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297 DAFTARY, A.; PADAYATCHI, N.; O'DONNELL, M. **Preferential adherence to antiretroviral therapy over tuberculosis treatment: a qualitative study of drug-resistant TB/HIV co-infected patients in South Africa.** *Global Public Health* (2014) **9**(9) 1107-1116 Abingdon, UK; Routledge [En, 17 ref.] ICAP, Mailman School of Public Health, Columbia University, New York, New York, USA. Email: ad2254@columbia.edu

Adherence to antiretroviral therapy (ART) and second-line antituberculosis medications is essential to achieve successful out-comes among individuals co-infected with HIV and multi or extensively drug-resistant TB (M/XDR-TB). In 2012-2013, we designed a qualitative study to explore barriers to adherence in KwaZulu-Natal, South Africa. We conducted six focus groups comprising 23 adults receiving treatment for either MDR-TB (n=2) or XDR-TB (n=21); 17 were on concurrent ART. Participants expressed a preference for ART over M/XDR-TB treatment as a result of greater tolerability, lower pill burden and a commitment to ART. Treatment outcomes and the social morbidity associated with M/XDR-TB, characterised by public notification, stigma and social isolation, were perceived to be worse than with HIV. Poor communication, low patient involvement and provider supervision of treatment exacerbated participants negative experiences with TB care. To improve adherence, it is critical that new regimens for drug-resistant

TB be developed with better efficacy, lower pill burden and fewer adverse effects. For the first time, such improved regimens are on the horizon. In parallel and equally important is the implementation of a cohesive approach that promotes patient involvement, empowerment and treatment literacy for HIV and for TB.

298 CHUNG, W. S.; CHEN, Y. F.; HSU, J. C.; YANG, W. T.; CHEN, S. C.; CHIANG, J. Y. **Inhaled corticosteroids and the increased risk of pulmonary tuberculosis: a population-based case control study.** *International Journal of Clinical Practice* (2014) **68** (10) 1193-1199 Oxford, UK; Wiley-Blackwell [En, 34 ref.] Department of Internal Medicine, Taichung Hospital, Ministry of Health and Welfare, No. 199, Seed, San-MM Road, Taichung 403, Taiwan. Email: chung.w53@msa.hinet.net

AIMS: The association between inhaled corticosteroid (ICS) use and pulmonary tuberculosis (TB) development is uncertain. We conducted a population-based case-control study to investigate whether ICS use increases the risk of developing TB. METHODS: Tuberculosis patients aged 18 years and older were identified using the National Health Insurance Research Database (NHIRD) in Taiwan between 2002 and 2010. Each TB patient was frequency matched to four control patients according to age, sex and index year. We retrospectively followed up the medications and comorbid medical conditions for the 5 years prior to the index date. We calculated the odds ratios

(ORs) and 95% confidence intervals (CIs) of TB development using multiple logistic regression models. RESULTS: Most of the study participants were men (68.7%), and the mean age among the 8091 TB patients and 32,364 comparison participants was 61.3±18.6 years. After adjusting for potential covariates, ICS use caused a 2.04-fold increased risk of developing TB (adjusted OR: 2.04, 95% CI: 1.78-2.33). When considering dose-response and adjusting for potential covariates, ICS and oral corticosteroids (OCS) use remained independent risk factors and exhibited a dose-response relationship of TB development. The multiplicative increased risk of TB was also significant in patients using ICS and OCS compared with patients not using ICS and OCS (adjusted OR: 4.31, 95% CI: 3.39-5.49). Previous TB history exhibited the greatest risk of TB development among the comorbidities (adjusted OR: 8.50, 95% CI: 7.52-9.61). CONCLUSION: Long-term ICS use may increase the risk of TB.

299 NYONATOR, F.; OFOSU, A.; SEGBAFAH, M.; D'ALMEIDA, S. **Monitoring and evaluating progress towards universal health coverage in Ghana.** *PLoS Medicine* (2014) **11** (9) e1001691 San Francisco, USA; Public Library of Sciences (PLoS) [En, 6 ref.] University of Health and Allied Sciences, Ho Volta Region, Ghana. Email: msegbafah@gmail.com

This article summarizes the policy context, monitoring and evaluation, and progress towards universal health coverage (UHC) in Ghana. The progress in child mortality trends and coverage for DPT immunization, antenatal care, skilled attendant at delivery and family planning, as well as inequalities in health worker distribution and health expenditures are discussed.

300 SHI KEHUI; WANG FEIQIAN; JIANG HONGLI; LIU HUA; WEI MENG; WANG ZHIGANG; XIE LI **Gut bacterial translocation May aggravate micro inflammation in hemodialysis**

patients. *Digestive Diseases and Sciences* (2014) **59** (9) 2109-2117 New York, USA; Springer [En, 28 ref.] Dialysis Centre of First Affiliated Hospital of Medicine School, Xian Jiaotong University, No. 277 West Yanta Road, Xi'an, 710061, Shaanxi, China. Email: hongli_jiang@sina.com

BACKGROUND/AIMS: Bacterial translocation (BT) promotes microinflammation in predialysis patients with end-stage renal disease (ESRD). However, the change in BT has not been reported in ESRD patients undergoing regular hemodialysis treatment. The present study investigated whether hemodialysis promotes gut BT and microinflammation. METHODS: The blood, gut, and dialysate of hemodialysis patients were analyzed using bacterial 16S rDNA amplification and DNA pyrosequencing to determine the presence of bacteria and alteration in gut microbiomes. High-sensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6), and endotoxin were also determined. Plasma d-lactate was tested for gut permeability. RESULTS: Bacteria were present in the plasma of 12 out of 52 ESRD patients. The majority of the bacteria detected in the blood were also distributed in the gut of ESRD patients on the basis of the phylogenetics of the blood and gut microbial specimens in the patients. In patient, groups treated with and without hemodialysis, the plasma hs-CRP, IL-6, and endotoxin levels differed between the positive and negative plasma bacterial DNA. In patients who were positive in blood bacteria, the bacterial DNA concentration was positively correlated with plasma levels of CRP and IL-6. The ESRD patients who underwent hemodialysis had a different flora and showed slightly higher levels of hs-CRP, IL-6, and plasma endotoxin, compared with those in ESRD patients who did not undergo hemodialysis. CONCLUSION: ESRD, rather than hemodialysis, primarily contributes to BT and microinflammation in ESRD patients. Hemodialysis may

exaggerate microinflammation in ESRD patients to some extent.

301 YOUNG, B. N.; BURGOS, M.; HANDAL, A. J.; BAKER, J.; RENDON, A.; ROSASTARACO, A.; LONG, J.; HUNLEY, K. **Social and clinical predictors of drug-resistant tuberculosis in a public hospital, Monterrey, Mexico.** *Annals of Epidemiology* (2014) **24** (10) 771-775 New York, USA; Elsevier [En, 25 ref.] Department of Anthropology, University of New Mexico, MSC01-1040, Albuquerque, NM 87131, USA. Email: byoung@unm.edu

PURPOSE: Drug-resistant tuberculosis (DRTB) is steadily increasing in Mexico, but little is known of patient risk factors in the Mexico-United States border region. This preliminary case-control study included 95 patients with active pulmonary TB with drug susceptibility results attending the Jose E. Gonzalez University Hospital in the urban hub of Nuevo Leon - the Monterrey Metropolitan Area. We report potential social and clinical risk factors of DRTB among this hospital-based sample. **METHODS:** We collected data through face-to-face interviews and medical record reviews from 25 cases with DRTB and 70 drug-sensitive controls. DNA was collected to assess an effect of genetic ancestry on DRTB by using a panel of 291,917 genomic markers. We calculated crude and multivariate logistic regression. **RESULTS:** After adjusting for potential confounding factors, we found that prior TB treatment (odds ratio, 4.5; 95% confidence interval, 0.9-21.1) and use of crack cocaine (odds ratio, 4.6; 95% confidence interval, 1.1-18.7) were associated with DRTB. No other variables, including genetic ancestry and comorbidities, were predictive. **CONCLUSIONS:** Health care providers may benefit from recognizing predictors of DRTB in regions where routine drug susceptibility testing is limited. Prior TB treatment and illicit drug use, specifically crack

cocaine, may be important risk factors for DRTB in this region.

302 SOH BEELENG [SOH, B. L. S.]; HAN PHEYYEN; TAM KAI-TONG; YUNG CHEEFU; LIEW WOEIKANG; TAN WOONHUI [TAN, W. H. N.]; CHONG CHIAYIN; THOON KOHCHENG **Investigations into an outbreak of suppurative lymphadenitis with BCG vaccine SSI® in Singapore.** *Vaccine* (2014) **32** (44) 5809-5815 Oxford, UK; Elsevier Ltd [En, 22 ref.] Vigilance and Compliance Branch, Health Products Regulation Group, Health Sciences Authority, 11 Biopolis Way #11-01 Helios, Singapore 138667, Singapore. Email: sally_soh@hsa.gov.sg

INTRODUCTION: From 2011 to 2012, we received an unexpectedly high number of reports of suppurative lymphadenitis following administration of a BCG vaccine used in our childhood vaccination programme in Singapore. We sought to determine the local incidence rates of BCG-associated suppurative lymphadenitis across the 2009 to 2012 vaccinated cohorts, and to analyse the potential factors contributing to this outbreak. **METHODS:** Reports of lymphadenitis following BCG vaccination from an AEFI active surveillance system at the KK Women's and Children's Hospital (KKH) and passive surveillance data from other healthcare institutions were reviewed. All valid reports received from January 2009 to December 2013 involving neonates vaccinated with the BCG vaccine in 2009 to 2012 that met case definitions were included in our analysis. Details of the demographics and vaccination history of the child, and statistics from the local vaccination programme were also obtained. Potential contributory factors were selected for further investigation based on a literature review of similar out-breaks overseas. **RESULTS:** We identified 283 cases of lymphadenitis, of which 76% were suppurative. A spike in suppurative lymphadenitis cases was seen in

the 2011 vaccinated cohort, with an incidence rate of 3.16 per 1000 vaccinees, as compared to 0.71 to 0.85 per 1000 in the 2009, 2010 and 2012 cohorts. Our investigations identified the likely cause of the outbreak to be batch-related, arising from manufacturing issues encountered by the manufacturer, after ruling out vaccine administration-related and host-related factors. CONCLUSIONS: The three-fold spike in BCG-associated suppurative lymphadenitis cases observed in the 2011 vaccinated cohort, possibly due to batch-to-batch variation of the vaccine, highlights that manufacturing controls can continue to be a challenge. Development of a more sensitive assay to test the reactogenicity of the BCG vaccine may help reduce the occurrence of such outbreaks and improve public confidence in the nation's vaccination programme.

303 ZHANG, Z.; LIU, M.; WANG, Y.; PANG, Y.; KAM, K. M.; ZHAO, Y. **Molecular and phenotypic characterization of multidrug-resistant *Mycobacterium tuberculosis* isolates resistant to kanamycin, amikacin, and capreomycin in China.** *European Journal of Clinical Microbiology & Infectious Diseases* (2014) **33** (11) 1959-1966 Berlin, Germany; Springer-Verlag GmbH [En, 33 ref.] Respiratory Diseases Department of Nanlou, Chinese People's Liberation Army General Hospital, Beijing, China. Email: pangyu@chinatb.org, kmkaml@gmail.com, zhaoyanlin@chinatb.org

Although second-line anti-tuberculosis (TB) injectable drugs have been widely used to improve treatment outcomes of multidrug resistant TB (MDR-TB), little is known about the prevalence and mechanism of second-line injectable drug resistance among MDR *Mycobacterium tuberculosis* isolates in China. Here, we found that 12.7% (20/158) of isolates showed resistance to at least one second-line injectable drug among 158 MDR isolates. At the

same time, there were 16 (10.1%) strains resistant to kanamycin (KAN), 9 (5.7%) to amikacin (AMK), and 12 (7.6%) to capreomycin (CAP). In addition, our data revealed no significant difference in the drug resistance patterns for Beijing versus non-Beijing genotype strains ($p > 0.05$). The most frequently observed mutation was A-to-G substitution at position 1401 of the rRs gene, conferring high-level resistance to KAN and AMK, but had varying minimum inhibitory concentrations (MICs) for CAP. The mutations in the eis promoter and tlyA gene were responsible for low-level resistance to CAP. 83.3% of A1401 G substitutions in the rRs gene was observed in Beijing genotype strains, while the difference was not significant ($p = 0.157$). Our data demonstrated that the hot-spot regions localized in the rRs gene serve as excellent markers for AMK, but is not a sensitive marker for KAN and CAP. In addition, the cross-resistance patterns and MICs differed among different genetic mutation types, which challenge the practice in China of generalizing resistance to AMK and CAP based on the resistance to KAN alone. Our findings suggested that the individualized drug susceptibility to three major second-line injectable drugs is essential in order to generate more effective treatment regimens for MDR patients.

304 STREICHER, E. M.; MAHARAJ, K.; YORK, T.; HEERDEN, C. VAN; BARNARD, M.; DIACON, A.; MENDEL, C. M.; BOSMAN, M. E.; HEPPLER, J. A.; PYM, A. S.; WARREN, R. M.; HELDEN, P. D. VAN **Rapid sequencing of the *Mycobacterium tuberculosis* pncA gene for detection of pyrazinamide susceptibility.** *Journal of Clinical Microbiology* (2014) **52** (11) 4056-4057 Washington, USA; American Society for Microbiology (ASM) [En, 13 ref.] DST/NRF Centre of Excellence for Biomedical Tuberculosis Research/MRC Centre for Tuberculosis Research,

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We developed a pyrazinamidase gene DNA-sequencing method to rapidly identify pyrazinamide resistance-causing mutations in GenoLyse-treated, smear-positive sputum specimens. The sensitivity and specificity were 90.9 and 100%, respectively, compared to those of MGIT drug susceptibility testing, after the exclusion of synonymous mutations and nonsynonymous mutations previously associated with susceptibility to pyrazinamide.

305 SHENOY, V. P.; SEEMA SHETTY; CHAITANYA TELLAPRAGADA; CHIRANJAY MUKHOPADHYAY LED **Fluorescence microscopy: leads the future of rapid and effective pulmonary tuberculosis diagnosis.** *International Journal of Pharma and Bio Sciences* (2014) 5 (3) B-752-B-756 Guntur, India; *International Journal of Pharma and Bio Sciences* [En, 18 ref.] Department of Microbiology, Kasturba Medical College, Manipal University, Manipal, India.

Early diagnosis and appropriate treatment play an important role in combating the mortality and morbidity caused by Tuberculosis and a rapid, reliable microscopy that can detect acid fast bacilli can be a very useful diagnostic modality. We have evaluated the performance of Light Emitting Diode Fluorescence Microscopy as an alternative to the existing conventional methods in the diagnosis of Pulmonary Tuberculosis. Total of 181 sputum samples received at the Microbiology laboratory of Kasturba Hospital, Manipal were examined by three different microbiologists using Ziehl-Neelsen's (ZN), Fluorescence microscopy (FM) and Light Emitting Diode fluorescence microscopy (LED). Results were independently tabulated by all the three

examiners for comparison of the efficacies of FM and LED in detecting the tubercle bacilli. Of the 181 samples, 25 (13.8%) were positive by all the three microscopic examinations. We did not observe any better sensitivity of the FM or the LED compared with the conventional ZN method. The measure of agreement between FM and LED was excellent and statistically significant (Kappa= 0.817; P value <0.01). LED is a promising reliable alternative that can replace both conventional ZN and FM. As it shortens the diagnostic process and being cost effective should be considered by all TB diagnostic laboratories for increased case finding and rapid diagnosis of Pulmonary Tuberculosis.

312 CHARLES, M.; VILBRUN, S. C.; KOENIG, S. P.; HASHIGUCHI, L. M.; MABOU, M. M.; OCHERETINA, O.; PAPE, J. W. **Treatment outcomes for patients with multidrug-resistant tuberculosis in post-earthquake Port-au-Prince, Haiti.** *American Journal of Tropical Medicine and Hygiene* (2014) 91 (4) 715-721 Deerfield, USA; *American Society of Tropical Medicine and Hygiene* [En, 33 ref.] Les Centres Groupe Hattien d'Etude du Sarcome de Kaposi et des Infections Opportunistes (GHESKIO), Port-au-Prince, Haiti. Email: makchuk@gmail.com

We report outcomes and 12-month survival for the first cohort of patients to undergo multidrug-resistant tuberculosis (MDR-TB) treatment after the earthquake in Haiti - From March 3, 2010 to March 28, 2013, 110 patients initiated treatment of laboratory-confirmed MDR-TB at the Groupe Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunistes (GHESKIO) Center in Port-au-Prince, Haiti. Twenty-seven patients (25%) were human immunodeficiency virus (HIV)-positive. As of October 31, 2013, 95 (86%) patients were either cured or alive on treatment, 4 (4%) patients defaulted, and 11 (10%) patients died. Culture conversion occurred by 30 days in 14 (13%) patients, 60 days in 49 (45%) patients,

and 90 days in 81 (74%) patients. The probabilities of survival to 12 months were 96% (95% confidence interval [95% CI]=89-99) and 85% (95% CI=64-94) for HIV-negative and - positive patients, respectively. Despite adverse conditions, outcomes for patients with MDR-TB are highly encouraging. Major efforts are underway to scale up community directly observed therapy and expand care to other regions of Haiti.

313 MONARREZ-ESPINO, J.; ENCISO-MORENO, J. A.; LAFLAMME, L.; SERRANO, C. J. **Serial QuantiFERON-TB Gold In-Tube assay and tuberculin skin test to diagnose latent tuberculosis in household Mexican contacts: conversion and reversion rates and associated factors using conventional and borderline zone definitions.** *Memorias do Instituto Oswaldo Cruz* (2014) **109** (7) 863-870 Rio de Janeiro, Brazil; Instituto Oswaldo Cruz [En, 36 ref.] Department of Public Health Sciences, Karolinska Institute, Stockholm, Sweden. Email: carmenyuyu2000@yahoo.com.mx

A cohort of 123 adult contacts was followed for 18-24 months (86 completed the follow-up) to compare conversion and reversion rates based on two serial measures of QuantiFERON (QFT) and tuberculin skin test (TST) (PPD from TUBERSOL, Aventis Pasteur, Canada) for diagnosing latent tuberculosis (TB) in household contacts of TB patients using conventional (C) and borderline zone (BZ) definitions. Questionnaires were used to obtain information regarding TB exposure, TB risk factors and socio-demographic data. QFT (IU/mL) conversion was defined as 0.35 to (C) or 0.70 (BZ) and reversion was defined as 1135 to 0.35 (C) or ≥ 0.35 to 0.20 (BZ); TST (mm) conversion was defined as 5 to (C) or 10 (BZ) and reversion was defined as to 5 (C). The QFT conversion and reversion rates were 10.5% and 7% with C and 8.1% and 4.7% with the BZ definitions, respectively. The TST rates were

higher compared with QFT, especially with the C definitions (conversion 23.3%, reversion 9.3%). The QFT conversion and reversion rates were higher for TST for TST, both rates were lower for QFT <0.35. No risk factors were associated with the probability of converting or reverting. The inconsistency and apparent randomness of serial testing is confusing and adds to the limitations of these tests and definitions to follow-up close TB contacts.

314 WAH WIN; SOURAV DAS; EARNEST, A.; LIM KANGYANG [LIM, K. Y. L.]; CHEE BINENG [GHEE, B. E. C.]; COOK, A. R.; WANG YEETANG; WIN KHINMARKYI; ONG ENGHOCK [ONG, E. H. M.]; HSU LIYANG **Time series analysis of demographic and temporal trends of tuberculosis in Singapore.** *BMC Public Health* (2014) **14** (1121) (31 October 2014) London, UK; BioMed Central Ltd [En, 31 ref.] Centre for Infectious Disease Epidemiology & Research, Saw Swee Hock School of Public Health, National University of Singapore and NUNS, Singapore, Singapore. Email: Liyang_hsu@yahoo.com

BACKGROUND: Singapore is an intermediate tuberculosis (TB) incidence country, with a recent rise in TB incidence from 2008, after a fall in incidence since 1998. This study identified population characteristics that were associated with the recent increase in TB cases, and built a predictive model of TB risk in Singapore. **METHODS:** Retrospective time series analysis was used to study TB notification data collected from 1995 to 2011 from the Singapore Tuberculosis Elimination Program (STEP) registry. A predictive model was developed based on the data collected from 1995 to 2010 and validated using the data collected in 2011. **RESULTS:** There was a significant difference in demographic characteristics between resident and non-resident TB cases. TB risk was higher in non-residents than in residents throughout the period. We found no

significant association between demographic and macro-economic factors and annual incidence of TB with or without adjusting for the population-at-risk. Despite growing non-resident population, there was a significant decrease in the non-resident TB risk ($p < 0.0001$). However, there was no evidence of trend in the resident TB risk over this time period, though differences between different demographic groups were apparent with ethnic minorities experiencing higher incidence rates. CONCLUSION: The study found that despite an increasing size of non-resident population, TB risk among non-residents was decreasing at a rate of about 3% per year. There was an apparent seasonality in the TB reporting.

670 PADAYATCHI, N.; GOPAL, M.; NAIDOO, R.; WERNER, L.; NAIDOO, K.; MASTER, I.; O'DONNELL, M. R. **Clofazimine in the treatment of extensively drug-resistant tuberculosis with HIV coinfection in South Africa: a retrospective cohort study.** *Journal of Antimicrobial Chemotherapy* (2014) **69** (11) 3103-3107 Oxford, UK; Oxford University Press [En, 20 ref.] Centre for the AIDS Programme of Research in South Africa (CAPRISA), Nelson R. Mandela School of Medicine, Doris Duke Medical Research Institute, University of KwaZulu-Natal, Private Bag X7, Congella, 4013, South Africa. Email: padayatchin@ukzn.ac.za

BACKGROUND: Extensively drug-resistant (XDR) tuberculosis (TB) and HIV coinfection is associated with low cure rates and high mortality. Clofazimine has shown activity in vitro against *Mycobacterium tuberculosis*, but clinical experience with clofazimine in XDR-TB and HIV coinfection is limited. METHODS: This was a retrospective cohort study of adult XDR-TB patients in Kwa-Zulu-Natal, South Africa, treated with either a clofazimine or non-clofazimine-containing XDR-TB treatment regimen. The primary outcome measure was TB culture

conversion at 6 months. Survival analysis and multivariate logistic regression compared time to event in different strata and identified risk factors for TB culture conversion. RESULTS: Between August 2009 and July 2011, eligible XDR-TB patients ($n=85$) were initiated on treatment for XDR-TB. Most patients (86%) were HIV-infected and receiving antiretroviral therapy (90%). Patients receiving a clofazimine-containing regimen ($n=50$) had a higher percentage of culture conversion (40%) compared with patients ($n=35$) receiving a non-clofazimine regimen (28.6%). On multivariate analysis, there was a 2-fold increase in TB culture conversion at 6 months (hazard rate ratio 2.54, 95% CI 0.99-6.52, $P=0.05$) in the group receiving a clofazimine-containing regimen. Adverse effects due to clofazimine were minor and rarely life-threatening. CONCLUSIONS: Clofazimine was associated with improved culture conversion in the treatment of XDR-TB/HIV. Adverse effects were minor and non-life-threatening. Based on these preliminary data, further study of clofazimine in XDR-TB/HIV treatment is warranted. Given the present low rates of culture conversion in XDR-TB treatment, we recommend empirical inclusion of clofazimine in treatment regimens for XDR-TB.

671 MAYOSI, B. M.; NTSEKHE, M.; BOSCH, J.; PANDIE, S.; JUNG, H.; GUMEDZE, F.; POGUE, J.; THABANE, L.; SMIEJA, M.; FRANCIS, V.; JOLDERSMA, L.; THOMAS, K. M.; THOMAS, B.; AWOTEDU, A. A.; MAGULA, N. P.; NAIDOO, D. P.; DAMASCENO, A.; BANDA, A. C.; BROWN, B.; MANGA, P.; KIRENGA, B.; MONDO, C.; MNTLA, P.; TSITSI, J. M.; PETERS, F.; ESSOP, M. R. (ET AL) **Prednisolone and *Mycobacterium indicus pranii* in tuberculous pericarditis.** *New England Journal of Medicine* (2014) **371** (12) 1121-1130 Waltham, USA; Massachusetts Medical Society [En, 37 ref.] Cardiac Clinic, Department of Medicine, Groote

Schuur Hospital and University of Cape Town, J Fl., Rm. J46-53, Groote Schuur Dr., Observatory, Cape Town, 7925, South Africa. Email: bongani.mayosi@uct.ac.za

BACKGROUND: Tuberculous pericarditis is associated with high morbidity and mortality even if antituberculosis therapy is administered. We evaluated the effects of adjunctive glucocorticoid therapy and *Mycobacterium indicus pranii* immunotherapy in patients with tuberculous pericarditis. **METHODS:** Using a 2-by-2 factorial design, we randomly assigned 1400 adults with definite or probable tuberculous pericarditis to either prednisolone or placebo for 6 weeks and to either *M. indicus pranii* or placebo, administered in five injections over the course of 3 months. Two thirds of the participants had concomitant human immunodeficiency virus (HIV) infection. The primary efficacy outcome was a composite of death, cardiac tamponade requiring pericardiocentesis, or constrictive pericarditis. **RESULTS:** There was no significant difference in the primary outcome between patients who received prednisolone and those who received placebo (23.8% and 24.5%, respectively; hazard ratio, 0.95; 95% confidence interval [CI], 0.77 to 1.18; P=0.66) or between those who received *M. indicus pranii* immunotherapy and those who received placebo (25.0% and 24.3%, respectively; hazard ratio, 1.03; 95% CI, 0.82 to 1.29; P=0.81). Prednisolone therapy, as compared with placebo, was associated with significant reductions in the incidence of constrictive pericarditis (4.4% vs. 7.8%; hazard ratio, 0.56; 95% CI, 0.36 to 0.87; P=0.009) and hospitalization (20.7% vs. 25.2%; hazard ratio, 0.79; 95% CI, 0.63 to 0.99; P=0.04). Both prednisolone and *M. indicus pranii*, each as compared with placebo, were associated with a significant increase in the incidence of cancer (1.8% vs. 0.6%; hazard ratio, 3.27; 95% CI, 1.07 to

10.03; P=0.03, and 1.8% vs. 0.5%; hazard ratio, 3.69; 95% CI, 1.03 to 13.24; P=0.03, respectively), owing mainly to an increase in HIV-associated cancer. **CONCLUSIONS:** In patients with tuberculous pericarditis, neither prednisolone nor *M. indicus pranii* had a significant effect on the composite of death, cardiac tamponade requiring pericardiocentesis, or constrictive pericarditis.

672 JINDANI, A.; HARRISON, T. S.; NUNN, A. J.; PHILLIPS, P. P. J.; CHURCHYARD, G. J.; CHARALAMBOUS, S.; HATHERILL, M.; GELDENHUYS, H.; MCILLERON, H. M.; ZVADA, S. P.; MUNGOF, S.; SHAH, N. A.; ZIZHOU, S.; MAGWETA, L.; SHEPHERD, J.; NYIRENDA, S.; DIJK, J. H. VAN; CLOUTING, H. E.; COLEMAN, D.; BATESON, A. L. E.; MCHUGH, T. D.; BUTCHER, P. D.; MUCHISON, D. A.

High-dose rifapentine with moxifloxacin for pulmonary tuberculosis.

New England Journal of Medicine (2014) **371** (17) 1599-1608 Waltham, USA; Massachusetts Medical Society [En, 30 ref.] St. George's, University of London, London, UK. Email: ajindani@sgul.ac.uk

BACKGROUND: Tuberculosis regimens that are shorter and simpler than the current 6-month daily regimen are needed. **METHODS:** We randomly assigned patients with newly diagnosed, smear-positive, drug-sensitive tuberculosis to one of three regimens: a control regimen that included 2 months of ethambutol, isoniazid, rifampicin, and pyrazinamide administered daily followed by 4 months of daily isoniazid and rifampicin; a 4-month regimen in which the isoniazid in the control regimen was replaced by moxifloxacin administered daily for 2 months followed by moxifloxacin and 900 mg of rifapentine administered twice weekly for 2 months; or a 6-month regimen in which isoniazid was replaced by daily moxifloxacin for 2 months followed by one weekly dose of both moxifloxacin

and 1200 mg of rifapentine for 4 months. Sputum specimens were examined on microscopy and after culture at regular intervals. The primary end point was a composite treatment failure and relapse, with noninferiority based on a margin of 6 percentage points and 90% confidence intervals. RESULTS: We enrolled a total of 827 patients from South Africa, Zimbabwe, Botswana, and Zambia; 28% of patients were coinfecting with the human immunodeficiency virus. In the per-protocol analysis, the proportion of patients with an unfavorable response was 4.9% in the control group, 3.2% in the 6-month group (adjusted difference from control, -1.8 percentage points; 90% confidence interval [CI], -6.1 to 2.4), and 18.2% in the 4-month group (adjusted difference from control, 13.6 percentage points; 90% CI, 8.1 to 19.1). In the modified intention-to-treat analysis these proportions were 14.4% in the control group, 13.7% in the 6-month group (adjusted difference from control, 0.4 percentage points; 90% CI, -4.7 to 5.6), and 26.9% in the 4-month group (adjusted difference from control, 13.1 percentage points; 90% CI, 6.8 to 19.4). CONCLUSIONS: The 6-month regimen that included weekly administration of high-dose rifapentine and moxifloxacin was as effective as the control regimen. The 4-month regimen was not noninferior to the control regimen.

673 WU CHENG; ZHOU XIAOHONG; LI CAIXIA [The expression and significance of TM, Th2 and Th17 cells related cytokines in peripheral blood of leprosy patients.] *Chinese Journal of Dermatovenereology* (2014) **28** (10) 998-1000 Shaanxi, China; Chinese Journal of Dermatovenereology [Ch, en, 12 ref.] The Dermatology Department, Suizhou Central Hospital, Suizhou 441300, China. Email: xiaohongzhou@126.com
OBJECTIVE: To explore the role of Th1, Th2 and Th17 related cytokines in leprosy. METHODS: The leprosy patients were 22, the cured leprosy

people were 43, the ENL were 4, and the normal persons were 20. We used the flow cytometry to test the IL-2, IL-4, IL-6, IL-10, TNF, IFN γ and IL-17 in four groups above mentioned. And use the SPSS - 19.0 to analysis the results. RESULTS: Concentrations of IL-2, IL-4, IL-6, IL-10, TNF, IFN γ and IL-17 in the leprosy patients group, the cured leprosy group and the ENL group were significantly higher level than the normal persons ($P < 0.05$). Concentrations of IL-10, IFN γ and IL-17 in the leprosy patients group were significantly higher level than the ENL group ($P < 0.05$). CONCLUSION: Th1, Th2 and Th17 cells related cytokines play an important role in the development of the leprosy. Although the cured leprosy patients with clinical symptoms have completely disappeared, but the body's immune function is still not back to normal, probably just a temporary state of relative balance. Concentrations of IFN γ , IL-10 and IL-17 may be associated with leprosy reaction. Relatively low levels of IFN γ , IL-10 and IL-17 are more likely to induce leprosy reaction. Th1, Th2 and Th17 related cytokines involved in the development of leprosy.

674 ADAMS, L. V.; MCQUILLAN, T.; NABURI, H. E.; LYATUU, G.; IPPOLITO, M. M.; SAUNDERS, A.; KIRAVU, A.; PALUMBO, P.; REYN, C. F. VON
Diagnosis and treatment of tuberculosis among children at an HIV Care Program in Dar es Salaam, Tanzania. *Pediatric Infectious Disease Journal* (2014) **33** (12) 1234-1236 Hagerstown, USA; Lippincott Williams & Wilkins, Inc. [En] Diagnosis and treatment of tuberculosis is challenging in children with human immunodeficiency virus (HIV) infection.

We describe the clinical features, diagnostic testing results, tuberculosis and HIV treatment and clinical outcomes of 57 HIV-infected children diagnosed with tuberculosis at the DarDar Pediatric Program in Dar es Salaam, Tanzania. In this cohort, tuberculosis was common, micro-

biologic studies were frequently negative and mortality was high.

675 ARAIJO E ARAUJO, A. E. R. DE; AQUINO, D. M. C. DE; GOULART, I. M. B.; PEREIRA, S. R. F.; FIGUEIREDO, I. A.; SERRA, H. O.; FONSECA, P. C. DE A.; CALDAS, A. DE J. M. **Neural complications and physical disabilities in leprosy in a capital of northeastern Brazil with high endemicity.** *Revista Brasileira de Epidemiologia* (2014) **17** (4) 899-910 Rio de Janeiro, Brazil; Associacao Brasileira de Pos-Graduacao em Saude Coletiva [En, Pt, 32 ref.] Universidade Ceuma - Sao Luis (MA), Brazil. Email: euggenia@hotmail.com

INTRODUCTION: Leprosy is an infectious disease whose etiologic agent is *Mycobacterium leprae*, manifested by dermatological and neurological signs and symptoms. OBJECTIVE: To investigate neural changes and the degree of physical disability in the eyes, hands and feet before and after treatment, as well as sociodemographic and clinical profile of patients affected by leprosy. METHOD: A longitudinal epidemiological study comprising 155 patients with leprosy, from a spontaneous demand, diagnosed between March 2010 and February 2011, and treated with multidrug therapy (MDT) between March 2010 and July 2012 in a program for leprosy eradication in Sao Luis (MA), Brazil. RESULTS: Before treatment, 46.5% of patients were considered as borderline, 51.6% had some alteration in the eyes and 52.3% in the feet, and the radial nerve (18.7%) was the most affected. There was a statistically significant difference between the changes in the radial nerve at the beginning of and after treatment. CONCLUSIONS: The analysis points to late diagnosis, as some patients have had abnormal neural and physical disabilities before treatment.

676 SRILOHASIN, P.; CHAI PRASERT, A.; TOKUNAGA, K.; NISHIDA, N.; PRAMMANANAN, T.; SMITTIPAT, N.; MAHASIRIMONGKOL, S.;

CHAIYASIRINROJE, B.; YANAI, H.; PALITTA-PONGARNPIM, P. **Genetic diversity and dynamic distribution of *Mycobacterium tuberculosis* isolates causing pulmonary and extrapulmonary tuberculosis in Thailand.** *Journal of Clinical Microbiology* (2014) **52** (12) 4267-4274 Washington, USA; American Society for Microbiology (ASM) [En, 40 ref.] Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Email: angkana.cha@mahidol.ac.th

This study examined the genetic diversity and dynamicity of circulating *Mycobacterium tuberculosis* strains in Thailand using nearly neutral molecular markers. The single nucleotide polymorphism (SNP)-based genotypes of 1,414 culture-positive *M. tuberculosis* isolates from 1,282 pulmonary tuberculosis (PTB) and 132 extrapulmonary TB (EPTB) patients collected from 1995 to 2011 were characterized. Among the eight SNP cluster groups (SCG), SCG2 (44.1%), which included the Beijing (BJ) genotype, and SCG1 (39.4%), an East African Indian genotype, were dominant. Comparisons between the genotypes of *M. tuberculosis* isolates causing PTB and EPTB in HIV-negative cases revealed similar prevalence trends although genetic diversity was higher in the PTB patients. The identification of 10 reported sequence types (STs) and three novel STs was hypothesized to indicate preferential expansion of the SCG2 genotype, especially the modern BJ ST10 (15.6%) and ancestral BJ ST19 (13.1%). An association between SCG2 and SCG1 genotypes and particular patient age groups implies the existence of different genetic advantages among the bacterial populations. The results revealed that increasing numbers of young patients were infected with *M. tuberculosis* SCGs 2 and 5, which contrasts with the reduction of the SCG1 genotype. Our results indicate the selection and dissemination of

potent *M. tuberculosis* genotypes in this population. The determination of heterogeneity and dynamic population changes of circulating *M. tuberculosis* strains in countries using the *Mycobacterium bovis* BCG (bacillus Calmette-Guerin) vaccine are beneficial for vaccine development and control strategies.

677 MEJIA, M. DEL C. C.; SANTOS, M. P. DOS; SILVA, G. A. V. DA; PASSOS, I. DA M.; NAVECA, F. G.; CUNHA, M. DA G. S.; MORAES, M. O.; PAULA, L. DE
Identification of primary drug resistance to rifampin in *Mycobacterium leprae* strains from leprosy patients in Amazonas State, Brazil. *Journal of Clinical Microbiology* (2014) **52** (12) 4359-4360 Washington, USA; American Society for Microbiology (ASM) [En, 17 ref.] Programa de Pós-Graduação em Imunologia Básica e Aplicada, Universidade Federal do Amazonas, Amazonas, Brazil. Email: 1paula.bio@hotmail.com

The aim of this study was to identify polymorphisms in the *folP1*, *gyrA*, and *rpoB* genes in leprosy patients treated in Amazonas State, Brazil. Among 197 slit-skin smear samples from untreated or relapsed patients, we found three cases of primary resistance to rifampin and one confirmed case of multidrug resistance.

678 MARION, E.; GANLONON, L.; CLACO, E.; BLANCHARD, S.; KEMPF, M.; ADEYE, A.; CHAUTY, A.
Establishment of quantitative PCR (qPCR) and culture laboratory facilities in a field hospital in Benin: 1-year results. *Journal of Clinical Microbiology* (2014) **52** (12) 4398-4400 Washington, USA; American Society for Microbiology (ASM) [En, 16 ref.] Centre de Diagnostic et de Traitement de l'Ulcer de Buruli, Fondation Raoul Follereau, Pobe, Benin. Email: estelle.marion@inserm.fr

No simple diagnostic tool is available to confirm *Mycobacterium ulcerans* infection, which is an emerging disease reported in many rural areas of Africa. Here, we report the 1-year results of a

hospital laboratory that was created in an area of endemicity of Benin to facilitate the diagnosis of *M. ulcerans* infection.

679 EKWUEME, O. C.; OMOTOWO, B. I.; AGWUNA, K. K. Strengthening contact tracing capacity of pulmonary tuberculosis patients in Enugu, southeast Nigeria: a targeted and focused health education intervention study. *BMC Public Health* (2014) **14** (1175) (18 November 2014) London, UK; BioMed Central Ltd [En, 38 ref.] Department of Community Medicine, University of Nigeria, Enugu Campus, PMB 01129, Enugu, Nigeria. Email: christiandolus@yahoo.com, omotowobabatunde@yahoo.com, ken.agwuna@unn.edu.ng

BACKGROUND: Nigeria ranks 10 out of the 22 countries in the world with the highest TB burden. Contact tracing enhances case finding and increases the probability of cure. The purpose of the study is to improve the contact tracing skills of tuberculosis patients at the major TB centre in Enugu State, Nigeria. Methods: The study is an educational intervention with a study and a control groups selected using multi-stage sampling techniques. A calculated sample size of 190 patients was used for each group. The instrument was a pre-tested semi-structured interviewer administered questionnaire. Data entry and analysis was done using Bpi-info version 3.3.2. Chi-square test and student t-test were used at $p < 0.05$ level of significance and 95 percent confidence interval. RESULTS: Awareness of contact tracing at baseline and post intervention were respectively 18.2% and 85.2% ($X^2 = 158.4$, $DF = 1$, $p = 0.000$; CI: 15.8-82.2) for the study group; 18.4% and 26.0% ($X^2 = 3.31$, $DF = 1$, $p = 0.069$; CI: -9.9-24.7) for the control group. Knowledge that contact tracing involve bringing all household contacts of TB patients for screening was 79 (44.9%) and 33 (19.2%) for the study and control groups at baseline ($X^2 = 26.32$,

$p=0.000$; CI: 7.2-44.1), but 151 (85.8%) and 36(20.9%) for the same at post-intervention ($X^2=147.22$, $p=0.000$; CI: 49.3-80.1). At baseline, only 5 (2.8%) of the study and 6(3.5%) of the control groups ($X^2=0.12$, $p=0.730$; CI: -14.2-12.8) brought two or more contacts for screening. At post-intervention, the figure rose to 114 (64.8%) and 9 (5.2%) ($X^2=134.94$, $p=0.000$; CI: 44.3-74.9) for the study and control groups respectively. Over 50% of the contacts brought for screening were less than 10 years; 31 (18.3%) at baseline to 138 (81.7%) post-intervention in the study group (CI: 47.6-79.2), and 26 (35.1%) to 38 (51.4%) for the control group ($X^2=12.472$, $p=0.000$; CI: 0.1 - 32.5). CONCLUSION: Intensive planned health education intervention has been used to improve the contact tracing skills of the TB patients in a major TB centre in Enugu State, Nigeria. Further training and re-training of TB patients on contact tracing is highly recommended.

680 MEMONA YASMIN; GOMGNIMBOU, M. K.; SIDDIQUI, R. T.; REFREGIER, G.; SOLA, C. **Multi-drug resistant *Mycobacterium tuberculosis* complex genetic diversity and clues on recent transmission in Punjab, Pakistan.** *Infection, Genetics and Evolution* (2014) **27**, 6-14 Amsterdam, Netherlands; Elsevier B.V. [En, 31 ref.] Health Biotechnology Division, National Institute for Bio-technology and Genetic Engineering (NIBGE), P.O. Box #577, Jhang Road, Faisalabad, Pakistan. Email: christophe.sola@upsud.fr

Multi-Drug Resistant Tuberculosis (MDR-TB), i.e. bacilli resistant to rifampicin (RIF) and isoniazid (INH), is a major Public Health concern in Pakistan according to WHO estimates (3.5% and 32% of new and retreated cases, respectively). Previous Pakistanis reports identified a correlation between being MDR and belonging to Beijing or EAI lineages in one study, and belonging to "H4" - Ural

Euro-American sublineage in another study. In addition, MDR-TB transmission was suspected in Karachi. We tested MDR characteristics on a Punjab sample of 278 clinical isolates (without selection for Multi-Drug Resistance) including new and retreated cases collected from 2008 to 2012. All samples were characterized by a new, microbead based method named "TB-SPRINT" (molecular diagnostic including spoligotype identification, and genetic resistance determinants to first-line anti-TB drugs RIF and INH). Isolates from 2011 to 2012 ($n=100$) were further analyzed using 24-loci MIRU-VNTR. We detected 8.7% MDR isolates (CI95%=[5.0; 12.5]), mainly among CAS lineage that predominates in this central-East region of Pakistan. Out of 20 MDR-TB cases, 12 different TB-SPRINT profiles were identified, limiting the suspicion of MDR-TB transmission. 24 MIRU-VNTR confirmed the unrelatedness of isolates with different TB-SPRINT profiles and discriminated 3 isolates with identical TB-SPRINT profiles. In conclusion, our study did not confirm any of the correlations between Multi-Drug Resistance and lineage or sublineage in Punjab, Pakistan. MDR-TB isolates were diverse indicating that transmission is not pervasive. TB-SPRINT proved useful as a first step for detecting MDR-TB likely transmission events, before more extensive genotyping such as 15 or 24 MIRU-VNTR and thorough epidemiological investigation.

681 LI DI; DONG CAIBO; CUI JIAYI; NAKAJIMA, C.; ZHANG CHUNLEI; PAN XINLING; SUN GAOXIANG; DAI ENYU; SUZUKI, Y.; ZHUANG MIN; LING HONG **Dominant modern sublineages and a new modern sublineage of *Mycobacterium tuberculosis* Beijing family clinical isolates in Heilongjiang Province, China.** *Infection, Genetics and Evolution* (2014) **27**, 294-299 Amsterdam, Netherlands; Elsevier B.V. [En, 35 ref.] Department of Microbiology, Harbin

Medical University, Heilongjiang Provincial Key Laboratory for Infection and Immunity, Key Laboratory of Etiology of Heilongjiang Province Education Bureau, Harbin, China. Email: lingh@ems.hrbmu.edu.cn

Mycobacterium tuberculosis Beijing family includes a variety of sublineages. Knowledge of the distribution of a certain sublineage of the Beijing family may help to understand the mechanisms of its rapid spread and to establish an association between a certain genotype and the disease outcome. We have previously found that *M. tuberculosis* Beijing family clinical isolates represent approximately 90% of the clinical isolates from Heilongjiang Province, China. To clarify the distribution of *M. tuberculosis* Beijing family sublineages in Heilongjiang Province, China and to investigate the regularity rule for their evolution, we examined single nucleotide polymorphisms (SNPs) of 250 *M. tuberculosis* Beijing family clinical isolates using 10 SNP loci that have been identified as appropriate for defining Beijing sublineages. After determining the sequence type (ST) of each isolate, the sublineages of all *M. tuberculosis* Beijing family isolates were determined, and phylogenetic analysis was performed. We found that 9 out of the 10 SNP loci displayed polymorphisms, but locus 1548149 did not. In total, 92.8% of the isolates in Heilongjiang Province are modern sublineages. ST10 is the most prevalent sublineage (ST10 and ST22 accounted for 63.2% and 23.6% of all the Beijing family isolates, respectively). A new ST, accounting for 4% of the Beijing family isolates in this area, was found for the first time. Each new ST isolate showed a unique VNTR pattern, and none were clustered. The present findings suggest that controlling the spread of these modern sublineages is important in Heilongjiang Province and in China.

682 ZHAO XIUQIN; WANG YUFENG; PANG YU
Antimicrobial susceptibility and molecular

characterization of *Mycobacterium intracellulare* in China. *Infection, Genetics and Evolution* (2014) **27**, 332-338 Amsterdam, Netherlands; Elsevier B.V. [En, 46 ref.] State Key Laboratory for Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China. Email: pangyu@chinatb.org

Mycobacterium avium complex (MAC) is the most common non-tuberculosis mycobacterial pathogen isolated from respiratory samples, mainly including two species, *Mycobacterium avium* (*M. avium*) and *Mycobacterium intracellulare* (*M. intracellulare*). Although these two species belong to the same group, *M. avium* and *M. intracellulare* reveal significant differences in pathogenicity and biology. Nevertheless, little is known regarding the drug resistant details profile of *M. avium* or *M. intracellulare* instead of MAC. Here, we examined the antimicrobial susceptibility profiles of 52 clinical *M. intracellulare* isolates against fourteen antimicrobial agents, which are widely selected for the treatment of nontuberculous mycobacteria (NTM) infection. The drug susceptibility test revealed that clarithromycin (47/52, 90.4%), rifampicin (41/52, 78.8%) and capreomycin (40/52, 76.9%) revealed highly antimicrobial activities against *M. intracellulare* isolates in vitro. Furthermore, all clarithromycin resistant isolates harbored mutations in the 23S rRNA gene, and the percentage of amikacin resistant ones with mutation in the *rrs* gene is 62.5% (10/16). The Hunter-Gaston Discriminatory Index (HGDI) value for the 16-loci Variable Number of Tandem Repeat (VNTR) typing of *M. intracellulare* isolates was 0.994, and *M. intracellulare* resistance to moxifloxacin was significantly more commonly found in clustered strains than in nonclustered strains ($\chi^2=5.551$, $P=0.040$). In conclusion, our data demonstrated

that clarithromycin and capreomycin revealed highly antimicrobial activities against *M. intracellulare* isolates, and clarithromycin and amikacin resistance could be detected more readily and rapidly using molecular scanning of corresponding drug target than conventional drug susceptibility testing. We also found that infection by clustered strains was significantly associated with resistance to moxifloxacin.

683 LEE SEUNGGUN; LEE SEUNGHUN; KIM YOUEUN; CHO YUJI; JEONG YIYEONG; KIM HOCHAEOL; LEE JONGDEOG; KIM JANGRAK; HWANG YOUNGSIL; KIM HEEJIN; MENZIES, D. **Risk factors for latent tuberculosis infection in close contacts of active tuberculosis patients in South Korea: a prospective cohort study.** *BMC Infectious Diseases* (2014) **14** (566) (18 November 2014) London, UK; BioMed Central Ltd [En, 27 ref.] Department of Internal Medicine, College of Medicine, Gyeongsang National University, 90 Chilam-Dong, Jinju, Gyeongnam 660-302, Korea Republic. Email: hochkim@gnu.ac.kr

BACKGROUND: The diagnosis and treatment of latent tuberculosis infection (LTBI) have become mandatory to reduce the burden of tuberculosis worldwide. Close contacts of active TB patients are at high risk of both active and LTBI. The aim of this study is to identify the predominant risk factors of contracting LTBI, persons in close contact with TB patients were recruited. This study also aimed to compare the efficacy of the tuberculin skin test (TST) and QuantiFERON®-TB GOLD (QFT-G) to diagnose LTBI. **METHODS:** Close contacts of active pulmonary TB patients visiting a hospital in South Korea were diagnosed for LTBI using TST and/or QFT-G. The association of positive TST and/or QFT-G with the following factors was estimated: age, gender, history of Bacillus Calmette-Guerin (BCG) vaccination, history of pulmonary TB, cohabitation status, the acid-fast bacilli smear status, and presence of

cough in source cases. **RESULTS:** Of 308 subjects, 38.0% (116/ 305) were TST positive and 28.6% (59/206) were QFT-G positive. TST positivity was significantly associated with male gender (OR: 1.734; 95% CI: 1.001-3.003, p=0,049), history of pulmonary TB (OR: 4.130; 95% CI: 1.441-11.835, p=0.008) and household contact (OR: 2.130; 95% CI: 1.198-3.786, p=0.01) after adjustment for confounding variables. The degree of concordance between TST and QFT-G was fair (70.4%, K=0,392). **CONCLUSIONS:** A prevalence of LTBI among close contacts of active pulmonary TB patients was high, and prior TB history and being a household contact were risk factors of LTBI in the study population.

684 BONURA, C.; GOMGNIMBOU, M. K.; REFREGIER, G.; ALEO, A.; FASCIANA, T.; GIAMMANCO, A.; SOLA, C.; MAMMINA, C. **Molecular epidemiology of tuberculosis in Sicily, Italy: what has changed after a decade?** *BMC Infectious Diseases* (2014) **14** (602) (19 November 2014) London, UK; BioMed Central Ltd [En, 19 ref.] Department of Sciences for Health Promotion and Mother-Child Care "G. D' Alessandro", University of Palermo, Palermo, Italy. Email: caterina.manunina@unipa.it

BACKGROUND: We aimed to investigate the molecular epidemiology of *Mycobacterium tuberculosis* complex (MTBC) isolates in the province of Palermo, Sicily, Italy, by characterizing 183 isolates identified in the years 2004-2012. A comparison with 104 MTBC strains identified in the same geographic area in the years 1994-2000 was also carried out. **METHODS:** One hundred eighty-three MTBC isolates identified in Palermo, Italy, in the years 2004-2012 were analyzed by spoligotyping and the 24 mycobacterial interspersed repetitive unit (MIRU)-variable-number tandem-repeat (VNTR) method typing. Susceptibility testing to streptomycin, isoniazid, rifampin and ethambutol was also performed.

Furthermore, the spoligotyping dataset obtained from 104 MTBC isolates identified from 1994 to 2000 was reanalyzed. Distribution into lineages and clustering of isolates in the two periods was compared. RESULTS: One hundred seventy-seven out of the 183 isolates of MTBC submitted to molecular typing were fully characterized. Of these, 108 were from Italian-born and 69 from foreign-born individuals. Eleven different lineages and 35 families-subfamilies were identified with the most represented lineages being Haarlem (26.5%), T (19.2%), LAM (13.6%) and S (8.5%). Except for the Haarlem lineage, where isolates from foreign-born patients were over represented, the distribution of isolates in the families belonging to the Euro-American clone reflected the proportions of the two subpopulations. A total of 27 (15.2%) strains were clustered and three clusters were mixed. Approximately 25% of the 183 MTBC isolates under study proved to be resistant to at least one antiTB drug, with only three isolates categorized as multidrug resistant (MDR). When MTBC isolates identified in the years 1994-2000 were reanalyzed, lineages T (30.8%), LAM (29.8%), Haarlem (16.3%) and S (13.5%) proved to be predominant. No MTBC isolates belonging to CAM, U, CAS, Turkish and Ural lineages were identified. CONCLUSIONS: A wide heterogeneity was detected among the MTBC strains isolated in the years 2004-2012. Six lineages were not present among the isolates of the period 1994-2000. Comparison between distribution of lineages in the two consecutive periods depicts rapid and deep changes in the TB epidemiology in Palermo, Italy. An universal and continued laboratory-based surveillance of TB in Sicily is required.

685 KATALE, B. Z.; MBUGI, E. V.; BOTHA, L.; KEYYU, I. D.; KEN-DALL, S.; DOCKRELL, H. M.; MICHEL, A. L.; KAZWALA, R. R.; RWEYEMAMU, M.

M.; HELDEN, P. VAN; MATEE, M. I. **Species diversity of non-tuberculous mycobacteria isolated from humans, livestock and wildlife in the Serengeti ecosystem, Tanzania.** *BMC Infectious Diseases* (2014) **14** (616) (18 November 2014) London, UK; BioMed Central Ltd [En, 40 ref.] Department of Microbiology and Immunology, School of Medicine, Muhimbili University of Health and Allied Sciences (MUHAS), Dar Es Salaam, Tanzania. Email: bugwesa2002@yahoo.co.uk

BACKGROUND: Non-tuberculous mycobacteria (NTM), which are ubiquitous micro-organisms occurring in humans, animals and the environment, sometimes receive public health and veterinary attention as opportunistic disease-causing agents. In Tanzania, there is limited information regarding the diversity of NTM species, particularly at the human-livestock-wildlife interface such as the Serengeti ecosystem, where potential for cross species infection or transmission may exist. METHODS: Mycobacterial DNA was extracted from cultured isolates obtained from sputum samples of 472 suspect TB patients and 606 tissues from wildlife species and indigenous cattle. Multiplex PCR was used to differentiate NTM from *Mycobacterium tuberculosis* complex (MTBC) members. NTM were further identified to species level by nucleotide sequencing of the 16S rRNA gene. RESULTS: A total of fifty five (55) NTM isolates representing 16 mycobacterial species and 5 isolates belonging to the MTBC were detected. Overall, *Mycobacterium intracellulare* which was isolated from human, cattle and wildlife, was the most frequently isolated species (20 isolates, 36.4%) followed by *M. lentiflavum* (11 isolates, 20%), *M. fortuitum* (4 isolates, 7.3%) and *M. chelonae-abscessus* group (3 isolates, 5.5%). In terms of hosts, 36 isolates were from cattle and 12 from humans, the balance being found in

various wildlife species. CONCLUSION: This study reveals a diversity of NTM species in the Serengeti ecosystem, some of which have potential for causing disease in animals and humans. The isolation of NTM from tuberculosis-like lesions in the absence of MTBC calls for further research to elucidate their actual role in causing disease. We are also suggesting a one health approach in identifying risk factors for and possible transmission mechanisms of the NTM in the agro-pastoral communities in the Serengeti ecosystem.

686 ARULANANTHAM, S. **Addressing inequality and exclusion - the opinion of people affected by leprosy in Africa and Asia, as to what should be included in any post Millennium Development Goal framework.** *Leprosy Review* (2014) **85** (3) 133-140 Colchester, UK; LEpra [En, 10 ref.] The Leprosy Mission England and Wales, Peterborough, Cambridgeshire, UK. Email: siana@tlmew.org.uk

With the Millennium Development Goals (MDGs) coming to an end in 2015 and recognizing that people affected by leprosy in most places have still to be mainstreamed into development programmes, the Leprosy Mission committed to advocate for a Post-2015 framework addressing the priorities of people affected by leprosy. In order to ensure its advocacy effort was legitimate, the Leprosy Mission consulted people affected by leprosy in 9 leprosy-endemic countries to ascertain the changes they have experienced over the last 10 years and identify their future development priorities. 95 group consultations with 4797 people affected by leprosy across 9 leprosy-endemic countries (Bangladesh, Congo Democratic Republic, Ethiopia, India, Mozambique, Myanmar, Nepal, Niger and Nigeria) were conducted. Focus group discussions and community meetings were used to gather qualitative data representing the development priorities of people affected by leprosy. General

development themes and recommendations were identified which could be included in the Leprosy Mission's positioning paper on Post-2015. Generally, the changes observed over the past 10 years were: improved access to education and health care; reduction in the number of new cases of leprosy; improvement in infrastructures; reduction in stigma and discrimination; greater awareness about leprosy; better employment opportunities; and greater awareness of human rights. However, some areas were still experiencing stigma and discrimination, few employment opportunities, and although general health services had improved, the quality of care was poor. The top 10 development priorities are: inclusive employment; affordable quality health care; education and training; stigma reduction; safety net support; disability-friendly infrastructure; awareness on leprosy; housing, water and sanitation; food security; and, technology and communication. It is recommended that these priorities, voiced by people affected by leprosy, be advocated for in the context of equity and inclusion, particularly under the banner of disability and neglected tropical diseases.

687 BASEL, P.; PAHAN, D.; MOET, F. J.; OSKAM, L.; RICHARDUS, J. H. **Leprosy incidence: six years follow-up of a population cohort in Bangladesh.** *Leprosy Review* (2014) **85** (3) 158-169 Colchester, UK; LEpra [En, 22 ref.] Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, Netherlands. Email: j.richardus@erasmusmc.nl

BACKGROUND: With approximately 250,000 new leprosy cases detected annually, transmission of *M. leprae* appears to be ongoing in many areas of the world. By studying prospectively the number of leprosy patients found in a population sample at the beginning of the study (prevalence) and the number of new patients found during the 6-year

observation period (incidence), we aim to understand better the transmission of *M. leprae* and the burden of disease. **METHODOLOGY:** To establish the prevalence and incidence rates of leprosy in the general population of a high endemic area in Bangladesh, we followed prospectively 20,218 individuals from a random cluster sample of the population and examined them at 2-yearly intervals for 6 years. **RESULTS:** At intake we found 27 new leprosy cases, indicating a prevalence of previously undiagnosed leprosy of 13-3/10,000. Follow-up at 2, 4 and 6 years revealed 17, 16, and eight new cases, respectively, representing incidence rates of 4.0, 4-5 and 2-3/10,000 PYAR, respectively. The incidence rate over 6 years was 3-7/10,000 PYAR. The observed incidence rate is three times higher than the new case detection rate in the same area. Of all 68 new leprosy cases, five (7%) had MB leprosy. The pro-portion of children under 15 years was 24%. The proportion of female patients was 60%, but the incidence rate of leprosy was the same for males and females. **CONCLUSIONS:** The decline in incidence of leprosy in a general population sample is less pronounced than routine data from a control programme led us to expect.

688 MALLIKA LAVANIA; JADHAV, R. S.; CHAITANYA, V. S.; RAVINDRA TURANKAR; SELVASEKHAR, A.; LOREITA DAS; FAM-KIMA DARLONG; HAMBROOM, U. K.; SANDIP KUMAR; UTPAL SENGUPTA **Drug resistance patterns in *Mycobacterium leprae* isolates from relapsed leprosy patients attending The Leprosy Mission (TLM) Hospitals in India.** *Leprosy Review* (2014) **85** (3) 177-185 Colchester, UK; LEPRO [En, 19 ref.] Stanley Browne Research Laboratory, The Leprosy Mission Community Hospital, Nand Nagri, New Delhi - 110 093, India. Email: mallikala-vania@gmail.com, mallika.lavania@tlmindia.org
Implementation of multidrug therapy (MDT) in

leprosy control programmes has significantly reduced the global prevalence of the disease in the last two decades. After many years of use of MDT, it is expected that drug resistance in *Mycobacterium leprae* may emerge. This is a major concern, especially during the stage of elimination. In the present study, slit-skin smears were collected from 140 leprosy relapse cases from different Leprosy Mission hospitals across India. DNA extracted from 111 (79%) of these samples was analysed for the genes associated with drug resistance in *M. leprae*. More than 90% of the patients relapsed as multibacillary (MB) cases. In our study, four (3.6%) of the DNA samples analysed showed mutations associated with rifampicin resistance. We also observed that mutations associated with resistance to dapsone and ofloxacin were observed in 9 (8.1%) of the DNA samples each; two samples had both dapsone and ofloxacin resistance. Further surveillance and appropriate interventions are needed to ensure the continued success of chemotherapy for leprosy.

689 CASTRO, L. E. DE; CUNHA, A. J. L. A. DA; FONTANA, A. P.; HALFOUN, V. L. R. DEC.; GOMES, M. K. **Physical disability and social participation in patients affected by leprosy after discontinuation of multidrug therapy.** *Leprosy Review* (2014) **85** (3) 208-217 Colchester, UK; LEPRO [En, 29 ref.] Departamento de Medicina de Família e Comunidade, Faculdade de Medicina da UFRJ. Rio de Janeiro, Rua Laura de Arai* 36-2° andar, CEP - 20211-170, Cidade Nova, Rio de Janeiro, RJ, Brazil. Email: gomes.mariakatia@gmail.com

OBJECTIVES: To describe the social participation frequency and the physical disability of patients who were discharged after the multidrug therapy (MDT/WHO) and factors associated with these variables. **METHOD:** A cross-sectional and analytical study, examining associations, which

took place Nova Iguagu/Brazil. A random sample of patients treated with multidrug therapy from 1997 to 2006 was selected. The rationale for sample size was determined by the estimated proportion of physical disability in the amount of 23%, with an acceptable sampling error rate of 5%; significance level was established as 5% among the 1080 patients finally a total sample of 225 patients. The evaluations were performed from January 2010 to December 2011 and Socio-demographic and clinical data were collected from the applications completed in the national notifiable diseases information system (SINAN). RESULTS: In the period of interest, 2179 cases were diagnosed with leprosy; 1080 met the criteria for inclusion. Of these, 225 were randomly selected patients who had mean age 56.12 (± 17.34 years), 55.6% were women, 39.9% went to high school and 28.9% were Caucasians. A total of 55.3% (125) showed multibacillary form, with a predominant dimorphous leprosy in 40.4%. Physical disability was present in 60.9% and social restrictions in 24.9% of patients. The variable physical disability was associated with the therapeutic regimen multibacillary and social participation. CONCLUSION: We observed a high frequency of disability and social restriction after long period after the start of MDT/WHO suggesting the late diagnosis of leprosy or inadequate follow-up after discharge. This study highlights the importance of systematic monitoring of these patients with their own criteria which could be held at the Family Health Strategy.

690 SOOKAN, L.; COOVADIA, Y. M. **A laboratory- based study to identify and speciate nontuberculous mycobacteria isolated from specimens submitted to a central tuberculosis laboratory from throughout KwaZulu-Natal Province, South Africa.** *SAMJ - South African Medical Journal* (2014) **104** (11) 766-768 Pretoria,

South Africa; SAMA Health and Medical Publishing Group [En, 12 ref.] Department of Medical Microbiology, Nelson Mandela School of Medicine, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa. Email: lishasookan@hotmail.com

BACKGROUND: Non-tuberculous mycobacteria (NTM) are important environmental pathogens capable of causing a spectrum of infection. The different species exhibit varied geographical prevalence worldwide. Identification of the infecting organism may be helpful in determining the clinical significance of the isolate. OBJECTIVE: To describe the spectrum of NTM isolated from clinical specimens received at the National Health Laboratory Service central tuberculosis laboratory in KwaZulu-Natal Province, South Africa. METHOD: In a laboratory-based prospective study, 200 suspected NTM were randomly selected over a period of 1 year and identified to species level using a commercially available DNA strip assay (GenoType Mycobacterium, CM/AS; Hain Lifescience, Germany). RESULTS: Of the 200 suspected NTM, 133 (66.5%) were confirmed to be NTM by the molecular test. The most frequently isolated NTM species were *Mycobacterium intracellulare* (45.9%), *M. avium* subspecies (11.3%), *M. goodii* (6.0%) and *M. kansasii* (4.5%). CONCLUSION: It is important for laboratories to document the local spectrum of NTM because of the geographical variation in the different NTM species isolated. Although molecular tests for identifying NTM are relatively expensive, they have the advantage of providing rapid and accurate identification of the various NTM species.

691 MOHAMED EL-HELALY; WASEEM KHAN; AIMAN EL-SAEED; BALKHY, H. H. **Pre-employment screening of latent tuberculosis infection among healthcare workers using tuberculin skin test and QuantiFERON-TB Gold**

test at a tertiary care hospital in Saudi Arabia.

Journal of Infection and Public Health (2014) **7** (6) 481-488 Oxford, UK; Elsevier Ltd [En] Infection Prevention and Control Department, King Abdulaziz Medical City, National Guard Health Affairs, Riyadh, Saudi Arabia. Email: mhelaly72@gmail.com, mhelaly72@yahoo.com

OBJECTIVE: To assess the agreement between the tuberculin skin test (TST) and the QuantiFERON-TB Gold test (QFT-G) as pre-employment screening tests for latent tuberculosis infection (LTBI) among healthcare workers. **METHODS:** A retrospective cross-sectional study was conducted among 1412 healthcare workers who were screened for LTBI during the period from August 2009 to May 2011 at a tertiary-care hospital in the Kingdom of Saudi Arabia (KSA). The studied population was screened for LTBI using both TST and QFT-G simultaneously. The agreement between both tests was quantified using the Kappa coefficient (K). **RESULTS:** Comparing the results of QFT-G with TST, the tests had a significant overall agreement of 73.7% (1040/1412; $K=0.33$; $p<0.01$). Negative concordance comprised 60.1% of the results, and positive concordance comprised 13.5%. However, positive TST but negative QFT comprised 16.3% of the results, and negative TST but positive QFT-G comprised 10.1%. Concordance was significantly associated with young age, female gender, Saudi-born nationals, and early career but not job type (clinical versus non-clinical) nor status of Bacillus Calmette-Guérin (BCG) vaccination. **CONCLUSIONS:** This study demonstrated 73.7% overall agreement between TST and QFT-G results among healthcare workers during pre-employment screening for LTBI. The results need to be confirmed in future studies before recommending QFT-G as a pre-employment screening test for LTBI.

692 LI YANGYANG; XIA YINYIN; DU XIN; CHEN WEI **[Analysis of characteristics of pulmonary**

tuberculosis patients registered in tuberculosis management information system from 2004 to 2013.]

Disease Surveillance (2014) **29** (8) 633-637 Beijing, China; Editorial Board of Disease Surveillance [Ch, en, 12 ref.] Public Health School, Peking Union Medical College, Beijing 100730, China. Email: chenwei@chiantb.org

OBJECTIVE: To understand the characteristics of pulmonary tuberculosis (TB) patients registered in the tuberculosis management information system (TBMIS). **METHODS:** The registration data of TB patient from 2004 to 2013 were collected from TBMIS to conduct descriptive and comparative analysis. **RESULTS:** The TB and smear positive registration rates showed upward and downward trends from 2004 to 2013. The annual TB registration rate declined by 3.62% from 2008 to 2013, and the annual smear positive registration rate declined by 6.33% from 2005 to 2013. In 2013, a total of 855 307 TB cases were registered in China with a registration rate of 62.86/100 000. Among these cases, 312 071 were smear positive and the registration rate was 22.93/100 000. The new smear positive case number was higher in males than in females in all age group except age group 0-14 years and the male to female ratio of the cases increased with age. The proportions of new smear positive cases were high in age groups >65, 55-64 years and 45-54 years and increased with year. **CONCLUSION:** The TB registration rate showed an upward trend before 2008 and a downward trend after 2008. The registration rate was higher in males than in females. The case number in middle aged and old people was high.

693 ACOSTA, L. M. W.; BASSANESI, S. L. **The Porto Alegre paradox: social determinants and tuberculosis incidence.** *Revista Brasileira de Epidemiologia* (2014) **17** (Suppl. 2) 88-101 Rio de Janeiro, Brazil; Associacao Brasileira de Pos-Graduacao em Saude Coletiva [En, Pt, 39 ref.]

Department of Health of Porto Alegre, Porto Alegre (RS), Brazil. Email: lisacosta@uol.com.br

INTRODUCTION: The incidence of tuberculosis (TB) is strongly associated with social and economic factors. The city of Porto Alegre, in the South of Brazil, has one of the highest Human Development Index and Gross Domestic Product per capita of the country. One would expect that the incidence of tuberculosis in such a place were low. However, the city has very high rates of incidence, the highest among Brazilian capitals. This paradox prompted this work, whose objectives were to analyze the spatial distribution of the incidence rate of bacilliferous pulmonary tuberculosis throughout the neighborhoods of Porto Alegre and its association with socioeconomic indicators. **METHODS:** Ecological non-concurrent cohort study. The units of analysis were the neighborhoods of the city. The average annual incidence of bacilliferous pulmonary tuberculosis for the period 2000 to 2005 and seven socioeconomic variables were analyzed, with information obtained from the IBGE and the Mortality Information System. **Spatial techniques and multivariate analyzes were used to check associations. Inequalities were also measured. RESULTS:** The spatial distribution of the incidence rate of bacilliferous pulmonary tuberculosis is very similar, i.e., associated with the distribution of socioeconomic factors. The Relative Index of Inequality was 7.9, showing the great difference in the incidence rate between neighborhoods. **CONCLUSION:** Porto Alegre presents high incidence rates of bacilliferous pulmonary tuberculosis, which distribution through the neighborhoods of the city is associated with socioeconomic factors. The city's high rate is due to the extremely high incidence rates in its poorest neighborhoods. The authors raise hypotheses and suggest interventions.

694 RODRIGUES-JUNIOR, A. L.; RUFFINO-

NETTO, A.; CASTILHO, E. A. DE **Spatial distribution of the human development index, HIV infection and AIDS-Tuberculosis comorbidity: Brazil, 1982-2007.** *Revista Brasileira de Epidemiologia* (2014) **17** (Suppl. 2) 204-215 Rio de Janeiro, Brazil; Associacao Brasileira de Pos-Graduacao em Saude Coletiva [En, Pt, 20 ref.] School of Medicine of Ribeirao Preto, Universidade de Sao Paulo, Ribeirao Preto (SP), Brazil. Email: alrj@fmrp.usp.br

INTRODUCTION: AIDS epidemic has given visibility to the incidence of tuberculosis, for being the most frequent opportunistic infection. It is known that individuals who are socially vulnerable are more susceptible to HIV transmission and tuberculosis as well. **OBJECTIVE:** This study aims to conduct a geoepidemiological study on HIV/AIDS, AIDS-Tuberculosis co-infection and social vulnerability. **METHOD:** This is an ecological study using incidence rates and the human development index to produce thematic maps and a descriptive analysis of epidemiology. The records of reported cases of HIV/AIDS from 1982 to 2007 were used, considering as cases of AIDS-Tuberculosis those records that were positively diagnosed with tuberculosis and those records with unknown diagnosis of tuberculosis, but showing compatible signs and symptoms with tuberculosis (fever, cough, cachexia and asthenia). **RESULTS:** The maps allowed the identification of areas with social differences and different patterns of incidence of HIV/AIDS and AIDS-Tuberculosis; regional differences were similar to those found by Josue de Castro, in 1940; regions with higher human development index values also showed higher incidence HIV/AIDS and AIDS-Tuberculosis. **CONCLUSION:** The prevention of HIV infection must be geographically specific, given socioeconomic and cultural differences. Although official records show decline in AIDS-TB co-infection, treatment

of cases of HIV/AIDS should observe the occurrence of opportunistic diseases, which should be notified and/or updated.

695 NGOYI, E. N. O.; OBENGUI; TATY, R. T.; KOU MBA, E. L.; NGALA, P.; IBARA, R. B. O. **[Mycobacterial species reparation: experience of the Antituberculosis Center in Pointe Noire (Republic of Congo).] Repartition des especes de mycobacteries dans une serie de tuberculoses pulmonaires au Centre antituberculeux de Pointe Noire (Republique du Congo).** *Bulletin de la Societe de Pathologie Exotique* (2014) **107** (5) 342-345 Paris, France; Springer-Verlag France [Fr, en, 5 ref.] Departement de microbiologie et hematologic, Faculte des sciences de la sante de Brazzaville, Brazzaville, Congo. Email: esther_mul1er2003@yahoo.fr

The aim of the present work was to describe mycobacteria species isolated in the antituberculosis center of Pointe-Noire city in Congo Brazzaville. It was a descriptive transversal study, conducted between September 2008 and April 2009 (7 months). A simple random sample was established from patients who came to the antituberculosis center of Pointe-Noire City (reference center on diagnosis and treatment of tuberculosis). To those patients consulting with symptoms leading to suspect pulmonary tuberculosis, a sputum sampling in three sessions was conducted. Staining techniques to Ziehl-Neelsen and auramine were performed in Pointe-Noire. Culture, molecular hybridization and antibiotic susceptibility testing to first-line antituberculosis drugs (isoniazid, rifampicin, ethambutol, pyrazinamide or streptomycin) using diffusion method on agar were performed in Cerba Pasteur laboratory in France. In 77 patients, 24 sputum (31.20%) were positive to the microscopic examination and 45 (58.44%) to the culture and identification by molecular hybridization. *Mycobacteria species* complex

isolated were *M. tuberculosis* with 31 cases (68.9%) and *M. africanum* with 3 cases (6.67%). Non-tuberculous mycobacteria (NMT) were isolated in association or not with *M. tuberculosis* in 9 cases (20%) and the most common species were *M. intracellulare*. In *M. tuberculosis* species, 7 strains (41.20%) were tested sensitive to the first-line antituberculosis drugs, 8 cases (47%) mono-resistance and 2 cases multidrug resistance at both isoniazide and rifampicine (12%) (MDR). This study showed the importance of Mycobacteria species complex and non-mycobacteria species in pulmonary tuberculosis. The data on resistance can help medical physicians in the treatment of pulmonary tuberculosis. Another study with a large population is required to confirm these data.

696 DOKUBO, E. K.; BADDELEY, A.; PATHMANATHAN, I.; COGGIN, W.; FIRTH, J.; GETAHUN, H.; KAPLAN, J.; DATE, A. **Provision of antiretroviral therapy for HIV-positive TB patients-19 countries, sub-Saharan Africa, 2009-2013.** *Morbidity and Mortality Weekly Report* (2014) **63** (47) 1104-1107 Atlanta, USA; Epidemiology Program Office, Centers for Disease Control and Prevention (CDC) [En, 10 ref.] Division of Global HIV/AIDS, Center for Global Health, CDC, Atlanta, Georgia, USA. Email: kdokubo@cdc.gov

Of the 9 million new cases of tuberculosis (TB) disease globally in 2013, an estimated 1.1 million (13%) were among persons living with HIV; of the 1.5 million deaths attributed to TB in 2013, a total of 360000 (24%) were among persons living with HIV. ART reduces the incidence of HIV-associated TB disease, and early initiation of ART after the start of TB treatment reduces progression of HIV infection and death among HIV-positive TB patients. To assess the progress in scaling up ART provision among HIV-positive TB patients in 19 countries in sub-Saharan Africa with high TB and HIV burdens, TB and HIV data collected by the

World Health Organization (WHO) were reviewed. The results found that the percentage of HIV-positive TB patients receiving ART increased from 37% in 2010 to 69% in 2013. However, many TB cases among persons who are HIV-positive go unreported, and only 38% of the estimated number of HIV-positive new TB patients received ART in 2013. Although progress has been made, the combination of TB and HIV continues to pose a threat to global health, particularly in sub-Saharan Africa.

697 ZEEUW, J. DE; DOUWSTRA, M.; OMANSEN, T. F.; SOPOH, G. E.; JOHNSON, C.; PHILLIPS, R. O.; ALFERINK, M.; SAUNDERSON, P.; WERF, T. S. VAN DER; DIJKSTRA, P. U.; STIENSTRA, Y. **Psychometric properties of the participation scale among former Buruli ulcer patients in Ghana and Benin.** *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3254 San Francisco, USA; Public Library of Sciences (PLoS) [En, 26 ref.] Department of Internal Medicine/Infectious Diseases, University Medical Center Groningen, University of Groningen, Groningen, Netherlands. Email: j.de.zeeuw@umcg.nl

BACKGROUND: *Buruli ulcer* is a stigmatising disease treated with antibiotics and wound care, and sometimes surgical intervention is necessary. Permanent limitations in daily activities are a common long term consequence. It is unknown to what extent patients perceive problems in participation in social activities. The psychometric properties of the Participation Scale used in other dis-abling diseases, such as leprosy, was assessed for use in former *Buruli ulcer* patients. **METHODS:** Former *Buruli ulcer* patients in Ghana and Benin, their relatives, and healthy community controls were interviewed using the Participation Scale, *Buruli ulcer* Functional Limitation Score, and the Explanatory Model Interview Catalogue to measure stigma. The Participation Scale was tested for the following psychometric properties:

discrimination, floor and ceiling effects, internal consistency, inter-item correlation, item-total correlation and construct validity. **RESULTS:** In total 386 participants (143 former *Buruli ulcer* patients with their relatives (137) and 106 community controls) were included in the study. The Participation Scale displayed good discrimination between former *Buruli ulcer* patients and healthy community controls. No floor and ceiling effects were found. Internal consistency (Cronbach's alpha) was 0.88. In Ghana, mean inter-item correlation of 0.29 and item-total correlations ranging from 0.10 to 0.69 were found while in Benin, a mean inter-item correlation of 0.28 was reported with item-total correlations ranging from -0.08 to 0.79. With respect to construct validity, 4 out of 6 hypotheses were not rejected, though correlations between various constructs differed between countries. **CONCLUSION:** The results indicate the Participation Scale has acceptable psychometric properties and can be used for *Buruli ulcer* patients in Ghana and Benin. Future studies can use this Participation Scale to evaluate the long term restrictions in participation in daily social activities of former BU patients.

698 BERRINGTON, W. R.; KUNWAR, C. B.; NEUPANE, K.; EEDEN, S. J. F. VAN DEN; VARY, J. C., J.R.; PETERSON, G. J.; WELLS, R. D.; GELUK, A.; HAGGE, D. A.; HAWN, T. R. **Differential dermal expression of CCL17 and CCL18 in tuberculoid and lepromatous leprosy.** *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3263 San Francisco, USA; Public Library of Sciences (PLoS) [En, 35 ref.] University of Washington School of Medicine, Seattle, Washington, USA. Email: berring@uw.edu

BACKGROUND: Leprosy is characterized by polar clinical, histologic and immunological presentations. Previous immunologic studies of leprosy polarity were limited by the repertoire of

cytokines known at the time. **METHODOLOGY:** We used a candidate gene approach to measure mRNA levels in skin biopsies from leprosy lesions. mRNA from 24 chemokines and cytokines, and 6 immune cell type markers were measured from 85 Nepalese leprosy subjects. Selected findings were confirmed with immunohistochemistry. **PRINCIPAL RESULTS:** Expression of three soluble mediators (CCL18, CCL17 and IL-10) and one macrophage cell type marker (CD14) was significantly elevated in lepromatous (CCL18, IL-10 and CD14) or tuberculoid (CCL17) lesions. Higher CCL18 protein expression by immunohistochemistry and a trend in increased serum CCL18 in lepromatous lesions was observed. No cytokines were associated with erythema nodosum leprosum or Type 1 reversal reaction following multiple comparison correction. Hierarchical clustering suggested that CCL18 was correlated with cell markers CD209 and CD14, while neither CCL17 nor CCL18 were highly correlated with classical TH1 and TH2 cytokines. **CONCLUSIONS:** Our findings suggest that CCL17 and CCL18 dermal expression is associated with leprosy polarity.

699 PETERS, R. M. H.; DADUN; BRAKEL, W. H. VAN; ZWEEKHORST, M. B. M.; DAMAYANTI, R.; BUNDERS, I. F. G.; IRWANTO **The cultural validation of two scales to assess social stigma in leprosy.** *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3274 San Francisco, USA; Public Library of Sciences (PLoS) [En, 55 ref.] Athena Institute, Faculty of Earth and Life Sciences, VU University, Amsterdam, Netherlands. Email: r.m.h.peters@vu.nl

BACKGROUND: Stigma plays an important role in the lives of persons affected by neglected tropical diseases, and assessment of stigma is important to document this. The aim of this study is to test the cross-cultural validity of the Community Stigma Scale (EMIC-CSS) and the

Social Distance Scale (SDS) in the field of leprosy in Cirebon District, Indonesia. **METHODOLOGY/PRINCIPLE FINDINGS:** Cultural equivalence was tested by assessing the conceptual, item, semantic, operational and measurement equivalence of these instruments. A qualitative exploratory study was conducted to increase our understanding of the concept of stigma in Cirebon District. A process of translation, discussions, trainings and a pilot study followed. A sample of 259 community members was selected through convenience sampling and 67 repeated measures were obtained to assess the psychometric measurement properties. The aspects and items in the SDS and EMIC-CSS seem equally relevant and important in the target culture. The response scales were adapted to ensure that meaning is transferred accurately and no changes to the scale format (e.g. layout, statements or questions) of both scales were made. A positive correlation was found between the EMIC-CSS and the SDS total scores ($r=0.41$). Cronbach's alphas of 0.83 and 0.87 were found for the EMIC-CSS and SDS. The exploratory factor analysis indicated for both scales an adequate fit as unidimensional scale. A standard error of measurement of 2.38 was found in the EMIC-CSS and of 1.78 in the SDS. The test-retest reliability coefficient was respectively, 0.84 and 0.75. No floor or ceiling effects were found. **CONCLUSIONS/SIGNIFICANCE:** According to current international standards, our findings indicate that the EMIC-CSS and the SDS have adequate cultural validity to assess social stigma in leprosy in the Bahasa Indonesia-speaking population of Cirebon District. We believe the scales can be further improved, for instance, by adding, changing and rephrasing certain items. Finally, we provide suggestions for use with other neglected tropical diseases.

700 GEORGE, P. J.; KUMAR, N. P.; RATHINAM

SRIDHAR; HANNA, L. E.; DINA NAIR; BANUREKHA, V. V.; NUTMAN, T. B.; SUBASH BABU
Coincident helminth infection modulates systemic inflammation and immune activation in active pulmonary tuberculosis. *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3289 San Francisco, USA; Public Library of Sciences (PLoS) [En, 41 ref.] National Institutes of Health-NIRT-International Center for Excellence in Research, Chennai, India. Email: sbabu@mail.nih.gov

BACKGROUND: Helminth infections are known to modulate innate and adaptive immune responses in active and latent tuberculosis (TB). However, the role of helminth infections in modulating responses associated with inflammation and immune activation (reflecting disease activity and/or severity) in TB is not known. **METHODOLOGY:** We measured markers of inflammation and immune activation in active pulmonary TB individuals (ATB) with co-incident *Strongyloides stercoralis* (Ss) infection. These included systemic levels of acute phase proteins, matrix metalloproteinases and their endogenous inhibitors and immune activation markers. As a control, we measured the systemic levels of the same molecules in TB-uninfected individuals (NTB) with or without Ss infection. **PRINCIPAL FINDINGS:** Our data confirm that ATB is associated with elevated levels of the various measured molecules when compared to those seen in NTB. Our data also reveal that co-incident Ss infection in ATB individuals is associated with significantly decreased circulating levels of acute phase proteins, matrix metalloproteinases, tissue inhibitors of matrix metalloproteinases as well as the systemic immune activation markers, sCD14 and sCD163. These changes are specific to ATB since they are absent in NTB individuals with Ss infection. **CONCLUSIONS:** Our data therefore reveal a profound effect of Ss infection on the

markers associated with TB disease activity and severity and indicate that co-incident helminth infections might dampen the severity of TB disease.

701 ZEEUW, J. DE; OMANSEN, T. F.; DOUWSTRA, M.; BAROGUI, Y. T.; AGOSSADOU, C.; SOPOH, G. E.; PHILLIPS, R. O.; JOHNSON, C.; ABASS, K. M.; SAUNDERSON, P.; DIJKSTRA, P. U.; WERF, T. S. VAN DER; STIENTSTRA, Y.
Persisting social participation restrictions among former *Buruli ulcer* patients in Ghana and Benin. *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3303 San Francisco, USA; Public Library of Sciences (PLoS) [En, 31 ref.] Department of Internal Medicine/Infectious Diseases, University Medical Center Groningen, University of Groningen, Groningen, Netherlands. Email: j.de.zeeuw@umcg.nl

BACKGROUND: *Buruli ulcer* may induce severe disabilities impacting on a person's well-being and quality of life. Information about long-term disabilities and participation restrictions is scanty. The objective of this study was to gain insight into participation restrictions among former *Buruli ulcer* patients in Ghana and Benin. **METHODS:** In this cross-sectional study, former *Buruli ulcer* patients were interviewed using the Participation Scale, the *Buruli ulcer* Functional Limitation Score to measure functional limitations, and the Explanatory Model Interview Catalogue to measure perceived stigma. Healthy community controls were also interviewed using the Participation Scale. Trained native interviewers conducted the interviews. Former *Buruli ulcer* patients were eligible for inclusion if they had been treated between 2005 and 2011, had ended treatment at least 3 months before the interview, and were at least 15 years of age. **RESULTS:** In total, 143 former *Buruli ulcer* patients and 106 community controls from Ghana and Benin were included in the study. Participation restrictions

were experienced by 67 former patients (median score, 30, IQR; 23;43) while 76 participated in social life without problems (median score 5, IQR; 2;9). Most restrictions encountered related to employment. Linear regression showed being female, perceived stigma, functional limitations, and larger lesions (category II) as predictors of more participation restrictions. **CONCLUSION:** Persisting participation restrictions were experienced by former BU patients in Ghana and Benin. Most important predictors of participation restrictions were being female, perceived stigma, functional limitations and larger lesions.

702 PIERI, F. M.; TOUSO, M. M.; RODRIGUES, L. B. B.; YAMAMURA, M.; PINTO, I. C.; DESSUNTI, E. M.; CRISPIM, J. DE A.; RAMOS, A. C. V.; ARROYO, L. H.; SANTOS NETO, M.; GARCIA, M. C. DA C.; POPOLIN, M. P.; SILVEIRA, T. R. DOS S.; ARCENCIO, R. A. **Patients perceptions on the performance of a local health system to eliminate leprosy, Parana State, Brazil.** *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3324 San Francisco, USA; Public Library of Sciences (PLoS) [En, 42 ref.] Department of Nursing, Universidade Estadual de Londrina, Londrina, Parana, Brazil. Email: ricardo@eerp.usp.br

BACKGROUND: In Brazil, leprosy has been listed among the health priorities since 2006, in a plan known as the "Pact for life" (Pactopela Vida). It is the sole country on the American continent that has not reached the global goal of disease elimination. Local health systems face many challenges to achieve this global goal. The study aimed to investigate how patients perceive the local health system's performance to eliminate leprosy and whether these perceptions differ in terms of the patients' income. **METHODOLOGY/PRINCIPAL FINDINGS:** A cross-sectional study was conducted in Londrina, State of Parana, Brazil. Interviews were performed with the leprosy patients. The local health system was assessed

through a structured and adapted tool, considering the domains judged as good quality of health care. The authors used univariate, bivariate and multivariate analyses. One hundred and nineteen patients were recruited for the study, 50.4% (60) of them were male, 54.0% (64) were between 42 and 65 years old and 66.3% (79) had finished elementary school. The results showed that patients used the Primary Health Care service near their place of residence but did not receive the leprosy diagnosis there. Important advances of this health system were verified for the elimination of leprosy, verifying protocols for good care delivery to the leprosy patients, but these services did not develop collective health actions and did not engage the patients' family members and community. **CONCLUSIONS/SIGNIFICANCE:** The patients' difficulty was observed to have access to the diagnosis and treatment at health services near their homes. Leprosy care is provided at the specialized level, where the patients strongly bond with the teams. The care process is individual, with limited perspectives of integration among the health services for the purpose of case management and social mobilization of the community to the leprosy problem.

703 NERY, J. S.; PEREIRA, S. M.; RASELLA, D.; PENNA, M. L. F.; AQUINO, R.; RODRIGUES, L. C.; BARRETO, M. L.; PENNA, G. O. **Effect of the Brazilian conditional cash transfer and primary health care programs on the new case detection rate of leprosy.** *PLoS Neglected Tropical Diseases* (2014) **8** (11) e3357 San Francisco, USA; Public Library of Sciences (PLoS) [En, 59 ref.] Federal University of Bahia, Institute of Collective Health, Salvador, Bahia, Brazil. Email: joilda_nery@yahoo.com.br

BACKGROUND: Social determinants can affect the transmission of leprosy and its progression to disease. Not much is known about the

effectiveness of welfare and primary health care policies on the reduction of leprosy occurrence. The aim of this study is to evaluate the impact of the Brazilian cash transfer (Bolsa Familia Program-BFP) and primary health care (Family Health Program-FHP) programs on new case detection rate of leprosy. **METHODOLOGY/ PRINCIPAL FINDINGS:** We conducted the study with a mixed ecological design, a combination of an ecological multiple-group and time-trend design in the period 2004-2011 with the Brazilian municipalities as unit of analysis. The main independent variables were the BFP and FHP coverage at the municipal level and the out-come was new case detection rate of leprosy. Leprosy new cases, BFP and FHP coverage, population and other relevant socio-demographic covariates were obtained from national databases. We used fixed-effects negative binomial models for panel data adjusted for relevant socio-demographic covariates. A total of 1,358 municipalities were included in the analysis. In the studied period, while the municipal coverage of BFP and FHP increased, the new case detection rate of leprosy decreased. Leprosy new case detection rate was significantly reduced in municipalities with consolidated BFP coverage (Risk Ratio 0.79; 95% CI=0.7470.83) and significantly increased in municipalities with FHP coverage in the medium (72-95%) (Risk Ratio 1.05; 95% CI=1.02-1.09) and higher coverage tertiles (>95%) (Risk Ratio 1.12; 95% CI=1.08-1.17). **CONCLUSIONS:** At the same time the Family Health Program had been effective in increasing the new case detection rate of leprosy in Brazil, the Bolsa Familia Program was associated with a reduction of the new case detection rate of leprosy that we propose reflects a reduction in leprosy incidence.

1068 BRATSCHI, M. W.; BOLZ, M.; GRIZE, L.; KERBER, S.; MINYEM, J. C.; BOOCK, A. U.; YEBOARMANU, D.; RUF, M. T.; PLUSCHKE, G.

Primary cultivation: factors affecting contamination and *Mycobacterium ulcerans* growth after long turnover time of clinical specimens. *BMC Infectious Diseases* (2014) **14** (636) (30 November 2014) London, UK; BioMed Central Ltd [En, 20 ref.] Swiss Tropical and Public Health Institute, Basel, Switzerland. Email: martin.bratschi@unibas.ch

BACKGROUND: While cultivation of pathogens represents a foundational diagnostic approach in the study of infectious diseases, its value for the confirmation of clinical diagnosis of *Buruli ulcer* is limited by the fact that colonies of *Mycobacterium ulcerans* appear only after about eight weeks of incubation at 30°C. However, for molecular epidemiological and drug sensitivity studies, primary isolation of *M. ulcerans* remains an essential tool. Since for most of the remote *Buruli ulcer* endemic regions of Africa cultivation laboratories are not easily accessible, samples from lesions often have to be stored for extended periods of time prior to processing. The objective of the current study therefore was to determine which transport medium, decontamination method or other factors decrease the contamination rate and increase the chance of primary isolation of *M. ulcerans* bacilli after long turnover time. **METHODS:** Swab and fine needle aspirate (FNA) samples for the primary cultivation were collected from clinically confirmed *Buruli ulcer* patients in the Mape Basin of Cameroon. The samples were either stored in the semi-solid transport media 71-19 or Amies or dry for extended period of time prior to processing. In the laboratory, four decontamination methods and two inoculation media were evaluated and statistical methods applied to identify factors that decrease culture contamination and factors that increase the probability of *M. ulcerans* recovery. **RESULTS:** The analysis showed: (i) that the use of moist transport media significantly increased the

recovery rate of *M. ulcerans* compared to samples kept dry; (ii) that the choice of the decontamination method had no significant effect on the chance of *M. ulcerans* isolation; and (iii) that Lowenstein-Jensen supplemented with antibiotics as inoculation medium yielded the best results. We further found that, ten extra days between sampling and inoculation lead to a relative decrease in the isolation rate of *M. ulcerans* by nearly 20%. Finally, collection and processing of multiple samples per patient was found to significantly increase the *M. ulcerans* isolation rate. CONCLUSIONS: Based on our analysis we suggest a procedure suitable for the primary isolation of *M. ulcerans* strains from patients following long delay between sample collection and processing to establish a *M. ulcerans* strain collection for research purposes.

1069 ABOUYANNIS, M.; DACOMBE, R.; DAMBE, L; MPUNGA, J.; FARAGHER, B.; GAUSI, F.; NDHLOVU, H.; KACHIZA, C.; SUAREZ, P.; MUNDY, C.; BANDA, H. T.; NYASULU, I.; SQUIRE, S. B. **Drug resistance of *Mycobacterium tuberculosis* in Malawi: a cross-sectional survey.** *Bulletin of the World Health Organization* (2014) **92** (11) 798-806 Geneva, Switzerland; World Health Organization [En, ar, ch, fr, ru, es, 28 ref.] Centre for Applied Health Research & Delivery, Department of Clinical Sciences, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, UK. Email: bertie.squire@lstm.ac.uk

OBJECTIVE: To document the prevalence of multidrug resistance among people newly diagnosed with - and those retreated for - tuberculosis in Malawi. METHODS: We conducted a nationally representative survey of people with sputum-smear-positive tuberculosis between 2010 and 2011. For all consenting participants, we collected demographic and clinical data, two sputum samples and tested for human immunodeficiency virus (HIV). The samples

underwent resistance testing at the Central Reference Laboratory in Lilongwe, Malawi. All *Mycobacterium tuberculosis* isolates found to be multidrug-resistant were retested for resistance to first-line drugs - and tested for resistance to second-line drugs - at a Supranational Tuberculosis Reference Laboratory in South Africa. FINDINGS: Overall, *M. tuberculosis* was isolated from 1777 (83.8%) of the 2120 smear-positive tuberculosis patients. Multidrug resistance was identified in five (0.4%) of 1196 isolates from new cases and 28 (4.8%) of 581 isolates from people undergoing retreatment. Of the 31 isolates from retreatment cases who had previously failed treatment, nine (29.0%) showed multidrug resistance. Although resistance to second-line drugs was found, no cases of extensive drug-resistant tuberculosis were detected. HIV testing of people from whom *M. tuberculosis* isolates were obtained showed that 577 (48.2%) of people newly diagnosed and 386 (66.4%) of people undergoing retreatment were positive. CONCLUSION: The prevalence of multidrug resistance among people with smear-positive tuberculosis was low for sub-Saharan Africa - probably reflecting the strength of Malawi's tuberculosis control programme. The relatively high prevalence of such resistance observed among those with previous treatment failure may highlight a need for a change in the national policy for retreating this subgroup of people with tuberculosis.

1070 SAURABH SINGH; KAVISH CHOUHAN; SOMESH GUPTA **Intralesional immunotherapy with killed *Mycobacterium indicus pranii* vaccine for the treatment of extensive cutaneous warts.** *Indian Journal of Dermatology, Venereology & Leprology* (2014) **80** (6) 509-514 Mumbai, India; Medknow Publications [En, 31 ref.] Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi - 110

029, India.

BACKGROUND: Multiple cutaneous warts in adults are often symptomatic, cosmetically disabling, and difficult to treat. Killed *Mycobacterium indicus pranii* (previously known as *Mycobacterium w*, popularly known as Mw) vaccine has earlier been investigated in genital warts with encouraging results. **OBJECTIVE:** To evaluate the efficacy and safety profile of intralesional injected killed Mw vaccine for the treatment of extensive extragenital cutaneous warts. **METHODS:** In this study, a retrospective analysis of medical records was performed in patients with cutaneous warts treated with intralesional Mw vaccine. Only patients with more than 5 extra-genital warts, involving at least two body sites and which had not shown any signs of spontaneous regression over 6 months were treated with the vaccine. **RESULTS:** Forty four patients were treated with intralesional Mw vaccine. The mean number of warts was 41.5 ± 25.7 with a disease duration of 3.1 ± 2.5 years. Complete clearance was achieved in 24 (54.5%) patients with a mean of 3.4 ± 1.1 intralesional injections. Cosmetically acceptable response to therapy (>75% clearance) was achieved in 37 (84.1%) patients. Wart response at distant sites was seen in 38 (86.3%) patients. Thirty-six patients (81.8%) experienced mild therapy-related side effects. Eighteen patients with complete response were followed up for 5.27 ± 1.7 months and none had recurrence of lesions. **CONCLUSIONS:** Killed Mw vaccine is safe and effective in the treatment of extensive cutaneous warts. Larger, preferably randomized controlled trials are needed to assess its efficacy vis a vis standard therapies for warts.

1071 IFFAT HASSAN; KAISAR AHMAD; ATIYA YASEEN **Pattern of pediatric dermatoses in Kashmir valley: a study from a tertiary care center.** *Indian Journal of Dermatology, Venereo-*

logy & Leprology (2014) **80** (5) 448-451 Mumbai, India; Medknow Publications [En, 7 ref.] Department of Dermatology, Sexually Transmitted Diseases and Leprosy and Pediatrics, Government Medical College Srinagar, University of Kashmir, Jammu and Kashmir, India.

A cross-sectional study was conducted to document the types of skin disorders prevalent among children aged up to 16 years in Kashmir Valley, Jammu and Kashmir, India. 1079 consecutive children attending the dermatology, STD and leprosy outpatient department of SMHS Hospital (672 children) and the paediatrics outpatient department of GB Pant Hospital (407 children) from December 2012 to July 2013 were enrolled. They were grouped as infants (day 1-1 year old), preschool children (2-5 years old), school children (6-10 years old) and adolescents (11-16 years old). A detailed general, systemic and cutaneous examination was done and relevant investigations were carried out when necessary. Of the 1079 patients examined, the preschool children comprised 35.5%, followed by infants (33.2%), school children (19%) and adolescents (12.3%). The male:female ratio was 1.4:1. Out of the 407 children attending the paediatrics outpatient department, 128 patients had no cutaneous findings. 76 dermatoses were recorded and divided into 16 groups. Considering the individual dermatoses, the top 10 were Mongolian spot (10.2%), papular urticaria (8.9%), tinea capitis (6.9%), pityriasis alba (5.2%), molluscum contagiosum (4.2%), scabies (3.9%), seborrhoeic eczema (3.9%), impetigo (3.7%), varicella (2.5%) and haemangiomas (1.9%). Among infections, viral infections were the most common, followed by fungal, bacterial, parasitic and mycobacterial. Mycobacterial infections consisted of one case each of lupus vulgaris and scrofuloderma. The most common type of eczema was pityriasis alba. Pigmentation disorders were seen in 14.1% cases,

with Mongolian spot being the most common (71.9%). Among other pigmentation disorders, vitiligo accounted for 42% of cases, followed by nevus anemicus, ephelides, lichen striatus and melasma. In the hypersensitivity disorder, papular urticaria (8.9% of all dermatoses) was predominantly seen in preschool children. Acne constituted 3.2% of all disorders. Keratinization disorders included cases of lamellar ichthyosis, non-bullous ichthyosiform erythroderma and diffuse palmoplantar keratodermas. Papulosquamous disorders accounted for 1.8% of all cases and included psoriasis, lichen planus and pityriasis rosea. Among hair disorders, alopecia areata (52.6%) was the most predominant followed by telogen effluvium (21%), canities (15.8%), androgenetic alopecia (5.3%) and monelithrix (5.3%). Sweat gland disorders included miliaria and hyperhidrosis. Neurocutaneous disorders encompassed Sturge-Weber syndrome, seen in 2 preschool boys, a single case of neurofibromatosis type 1 in a pre-school boy and 4 cases of tuberous sclerosis in school children and adolescents. Among photodermatoses, polymorphic light eruption was the most common. A case of Kindler's syndrome in a 3-year-old girl was also documented. Five cases of epidermolysis bullosa were. Nutritional and metabolic disorders such as acrodermatitis enteropathica and congenital erythropoietic porphyria comprised 0.4% of all disorders. Miscellaneous disorders (7.7%) included acanthosis nigricans, infantile haemangiomas, milia, Epstein pearls, lanugo hairs, toxic erythema of the neonate, aphthous ulcers, physiological changes of the neonate like desquamation, steroid rosacea, keloids, lipoma, morphea, collodion baby with polydactyly, congenital geographic tongue and haemosiderosis. It is concluded that skin disorders are common in children in the Kashmir valley with infections forming the largest

group, followed by pigmentary disorders and eczemas.

1072 COX, H. S.; MBHELE, S.; MOHESS, N.; WHITELAW, A.; MULLER, O.; ZEMANAY, W.; LITTLE, F.; AZEVEDO, V.; SIMPSON, J.; BOEHME, C. C.; NICOL, M. P. **Impact of Xpert MTB/RIF for TB diagnosis in a primary care clinic with high TB and HIV prevalence in South Africa: a pragmatic randomised trial.** *PLoS Medicine* (2014) **11** (11) e1001760 San Francisco, USA; Public Library of Sciences (PLoS) [En, 22 ref.] Division of Medical Microbiology and Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa. Email: Helen.cox@uct.ac.za

BACKGROUND: Xpert MTB/RIF is approved for use in tuberculosis (TB) and rifampicin-resistance diagnosis. However, data are limited on the impact of Xpert under routine conditions in settings with high TB burden. **METHODS AND FINDINGS:** A pragmatic prospective cluster-randomised trial of Xpert for all individuals with presumptive (symptomatic) TB compared to the routine diagnostic algorithm of sputum microscopy and limited use of culture was conducted in a large TB/HIV primary care clinic. The primary out-come was the proportion of bacteriologically confirmed TB cases not initiating TB treatment by 3 mo after presentation. Secondary outcomes included time to TB treatment and mortality. Unblinded randomisation occurred on a weekly basis. Xpert and smear microscopy were performed on site. Analysis was both by intention to treat (ITT) and per protocol. Between 7 September 2010 and 28 October 2011, 1,985 participants were assigned to the Xpert (n=982) and routine (n=1,003) diagnostic algorithms (ITT analysis); 882 received Xpert and 1,063 routine (per protocol analysis). 13% (32/257) of individuals with bacteriologically confirmed TB (smear, culture, or Xpert) did not

initiate treatment by 3 mo after presentation in the Xpert arm, compared to 25% (41/167) in the routine arm (ITT analysis, risk ratio 0.51, 95% CI 0.33-0.77, $p=0.0052$). The yield of bacteriologically confirmed TB cases among patients with presumptive TB was 17% (167/1,003) with routine diagnosis and 26% (257/982) with Xpert diagnosis (ITT analysis, risk ratio 1.57, 95% CI 1.32-1.87, $p<0.001$). This difference in diagnosis rates resulted in a higher rate of treatment initiation in the Xpert arm: 23% (229/1,003) and 28% (277/982) in the routine and Xpert arms, respectively (ITT analysis, risk ratio 1.24, 95% CI 1.06-1.44, $p=0.013$). Time to treatment initiation was improved overall (ITT analysis, hazard ratio 0.76, 95% CI 0.63-0.92, $p=0.005$) and among HIV-infected participants (ITT analysis, hazard ratio 0.67, 95% CI 0.53-0.85, $p=0.001$). There was no difference in 6-mo mortality with Xpert versus routine diagnosis. Study limitations included incorrect intervention allocation for a high proportion of participants and that the study was conducted in a single clinic. CONCLUSIONS: These data suggest that in this routine primary care setting, use of Xpert to diagnose TB increased the number of individuals with bacteriologically confirmed TB who were treated by 3 mo and reduced time to treatment initiation, particularly among HIV-infected participants.

1073 HOLM, L. L.; ROSE, M. V.; KIMARO, G.; BYGBJERG, I. C.; MFINANGA, S. G.; RAVN, P.; RUHWALD, M. **A comparison of interferon- γ and IP-10 for the diagnosis of tuberculosis.** *Pediatrics* (2014) **134** (6) e1568-e1575 Elk Grove Village, USA; American Academy of Pediatrics [En] Clinical Research Centre, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark. OBJECTIVE: Interferon- γ and IP-10 release assays are diagnostic tests for tuberculosis infection. We have compared the accuracy of IP-10 and

QuantiFERON-TB Gold In-tube [QFT-IT] in Tanzanian children suspected of having active tuberculosis (TB). METHODS: Hospitalized Tanzanian children with symptoms of TB were tested with the QFT-IT and IP-10 tests and retrospectively classified into diagnostic groups. Adults with confirmed TB were assessed in parallel. RESULTS: A total of 203 children were included. The median age was 3.0 years (interquartile range: 1.2-7.0), 38% were HIV infected, 36% were aged <2 years, and 58% had a low weight-for-age. IP-10 and QFT-IT test performance was comparable but sensitivity was low: 33% (1 of 3) in children with confirmed TB and 29% (8 of 28) in children with probable TB. Rates of indeterminate responders were high: 29% (59 of 203) for IP-10 and 26% (53 of 203) for QFT-IT. Age <2 years was associated with indeterminate test outcome for both IP-10 (adjusted odds ratio [aOR]: 2.2; $P=.02$) and QFT-IT (aOR: 2.4; $P=.01$). TB exposure was associated with positive IP-10 test out-come (aOR: 3.6; $P=.01$) but not with positive QFT-IT outcome (aOR 1.4; $P=.52$). In 102 adults, test sensitivity was 80% for both tests ($P=.248$). CONCLUSIONS: Although IP-10 and QFT-IT performed well in Tanzanian adults, the tests exhibited an equally poor performance in diagnosing active TB in children. Test performance was especially compromised in young children. Neither test can be recommended for use in hospitalized children in high-burden settings.

1074 WASSERMAN, S.; MEINTJES, G. **The diagnosis, management and prevention of HIV-associated tuberculosis.** *SAMJ - South African Medical Journal* (2014) **104** (12) 886-893 Pretoria, South Africa; S AMA Health and Medical Publishing Group [En] Division of Infectious Diseases and HIV Medicine, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa. Email:

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Tuberculosis (TB) and its strong association with HIV infection are the most important causes of the high rates of infectious morbidity and mortality in South African adults. The interaction between HIV and TB leads to more frequent smear-negative and extrapulmonary disease, resulting in atypical clinical presentations and altered performance characteristics of diagnostic tests. New and emerging diagnostics are being used to support earlier initiation of therapy and detection of drug resistance, although these have inherent limitations and empirical therapy is often still required. The management of HIV-associated TB is complicated by rapid clinical progression of disease, immune reconstitution inflammatory syndrome, drug-drug interactions and shared toxicities. A strong evidence base now provides guidance on the timing of initiation of antiretroviral therapy, the use of corticosteroids in TB and the use of isoniazid preventive therapy. This article provides a clinically oriented overview of the diagnosis, management and prevention of HIV-associated TB, with a focus on recent evidence in the field.

1075 KASSIM, M. A.; BAUNATH, H.; ODHAV, B. **Effect of traditional leafy vegetables on the growth of lactobacilli and bifidobacteria.** *International Journal of Food Sciences and Nutrition* (2014) **65** (8) 977-980 London, UK; Informa Healthcare [En] Department of Biotechnology and Food Technology, Durban University of Technology, Durban, South Africa. Email: muhammad.kassim@wits.ac.za

Traditional leafy vegetables, apart from being a staple in the diet of most of sub-Saharan Africa, are an essential part of traditional medicine and are used daily by traditional healers in the region to treat a wide variety of ailments. In this study, a batch culture technique was used to investigate whether 25 infusions from 22 traditional leafy

vegetables stimulated the growth of *Lactobacillus bulgaricus*, *Lactobacillus lactis*, *Lactobacillus reuteri* and *Bifidobacterium longum* in pure culture. High performance liquid chromatography was used to determine the inulin content of the infusions. *Sonchus oleraceus* stimulated all four strains and *Taraxacum officinale* stimulated three strains. In total, 18 plants stimulated at least one of the four probiotic strains. The inulin content of the infusions varied between 2.5% and 3.6%, with *Asparagus sprengeri* containing the highest percentage. These results indicate that traditional leafy vegetables do stimulate the growth of the selected lactobacilli and bifidobacteria in pure culture and contain inulin. These infusions can now be tested for prebiotic potential using mixed culture systems or human hosts.

1076 INGRAM, P. R.; CHENG, A. C.; MURRAY, R. J.; BLYTH, C. C.; WALLS, T.; FISHER, D. A.; DAVIS, J. S. **What do infectious diseases physicians do? A 2-week snapshot of inpatient consultative activities across Australia, New Zealand and Singapore.** *Clinical Microbiology and Infection* (2014) **20** (10) 0737-0744 Oxford, UK; Wiley-Blackwell [En, 26 ref.] Department of Microbiology and Infectious Diseases, Royal Perth Hospital, Perth, 6000 WA, Australia. Email: paul.ingram@health.wa.gov.au

The practice of an infectious diseases (ID) physician is evolving. A contemporary understanding of the frequency and variety of patients and syndromes seen by ID services has implications for training, service development and setting research priorities. We performed a 2-week prospective survey of formal ID physician activities related to direct inpatient care, encompassing 53 hospitals throughout Australia, New Zealand and Singapore, and documented 1722 inpatient interactions. Infections involving the skin and soft tissue, respiratory tract and

bone/joints together accounted for 49% of all consultations. Susp & tedkonfirmed pathogens were primarily bacterial (60%), rather than viral (6%), fungal (4%), mycobacterial (2%) or parasitic (1%). *Staphylococcus aureus* was implicated in 409 (24%) episodes, approximately four times more frequently than the next most common pathogen. The frequency of healthcare-related infections (35%), immunosuppression (21%), diabetes mellitus (19%), prosthesis-related infections (13%), multiresistant pathogens (13%) and non-infectious diagnoses (9%) was high, although consultation characteristics varied between geographical settings and hospital types. Our study highlights the diversity of inpatient-related ID activities and should direct future teaching and research. 1D physicians ability to offer beneficial consultative advice requires broad understanding of, and ability to interact with, a wide range of referring specialities.

1077 ERDEM, H.; OZTURK-ENGİN, D.; ELALDI, N.; GULSUN, S.; SENGOZ, G.; CRISAN, A.; JOHANSEN, I. S.; NAN, A.; NECHIFOR, M.; ALMAHDAWI, A.; CIVLJAK, R.; OZGULER, M.; SAVIC, B.; CERAN, N.; CACOPARDO, B.; INAL, A. S.; NAMIDURU, M.; DAYAN, S.; KAYABAS, U.; PARLAK, E.; KHALIFA, A.; KURSUN, E.; SIPAHI, O. R.; YEMISEN, M.; AKBULUT, A.; BITIRGEN, M. (ET AL) **The microbiological diagnosis of tuberculous meningitis: results of Haydarpasa-1 study.** *Clinical Microbiology and Infection* (2014) **20** (10) 0600-0608 Oxford, UK; Wiley-Blackwell [En, 27 ref.] Department of Infectious Diseases and Clinical Microbiology, GATA Haydarpasa Training Hospital, Istanbul, Turkey. Email: hakanerdem1969@yahoo.com

We aimed to provide data on the diagnosis of tuberculous meningitis (TBM) in this largest case series ever reported. The Haydarpasa-1 study involved patients with microbiologically confir-

med TBM in Albania, Croatia, Denmark, Egypt, France, Hungary, Iraq, Italy, Macedonia, Romania, Serbia, Slovenia, Syria and Turkey between 2000 and 2012. A positive culture, PCR or Ehrlich-Ziehl-Neelsen staining (EZNs) from the cerebrospinal fluid (CSF) was mandatory for inclusion of meningitis patients. A total of 506 TBM patients were included. The sensitivities of the tests were as follows: interferon- γ release assay (Quantiferon TB gold in tube) 90.2%, automated culture systems (ACS) 81.8%, Lowenstein Jensen medium (L-J) 72.7%, adenosine deaminase (ADA) 29.9% and EZNs 27.3%. CSF-ACS was superior to CSF L-J culture and CSF-PCR ($p < 0.05$ for both). Accordingly, CSF L-J culture was superior to CSF-PCR ($p < 0.05$). Combination of L-J and ACS was superior to using these tests alone ($p < 0.05$). There were poor and inverse agreements between EZNs and L-J culture ($K = -0.189$); ACS and L-J culture ($K = -0.172$) ($p < 0.05$ for both). Fair and inverse agreement was detected for CSF-ADA and CSF-PCR ($c = -0.299$, $p < 0.05$). Diagnostic accuracy of TBM was increased when both ACS and L-J cultures were used together. Non-culture tests contributed to TBM diagnosis to a degree. However, due to the delays in the diagnosis with any of the cultures, combined use of non-culture tests appears to contribute early diagnosis. Hence, the diagnostic approach to TBM should be individualized according to the technical capacities of medical institutions particularly in those with poor resources.

1078 GOK, S. E.; KAPTANOGLU, E.; CELIKBAS, A.; ERGONUL, O.; BAYKAM, N.; EROGIU, M.; DOKUZOGUZ, B. **Vertebral osteomyelitis: clinical features and diagnosis.** *Clinical Microbiology and Infection* (2014) **20** (10) 1055-1060 Oxford, UK; Wiley-Blackwell [En, 20 ref.] Infectious Diseases and Clinical Microbiology Clinic, Ankara Numune Training and Research Hospital, Ankara, Turkey. Email- oergonul@ku.edu.tr

We aimed to describe clinical and diagnostic features of vertebral osteomyelitis for differential diagnosis and treatment. This is a prospective observational study performed between 2002 and 2012 in Ankara Numune Education and Research Hospital in Ankara, Turkey. All the patients with vertebral osteomyelitis were followed for from 6 months to 3 years. In total, 214 patients were included in the study, 113 out of 214 (53%) were female. Out of 214 patients, 96 (45%) had brucellar vertebral osteomyelitis (BVO), 63 (29%) had tuberculous vertebral osteomyelitis (TVO), and 55 (26%) had pyogenic vertebral osteomyelitis (PVO). Mean number of days between onset of symptoms and establishment of diagnosis was greater with the patients with TVO (266 days) than BVO (115 days) or PVO (151 days, $p < 0.001$). In blood cultures, *Brucella* spp. were isolated from 35 of 96 BVO patients (35%). Among 55 PVO patients, the aetiological agent was isolated in 11 (20%) patients. For tuberculin skin test >15 mm, sensitivity was 0.66, specificity was 0.97, positive predictive value was 0.89, negative predictive value was 0.88, and receiver operating characteristics area was 0.8. Tuberculous and brucellar vertebral osteomyelitis remained the leading causes of vertebral osteomyelitis with delayed diagnosis. In differential diagnosis of vertebral osteomyelitis, consumption of unpasteurized cheese, dealing with husbandry, sweating, arthralgia, hepatomegaly, elevated alanine transaminase, and lumbar involvement in magnetic resonance imaging were found to be predictors of BVO, thoracic involvement in magnetic resonance imaging and tuberculin skin test >15 mm were found to be predictors of TVO, and history of spinal surgery and leucocytosis were found to be predictors of PVO.

1079 WAH WAR AUNG; THANDAR LWIN; PHYU WIN EI; FONG HORWAI; THIRUCHELVAN

NADARAJAN; TIN TIN MAR; WINT WINT NYUNT; NAN AYE THIDAR OO; MI MI HTWE
Evaluation of a microarray nanotechnology-based test for diagnosis of tuberculosis.

Myanmar Health Sciences Research Journal (2014) **26** (1) 81-82 Yangon, Myanmar; Department of Medical Research, Ministry of Health [En, 2 ref.] Bacteriology Research Division, Department of Medical Research, Lower Myanmar, Myanmar. This study was carried out to evaluate the validity of TB protein biochip test for the diagnosis of tuberculosis (TB) in a clinical setting, and to determine the presence and relevance of TB-specific antigenic protein markers among TB patients in Myanmar. Blood serum samples were collected from new TB patients (aged 12 years) attending a TB health centre in Yangon, Myanmar during 2010-2011. All patients showed reactivity to all 5 antigenic markers tested, namely liparabinomannan, polyclonal 38 KDa, polyclonal 16 KDa, early secretory antigenic target 6, and culture filtrate protein 10. The sensitivity, specificity, and positive and negative predictive values of the TB protein biochip test were 60.25%, 67.84%, 62.0% and 66.44%, respectively.

1080 NDWANDWE, Z. S. I.; MAHOMED, S.; LUTGE, E.; KNIGHT, S. E. **Factors affecting nonadherence to tuberculosis treatment in uMgungundlovu Health District in 2010.** *Southern African Journal of Epidemiology & Infection* (2014) **29** (2) 56-59 Johannesburg, South Africa; South African Institute for Medical Research [En, 20 ref.] School of Laboratory Medicine and Medical Science, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa. Email: mahomeds@ukzn.ac.za

KwaZulu-Natal has a high burden of tuberculosis disease, and is currently not meeting national and international treatment out-come targets. The aim of this study was to investigate patient-related and socio-economic factors that affect

treatment adherence in patients on tuberculosis treatment in uMgungundlovu Health District. A case-control study design was used. Three hundred cases (treatment interruption) and 300 controls (treatment completed) were interviewed by trained fieldworkers using a structured questionnaire. In bivariate analysis, lack of education, unemployment and other socio-economic indicators (low income, type of housing, sanitation and residential area) were associated with an increased risk of treatment interruption. Personal factors [smoking, drug and alcohol use, human immunodeficiency virus (HIV) co-infection and perceived severity of illness] were also risk factors for treatment interruption. In multivariate analysis, distance from the clinic was significantly associated with treatment interruption [adjusted odds ratio (OR) 1.3, 95% confidence interval (CI): 1.3-1.6, (p-value <0.005)], as well as residing in a rural area (adjusted OR 1.4, 95% CI: 1.1-1.8, p-value <0.005). Patients co-infected with HIV were twice as likely to interrupt treatment (adjusted OR 2.3, 95% CI: 1.1-4.7, p-value <0.005), and feeling very or fairly ill during tuberculosis treatment was also significantly associated with treatment interruption (adjusted OR 5.0, 95% CI: 2.1-11.9, p-value <0.005). The results highlight the complex interaction between personal and socio-economic risk factors for treatment interruption.

1081 TSHITANGANO, T. G. **Measures practised by healthcare workers to prevent tuberculosis transmission at rural hospitals in Vhembe district.** *Southern African Journal of Epidemiology & Infection* (2014) **29** (2) 65-69 Johannesburg, South Africa; South African Institute for Medical Research [En, 25 ref.] Department of Public Health, University of Venda, Thohoyandou, South Africa. Email: takalani.tshitangano@univen.ac.za

The risk of becoming infected with tuberculosis in healthcare settings is increasing daily. Of every 100 hospitalised patients at any given time, seven in developed, and 10 in developing, countries, will acquire at least one infection in a health-care setting, including tuberculosis. This study assessed measures practised by healthcare workers (HCWs) to prevent tuberculosis transmission at rural hospitals of Vhembe district. A qualitative approach using a cross-sectional descriptive phenomenology design was adopted. Purposive sampling was used to select 57 participants for focus group discussions. The necessary approval, permission and clearance were obtained. Participants rights were respected. The findings of this study revealed that the majority of tuberculosis infection control measures practised by HCWs were incorrect, and not aligned with national and international tuberculosis infection control standards. It was concluded that the incorrect measures that were practised might increase the risk of HCWs becoming infected with tuberculosis at rural hospitals in Vhembe district. The development and implementation of a tuberculosis infection control plan at hospital level would ensure that tuberculosis infection control measures practised by HCWs at hospitals in Vhembe district would reduce the chance of them acquiring tuberculosis at these hospitals.

1082 MALANGU, N.; NTULL S. T.; ALBERTS, M. **Causes of death in patients treated at a tertiary hospital in the Limpopo province: a retrospective study from 2008-2010.** *Southern African Journal of Epidemiology & Infection* (2014) **29** (2) 80-86 Johannesburg, South Africa; South African Institute for Medical Research [En, 22 ref.] Department of Epidemiology and Biostatistics, University of Limpopo, Medunsa Campus, Gauteng, South Africa. Email: gustavmalangu@gmail.com

The aim of this study was to determine mortality rates and identify associated causes at a tertiary hospital situated in the Limpopo province of South Africa. Death notification forms from Pietersburg Mankweng Hospital Complex were retrieved and reviewed for the period 1 January 2008-31 December 2010 in this cross-sectional study. Data were collected using a data collection form designed for the study. There were 5 232 deaths, on which there was complete information for 5 147, which was then analysed. The average death rate was 6.8 deaths per 1 000 patients, based on the number of patients admitted during the study period. The age of the deceased ranged from 15-104 years, with a mean of 49.1±18.6 years. While only 2.4% of deaths occurred in teenagers, over two thirds occurred in people aged 20-59 years. Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS), cancer, cardiovascular disease, trauma and tuberculosis were the top five most common causes of death, and were responsible for 61.2% of all recorded deaths. Trauma was the most common cause of death in teenagers, and HIV/AIDS the most common cause in young adults and adults. Cardiovascular disease was the main cause of death in the elderly. Overall, the triple burden of infectious diseases, noncommunicable diseases (NCDs) and injury remain the leading causes of death in patients at the study site. Innovative injury prevention strategies and interventions to control the spread of infectious diseases are urgently required. Cancer screening services and culturally appropriate lifestyle programmes are needed to address NCDs.

1083 LOUWAGIE, G.; AYOYUSUF, O.A. **Factors associated with retreatment tuberculosis in tshwane, South Africa: the role of tobacco smoking.** *Southern African Journal of Epidemiology & Infection* (2014) **29** (2) 87-90 Johannesburg, South Africa; South African Institute for

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There is evidence from international studies that tobacco smoking increases the risk of tuberculosis recurrence through its effects on the immunological and barrier functions of the airways. In this cross-sectional study, the association between current tobacco smoking and retreatment tuberculosis was studied in a population of 1 926 South African tuberculosis patients with high human immunodeficiency virus (HIV) co-infection rates. Retreatment tuberculosis was more common in male and among HIV-positive participants currently on antiretroviral treatment, or with unknown antiretroviral treatment status. However, we did not find an association between smoking and retreatment tuberculosis. A longitudinal study is needed to confirm these findings.

1084 NGAIMISI, E.; MINZI, O.; MUGUSI, S.; SASI, P.; RIEDEL, K. D.; SUDA, A.; UEDA, N.; BAKARI, M.; JANABI, M.; MUGUSI, F.; BERTILSSON, L.; BURHENNE, J.; AKLILLU, E.; DICZFALUSY, U. **Pharmacokinetic and pharmacogenomic modelling of the CYP3A activity marker 40-hydroxycholesterol during efavirenz treatment and efavirenz/rifampicin co-treatment.** *Journal of Antimicrobial Chemotherapy* (2014) **69** (12) 3311-3319 Oxford, UK; Oxford University Press [En, 34 ref.] Department of Pharmacognosy, Unit of Pharmacology and Therapeutics, School of Pharmacy, Muhimbili University of Health and Allied Sciences, PO Box 65013, Dar es Salaam, Tanzania. Email: engaimisi@gmail.com

OBJECTIVES: To assess the effect of the major efavirenz metabolizing enzyme (CYP2 B6) genotype and the effects of rifampicin co-treatment on induction of CYP3A by efavirenz.

PATIENTS AND METHODS: Two study arms (arm 1, n=41 and arm 2, n=21) were recruited into this study. In arm 1, cholesterol and 413-hydroxycholesterol were measured in HIV treatment-naive patients at baseline and then at 4 and 16 weeks after initiation of efavirenz-based antiretroviral therapy. In arm 2, cholesterol and 413-hydroxycholesterol were measured among patients taking efavirenz during rifampicin-based tuberculosis (TB) treatment (efavirenz/rifampicin) just before completion of TB treatment and then serially following completion of TB treatment (efavirenz alone). Nonlinear mixed-effect modelling was performed. **RESULTS:** A one-compartment, enzyme turnover model described 4[3-hydroxycholesterol kinetics adequately. Efavirenz treatment in arm 1 resulted in 1.74 (relative standard error=15%), 3.3 (relative

standard error=33.1%) and 4.0 (relative standard error=37.1%) average fold induction of CYP3A for extensive (CYP2 B6*1/*1), intermediate (CYP2 B6*1/*6) and slow (CYP2 B6*6/*6) efavirenz metabolizers, respectively. The rate constant of 40-hydroxycholesterol formation [mean (95% CI)] just before completion of TB treatment [efavirenz/rifampicin co-treatment, 7.40×10^{-7} h⁻¹ (5.5×10^{-7} - 1.0×10^{-6})] was significantly higher than that calculated 8 weeks after completion [efavirenz alone, 4.50×10^{-7} h⁻¹ (4.40×10^{-7} - 4.52×10^{-7})]. The CYP3A induction dropped to 62% of its maximum by week 8 of completion. **CONCLUSIONS:** Our results indicate that efavirenz induction of CYP3A is influenced by CYP2 B6 genetic polymorphisms and that efavirenz/rifampicin co-treatment results in higher induction than efavirenz alone.