidomycosis) infections, as well as other opportunistic infections. The use of BRMs warrants careful determination of infectious risk on the basis of history (including exposure, residence, and travel and immunization history) and selected baseline screening test results. Routine immunizations should be given at least 2 weeks (inactivated or subunit vaccines) or 4 weeks (live vaccines) before initiation of BRMs whenever feasible, and inactivated influenza vaccine should be given annually. Inactivated and subunit vaccines should be given when needed while taking BRMs, but live vaccines should be avoided unless under special circumstances in consultation with an infectious diseases specialist. If the patient develops a febrile or serious respiratory illness during BRM therapy, consideration should be given to stopping the BRM while actively searching for and treating possible infectious causes.