

Tropical Diseases Bulletin

Vol 106 No 10-11 October-November 2009

637 MESFIN, M. M.; NEWELL, J. N.; WALLEY, J. D.; AMANUEL GESSESSEW; TASSEW TESFAYE; LEMMA, F.; MADELEY, R. J. **Quality of tuberculosis care and its association with patient adherence to treatment in eight Ethiopian districts.** *Health Policy and Planning* (2009) **24** (0) 457-406 Oxford, UK; Oxford University Press [En, 40 ref.] Nuffield Centre for International Health and Development, Leeds Institute of Health Sciences, University of Leeds, Charles Thackrah Building, 101 Clarendon Road, Leeds LS2 9JL, UK. Email: M.melese@leeds.ac.uk

Background: Little is known about the quality of tuberculosis (TB) service delivery in public health facilities in Ethiopia and its association with patients non-adherence to TB treatment. This study assessed the organization, management and processes of TB care delivery, and their effects on patients' adherence to TB treatment. Methods: The quality of TB care was investigated in 44 public health facilities from three perspectives: structure, processes of TB care delivery and patient treatment outcome. Quality of care was determined by adherence to national TB guidelines. On-site observations of TB service delivery and interviews with health providers were conducted to evaluate structural factors. Patients ($n=237$) in the health facilities were interviewed prospectively at completion of their treatment to determine the quality of tuberculosis care delivered. Three measures of treatment adherence [treatment interruption (~2 weeks), availability of unused TB drugs and treatment default] were quantified from a review of patient treatment registers and an audit of unused TB

drugs at patients' homes. Effects were identified of poor quality structures and processes of service delivery on these three measures of adherence. Results: TB care providers were untrained in 18 (44%) of 44 facilities and daily outpatient TB care was not given in 13 of 44 (25%). Among the 237 patients, 43% attempted treatment for ~15 days and 30% had at least 1 day's dose of TB drugs unused. Patients tended to interrupt and default from treatment when their care provider had been inadequately supervised by district TB control experts and was incapable of dealing with patients' minor illnesses. Unavailability of daily TB care in health facilities was associated with missing daily doses. Conclusion: Better training of TB care providers and district supervisory support could be important interventions to improve the quality of care delivery and patient adherence to treatment.

638 GANIEM, A. R.; PARWATI, I.; WISAKSANA, R.; ZANDEN, A. VAN DER; DE BEEK, D. VAN; STURM, P.; VEN, A. VAN DER; ALISJAHBANA, B.; BROUWER, A. M.; KURNIANI, N.; GANS, J. DE; CREVEL, R. VAN **The effect of HIV infection on adult meningitis in Indonesia: a prospective cohort study.** *AIDS* (2009) **23** (17) 2309-2316 Hagerstown, USA; Lippincott Williams & Wilkins [En, 29 ref.] Department of Neurology, Hasan Sadikin Hospital. Jalan Pasteur 38, Bandung 40161, Indonesia. Email: rizalbdg@gmail.com

Objective: Indonesia has a concentrated but rapidly growing HIV epidemic. We examined the effect of HIV on causative organisms, clinical

features and prognosis of adult meningitis. Design: A prospective cohort study. Methods: All adult patients at a referral hospital who underwent cerebrospinal fluid examination for suspected meningitis were examined for HIV and included in a prospective cohort study. Microbiological testing was done for common bacterial pathogens, mycobacteria and fungi. Patients were followed for at least 6 months, and logistic regression models were used to identify risk factors for mortality. Results: Among 185 patients who mostly presented with subacute meningitis, 60% were male and the median age was 30 years. HIV infection was present in 25% of the patients; almost two-thirds were newly confirmed, and all presented with severe immunosuppression (median CD4 cell count $13/\mu\text{l}$, range 2-98). One-third of HIV-infected patients had cryptococcal meningitis whereas two-thirds suffered from tuberculosis. After 1 month, 41 % of patients had died. HIV infection was strongly associated with 1-month mortality (adjusted odds ratio 12.15; 95% confidence interval 3.04-15.72) and death during extended follow-up (hazard ratio 2.48; 95% confidence interval 1.97-5.74). Conclusion: Although HIV is still uncommon in the general population in Indonesia, its prevalence among adult meningitis cases already seems high. *Mycobacterium tuberculosis* and *Cryptococcus neoformans* are the main causes of meningitis in this setting, and mortality is very high, especially in HIV-infected patients. Our data suggest that adult meningitis cases in Indonesia should be screened routinely for HIV infection. Further studies are needed to address the high mortality.

639 PARK SANGHYOUNG; YANG SUKKYUN; YANG DONGHOON; KIM KYUNGJO; YOON SOONMAN; CHOE JAEWON; YE BYONGDUK; BYEON JEONGSIK; MVUNG SEUNGJAE; KIM JINHO **Prospective randomized trial of six-month versus nine-month therapy for intestinal tuberculosis.** *Antimicrobial Agents and Chemotherapy* (2009) **53** (10) 4167-4171 Washington, USA; American Society for

Microbiology (ASM) [En, 35 ref.] Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, 388-1 Pungnap-dong, Songpa-gu, Seoul 138-736, Korea Republic. Email: sky@amc.seoul.kr

Intestinal tuberculosis (TB) continues to be a common disease worldwide. However, the optimal duration of anti-TB medication has not been well established. We therefore compared the efficacy of 6-month and 9-month therapy in the treatment of intestinal TB. Ninety patients definitely diagnosed with intestinal TB were randomized into 6-month ($n=45$) or 9-month ($n=45$) treatment groups, prospectively. The primary end point was complete response, defined as endoscopic healing of active lesions. Patients were followed up monthly for 3 months after therapy initiation, then every 3 months until the end of therapy, and finally 1 year later. Relapse was assessed 1 year after the end of therapy by patient interview and colonoscopy. Baseline characteristics were similar in the 6-month and 9-month groups. Intention-to-treat analysis revealed no significant differences between the two groups in complete response (6-month group, 93.3%; 9-month group, 91.1%; $P=1.00$) or recurrence rate (6-month group, 2.4%; 9-month group, 0.0%; $P=1.00$). Median follow-up duration was 39 months in the 6-month group and 32 months in the 9-month group. No surgery was performed on any patient in either group. In conclusion, the 6-month therapy was as effective as 9-month therapy in patients with intestinal TB and may have the additional benefits of reduced treatment cost and increased compliance.

640 REVEIZ, L.; BUENDÍA, J. A.; TÉLLEZ, D. **Chemoprophylaxis in contacts of patients with leprosy: systematic review and meta-analysis.** *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* (2009) **26** (4) 341-349 Washington, USA; Pan American Health Organization [En, es] Cochrane Collaboration Branch, Sanitas University Foundation, Avenida Calle 127, no. 21-60, Bogota, Colombia. Email:

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Objective. To identify and summarize randomized clinical trials (RCTs) that assessed the effectiveness of chemoprophylaxis to prevent leprosy in contacts of patients newly diagnosed with the disease. **Methods.** All studies were extracted from Medline (PubMed 1966 to November 200~), the Cochrane Controlled Trials Register (number 32008), LILACS (1982 to November 2008), and Scirus (November 2008). Manual searches and searches of crossed references of assessed articles were also done. RCTs' risk of bias was assessed according to the methodology proposed by the Cochrane Collaboration. The main outcome measure was diagnosis of leprosy (secondary cases) in contacts of patients with the disease (primary cases). **Results.** The search identified 320 references, from which 7 RCTs with a total of 66 311 participants were included and evaluated. The combined results from the RCTs favored chemoprophylaxis to placebo with 2-4 years of follow-up (6 RCTs, 66 107 participants, relative risk (RR) 0.59, 95% confidence interval (CI) 0.50-0.70, 12=0 (12 describes percent total variation across studies caused by heterogeneity)). Single-dose rifampicin (21 711 participants, RR 0.43, 95% CI 0.28-0.07, number needed to treat 285), dapson once or twice weekly for at least 2 years (3 RCTs, 43 137 participants, RR 0.60, 95% CI 0.48-0.76, 12=0), and acedapson every 10 weeks for 7 months (2 RCTs, 1 259 participants, RR 0.49, 95% CI 0.33-0.72, 12=0) were significantly superior to placebo in preventing secondary cases of leprosy. **Conclusion.** Chemoprophylaxis is effective in lowering the incidence of leprosy in contacts of patients diagnosed with the disease.

641 RICHARDUS, J. H. **Special Issue: Epidemiology in leprosy.** *Leprosy Review* (2009) **80** (3) 235-344 Colchester, UK; LEPRO [En]

This special issue focuses on 2 important developments in the epidemiological study of leprosy: molecular epidemiology (Part I) and

spatial-temporal analysis of leprosy using the geographical information system (GIS) technology (Part II). Part I includes 8 articles that characterize the short tandem repeat genotypes of *Mycobacterium leprae* and used as basis for a strain typing tool to establish linkage between leprosy cases and understand leprosy transmission in Asia (China, Philippines, Thailand and India) and South America (Brazil, Colombia and Mexico). The articles are accompanied by an editorial providing an insightful historic perspective of the IDEAL consortium and the development of molecular epidemiological tools, as well as a commentary on the articles. Part II contains an article analysing the spatial distribution allid tirne trends of leprosy patients in Brazil, and an editorial describing the practical applications for GIS in leprosy control.

642 FATIREGUN, A. A.; OJO, A. S.; BAMGBOYE, A. E. Treatment outcomes among pulmonary tuberculosis patients at treatment centers in Ibadan, Nigeria. *Annals of African Medicine* (2009) **8** (2) 100-104 Mumbai, India; Medknow Publications [En, fr, 18 ref.] Department of Epidemiology. Medical Statistics and Environmental Health, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria. Email: akinfati@yahoo.com

Objective: To assess the treatment outcomes and determinants of outcome among tuberculosis patients. **Design:** A longitudinal study design involving a cohort of sputum smear-positive pulmonary tuberculosis patients at Initiation of therapy, who were followed up to the end of treatment at eighth month. **Setting:** Tuberculosis treatment centres in Ibadan, Nigeria. **Results:** A total of 1254 patients with a mean age of 35.0±3.3 years were followed up. The percentages of patients with treatment outcomes assessed in the study were as follows: cure (76.6%), failure (8.1%), default (6.6%), transferred out (4.8%), and death (1.9%). The cure rate varied significantly between treatment centres from 40 to 94.4% ($P<0.05$). The treatment centres located within the specialist health centres at Jericho and the

University College Hospital had 50 and 75% cure rates, respectively. The mean age of cured patients was 31.2 ± 3.1 years, which was significantly lower than the mean age of those with poor treatment outcomes (36.7 ± 3.5 years: $P < 0.05$). Males had a higher risk of a poor treatment outcome (RR=1.8; 95% CI: 1.02-1.94) than females. Also, patients with a poor knowledge of tuberculosis had a higher risk of having a poor treatment outcome (RR=1.35; 95% CI: 1.25-1.46) compared to those with a good knowledge. Conclusion: Variations in health centre treatment outcomes and poor knowledge of tuberculosis among patients suggest that poor programme implementation quality may be a major modifiable determinant of treatment outcomes in our setting.

643 GAUTAM, V. P. **Treatment of leprosy in India.** *Journal of Postgraduate Medicine* (2009) **55** (3) 220-224 Mumbai, India; Medknow Publications [En, 55 ref.] Netherlands Leprosy Relief India, B-38, Panchsheel Enclave, New Delhi - 110 017, India. Email: virendragautam_1@rediffmail.com

Introduction of multi-drug therapy (MDT) into the National Leprosy Eradication Program (NLEP) of India has brought a decline in both the burden of the disease and the detection of new cases in the country. Despite this success, MDT has had many problems like remarkable relapse rate, non-adherence to the MDT and the emergence of drug resistance associated with it. Moreover, there is no new MDT regimen at present, which could solve all these problems. The current situation suggests that we should look for alternative solutions in the delivery of leprosy-related services. With the introduction of Accredited Social Health Activists under the National Rural Health Mission, there is an opportunity to control some of these problems associated with MDT. In addition, the District Nucleus should take initiatives and actively participate in the establishment of coordination between the departments of Health, Social welfare and justice, education and various non-governmental

agencies working in the field of leprosy and disability in order to deliver the best of services to the persons affected by leprosy.

644 SCHURING, R. P.; RICHARDUS, J. H.; PAHAN, D.; OSKAM, L. **Protective effect of the combination BCG vaccination and rifampicin prophylaxis in leprosy prevention.** *Vaccine* (2009) **27** (50) 7125-7128 Amsterdam, Netherlands: Elsevier [En, 16 ref.] KIT (Royal Tropical Institute) Biomedical Research, Meibergdreef 39, 1105 AZ Amsterdam, Netherlands. Email: l.oskam@kit.nl

BCG vaccination and rifampicin chemoprophylaxis are both strategies for leprosy prevention. While the combined effect is unknown, the combination may give the desired push to halt leprosy transmission. Secondary analysis was done on results from a single centre, double blind, cluster randomized, and placebo-controlled trial. Individually, BCG (given at infancy) and rifampicin showed to protect against leprosy (57% [95% CI: 24-75%] and 58% [95% CI: 30-74%], respectively). The combined strategies showed a protective effect of 80% (95% CI: 50-92%). This is the first time that the additive effect of BCG and rifampicin are shown; the combined strategies can possibly lower leprosy incidence.

645 DUONG DUY AN; NGUYEN THI HONG DUYEN; NGUYEN THI NGOC LAN; DAI VIET HOA; DANG THI MINH HA; VO SY KIET; DO DANG ANH THU; NGUYEN VAN VINH CHAU; NGUYEN HUY DUNG; DINH NGOC SY; FARRAR, J.; CAWS, M. **Beijing genotype of *Mycobacterium tuberculosis* is significantly associated with high-level fluoroquinolone resistance in Vietnam.** *Antimicrobial Agents and Chemotherapy* (2009) **53** (11) 4835-4839 Washington, USA; American Society for Microbiology (ASM) [En, 31 ref.] Hospital for Tropical Diseases, Oxford University Clinical Research Unit, 190 Ben Ham Tu, District 5, Ho Chi Minh City, Vietnam. Email: mcaws@hotmail.com

Consecutive fluoroquinolone (FQ)-resistant isolates (11= 109) identified at the Pham Ngoc

Thach Hospital for Tuberculosis, Ho Chi Minh City, Vietnam, were sequenced in the quinolone resistance-determining regions of the *gyrA* and *gyrB* genes and typed by large sequence polymorphism typing and spoligotyping to identify the Beijing genotype of *Mycobacterium tuberculosis*. Beijing genotype prevalence was compared with 109 consecutive isolates from newly presenting patients with pulmonary tuberculosis from the hospital outpatient department. Overall, 82.6% ($n=90/109$) of isolates had mutations in *gyrAB*. Nine novel mutations were identified in *gyrB* (S486F, N538T, T539P, D500A, D500H, D500N, G509A, E540V, and E540D). The influence of these novel *gyrB* mutations on FQ resistance is not proven. The Beijing genotype was significantly associated with FQ resistance (odds ratio [OR], 2.39 [95% confidence interval {CI}, 1.34 to 4.25]; $P=0.003$). Furthermore, Beijing genotype FQ-resistant isolates were significantly more likely than FQ-resistant isolates of other genotypes to have *gyrA* mutations. (OR, 7.75 [95% CI, 2.84 to 21.15]; $P=0.0001$) and high level ($>8 \mu\text{g/ml}$) FQ resistance (OR, 11.0 [95% CI, 2.6 to 47.0]; $P=0.001$). The underlying mechanism of the association of the Beijing genotype with high-level FQ resistance in this setting remains to be determined. The association of the Beijing genotype with relatively high level FQ resistance conferred by specific *gyrA* mutations reported here is of grave concern given the epidemic spread of the Beijing genotype and the current hopes for shorter first-line treatment regimens based on FQs.

646 KHAN, M. S.; SHOAIB KHAN; GODFREY-FAUSSETT, P. **Default during TB diagnosis: quantifying the problem.** *Tropical Medicine and International Health* (2009) **14** (12) 1437-1441 Oxford, UK, Blackwell Publishing [En, fr, pt, 14 ref.] London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. Email: mishalk@cantab.net

OBJECTIVES: To quantify default during diagnosis in TB suspects and in smear-positive cases; to investigate sex differences in default during

diagnosis, in all of Pakistan. METHODS: Data from laboratory registers were collected on 12 216 suspects in nine districts over the period July-September 2008. RESULTS: A total of 1573 TB suspects (12.9%, 95% CI=12.3-13.5) dropped out of the diagnostic process after initial sputum submission. A total of 2058 smear positive cases were detected, and of these 107 (5.2%, 95% CI=4.2-6.2) defaulted during diagnosis and therefore could not be started on treatment. Male suspects defaulted slightly more frequently than female suspects ($P=0.0268$). CONCLUSION: Default during diagnosis is a frequent occurrence in Pakistan that should be monitored and addressed by TB control programs.

647 AMUHA, M. G.; KUTYABAMI, P.; KITUTU, F. E.; ODOI-ADOME, R.; KALYANGO, J. N. **Non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara Hospital Uganda: prevalence and associated factors.** In *Makerere Faculty of Medicine Annual Scientific Conference, Munyonyo, Kampala, Uganda, September 2009.* [Edited by Tumwine, J. K.]. African Health Sciences (2009) **9** (s1) S8-S15 Kampala, Uganda; Makerere University Medical School [En, 20 ref.] Department of Pharmacy, Faculty of Medicine, Makerere University, Kampala, Uganda. Email: nakayaga2001@yahoo.com

Background: Non-adherence to treatment remains a major obstacle to efficient tuberculosis control in developing countries. The dual infection of Tuberculosis and HIV presents further adherence problems because of high pill burden and adverse effects. This poses a risk of increased multi-drug resistant TB. However, the prevalence of non adherence and its associated factors have not been studied in these patients in Uganda. Objectives: To determine the prevalence and factors associated with non-adherence to anti-TB drugs among TB/HIV co-infected patients in Mbarara hospital. Methods: A cross sectional study with qualitative and quantitative data collection methods was conducted among TB/HIV co-infected adults in Mbarara hospital from January to March 2008. Consecutive

sampling was used to select 140 participants. Adherence was assessed over a 5 day period prior to the interview using patients self-reports. Data was collected using an interviewer administered questionnaire. Qualitative data was collected through key informant interviews using a topic guide and was analyzed manually. Quantitative data was analyzed using STATA version 8. Logistic regression was used to determine factors associated with non-adherence. Results: The prevalence of non-adherence was 25% (95% CI=17.8-32%). Being on continuous phase of the TB regimen was significantly associated with non-adherence (OR=6.24, $p < 0.001$). Alcohol consumption, being on antiretroviral therapy and smoking confounded the relationship between stage of the TB regimen and non-adherence. Conclusion: The prevalence of non-adherence was high. Patients that are on continuous phase of TB treatment should be supported to continue taking their drugs. In addition, patients that drink alcohol; smoke and those not on ART should be targeted with interventions to improve adherence.

1047 ABADIA. E.; SEQUERA, M.; ORTEGA. D.; MENDEZ. M. V.; ESCALONA. A; MATA, O. DA; IZARRA, E.; ROJAS, Y; JASPE. R.; MOTIWALA, A. S.; ALLAND, D.; WAARD, J. DE; TAKIFF. H. E. *Mycobacterium tuberculosis* ecology in Venezuela: epidemiologic correlates of common spoligotypes and a large clonal cluster defined by MIRU-VNTR-24. *BMC Infectious Diseases* (2009) 9 (122) (06 August 2009) London, UK; BioMed Central Ltd [En, 39 ref.] Laboratorio de Genetica Molecular, CMBC, Instituto Venezolano de Investigaciones Cientificas (IVIC), 1020A Caracas, Venezuela. Email: eabadia@gmail.com, moniquita4@gmail.com, dagmarys@gmail.com, mvmendez@ivic.ve, leeuwenhoek@hotmail.com, odamata78@yahoo.com, elixjosei@yahoo.es, yeimyrojas@hotmail.com. rjaspe@ivic.ve, ghadiaah@umdnj.edu, allandda@umdnj.edu, jacobusdeward@gmail.com, htakiff@ivic.ve.

Background: Tuberculosis remains an endemic

public health problem, but the ecology of the TB strains prevalent, and their transmission, can vary by country and by region. We sought to investigate the prevalence of *Mycobacterium tuberculosis* strains in different regions of Venezuela. A previous study identified the most prevalent strains in Venezuela but did not show geographical distribution nor identify clonal genotypes. To better understand local strain ecology, we used spoligotyping to analyze 1298 *M. tuberculosis* strains isolated in Venezuela from 1997 to 2006, predominantly from two large urban centers and two geographically distinct indigenous areas, and then studied a subgroup with MIRUVNTR 24 loci. Results: The distribution of spoligotype families is similar to that previously reported for Venezuela and other South American countries: LAM 53%, T 10%, Haarlem 5%, S 1.9%, X 1.2%, Beijing 0.4%, and EAI 0.2%. The six most common shared types (SIT's 17,93,605,42,53,20) accounted for 49% of the isolates and were the most common in almost all regions, but only a minority were clustered by MIRU- VNTR 24. One exception was the third most frequent overall, SIT 605, which is the most common spoligotype in the state of Carabobo but infrequent in other region. MIRU-VNTR homogeneity suggests it is a clonal group of strains and was named the "Carabobo" genotype. Epidemiologic comparisons showed that patients with SIT 17 were younger and more likely to have had specimens positive for Acid Fast Bacilli on microscopy, and patients with SIT 53 were older and more commonly smear negative. Female TB patients tended to be younger than male patients. Patients from the high incidence, indigenous population in Delta Amaeuro state were younger and had a nearly equal male:female distribution. Conclusion: Six SIT's cause nearly half of the cases of tuberculosis in Venezuela and dominate in nearly all regions. Strains with SIT 17, the most common pattern overall, are more actively transmitted and SIT 53 strains may be less virulent and associated with reactivation of past infections in older patients. In contrast to other

common spoligotypes, strains with SIT 605 form a clonal group centered in the state of Carabobo.

1048 ERMERTCAN. Ş.: HOSGOR-LİMONCU, M.: ERAÇ; B.: TASILİ. H.: A VUSOĞLU. C: BOZKURT. H. In vitro activity of linezolid against *Mycobacterium tuberculosis* strains isolated from Western Turkey. *Japanese Journal of Infectious Diseases* (2009) 62(5) 384-385 Tokyo, Japan; National Institute of Infectious Diseases (NIID) [En, 14 ref.] Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Ege University, 35100, Bornova, Izmir, Turkey. Email: safak.ermertcan@ege.edu.tr. sermertcan@gmail.com.

We investigated the linezolid susceptibility of *Mycobacterium tuberculosis* strains isolated from a tertiary care hospital in Izmir. A total of 67 *M. tuberculosis* strains (33 multidrug-resistant [MDR] and 34 non-MDR) were isolated and identified by the Tuberculosis Laboratory, Department of Microbiology and Clinical Microbiology, Faculty of Medicine, Ege University. The activity of linezolid was studied by the standard agar proportion method. For all of the strains, the MIC range was 0.06-1 mg/L, and the MIC₅₀ and MIC₉₀ values were 0.5 mg/L. No differences were observed between the MDR and non-MDR isolates. In general, linezolid was found to be effective for both the non-MDR and MDR *M. tuberculosis* strains.

1049 ZHANG Q/NG; XIAO HEPING; SUGAWARA. J. Tuberculosis complicated by diabetes mellitus at Shanghai Pulmonary Hospital, China. *Japanese Journal of Infectious Diseases* (2009) 62 (5) 390-391 Tokyo, Japan; National Institute of Infectious Diseases (NIID) [En, 14 ref.] Department of Tuberculosis, Shanghai Pulmonary Hospital, Shanghai. China. Email: sugawara@jata.or.jp

An association between diabetes mellitus (DM) and tuberculosis (TB) has been implied for a long time. We previously reported that KDP type 1 diabetic rats and OK type 2 diabetic rats are highly susceptible to *Mycobacterium tuberculosis*

infection. As a next step, we conducted a retrospective analysis of 2,141 patients with pulmonary TB newly diagnosed during the period from 2008 to 2009 to evaluate the influence of DM on the drug response rate and the long-term relapse rate of TB. There were 203 DM patients with TB (type 1 DM, 7 [3.4%]; type 2 DM, 196 [96.6%]). The TB relapse rate (2 years after discharge) was higher in DM patients than in non-diabetic patients (20% versus 5.3%). The frequency of multidrug-resistant-TB among DM patients with TB was higher than that among TB patients (17.7% versus 8.4%, $P < 0.01$). These results suggest that the period of TB treatment should be prolonged, and that in the meantime the blood glucose level should be maintained within a reference value range.

1050 ZHANG FuREN; HUANG WEI; CHEN SHuMIN; SUN LIANGDAN; LIU HONG; Li Yi; CUI YONG; YAN XIAOXIAO; YANG HAITAO; YANG RONGDE; CHU TONGSHENG; ZHANG CHI; ZHANG LiN; HAN JIANWEN; Yu GONGQI; QUAN CHENG; Yu YONGXIANG; ZHANG ZHENG; SHI BENQING; ZHANG LIANHUA; CHENG HUI; WANG CHANGYUAN; LiN Y AN; ZHENG HouFENG; Fu XIAN; Zuo XIANBO (ET AL) Genomewide association study of leprosy. *New England Journal of Medicine* (2009) 361(27) 2609-2618 Waltham, USA; Massachusetts Medical Society [En, 38 ref.] Shandong Provincial Institute of Dermatology and Venereology, Shandong Academy of Medical Science, 57, Jiyan Lu, Jinan, Shandong 250022, China. Email: zhangfuren@hotmail.com. ayzxj@vip.sina.com, liuj3@gis.a-star.edu.sg.

BACKGROUND: The narrow host range of *Mycobacterium leprae* and the fact that it is refractory to growth in culture has limited research on and the biologic understanding of leprosy. Host genetic factors are thought to influence susceptibility to infection as well as disease progression. METHODS: We performed a two-stage genomewide association study by genotyping 706 patients and 1225 controls using the Human 610-Quad BeadChip (Illumina). We

then tested three independent replication sets for an association between the presence of leprosy and 93 single-nucleotide polymorphisms (SNPs) that were most strongly associated with the disease in the genomewide association study. Together, these replication sets comprised 3254 patients and 5955 controls. We also carried out tests of heterogeneity of the associations (or lack thereof) between these 93 SNPs and disease, stratified according to clinical subtype (Multibacillary VS. paucibacillary). RESULTS: We observed a significant association ($P < 1.00 \times 10^{-6}$) between SNPs in the genes *CCDC122*, *C13orf31*, *NOD2*, *TNFSF15*, *HLA-DR*, and *RIPK2* and a trend toward an association ($P = 5.1 \times 10^{-4}$) with a SNP in *LRRK2*. The associations between the SNPs in *C13orf31*, *LRRK1*, *NOD2*, and *RIPK2* and Multibacillary leprosy were stronger than the associations between these SNPs and paucibacillary leprosy. CONCLUSIONS: Variants of genes in the NOD2-mediated signaling pathway (which regulates the innate response) are associated with susceptibility to infection with *M. leprae*.

1051 LAKSHMI RAJESH, RAMESH KARUNAIANANTHAM, NARAYANAN, P. R.: SOUMYA SWAMINATHAN Antiretroviral drug resistant mutations at baseline and at time of failure of antiretroviral therapy in HIV type I-coinfected TB patients. *AIDS Research and Human Retroviruses* (2009) 25 (11) 1179-1185 New Rochelle, USA: Mary Ann Liebert, Inc. [Enj] Tuberculosis Research Centre (ICMR), Chetput, Chennai 600 031. India.

There is limited information on the prevalence and pattern of HIV drug-resistant mutations (DRMs) among HIV-I-coinfected tuberculosis (TB) patients before and after antiretroviral treatment. Patients with HIV-I and TB were recruited into a clinical trial from two different once-daily antiretroviral regimens and followed for a period of 6 months after ART initiation. Patients were treated with standard short-course anti-TB treatment (2EHRZ/4RH.) and were randomized to receive ddI/3TC with either

nevirapine or efavirenz, once daily. Genotypic drug resistance (DR) testing was carried out for the *pol* gene at baseline and at the time of virological failure. At baseline, major DRMs with respect to NNRTIs (G190GA) and TAMs (T215S and I) were observed in 3 out of 107 patients. Of 15 treatment failures, 14 had more than one major NRTI and NNRTI mutation. V106M was the major NNRTI mutation that emerged in EFZ and Y181C in the NVP group. Among NRTI mutations, M184V was the commonest followed by L75V. Primary drug resistance to antiretroviral drugs was low among HIV-1 co-infected TB patients in south India. A once-daily regimen of ddI/3TC/EFZ or NVP results in a specific pattern of NNRTI mutations and negligible thymidine analog mutations (TAMs).

1052 LIAO. C. H.: CHOU. C. H.: LAI. C. C.: HANG. Y. T.: TAN. C. K.: HSU. H. L.: HSUEH. P. R. Diagnostic performance of an enzyme-linked immunospot assay for interferon-gamma in extrapulmonary tuberculosis varies between different sites of disease. *Journal of Infection* (2009) 59 (6) 402-408 Amsterdam, Netherlands; Elsevier [En. 37 ref.] Department of Internal Medicine, Far Eastern Memorial Hospital, Taipei, Taiwan. Email: hsporen@ntu.edu.tw

Objectives: To evaluate diagnostic performance of an enzyme-linked immunospot assay for interferon-gamma (T-SPOT-TB) in patients with suspected extrapulmonary tuberculosis (TB). Methods: From January 2007 to December 2008, patients with suspected extrapulmonary TB were prospectively enrolled from 2 tertiary care hospitals. Results: A total of 138 patients with suspected extrapulmonary TB were enrolled; 50 patients had positive culture for *Mycobacterium tuberculosis* and 39 patients had probable TB. The sites of infection were lymph node ($n=20$), pleura ($n=19$), bone/joint ($n=15$), urinary tract ($n=7$), peritoneum ($n=7$), meninges ($n=6$), disseminated ($n=5$), intestine ($n=3$), pericardium ($n=2$), skin ($n=2$), throat ($n=1$), neck ($n=1$), and genitalia ($n=1$). The overall sensitivity

and specificity were 79.8% (71/89) and 81.6% (40/49). The sensitivity ranged from 100% for tuberculous meningitis, tuberculous pericarditis, and intestinal TB, 95% for lymphadenitis, to 42.9% for tuberculous peritonitis. The sensitivity of the T SPOT-TB assay was 70.6% in immunocompromised patients and 85.5% in immunocompetent patients ($p=0.09$). Conclusions: The T SPOT-TB assay can be a useful tool for diagnosing extra-pulmonary TB in immunocompetent and immunocompromised patients, particularly for tuberculous meningitis, pericarditis, lymphadenitis, and intestinal TB.

1053 KIM SUNGHAN; CHO OHHYUN; PARK SUJIN; YE BYONGDUK; SUNG HEUNGSUP; KIM MINA; LEE SUNGOH; CHOI SANGHO; Woo JUNHEE; KIM Y ANGSoo Diagnosis of abdominal tuberculosis by T-cell-based assays on peripheral blood and peritoneal fluid mononuclear cells. *Journal of Infection* (2009) 59(6) 409-415 Amsterdam, Netherlands; Elsevier [En. 28 ref.] Department of Infectious Diseases, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-dong, Songpagu, Seoul 138-736, Korea Republic. Email: yskim@www.amc.seoul.kr

Objectives: Diagnosing abdominal tuberculosis (TB) remains a challenge. A recently developed RD-1 gene-based assay for diagnosing tuberculosis infection shows promising results. We evaluated the diagnostic usefulness of this assay compared with conventional tests in patients with suspected abdominal TB in clinical practice. Methods: All patients with suspected abdominal TB were prospectively enrolled in a tertiary hospital during a 1-year period. In addition to the conventional tests for diagnosing TB, the IFN- γ -producing T-cell response to ESAT-6 and CFP-10 by ELISPOT assay using peripheral blood mononuclear cells (PBMC) and peritoneal fluid mononuclear cells (PF-MC) were performed. Results: Forty eight patients with suspected abdominal TB were enrolled. Of these patients, 30 (63%) were classified as abdominal TB including 14 TB peritonitis (12 confirmed + 1 probable + 1 possible), 6 abdominal TB

lymphadenitis (3 confirmed + 3 probable), 4 hepatic TB (3 confirmed + 1 possible), 2 intestinal TB (1 confirmed + 1 probable), 3 renal TB (1 confirmed + 2 probable), and 1 pancreatic TB (1 confirmed). Eighteen (38%) were classified as not TB. ELIS POT assay using PBMC was performed on samples from all 48 subjects. The sensitivity and specificity of the PBMC ELISPOT assay were 89% (95% CI, 71-98%) and 78% (95% CI, 52-94%), respectively. In the 11 patients in whom PF-MC ELISPOT assay was performed, it was positive in 5 of 6 patients with TB peritonitis, and negative in all 5 patients with not TB. Conclusions: The ELIS POT assay using PBMC and PF-MC is a useful adjunct to the current tests for diagnosing abdominal TB.

1054 LIAO. C. H.; LAI. C. C.; TAN, C. K.; CHOU. C. H.; HSU, H. L.; TASI, T. H.; HUANG. Y. T.; HSUEH. P. R. False-negative results by enzyme-linked immunospot assay for interferon- γ among patients with culture-confirmed tuberculosis. *Journal of Infection* (2009) 59 (6) 421-423 Amsterdam, Netherlands: Elsevier [En, 12 ref.] Department of Internal Medicine, Far Eastern Memorial Hospital, Taipei County, Taiwan. Email: hsporen@ntu.edu.tw

During January 2007-December 2008, a total of 582 patients suspected of having tuberculosis underwent ELIS POT assay at two tertiary care facilities in Taiwan. These patients included 232 patients with culture-confirmed tuberculosis who underwent the ELIS POT assay. Most of the patients were male (62%), with mean, age of 54.4 ± 20.7 years. Diabetes mellitus was the most common concurrent disease, followed by malignancy. 26 patients received prior antituberculous treatment before the examination with the assay. Extrapulmonary tuberculosis was observed in 70 patients. Of the 232 culture-confirmed cases, 199 (85.8%) had positive ELISPOT results and 33 patients had false-negative ELIS POT results. There were no significant differences with regard to gender and concurrent disease between the patients with true positive results and those with false-positive

results. In univariate analysis, patients with false-negative ELIS POT results were more likely to be older, had liver cirrhosis, and had received steroids at the time of enrolment. Multivariate analyses showed that increased age and daily steroid use ≥ 10 mg were associated with false negative results. Thus, ELISPOT assay can be a useful adjuvant tool for diagnosing active tuberculosis. However, a negative ELIS POT assay cannot totally rule out tuberculosis, especially in elderly patients and in those receiving steroid treatment.

1055 JIMENEZ-CORONA. M. E; GARCIA-GARCIA. L. LEON, A. P. DE; BOBADILLA-DEL VALLE. M; TORRES. M.; CANIZALES-QUINTERO. S. : PALACIOS-MERINO, C.; MOLINA-HERNANDEZ. S.: MARTINEZ-GAMBOA. R. A.; JUAREZ-SANDINO. L; CANO-ARELLANO. B.; FERREYRA-REYER. L. CRUZ-HERVERT. L P.; BAEZ-SALDANA. R.: FERREIRA-GUERRERO. E.: SADA. E.: MARQUINA. B.: SIFUENTESOSORNIO, J. [Research on conventional and molecular epidemiology of tuberculosis in Orizaba. Veracruz, 1995-2008.] Investigacion sobre epidemiologia convencional y molecular de tuberculosis en Orizaba. Veracruz, 1995-2008. *Salud Publica de Mexico* (2009) 51 (Suplemento 3) S470-S478 Cuernavaca, Mexico; Instituto Nacional de Salud Publica [Es, en, 49 ref., *Genomica y proteomica en enfermedades infecciosas.*] Centro de Investigacion sobre Enfermedades Infecciosas, Instituto Nacional de Salud Publica, Av. Universidad 655, col. Santa Marfa Ahuacatithin, 62100. Cuernavaca, Mor., Mexico. Email: garcigarm@gmail.com

This study describes the achievements of the Mexican Consortium against Tuberculosis, in the Sanitary District of Orizaba. Veracruz, Mexico between 1995 and 2008. In brief, the main results can be classified as follows: (1) Conventional and molecular epidemiology (measurement of burden of disease, trends, risk factors and vulnerable groups, consequences of drug resistance, identification of factors that favor nosocomial and community transmission): (2) Development of diagnostic techniques to detect

drug resistance, description of circulating clones and adaptation of simple techniques to be used in the field: (3) Evaluation of usefulness of tuberculin skin test, immunologic responses to BCG, impact of directly observed therapy for tuberculosis' (DOTS), and study of immunological biomarkers and (4) Comments on ethical aspects of tuberculosis research. Additionally, we describe the impact on public policies, transfer of technology, capacity building and future perspectives.

1056 AKKSILP. S.; WAITANAAMORNKIAT. W.; KRRIKRAISAK. W.; NATENIYOM. S.; RIENTHONG. S.; SIRINAK. C; NGAMLERT. K; MANKATIITHAM. W.; SAITAYAWUTHIPONG. W.; SUMNAPUN, S.; YAMADA, N.; MONKONGDEE. P.: ANUWATNONTTHAKATE. A.; BURAPAT. C; WELLS. CD.; TAPPERO, W.; VARMA. J. K Multi-drug resistant TB and HIV in Thailand: overlapping, but not independently associated risk factors. *Southeast Asian Journal of Tropical Medicine and Public Health* (2009) 40 (6) 1264-1278 Bangkok, Thailand; SEAMEO TROPMED Network [En, 31 ref] Office of Disease Prevention and Control 7. Ubon Ratchathani, Thailand. Email: jvarma@cdc.gov

The HIV and multi-drug resistant tuberculosis (MDR-TB) epidemics are closely linked. In Thailand as part of a sentinel surveillance system, we collected data prospectively about pulmonary TB cases treated in public clinics. A subset of HIV infected TB patients identified through this system had additional data collected for a research study. We conducted multivariate analysis to identify factors associated with MDR-TB. Of 10,428 TB patients, 2,376 (23%) were HIV-infected; 145 (1.3%) had MDRTB. Of the MDRTB cases, 52 (37%) were HIV-infected. Independent risk factors for MDR-TB included age 18-29 years old, male sex, and previous TB treatment, but not HIV infection. Among new patients, having an injection drug use history was a risk factor for MDR-TB. Of 539 HIV-infected TB patients in the research study, MDR-TB was diagnosed in 19 (4%); the only significant risk factors were previ-

ous TB treatment and previous hepatitis. In Thailand, HIV is common among MDR-TB patients, but is not an independent risk factor for MDR-TB. Populations at high risk for HIV - young adults, men, injection drug users - should be prioritized for drug susceptibility testing.

1057 BURAPAT. C.; KJITIKRAISAK, W.; CAIN, K P.; TASANEYAPAN. T.; NATENIYOM. S.; AKKSILP. S.; MANKATILTHAM. W.; SIRINAK. C.; SAITAYAWUTHIPONG. W.; VARMA. J. K. Health-seeking behavior among HIV-infected patients treated for TB in Thailand. *Southeast Asian Journal of Tropical Medicine and Public Health* (2009) 40 (6) 1335-1346 Bangkok, Thailand: SEAMEO TROPMED Network [En, 30 ref] Thailand Ministry of Public Health-US Centers for Disease Control and Prevention Collaboration. Nonthaburi. Thailand. Email: jvarma@cdc.gov

In Asia, patients increasingly seek tuberculosis (TB) treatment in the private sector; however, few private sector practices follow international TB management guidelines. We conducted a study to measure the frequency and predictors of seeking TB diagnosis in the private sector among 756 HIV-infected TB patients in four Thai provinces during 2005-2006. Of enrolled patients, 97 (13%) first sought care at a private provider and 83 (11%) at a pharmacy. In multi variable analysis, the only factor independently associated with seeking care at a private provider was having a high TB stigma score. Factors independently associated with seeking care at a pharmacy included not knowing that TB can be cured and that TB care can be provided close to home. Patients reported that the most influential factor in choosing a provider was confidentiality (46%; 62%). Further research is needed to evaluate whether educating the community about the confidentiality, availability, and success of curing TB at government health facilities can promote prompt utilization of public TB treatment services by HIV-infected patients in Thailand.

1058 SYRE. H.; MYNEEDU. V. P.; ARORA. V. K.; GREWAL. H. M. S. Direct detection of

mycobacterial species in pulmonary specimens by two rapid amplification tests, the Gen-Probe Amplified *Mycobacterium tuberculosis* direct test and the GenoType Mycobacteria Direct test. *Journal of Clinical Microbiology* (2009) 47 (11) 3635-3639 Washington. USA:

American Society for Microbiology (ASM) [En, 25 ref] The Gade Institute. Section of Microbiology and Immunology, University of Bergen, N-5021 Bergen. Norway. Email: Heidi.Syre@gades.uib.no

Nucleic acid amplification tests have improved tuberculosis diagnostics considerably. This study evaluates a new amplification test, the GenoType Mycobacteria Direct (GTMD) test for detection of the *Mycobacterium tuberculosis* complex, *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium kansasii*, and *Mycobacterium Malmoeense* directly in 61 sputum samples. Thirty (49.2%) samples were auramine smear positive and 31 (50.8%) were smear negative. The GTMD results were compared to the Gen-Probe Amplified *M. tuberculosis* Direct (MTD) test results, using culturing and sequencing of the 16S rRNA gene as reference methods. The GTMD test could identify 28 of 29 samples containing the *M. tuberculosis* complex and was negative in a sputum sample containing *M. intracellulare*. The overall sensitivity and specificity results were 93.3% and 90.0% for the GTMD test, respectively, and 93.1% and 93.5% for the MTD test, respectively. The GTMD test is rapid and can be easily included in routine clinical laboratories for the direct detection of the *M. tuberculosis* complex in smear-positive sputum samples as an adjunct to microscopy and culture. Further studies are needed to evaluate the performance of the GTMD test for the detection of atypical mycobacteria.

1059 KASER, M.; GUTMANN, O.; HAUSER, J.; STINEAR, T.; COLE, S.; YEBOAH-MANU, D.; DERNTCK, G.; CERTA, U.; PLUSCHKE, G. Lack of insertional-deletional polymorphism in a collection of *Mycobacterium ulcerans* isolates from Ghanaian Buruli ulcer patients. *Journal of*

Clinical Microbiology (2009) 47(II) 3640-3646 Washington, USA; American Society for Microbiology (ASM) [En, 63 ref.] Swiss Tropical Institute, Molecular Immunology, Socinstrasse 57, 4002 Basel, Switzerland. Email: m.kaeser@unibas.ch

Mycobacterium ulcerans causes the devastating infectious skin disease Buruli ulcer and has a monomorphic population structure. The resolution of conventional genetic fingerprinting methods is therefore not sufficient for microepidemiological studies aiming to characterize transmission pathways. In a previous comparative genomic hybridization analysis with a microarray covering part of the *M. ulcerans* genome, we have found extensive insertional-deletional sequence polymorphisms among *M. ulcerans* isolates of diverse geographic origins that allowed us to distinguish between strains coming from different continents. Since large numbers of insertion sequences are spread over the genome of African *M. ulcerans* strains, we reasoned that these may drive large sequence polymorphisms in otherwise clonal local mycobacterial populations. In this study, we used a printed DNA microarray covering the whole genome of the Ghanaian *M. ulcerans* reference strain Agy99 for comparative genomic hybridization. The assay identified multiple regions of difference when DNA of a Japanese *M. ulcerans* strain was analyzed. In contrast, not a single insertional-deletional genomic variation was found within a panel of disease isolates coming from an area of Ghana where Buruli ulcer is endemic. These results indicate that, despite the expectations deduced from other mycobacterial pathogens, only analyses of single nucleotide polymorphisms will have the potential to differentiate local populations of *M. ulcerans*.

1060 KASER, M.; HAUSER, L PLUSCHKE, G. Single nucleotide polymorphisms on the road to strain differentiation in *Mycobacterium ulcerans*. *Journal of Clinical Microbiology* (2009) 47 (II) 3647-3652 Washington, USA; American Society

for Microbiology (ASM) [En, 40 ref.] Swiss Tropical Institute, Molecular Immunology, Socinstrasse 57, 4002 Basel, Switzerland, Email: m.kaeser@unibas.ch

The genomic fine-typing of strains of *Mycobacterium ulcerans*, the causative agent of the emerging human disease Buruli ulcer, is difficult due to the clonal population structure of geographical lineages. Although large sequence polymorphisms (LSPs) resulted in the clustering of patient isolates originating from across the globe, differentiation of strains within continents using conventional typing methods is very limited. In this study, we analyzed *M. ulcerans* LSP haplotype-specific insertion sequence elements among 83 *M. ulcerans* strains and identified single nucleotide polymorphisms (SNPs) that differentiate between regional strains. This is the first genetic discrimination based on SNPs of *M. ulcerans* strains from African countries where Buruli ulcer is endemic, resulting in the highest geographic resolution of genotyping so far. The findings support the concept of genome-wide SNP analyses as tools to study the epidemiology and evolution of *M. ulcerans* at a local level.

1061 MILLET, L BABOOLAL, S.; AKPAKA, P. E.; RAMOUTAR, D.; RASTOGI, N. Phylogeographical and molecular characterization of an emerging *Mycobacterium tuberculosis* clone in Trinidad and Tobago. *Infection, Genetics and Evolution* (2009) 9 (6) 1336-1344 Amsterdam, Netherlands; Elsevier [En, 33 ref.] Unite de la Tuberculose et des Mycobacteries, Institut Pasteur de Guadeloupe, Abymes. Guadeloupe, Email: nrastogi@pasteur-guadeloupe.fr

We report on a fine molecular and phylogenetical characterization of circulating *Mycobacterium tuberculosis* strains isolated from patients during a 1-year period in Trinidad and Tobago (T&T). The spoligotyping data coupled to minisatellite typing and available epidemiological data showed that a single major clone of "evolutionary 111001crn" tubercle bacilli (SIT566) was responsible for more than half of the tuberculosis (TB) cases. II

preferentially infected younger age groups (mean 39.1 years versus 47.7 years for other genotypes, $p < 0.005$), and was overrepresented in Port-of Spain (1 out of 3 patients). A comparison of genotyping results to data gathered for 6 Caribbean countries ($n = 2653$ clinical isolates) showed that the overall lineage distribution in T & T was completely different from its neighbors, e.g., T & T was the only country harboring a unique sublineage of the Latin American & Mediterranean (LAM) family, designated LAM-IOCAM with phylogeographical specificity for Cameroon and neighboring countries in West Africa; interestingly 3/4 of the patients within this group in T & T were African descendants. Similarly, strains belonging to East African Indian (EAI) lineage with phylogeographical specificity for the Indian subcontinent, were found in T & T (13% of all strains), but were absent among the neighboring countries. Although the predominant SIT566 was not yet detected elsewhere in the Caribbean, available information underlined that this genotype was already present in the United States as imported cases of disease among T & T-born patients. Characterization of SIT566 strains using 12-, 15- and 24-loci MIRU typing, and comparison of results to international databases showed that these isolates were characterized by a common 12-loci MIRU pattern 224315153324 corresponding to MIRU International Type-MIT633 in 21/25 strains tested, as well as its 4 variants; an orphan pattern 224315153424, MIT27-2243 15 153323, MIT117-224325143324, and MIT1158-224215153324. Extended 24-loci MIRU typing led to a predominant pattern 224315153324323483334323 in a total of 16/21 MIT633 isolates, as well as identification of 3 supplemental patterns. Comparison of 24-loci MIRU data with the international database MIRU-VNTRplus showed the unique nature of the patterns obtained in T & T. Further analysis using the Levenshtein algorithm showed that the first 2 closest matches with the SIT566/ MIT633 clone belonged to the X lineage strains in MIRU-

VNTRplus. This observation corroborates our preliminary spoligotyping-based analysis using minimum spanning and neighborjoining trees, which suggested a phylogenetical relatedness of the SIT566 clone with SIT119, which represents X 1 lineage prototype in SpolDB4 database. We hypothesize that the predominant SIT566 clone might have evolved from a pool of X lineage *M. tuberculosis* strains with phylogeographical affinity for Anglo-Saxon descendants.

1062 MATHURIA.J. P.: GOPAL NATH: SAMARIA. J. K.: SHAMPA ANUPURBA Molecular characterization of INH-resistant *Mycobacterium tuberculosis* isolates by PCR-RFLP and multiplex-PCR in North India. *Infection, Genetics and Evolution* (2009) 9 (6) 1352-1355 Amsterdam, Netherlands; Elsevier [En, 38 ref.] Department of Microbiology, Institute of Medical Sciences, Banara-Hindu University, Varanasi 221 005, Uttar Pradesh, India. Email: jiteshl41@gmail.com.shampa_anupurba@yahoo.co.in

In the present study, among 327 *Mycobacterium tuberculosis* (MTB) isolates collected from patients attending three different centres of North India, we attempted to find out the most common mutations occurring both at the Ser315 codon of *katG* and at the regulatory region of the *mabA-inhA* operon to evaluate their role for INH drug resistance in India. Out of 121 phenotypically INH-resistant MTB isolates, 88 (72.7%) were resistant to INH by genotypic methods viz., PCR-RFLP with MspI and SatI digestion and multiplex-PCR. PCR-RFLP results showed that 67 (55.4%) isolates had mutation in codon 315 of *katG* by SatI endonuclease. Among these, eight isolates that were found resistant by SatI PCR-RFLP were found to be sensitive by MspI PCR-RFLP. By multiplex-PCR we found 49 (40.5%), 21 (17.4%) and 10 (8.3%) isolates having AGC ACC substitution in *katG* only, mutation in *inhA* only and mutation in both respectively. Simultaneous use of both PCR-RFLP and multiplex-PCR can improve the detection rate of INH-resistant strains and may have an advantage

over the liquid culture system of detecting drug resistance. These findings also enhanced our understanding about potential of resistance-related mutations in *M. tuberculosis*. clinical isolates in India and could help in development and designing of molecular methods for evaluating the drug susceptibility profiles of *M. tuberculosis* clinical isolates.

1063 MOKROISOV. I.; VAICUEVA. V.; SOVHOZOVA, N.; ALDASUEY. A.; RASTOGI. N.; ISAKOVA, J. Penitentiary population of *Mycobacterium tuberculosis* in Kyrgyzstan: exceptionally high prevalence of the Beijing genotype and its Russia-specific subtype. *Infection, Genetics and Evolution* (2009) 9 (6) 1400-1405 Amsterdam, Netherlands; Elsevier [En, 41 ref.] Unite de la Tuberculose et des Mycobactéries, Institut Pasteur de Guadeloupe, Aymes 971 X3, Guadeloupe. Email: imokrousov@mail.ru.jainagul@mail.ru

Here, we present results of the first study of the *Mycobacterium tuberculosis* genotypes circulating in Kyrgyzstan. We focused on the incarcerated population known to be at high-risk for tuberculosis (TB) and with a significant impact on TB incidence in the general population. Beijing genotype was detected in 42 of 56 *M. tuberculosis* sputum-extracted DNA samples from newly-diagnosed adult pulmonary TB patients. RIP and INH resistance was genotypically detected in 28% and 55% samples; 13 of 15 MDR strains belonged to Beijing genotype. 12-locus MIRU-VNTR typing showed 8 of 56 samples to be mixed cases; 7 of them contained a Beijing strain. MIRU analysis demonstrated a high homogeneity of the studied collection (HGI=0.66) while 28 of 56 strains had a profile 223325153533 corresponding to BeijingIM2 subtype highly prevalent in different Russian settings. Three hypervariable loci, QUB-3232, VNTR-3820 and VNTR-4120, permitted to further subdivide 28 BeijingIM2 strains into 11 subtypes shared by 1 to 9 strains. To conclude, all markers taken together, the penitentiary population of *M. tuberculosis* in Kyrgyzstan exhibited a strong genetic affinity to Russia and a weak

relatedness to East Asia.

1064 Mvusi. L. Collaborative push to address TB crisis on mines. *SAMJ - South African Medical Journal* (2009) 99 (12) 852855 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En]

This article features the health policy measures being developed and implemented to combat the growing problem of mycobacterium tuberculosis epidemic in miners in South Africa. Following a history of failed TB control strategies, a government-led "TB in Mines Task Team" was set up to address the deepening crisis. The importance of offering isoniazid preventive therapy, as well as continuing data collection on disease epidemiology, is stressed.

1065 JEESUNHA; GOLUB, J.E.; JOJAESEONG; PARKILSU; OHRR HEECHOUL; SAMET. J. M. Smoking and risk of tuberculosis incidence, mortality, and recurrence in South Korean men and women. *American Journal of Epidemiology* (2009) 170 (12) 14781485 Cary, USA; Oxford University Press [En, 34 ref.] Department of Preventive Medicine and Public Health, Yonsei University College of Medicine, Seoul, Korea Republic. Email: ohrr@yuhs.ac

The authors explored the association of cigarette smoking with tuberculosis incidence; recurrence, and mortality. A 14-year prospective cohort study (1992-2006) was carried out in 1,294,504 South Koreans. Participants were grouped by smoking history, and the authors assessed tuberculosis incidence, mortality, and recurrence risk for each group. Unadjusted and adjusted Cox proportional hazards models were used to investigate the association between smoking history and the 3 outcomes of interest, adjusting for age and alcohol use. Compared with never smokers, current smokers had increased mortality from tuberculosis among both men (adjusted hazard ratio (HR)=1.6, 95% confidence interval (CI): 1.3, 2.0) and women (HR=1.6, 95% CI: 1.0, 2.4). Current male smokers had greater risk of incident tuberculosis than former smokers (HR=1.4, 95%

CI: 1.3, 1.5), and risk among current smokers increased with number of cigarettes smoked daily. In females, cigarette smoking was not associated with incident tuberculosis. There was interaction between smoking and sex for incidence ($P=0.00047$). The effect of smoking was generally reduced with adjustment for body mass index. Among men, the highest alcohol consumption category (2100 g/day) was associated with risk of incident tuberculosis (HR=1.5, 95% CI: 1.3, 1.7). This study provides longitudinal evidence that smoking increases risk of incident tuberculosis, mortality from tuberculosis, and tuberculosis recurrence.

1066 YIMER, S.: HOLM-HANSEN. C. YIMALDU. TO BJUNE, G. Health care seeking among pulmonary tuberculosis suspects and patients in rural Ethiopia: a community-based study. *BMC Public Health* (2009) 9 (454) (9 December 2009) London, UK; BioMed Central Ltd [En, 25 ref.] Department of General Practice and Community Medicine, University of Oslo, Oslo, Norway. Email: yim solo@yahoo.com. carol.holm-hansen@fhi.no. tilahunyi maldu2003@yahoo.it, g.a.bjune@medisin.uio.no

Background: Health care seeking is a dynamic process that is influenced by socio-demographic, cultural and other factors. In Ethiopia, there are limited studies regarding the health seeking behaviour of tuberculosis (TB) suspects and TB patients. However, a thorough understanding of patients' motivation and actions is crucial to understanding TB and the treatment of disease. Such insights would conceivably help to reduce delay in diagnosis, improve treatment adherence and thereby reduce transmission of TB in the community. The objective of this study was to describe and analyze health care seeking among TB suspects and pulmonary TB (PTB) cases in a rural district of the Amhara Region in Ethiopia. Methods: Study *kebeles* were randomly selected in a cross-sectional study design. House-to-house visits were conducted in which individuals aged 15 years and above in all households of the

kebeles were included. Subjects with symptoms suggestive of TB were interviewed about their health seeking behaviour, socio-demographic and clinical factors using a semi-structured questionnaire. Logistics regression analysis was employed to assess associations between the independent and outcome variables. Results: The majority, 787 (78%), TB suspects and 33 (82.5%) PTB cases had taken health care actions for symptoms from sources outside their homes. The median delay before the first action was 30 days. In logistics regression, women (AOR 0.8, 95% CI 0.6, 0.9) were found to be less likely to visit a medical health provider than men. Those with a long duration of cough (AOR 1.5, 95% CI 1.03, 2.1) and those with a previous history of TB (AOR 1.5, 95% CI 1.03, 2.3) were more likely to visit a medical health provider compared to those with a shorter duration of cough and with no history of TB. Conclusion: The majority of TB suspects and PTB cases had already taken health care actions for their symptoms at the time of the survey. The availability of a simple and rapid diagnostic TB test for use at the lowest level of health care and the involvement of all health providers in case finding activities are imperative for early TB detection.

1067 TSAI PUIJEN; LIN MENLUNG; CHU CHIENMIN; PERNG CHENGHW ANG Spatial autocorrelation analysis of health care hotspots in Taiwan in 2006. *BMC Public Health* (2009) 9 (464) (14 December 2009) London, UK; BioMed Central Ltd [En, 42 ref.] College of Liberal and General Education, Aletheia University, Taipei, Taiwan. Email: puijentsai@gmail.com. mllin1976@mail.aue.du.tw, d91228003@ntu.edu.tw, chperng@gmail.com
Background: Spatial analytical techniques and models are often used in epidemiology to identify spatial anomalies (hotspots) in disease regions. These analytical approaches can be used to not only identify the location of such hotspots, but also their spatial patterns. Methods: In this study, we utilize spatial autocorrelation methodologies, including Global Moran's I and Local Getis-Ord

statistics, to describe and map spatial clusters, and areas in which these are situated, for the 20 leading causes of death in Taiwan. In addition, we use the fit to a logistic regression model to test the characteristics of similarity and dissimilarity by gender. Results: Gender is compared in efforts to formulate the common spatial risk. The mean found by local spatial autocorrelation analysis is utilized to identify spatial cluster patterns. There is naturally great interest' in discovering the relationship between the leading causes of death and well-documented spatial risk factors. For example, in Taiwan, we found the geographical distribution of clusters where there is a prevalence of tuberculosis to closely correspond to the location of aboriginal townships. Conclusions: Cluster mapping helps to clarify issues such as the spatial aspects of both internal and external correlations for leading health care events. This is of great aid in assessing spatial risk factors, which in turn facilitates the planning of the most advantageous types of health care policies and implementation of effective health care services.

4578 KARIM, S. S. A.; CHURCHYARD, G. J.; Q. A.; LAWN, S. D. **HIV infection and tuberculosis in South Africa : an urgent need to escalate the public health response.** *Lancet (British edition)* (2009) **374** (9693) 921-933 London, UK; Elsevier Ltd [En. 63 ref.] CAPRISA-Centre for the AIDS Programme of Research in South Africa, 2nd Floor Doris Duke Medican Research Institute, Nelson R Mandela School of medicine, University of KwaZulu Natal, Private Bag X7, Congella 4013, South Africa. Email : Karimsl@ukzn.ac.za

One of the greatest challenges facing post-apartheid South Africa is the control of the concomitant HIV and tuberculosis epidemics. HIV continues to spread relentlessly, and tuberculosis has been declared a national emergency. In 2007, South Africa, with 0.7% of the world's population, had 17% of the global burden of HIV infection and one of the world's worst tuberculosis epidemics, compounded by rising drug resistance and HIV co-

infection. Until recently, the South African Government's response to these diseases has been marked by denial, lack of political will, and poor implementation of policies and programmes. Nonetheless, there have been notable achievements in disease management, including substantial improvements in access to condoms, expansion of tuberculosis control efforts, and scale-up of free antiretroviral therapy (ART), Care for acutely ill AIDS patients and long-term provision of ART are two issues that dominate medical practice and the health care system. Decisive action is needed to implement evidence based priorities for the control of the HIV and tuberculosis epidemics. By use of the framework of the Strategic Plans for South Africa for tuberculosis and HIV/AIDS, we provide prioritised four step approaches for tuberculosis control, HIV prevention and HIV treatment. Strong leadership, political will, social mobilisation, adequate human and financial resources, and sustainable development of health-care services are needed for successful implementation of these approaches.

4579 MALLARD, K.; ELDIN, G. S. S.; MCNERNEY, R. **Screen-Tape as a tool for the rapid differentiation of *Mycobacterium tuberculosis* isolates.** *Journal of Medical Microbiology* (2009) **58** (9) 1266-1268 Reading, UK; Society for General Microbiology [En. 12 ref.] London School of Hygiene and Tropical Medicine, London, UK. Email : kim.mallard@lshtm.ac.uk

This paper describes a novel technique that combined MIRU-VNTR typing with a new electrophoretic technology, i.e., Screen-Tape (Lab901), for differentiating 20 drug-resistant strains of *M. tuberculosis* from Sudan. Typing these 20 drug-resistant strains by MIRU-VNTR analysis provided 13 different genotypes. In addition. ScreenTape yielded 272 different amplicons from these strains, with a correlation coefficient of 0.9911 when compared to those obtained from GenoScreen, as 264 (97.1%) of the yielded alleles were correctly assigned.

4580 ABADÍA, E.; SEQUERA, M.; ORTEGA, D.; MÉNDEZ, M. V.; ESCALONA, A.; MATA, O. DA; IZARRA, E.; ROJAS, Y.; JASPE, R.; MOTIWALA, A. S.; ALLAND, D.; WAARD, J. DE; TAKIFF, H. E. ***Mycobacterium tuberculosis* ecology in Venezuela: epidemiologic correlates of common spoligotypes and a large clonal cluster defined by MIRU-VNTR-24.** *BMC Infectious Diseases* (2009) **9** (122) (06 August 2009) London, UK; BioMed Central Ltd [En, 39 ref.] Laboratorio de Genética Molecular. CMBC, Instituto Venezolano de Investigaciones Científicas (IVIC), 1020A Caracas, Venezuela. Email: eabadia@gmail.com, moniquita4@gmail.com, dagmarys@gmail.com, mvmendez@ivic.ve, leeuwenhoek@hotmail.com, odamata78@yahoo.com, elixjosei@yahoo.es, yeimyrojas@hotmail.com, rjaspe@ivic.ve, ghadiaah@umdnj.edu, allandda@umdnj.edu, jacobusdeward@gmail.com, htakiff@ivic.ve

Background: Tuberculosis remains an endemic public health problem, but the ecology of the TB strains prevalent, and their transmission, can vary by country and by region. We sought to investigate the prevalence of *Mycobacterium tuberculosis* strains in different regions of Venezuela. A previous study identified the most prevalent strains in Venezuela but did not show geographical distribution nor identify clonal genotypes. To better understand local strain ecology, we used spoligotyping to analyze 1298 *M. tuberculosis* strains isolated in Venezuela from 1997 to 2006, predominantly from two large urban centers and two geographically distinct indigenous areas, and then studied a subgroup with MIRU-VNTR 24 loci. Results: The distribution of spoligotype families is similar to that previously reported for Venezuela and other South American countries: LAM 53%, T 10%, Haarlem 5%, S 1.9%, X 1.2%, Beijing 0.4%, and EAI 0.2%. The six most common shared types (SIT's 17,93,605,42,53,20) accounted for 49% of the isolates and were the most common in almost all regions, but only a minority were clustered by MIRU-VNTR 24. One exception was the third most frequent overall. SIT 605, which is the most

common spoligotype in the state of Carabobo but infrequent in other regions. MIRU-VNTR homogeneity suggests it is a clonal group of strains and was named the "Carabobo" genotype. Epidemiologic comparisons showed that patients with SIT 17 were younger and more likely to have had specimens positive for Acid Fast Bacilli on microscopy, and patients with SIT 53 were older and more commonly smear negative. Female TB patients tended to be younger than male patients. Patients from the high incidence, indigenous population in Delta Amacuro state were younger and had a nearly equal male:female distribution. Conclusion: Six SIT's cause nearly half of the cases of tuberculosis in Venezuela and dominate in nearly all regions. Strains with SIT 17, the most common pattern overall may be more actively transmitted and SIT 53 strains may be less virulent and associated with reactivation of past infections in older patients. In contrast to other common spoligotypes, strains with SIT 605 form a clonal group centered in the state of Carabobo.

4581 MIOTTO, P.; SALERI, N.; DEMBELÉ, M.; OUEDRAOGO, M.; BADOUM, G.; PINSI, G.; MIGLIORI, G. B.; MATIEELLI, A.; CIRILLO, D. M. **Molecular detection of rifampin and isoniazid resistance to guide chronic TB patient management in Burkina Faso.** *BMC Infectious Diseases* (2009) **9** (142) (28 August 2009) London, UK; BioMed Central Ltd [En, 30 ref.] Emerging Bacterial Pathogens Unit, San Raffaele Scientific Institute, Milan, Italy. Email: miotto.paolo@hsr.it, nuccia75@hotmail.com, mathurin_dembele@hotmail.com, patindaom@yahoo.fr, gisebad@yahoo.fr, gpinsi@libero.it, giovannibattista.migliori@fsm.it, amatteelli@bsnet.it, cirillo.daniela@hsr.it

Background: Drug-resistant tuberculosis (DR-TB) is considered a real threat to the achievement of TB control. Testing of mycobacterial culture and testing of drug susceptibility (DST) capacity are limited in resource-poor countries, therefore inadequate treatment may occur, favouring resistance development. We evaluated the

molecular assay GenoType® MTBDRplus (Hain Lifescience, Germany) in order to detect DR- TB directly in clinical specimens as a means of providing a more accurate management of chronic TB patients in Burkina Faso, a country with a high TB-HIV co-infection prevalence. Methods: Samples were collected in Burkina Faso where culture and DST are not currently available, and where chronic cases are therefore classified and treated based on clinical evaluation and sputum-smear microscopy results. One hundred and eight chronic TB patients (sputum smear-positive, after completing a re-treatment regimen for pulmonary TB under directly observed therapy) were enrolled in the study from December 2006 to October 2008. Two early morning sputum samples were collected from each patient, immediately frozen, and shipped to Italy in dry ice. Samples were decontaminated, processed for smear microscopy and DNA extraction. Culture was attempted on MGIT960 (Becton Dickinson, Cockeysville, USA) and decontaminated specimens were analyzed for the presence of mutations conferring resistance to rifampin and isoniazid by the molecular assay GenoType® MTBDRplus. Results: We obtained a valid molecular test result in 60/61 smear-positive and 47/47 smear-negative patients. Among 108 chronic TB cases we identified patients who (i) harboured rifampin- and isoniazid-susceptible strains (n 21). (ii) were negative for MTB complex DNA (n 24). and (iii) had non-tuberculous mycobacteria infections (n 13). The most represented mutation conferring rifampin-resistance was the D516V substitution in the hotspot region of the *rpoB* gene (43.8% of cases). Other mutations recognized were the H526D (15.6%), the H526Y (15.6%), and the S531L (9.4%). All isoniazid-resistant cases (n 36) identified by the molecular assay were carrying a S315T substitution in the *katG* gene. In 41.7% of cases, a mutation affecting the promoter region of the *inhA* gene was also detected. Conclusion: The GenoType® MTBDRplus assay performed directly on sputum specimens improves the

management of chronic TB cases allowing more appropriate anti-TB regimens.

4582 VANDAN, N.; ALI, M.; PRASAD, R.; KUROIWA, C. **Assessment of doctors' knowledge regarding tuberculosis management in Lucknow, India: a public-private sector comparison.** *Public Health* (2009) **123** (7) 484-489 Oxford, UK; Elsevier [En, 30 ref.] Global Health Policy, Graduate School of Medicine. The University of Tokyo, Hongo, Bunkyo Ku, Tokyo 113-0033, Japan. Email: denube5@yahoo.com

Objective: India tops the list of 22 high-burden tuberculosis (TB) countries. India adopted directly observed treatment – short course (DOTS) under the Revised National Tuberculosis Control Programme (RNTCP) in 1992 and public-private mix DOTS in 2002. This study was conducted to assess the knowledge of doctors in the public and private sectors regarding TB control and management. Study design: Cross-sectional study. Methods: This study used a self-reported questionnaire based on the RNTCP technical and operational guidelines. One hundred and forty-one doctors were recruited through census sampling; all were registered with the Chest Physicians Association. This study was conducted in Lucknow, India in February-March 2007. Results: Of 141 doctors, 71% had specialized medical education for treating TB, 60% had received RNTCP training and 69% reported that they follow DOTS methodology for TB treatment. Fifty-six percent of doctors worked in the public sector and 44% worked in the private sector. Forty-nine percent of doctors working in the public sector and 53% working in the private sector correctly reported all TB symptoms as per the RNTCP guidelines. Sixty-six percent of doctors in the public sector and 39% in the private sector reported the correct technique for sputum sampling. Public sector doctors demonstrated better knowledge of drug regimens for sputum smear-positive and sputum smear-negative TB than private sector doctors. Statistical analysis indicated that doctors in the public sector had 2.1

times better knowledge than private sector doctors (odds ratio 2.1; $P=0.05$). Conclusion: Health policy managers and Dots implementers should encourage all doctors, particularly private sector doctors, to receive RNTCP training and follow DOTS methodology. Improvement is needed in RNTCP training, and emphasis needs to be given to correct diagnosis, management and follow-up of TB patients.

4583 KHAING WIN HTUN; KHIN NWE OO **Serological response of chemoprophylaxis on high risk contacts of new leprosy cases in Nyaungdon Township.** *Myanmar Health Sciences Research Journal* (2009) **21** (1) 7-11 Yangon, Myanmar; Department of Medical Research, Ministry of Health [En, 12 ref.] Bacteriology Research Division, Department of Medical Research (Central Myanmar), Myanmar.

This study was carried out in one of the leprosy endemic townships, Nyaungdon Township, Ayeyawady Division. The aim was to study the serological response of chemoprophylaxis by using a single dose of ROM (rifampicin, onoxacin and rinocycline), which is WHO recommended regime for single ksion of leprosy, on high risk extended contacts of new leprosy cases. The blood samples were collected from extended contacts two times before and six months after the chemoprophylaxis. Indirect. NTP-BSA ELISA test was carried out on samples. Determination of the baseline seropositivity rate of extended contacts of new leprosy case was also carried out. Seropositive contacts were assumed as high risk group. In the baseline study, the seropositivity rate is significantly higher in household (contacts of multibacillary (MB) leprosy cases. The seropositivity rate of children contacts under 15 years of age is higher than that of adult contacts, $X^2=31.58$, $p<0.001$. The difference of mean OD titers in treated group before and after chemoprophylaxis is significantly reduced compared to non-treated group in adult, $p=0.004$. However, it is not significant in children. The difference of seropositivity rate before and six

months after chemoprophylaxis is not significantly reduced in treated group compared to non-treated group.

4584 HAN WIN; YAE CHAN; SANDAR KYI; KHIN MAY THI; MYO ZAW; KHIN MYAT TUN **Smoking as a risk factor for pulmonary tuberculosis in adults.** *Myanmar Health Sciences Research Journal* (2009) **21** (1) 38-43 Yangon, Myanmar; Department of Medical Research, Ministry of Health [En, 17 ref.] Clinical Research Division, Department of Medical Research (Lower Myanmar), Myanmar.

Tobacco use, particularly smoking, is widely recognized by the medical community as well as the general public as a major public health problem. The aim of this study was to determine tobacco smoking as a behavioral risk factor associated with pulmonary tuberculosis in adults. A case-control study design was used. The study subjects were 100 new pulmonary TB patients (cases) and age-sex matched 100 non-TB cases and healthy subjects (controls) attending Township TB Centre in Kyimyindine Township, Yangon from November 2006 to June 2007. Data were collected by face-to-face interview using questionnaires. Among the cases, proportion of non-smokers, current active smokers and ex-active smokers were 39%, 41 % and 20%, respectively. Among the controls, they were 60%, 27% and 13%. It was found that current active smoking was associated with development of pulmonary TB (OR=2.15, 95% CI=1.05-4.38). Moreover, active smokers who started smoking at ~20 years of age (OR=4.12, 95% CI=1.7-9.99), or had a duration of >10 yrs (OR=4.18, 95% CI=1.63-10.73), or smoked more than 10 cigarettes/day (OR=3.13, 95% CI=1.47-6.66), were at a higher risk of pulmonary TB compared to non-smokers. Therefore, an effective anti-smoking campaign is needed to have a positive repercussion on TB incidence.

4585 TABARSI, P.; CHITSAZ, E.; MORADI, A.; BAGHAEI, P.; FARNIA, P.; MARJANI, M.; IRANNEJAD, P.; MANSOURI, D.; MASJEDI, M. **First-**

line antituberculosis drug resistance prevalence and its pattern among HIV -infected patients in the national referral tuberculosis centre, Iran.

International Journal of STD & AIDS (2009) **20** (8) 566-570 London, UK; RSM Press Ltd [En, 21 ref.] Mycobacteriology Research Center, National Research Institute of Tuberculosis and Lung Disease, Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Darabad, Niavaran Sq, Tehran 1955841452, Iran. Email: ehchitsaz@nritld.ac.ir

The objective of this study was to determine the drug resistance prevalence and its pattern among tuberculosis (TB)-HIV patients in Iran. In this retrospective study, all admitted TB/HIV patients presenting to our tertiary centre during 2005-2007 were considered. After confirmation for TB-HIV, first-line DST was performed for culture-positive patients. The drug resistance patterns and the treatment outcomes were analysed. Of the total 92 TB/HIV patients, 27 were culture negative, and DST were available in 65. Intravenous drug abuse was seen in 59 (90.8%). Thirty-seven (57%) were 'sensitive' cases and 28 (43%) were 'any drug resistance' cases. Twenty-one (32.3%) were mono-drug, three (4.6%) poly-drug and four (6.1%) were multidrug-resistant TB patients. Previous anti-TB medication was significantly associated with any drug resistance ($P=0.041$; 95% confidence interval=0.086-0.984): however, having any drug resistance did not affect the treatment outcome ($P=0.56$). Streptomycin showed the highest resistance rate (27%) followed by isoniazid (20%), pyrazinamide (9.8%), rifampin (9.2%) and ethambutol (3%). Drug resistance to antitubercular agents in TB-HIV co-infected patients in Iran is high compared with other reports. Drug resistance is higher among those who have had prior anti-TB medication.

4586 KIBADI, K.; BOELAERT, M.; KAVINUA, M.; MINUKU, J. B.; MUVEMBE-TAMFUM, J. J.; PORTAELS, F.; LEFÈVRE, P. **Therapeutic itineraries of patients with ulcerated forms of *Mycobacterium ulcerans* (Buruli ulcer) disease in a rural health zone in the Democratic Republic of**

Congo. *Tropical Medicine and International Health* (2009) **14** (9) 1110-1116 Oxford, UK; Blackwell Publishing [En, 30 ref.] Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium. Email: plefevre@itg.be

OBJECTIVE: To describe lay perceptions of the ulcerated forms of *Mycobacterium ulcerans*, commonly called Buruli ulcer (BU), and therapeutic itineraries of BU patients in a rural area of the Democratic Republic of Congo. **METHODS:** Qualitative research consisting of semi-structured interviews of 19 patients with clinical signs of BU and 12 in-depth interviews of confirmed cases allowing for a detailed reconstruction of the itineraries followed. **RESULTS:** The first symptoms of BU are perceived as mild. The perceived seriousness of the disease increases as the ulceration persists, increases in size or results in complications. Knowledge about the biomedical aetiology of the disease is scarce; it is commonly believed to be due to witches' attacks or bad fate. Four therapeutic paths are taken: self-medication, traditional therapy, the church and the health centre. However lay perception, recourse to traditional treatments and self-medication only partially explain the long delays in diagnosis (on average 6 months); the main problem lies with health providers, particularly the lack of proper diagnostic capability. **CONCLUSIONS:** Diagnostic capabilities at health centre level need to be strengthened through training and supervision. Engaging with the population and the traditional healers would render health promotion messages on BU more relevant and culturally acceptable.

4587 LAWN, S. D.; EDWARDS, D. J.; KRANZER, K.; VOGT, M.; BEKKER L. G.; WOOD, R. **Urine lipoarabinomannan assay for tuberculosis screening before antiretroviral therapy diagnostic yield and association with immune reconstitution disease.** *AIDS* (2009) **23** (14) 1875-1880 Hagerstown, USA; Lippincott Williams & Wilkins [En, 27 ref.] Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University

of Cape Town, Anzio Road, Observatory 7925, Cape Town, South Africa. Email: stevelawn@yahoo.co.uk

Objective: To assess the utility of urine lipoarabinomannan (LAM) detection as a diagnostic screening test for tuberculosis (TB) in HIV infected patients with advanced immunodeficiency and high prevalence of sputum smear-negative pulmonary disease. **Design:** Cross-sectional survey. **Methods:** Unselected adults enrolling for antiretroviral therapy (ART) in a South African clinic were screened for TB with two sputum samples for fluorescence microscopy and mycobacterial liquid culture. LAM was measured in urine samples using a commercially available enzyme-linked immunosorbent assay. **Results:** Sputum culture-positive TB was diagnosed in 58 patients (median CD4 cell count=78 cells/ μ l) out of 235 patients screened (TB prevalence=0.25). Cultures were identified as positive after a mean of 24 days (SD=9 days). The sensitivity of sputum microscopy was just 0.14 (specificity=1.00), whereas that of LAM in concentrated urine was 0.38 ($P<0.01$; specificity=1.00). In those with CD4 cell counts of less than 50, 50-100 and more than 150 cells/ μ l, the LAM assay sensitivities were 0.67, 0.41 and 0.13, respectively. Corresponding values for the combined use of the LAM assay and microscopy were 0.67, 0.53 and 0.21, respectively. Among TB patients, detectable LAM was very, strongly associated with low CD4 cell counts and advanced clinical stage. All patients who developed TB immune reconstitution disease ($n=5$) had detectable urinary LAM at baseline. **Conclusion:** The LAM assay has substantially superior sensitivity to sputum microscopy as a routine diagnostic TB screening test among patients with CD4 cell counts less than 100 cells/ μ l. In one half

of such patients, this assay could reduce the mean time to diagnosis by approximately 3 weeks. Furthermore, detectable urinary LAM may predict the development of TB immune reconstitution disease.

4588 SAEED AKHTAR; RATHI, A. S. K. Multilevel modeling of household contextual determinants of tuberculin skin test positivity among contacts of infectious tuberculosis patients, Umerkot, Pakistan. *American Journal of Tropical Medicine and Hygiene* (2009) **80** (3) 351-358 Northbrook, USA; American Society of Tropical Medicine and Hygiene [En] Department of Community Medicine and Behavioral Sciences, Kuwait University, PO Box 24923, Safat 13110, Kuwait. Email: saeed.akhtar@hsc.edu.kw

This cross-sectional study sought to identify household contextual determinants that might be associated with *Mycobacterium tuberculosis* infection as assessed by tuberculin skin test (TST) positivity among familial contacts of index patients of infectious pulmonary tuberculosis (TB) while controlling for the effects of individual-level factors. We analysed data on TST results on 359 household contacts of 77 index cases with acid-fast bacilli (AFB) sputum smear-positive pulmonary TB using multilevel logistic regression analysis with characteristics of household contacts at the first level and that of households at the second level. The prevalence of *M. tuberculosis* infection as assessed by TST positivity among household contacts of index TB patients was 49.9% (179/35). After taking into account the individual-level risk factors, the household-level contextual determinants significantly associated with TST positivity of the contacts were the gender of the index TB patient (adjusted odds ratio [OR]=2.2; 95% confidence interval