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2559 KARSTAEDT, A. S. **Extrapulmonary tuberculosis among adults: experience at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa.** *SAMJ - South African Medical Journal* (2014) **104** (1) 22-24 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 14 ref.] Division of Infectious Diseases, Department of Medicine, Chris Hani Baragwanath Hospital and University of the Witwatersrand, Johannesburg, South Africa. Email: karstaedt@mweb.co.za

BACKGROUND: Extrapulmonary tuberculosis (EPTB) occurs in 15-20% of immunocompetent and 20-70% of HIV-infected patients with tuberculosis. There are few recent incidence data for EPTB. **METHODS:** Adults (N=2 963) with culture-proven EPTB seen over 2 years at Chris Hani Baragwanath Academic Hospital, the main referral hospital serving Soweto, Johannesburg, South Africa, were retrospectively studied for pattern and incidence. **RESULTS:** The commonest sites of EPTB were the pleura (39.1%), lymph nodes (31.0%), blood (21.8%), meninges (7.3%), and peritoneum (2.9%). Disseminated tuberculosis occurred in 25.0%. The median age was 33 years (range 18-87 years). Males comprised 53.2% overall, with a female majority in the peritonitis group. For Soweto, the incidence of adult EPTB was 88.6/100 000 population, rising to 139.4/100 000 and 125.7/100 000 in the 25-34-year and 35-44-year age groups,

respectively. There was no secondary peak in the elderly (17.9/100 000). **CONCLUSIONS:** This retrospective cohort showed a high incidence of EPTB, most marked in the 25-44-year age group. Culture of extrapulmonary sites is of importance to confirm diagnosis of tuberculosis and to ensure antituberculosis drug susceptibility testing.

2560 WATT, J. P.; DAVIS, J. H. **Percutaneous core needle biopsies: the yield in spinal tuberculosis.** *SAMJ - South African Medical Journal* (2014) **104** (1) 29-32 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 15 ref.] Department of Orthopaedic Surgery, Stellenbosch University, Stellenbosch Central, Stellenbosch 7600, South Africa. Email: johanhedavis@gmail.com

BACKGROUND: Current recommendations for spinal tuberculosis (TB) not requiring open surgery include core needle biopsy to confirm TB and determine drug sensitivity. International figures show the positive culture yield from core needle biopsies is 50-83%. **OBJECTIVES:** To (i) assess the yield of percutaneous needle biopsies; (ii) identify factors that may lead to a negative result; and (iii) determine whether, TB being suspected, needle biopsy is justified. **METHODS:** We conducted a multicentre retrospective review of 44 patients treated for suspected spinal TB between January 2009 and April 2012, who did not require open surgery. Data captured included demographics, relevant history, outcome of

investigations and histopathological findings in patients. RESULTS: The overall positive TB culture rate was 59%. Age, duration of symptoms, HIV and neurological status, erythrocyte sedimentation rate and cell count had no statistical influence. Of the 7 patients receiving TB treatment at the time of biopsy, 3 were culture-positive. Multidrug resistance was evident in 12% of positive cultures. The positive culture yield was 40% at Tygerberg Hospital and 75% at Groote Schuur Hospital, with no difference in histological yield. This was attributed to the practice of decontaminating specimens prior to culture at Tygerberg Hospital. The highest culture yield (32%) came from samples showing non-necrotising chronic inflammatory changes. Conclusion. Percutaneous biopsy remains an important tool to diagnose and manage spinal TB. The yield of transpedicular biopsies in this study was comparable with international figures. Specimen decontamination prior to culture had a direct negative influence on biopsy culture yield, as did prior TB treatment.

2561 GRINSZTEJN, B.; HOSSEINIPOUR, M. C.; RUIBAUDO, H. J.; SWINDELLS, S.; ERON, J.; CHEN, Y. Q.; WANG, L.; OU, S. S.; ANDERSON, M.; MCCAULEY, M.; GAMBLE, T.; KUMARASAMY, N.; HAKIM, J. G.; KUMWENDA, J.; PILOTO, J. H. S.; GODBOLE, S. V.; CHARIYA-LERTSAK, S.; MEMO, M. G. DE; MAYER, K. H.; ESHLEMAN, S. H.; PIWOWAR-MANNING, E.; MAKHEMA, J.; MILLS, L. A.; PANCHIA, R.; SANNE, I.; GALLANT, J. (ET AL)
Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. *Lancet Infectious Diseases* (2014) **14** (4) 281-290 Oxford, UK; Elsevier Ltd [En, 32 ref.] Fred Hutchinson Cancer Research Center, Seattle, Washington, USA. Email: mscohen@med.unc.edu

BACKGROUND: Use of antiretroviral treatment for HIV-1 infection has decreased AIDS-related morbidity and mortality and prevents sexual transmission of HIV-1. However, the best time to initiate antiretroviral treatment to reduce progression of HIV-1 infection or non-AIDS clinical events is unknown. We reported previously that early antiretroviral treatment reduced HIV-1 transmission by 96%. We aimed to compare the effects of early and delayed initiation of antiretroviral treatment on clinical outcomes. METHODS: The HPTN 052 trial is a randomised controlled trial done at 13 sites in nine countries. We enrolled HIV-1-serodiscordant couples to the study and randomly allocated them to either early or delayed antiretroviral treatment by use of permuted block randomisation, stratified by site. Random assignment was unblinded. The HIV-1-infected member of every couple initiated antiretroviral treatment either on entry into the study (early treatment group) or after a decline in CD4 count or with onset of an AIDS-related illness (delayed treatment group). Primary events were AIDS clinical events (WHO stage 4 HIV-1 disease, tuberculosis, and severe bacterial infections) and the following serious medical conditions unrelated to AIDS: serious cardiovascular or vascular disease, serious liver disease, end-stage renal disease, new-onset diabetes mellitus, and non-AIDS malignant disease. Analysis was by intention-to-treat. This trial is registered with ClinicalTrials.gov, number NCT00074581. FINDINGS: 1763 people with HIV-1 infection and a serodiscordant partner were enrolled in the study; 886 were assigned early antiretroviral treatment and 877 to the delayed treatment group (two individuals were excluded from this group after randomisation). Median CD4 counts at randomisation were 442 (IQR 373-522) cells per μm^3 in patients assigned to the early treatment

group and 428 (357-522) cells per μL in those allocated delayed antiretroviral treatment. In the delayed group, antiretroviral treatment was initiated at a median CD4 count of 230 (IQR 197-249) cells per μL . Primary clinical events were reported in 57 individuals assigned to early treatment initiation versus 77 people allocated to delayed antiretroviral treatment (hazard ratio 0.73, 95% CI 0.52-1.03; $p=0.074$). New-onset AIDS events were recorded in 40 participants assigned to early antiretroviral treatment versus 61 allocated delayed initiation (0.64, 0.43-0.96; $p=0.031$), tuberculosis developed in 17 versus 34 patients, respectively (0.49, 0.28-0.89, $p=0.018$), and primary non-AIDS events were rare (12 in the early group vs nine with delayed treatment). In total, 498 primary and secondary outcomes occurred in the early treatment group (incidence 24.9 per 100 person-years, 95% CI 22.5-27.5) versus 585 in the delayed treatment group (29.2 per 100 person-years, 26.5-32.1; $p=0.025$). 26 people died, 11 who were allocated to early antiretroviral treatment and 15 who were assigned to the delayed treatment group. INTERPRETATION: Early initiation of antiretroviral treatment delayed the time to AIDS events and decreased the incidence of primary and secondary outcomes. The clinical benefits recorded, combined with the striking reduction in HIV-1 transmission risk previously reported, provides strong support for earlier initiation of antiretroviral treatment.

2562 PEREZ-GUZMAN, C.; VARGAS, M.H.; ARELLANO-MACIAS, M. R.; HERNANDEZ-COBOS, S.; GARCIA-ITUARTE, A. Z.; SERNA-VELA, F. J. **Clinical and epidemiological features of extrapulmonary tuberculosis in a high incidence region.** *Salud Publica de Mexico* (2014) **56** (2) 189-196 Cuernavaca, Mexico; Instituto Nacional de Salud Publica [En, es, 36 ref.] Secretaria de Salud

del Estado de Aguascalientes, Aguascalientes, Mexico. Email: mhvargasb@yahoo.com.mx

OBJECTIVE: To describe the clinical features of extrapulmonary tuberculosis (EXPTB) and to evaluate epidemiological data to search for potential explanations for its high frequency in the state of Aguascalientes, Mexico. MATERIALS AND METHODS: Clinical records of all patients with tuberculosis seen in Aguascalientes in 2008 were reviewed, and official databases were analyzed. RESULTS: EXPTB comprised 60.5% of the 86 cases evaluated, being lymph nodes the main site affected. Patients with EXPTB were younger and more obese than subjects with pulmonary tuberculosis (PTB). One third of cases in either group had diabetes, a frequency much higher than expected. Epidemiological analysis showed that PTB incidence, but not EXPTB incidence, decreases as geographical altitude increases, and had a descendent trend from 1997 to 2011. CONCLUSIONS: The lower frequency of PTB (due to its inverse relationship with altitude and its descendent trend in last years) might explain the high frequency of EXPTB. Obesity appeared to protect against developing pulmonary involvement, and diabetes was more frequent than expected among PTB and EXPTB cases.

2563 JEONG, J. C.; KOO, T. Y.; JEON, H. J.; PARK, H. C.; RYU, H. J.; LEE, J. P.; MIN, S. I.; HWANG, Y. H.; HA, J.; AHN, C.; YANG, J. **Utility of QuantiFERON-TB assay for prediction of tuberculosis development in kidney transplant patients in an intermediate-tuberculosis burden country: lack of evidence for enhanced prediction for short-term tuberculosis development.** *In 13th Congress of the Asian Society of Transplantation: Advances in Kidney Transplantation, Kyoto, Japan, 3-6 September 2013. Transplantation*

Proceedings (2014) **46** (2) 583-587 New York, USA; Elsevier [En] Transplantation Center, Seoul National University Hospital, 101 Daehak-no, Jongno-gu, Seoul 110-744, Korea Republic. Email: jcyjs@dreamwiz.com, jcyjs@snu.ac.kr

INTRODUCTION: Although a latent tuberculosis (TB) infection is a risk factor for active TB, the diagnosis of latent TB infection is difficult in end-stage renal disease patients. **PATIENTS AND METHODS:** We retrospectively compared the results of the QuantiFERON-TB (QFT) test and the tuberculin skin test in patients on the waiting list for kidney transplantation (KT), and investigated whether the QFT test can predict TB development in KT recipients in an intermediate-TB-burden country. **RESULTS:** The incidence of post-KT TB was 283 cases/100,000 patient-years among 1274 KT recipients at the Seoul National University Hospital. The overall standardized incidence ratio of TB was 4.358 compared with the general population. A past history of TB infection, smoking history, myocardial infarction after KT, and pneumocystis infection were significant predictors of subsequent TB development (adjusted odds ratios were 3.618, 2.959, 9.993, and 5.708, respectively). Among the 129 recipients who had the QFT test, 42 patients (32.5%) had positive a QFT. At a median follow-up of 8.4±6.8 months, 1 patient with positive QFT results developed TB after KT, and 1 of the 87 patients with negative QFT results developed TB after KT. In both of these 2 cases, active TB developed despite isoniazid prophylaxis. Among 272 patients on the waiting list for KT, the tuberculin skin test and QFT were positive in 22.8% and 35.3%, respectively. The degree of agreement between the 2 tests was poor ($\kappa=0.352$). **CONCLUSIONS:** The QFT test did not predict subsequent short-term TB development.

Furthermore, a long-term and larger-scale study is needed to confirm our results.

2564 NIEKERK, L. VAN; RAUBENHEIMER, P. J. **A point-prevalence survey of public hospital inpatients with palliative care needs in Cape Town, South Africa.** *SAMJ - South African Medical Journal* (2014) **104** (2) 138-141 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 19 ref.] Department of Medicine, University of Cape Town and Groote Schuur Hospital, Cape Town, South Africa. Email: peter.raubenheimer@uct.ac.za

OBJECTIVES: To assess the need for palliative care among inpatients occupying acute beds in the public sector hospitals of the Cape Town Metropole. **METHODS:** A cross-sectional, contemporaneous, point-prevalence study was performed at 11 public sector hospitals in the Cape Town Metropole using a standardised palliative care identification tool. Data were collected on the socio-demographic characteristics, diagnoses, and prior and current care planning of patients. **RESULTS:** The case notes of 443 hospital inpatients were surveyed, and 16.6% were found to have an active life-limiting disease. The mean age of the group was 56 years. The diagnoses were cancer in 50.8%, organ failure in 32.5%, and HIV/ tuberculosis in 9.6%. The greatest burden of disease was in the general medical wards, to which an overall 54.8% of patients meeting the requirements for palliative care were admitted. **CONCLUSIONS:** This study provides evidence for the need for palliative care services in public sector hospitals and in the health system as a whole. The young age of patients and the high prevalences of end-stage renal failure and HIV are unique, and the burden in the general medical wards suggests a focus for initial inpatient programmes.

2565 CONRADIE, F.; MEINTJES, G.; HUGHES, J.; MAARTENS, G.; FERREIRA, H.; SIWENDU, S.; MASTER, I.; NDJEKA, N. **Clinical Access to Bedaquiline Programme for the treatment of drug-resistant tuberculosis.** *SAMJ - South African Medical Journal* (2014) **104** (3) 164-166 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 5 ref.] School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa. Email: fconradie@witshealth.co.za

While clinical disease caused by drug-sensitive *Mycobacterium tuberculosis* (MTB) can usually be treated successfully, clinical disease caused by drug-insensitive MTB is associated with a poorer prognosis. In December 2012, a new drug, bedaquiline, was approved by the US Food and Drug Administration. This article documents the process whereby the National Department of Health, Right to Care and Medecins Sans Frontieres obtained access to this medication for South Africans who might benefit from subsequent implementation of the Clinical Access to Bedaquiline Programme.

2566 ONYENEKWU, C. P.; ZEMLIN, A. E.; ERASMUS, R. T. **High pleural fluid adenosine deaminase levels: a valuable tool for rapid diagnosis of pleural TB in a middle-income country with a high TB/HIV burden.** *SAMJ - South African Medical Journal* (2014) **104** (3) 200-203 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 17 ref.] Division of Chemical Pathology, Faculty of Health Sciences, National Health Laboratory Service, Stellenbosch University, Cape Town, South Africa. Email: azemlin@sun.ac.za

BACKGROUND: South Africa has the highest burden of tuberculosis (TB) in the World Health Organization (WHO) African region. Using

traditional TB diagnostic tools, the diagnosis of pleural TB (PTB) is highly unrewarding. Elevated levels of pleural fluid adenosine deaminase (FADA) have been shown to be useful in the diagnosis of PTB; however, similar levels may be found in some other medical conditions leading to misdiagnosis. Following queries from clinicians concerning the likely high false-positive (FP) rate of FADA from our laboratory, we performed a retrospective audit of all high FADA results generated over a 12-month period. OBJECTIVES: To determine the positive predictive value (PPV) of FADA, the frequent causes of FPs in our laboratory and the demographic characteristics of tuberculous pleural effusions (TPEs) and non-tuberculous pleural effusions (NTPEs). METHODS: High FADA results generated in the past year were extracted with corresponding TB culture results, fluid cell count, cytology/histology results, radiology reports and HIV results. Hospital records were reviewed for the final diagnosis in each case. Diagnosis of PTB was based on the WHO case definition of TB. RESULTS: A total of 159 results were reviewed: 133 (83.6%) were TPE, hence. FADA had a PPV of 83.6%. Neoplasm was the most common cause of an FP in 13/26 (50%) NTPEs. While TPE was more common than NTPE in younger people, both groups had an equal gender distribution. CONCLUSION: FADA had a high PPV for PTB in our laboratory. We recommend its continued use as a rapid and reliable diagnostic tool for PTB.

2567 NOESKE, J.; NDI, N.; ELO, G. A.; MFONDIH, S. M. **Tuberculosis incidence in Cameroonian prisons: a 1-year prospective study.** *SAMJ - South African Medical Journal* (2014) **104** (3) 209-211 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 11 ref.] National Tuberculosis Programme,

Yaounde, Cameroon. Email: juergennoeske@yahoo.fr

BACKGROUND: Rates of tuberculosis (TB) transmission in prisons are reported to be high worldwide. However, a recent systematic review identified only 19 published studies reporting TB incidence in prisons, most of them from the last century and only one from sub-Saharan Africa. **OBJECTIVES:** To assess the persisting risk of smear-positive pulmonary tuberculosis (PTB) among prison populations benefiting from a comprehensive TB/HIV control programme in Cameroon, compared with that in the community. **METHODS:** This descriptive and prospective study evaluated PTB incidence rates over a year period. The study population was inmates of 10 major prisons, sampled by convenience, comprising about 45% of the country's prison population. As PTB incident cases, all prisoners with incident PTB after a prison stay of days were considered. The prison TB incidence rate was compared with that of the corresponding male population in the community. **RESULTS:** The mean annual PTB incidence in Cameroonian prisons in this study was 1700 cases in 100 000 person-years at risk, the incidence rate ratio being 9.4 (95% confidence interval 8.1-10.9). **CONCLUSION:** Findings suggest that internationally recommended prison TB control measures alone may not help protect prisoners from within-prison spread of TB. Imprisonment policies and conditions therefore require fundamental changes.

2568 ABRAHAM, P. R.; LATHA, G. S.; VALIURI, V. L.; SANGITA MUKHOPADHYAY ***Mycobacterium tuberculosis* PPE protein Rv0256c induces strong B cell response in tuberculosis patients. In 11^o congress Molecular Epidemiology and**

Evolutionary Genetics of Infectious Diseases, Louisiana, USA, 30 October-2 November 2012. *Infection, Genetics and Evolution* (2014) 22 244-249 Amsterdam, Netherlands; Elsevier B.V. [En, 41 ref.] Laboratory of Molecular Cell Biology, Centre for DNA Fingerprinting and Diagnostics (CDFD), Gruhakalpa Building, Nampally, Hyderabad 500 001, India. Email: sangita@cdfd.org.in, kashbon@yahoo.com

Tuberculosis (TB) is one of the most important diseases of humans and major public health problem worldwide. Early and accurate diagnosis of TB is necessary for the treatment, prevention, and control of TB. Therefore, it is important to identify suitable antigens that can differentiate active tuberculosis patients from BCG-vaccinated individuals. In the present study, we have used Rv0256c (PPE2) protein of *Mycobacterium tuberculosis* to screen the sera of infected patients belonging to different clinical TB presentations, and BCG-vaccinated clinically healthy individuals by enzyme immunoassay. Our results demonstrated that Rv0256c displayed stronger and specific immunoreactivity against the sera obtained from clinically active tuberculosis patients compared to PPD and ESAT-6 and could differentiate the TB-patients from the BCG-vaccinated controls. Importantly, Rv0256c was also found to detect even the extrapulmonary and smear-negative pulmonary cases which often are tedious and difficult to detect using conventional diagnostic methods. This study suggests that Rv0256c can be used as a potential marker for the serodiagnosis of tuberculosis patients.

2569 AKINTOLA, O.; HANGULU, L. **Infection control in homebased care for people living with HIV/AIDS/TB in South Africa: An exploratory study. *Global Public Health* (2014) 9 (4) 382-393**

Abingdon, UK; Routledge [En, 19 ref.] School of Applied Human Sciences, University of KwaZulu-Natal, Durban, South Africa. Email: akintolao@ukzn.ac.za

The majority of HIV and AIDS patients in sub-Saharan African countries receive health care services at home. Yet research on infection control in home-based care settings is virtually non-existent. This study explored infection control practices in home-based care in a South African province with a high HIV/TB prevalence. We conducted interviews with 10 managers of home-based care organizations and 10 focus group discussions with 80 volunteer caregivers working in high HIV/TB prevalent communities in South Africa. Findings show that volunteers had insufficient training on infection control. Materials necessary for the maintenance of hygiene and protective equipment were in short supply and the protective equipment supplied was of poor quality. Home-based care patients lived in crowded and poor conditions, and family members were negatively disposed to the use of protective devices. Together, these factors put volunteers and family caregivers at risk of infection with HIV and TB. Health policy should address the training of volunteer caregivers and the regular supply of good quality materials to ensure effective infection control. It is also important to educate families on infection control. Finally, there is a need to integrate HIV and TB control at the community level.

2570 FAURHOLT-JEPSEN, M.; FAURHOLT-JEPSEN, D.; RANGE, N.; PRAYGOD, G.; JEREMIAH, K.; AABYE, M. G.; CHANGALUCHA, J.; KRARUP, H.; CHRISTENSEN, D. L.; ANDERSEN, A. B.; BRAGE, S.; FRIIS H. **The use of combined heart rate response and accelerometry to assess the level and predictors of physical activity in tuberculosis**

patients in Tanzania. *Epidemiology and Infection* (2014) **142** (6) 1334-1342 Cambridge, UK; Cambridge University Press [En, 22 ref.] Department of Nutrition, Exercise and Sports, University of Copenhagen, Rolighedsvej 30, 1958 Frederiksberg C, Denmark. Email: maria@faurholt-jepsen.dk

We assessed the role of tuberculosis disease and HIV infection on the level of physical activity. A combined heart rate and movement sensor was used to assess habitual physical activity in TB patients and non-TB controls. The association between sputum-negative TB, sputum positive TB, HIV and physical activity estimates were assessed in multivariable linear regression models adjusted for age, sex, haemoglobin and alpha-1-acid glycoprotein (AGP). Sputum positive [e^{β} 0.43, 95% confidence interval (CI) 0.29-0.64] and sputum-negative (e^{β} 0.67, 95% CI 0.47-0.94) TB as well as HIV infection (e^{β} 0.59, 95% CI 0.46-0.75) were associated with reduced activity compared to controls. Anaemia accounted for a substantial part of the effects of HIV, while elevated A (11) primarily mediated the TB effect. The level of physical activity is highly influenced by TB and HIV, and mainly mediated through anaemia of infection and associated with elevated acute phase response.

2571 RIPAMONTI, D.; BENATTI, S. V.; FILIPPO, E. DI; RAVASIO, V.; RIZZI, M. **Drug reaction with eosinophilia and systemic symptoms associated with raltegravir use: case report and review of the literature.** *AIDS* (2014) **28** (7) 1077-1079 Hagerstown, USA; Lippincott Williams & Wilkins, Inc. [En, 13 ref.] Ospedale Papa Giovanni XXIII, Bergamo, Italy. Email: diego.ripamonti@hotmail.com

A 39-year-old man from Cote d'Ivoire was admitted to hospital in January 2013 for low-

grade fever, weight loss and abdominal pain. He tested positive for HIV and his CD4 T-lymphocyte count was 3 cells/ μ l, HIV RNA was 4.5x10⁶ copies/ml, whereas urinalysis showed a heavy proteinuria (3 g/day), interpreted as HIV-associated nephropathy. He was empirically treated for atypical mycobacteriosis with ethambutol, azithromycin, and rifabutin (blood cultures yielded *Mycobacterium avium* few weeks later) for 6 months, and he was put on highly active antiretroviral therapy (HAART; zidovudine/lamivudine + darunavir/ritonavir) along with co-trimoxazole prophylaxis. His viral load decreased to less than 50 copies/ml and CD4+ cell count was 30 cells/ μ l at week 24 after HAART initiation. In July 2013, he developed symptomatic muscular toxicity and zidovudine/lamivudine was replaced by raltegravir (RAL), in the hypothesis of zidovudine-induced myopathy, whereas for concomitant neutropenia, co-trimoxazole was switched to atovaquone. After 4 weeks since RAL introduction, he developed fever with an itchy rash on the limbs and scalp, and painful oral aphthae. He was admitted to hospital in August 2013 and his blood tests showed an icteric cholestatic hepatitis and low-grade anaemia. In the following days, he developed a high-grade fever associated with a sharp increase in inflammatory markers and increased jaundice. Eosinophilia increased to 1320 cells. His liver biopsy showed an inflammatory infiltration, but was inconclusive. He developed severe anaemia with a haemolytic pattern, which was attributed to intravenous piperacillin/tazobactam, which he was receiving for a provisional diagnosis of bacterial cholecystitis. In suspicion of a drug reaction, he was treated with oral prednisone (0.5 mg/kg daily) for 5 days, with a rapid improvement and sudden relapse of symptoms at withdrawal. He

was restarted on prednisone (1 mg/kg daily), with prompt resolution of symptoms and a gradual improvement of the biochemical abnormalities. He was discharged home after 2 weeks in good clinical conditions. The prednisone was tapered over 8 weeks, without recurrence of symptoms. He was switched to darunavir/ritonavir and abacavir/lamivudine. He was healthy at the last follow-up visit in November 2013. A review of literature on this topic follows.

2572 YANG YING; ZHOU CHENQING; SHI LEI; MENG HECHENG; YAN HE **Prevalence and characterization of drug-resistant tuberculosis in a local hospital of northeast China.** *International Journal of Infectious Diseases* (2014) **22**, 83-86 Oxford, UK; Elsevier Ltd [En, 25 ref.] College of Light Industry and Food Sciences, South China University of Technology, Guangzhou 510640, China. Email: yanhe@scut.edu.cn

OBJECTIVES: To investigate the distribution and risk factors associated with drug-resistant tuberculosis (TB) at a local hospital in Northeast China. **METHODS:** A total of 205 patients with TB were enrolled in the study from March 8, 2010 to July 13, 2011. *Mycobacterium tuberculosis* (MTB) strains isolated from patients were subjected to drug susceptibility testing by proportion method. **Results:** Among the 205 patients with MTB, 54 (26.3%) had isolates that showed resistance to at least one drug. The overall prevalence of multidrug-resistant TB (MDR-TB) was 6.8% (n=14) (3.0% of newly diagnosed patients and 22.0% of previously treated cases). Importantly, an extensively drug-resistant TB (XDR-TB) isolate was found, which was isolated from a newly treated patient. Eleven (5.4%) were infected with a poly-resistant strain of MTB (5.5% of newly diagnosed patients and 4.9% of previously treated cases). The mono-resistance rates of

isoniazid, rifampin, ethambutol, streptomycin, ofloxacin, and kanamycin were 3.4%, 1.5%, 2.4%, 3.9%, 2.4% and 0.5%, respectively. Certain groups, including previously treated patients and male patients, were more likely to develop chug-resistant TB. CONCLUSIONS: The results of this analysis of drug resistance in MTB reflect the situation in a local hospital and indicate that the morbidity related to TB, especially M DR-TB, is still a serious health problem. Thus, the timely detection of drug resistance is of great importance to optimize treatment and to direct infection control measures to block the transmission of MDR-TB.

2573 PIETERSEN, E.; IGNATIUS, E.; STREICHER, E. M.; MASTRAPA, B.; PADANILAM, X.; POORAN, A.; BADRI, M.; LESOSKY, M., HELDEN, P VAN; SIRGEL, F. A.; WARREN, R.; DIAEDA, K. **Long-term out-comes of patients with extensively drug-resistant tuberculosis in South Africa: a cohort study.** *Lancet (British edition)* (2014) **383** (9924) 1230-1239 Oxford, UK; Elsevier Ltd [En] Lung Infection and Immunity Unit, Department of Medicine, Division of Pulmonology and University of Cape Town Lung Institute, University of Cape Town, Cape Town, South Africa. Email: keertan.dheda@uct.ac.za

BACKGROUND: Long-term treatment-related outcomes in patients with extensively drug-resistant (XDR) tuberculosis are unknown. We followed up a cohort of patients to address knowledge gaps. METHODS: Between March, 2008, and August, 2012, we prospectively followed up a cohort of 107 patients from three provinces in South Africa, who had been diagnosed with XDR tuberculosis between August 2002, and February, 2008. Available isolates from 56 patients were genotyped to establish strain type and used for extended susceptibility testing.

FINDINGS: All patients were treated empirically as inpatients with a median of eight drugs (IQR six to ten). 44 patients (41%) had HIV. 36 (64%) of 56 isolates were resistant to at least eight drugs, and resistance to an increasing number of drugs was associated with the Beijing genotype ($p=0.01$). After 24 months of follow-up, 17 patients (16%) had a favourable outcome (ie, treatment cure or completion), 49 (46%) had died, seven (7%) had defaulted (interruption of treatment for at least 2 consecutive months), and 25 (23%) had failed treatment. At 60 months, 12 patients (11%) had a favourable outcome, 78 (73%) had died, four (4%) had defaulted, and 11 (10%) had failed treatment. 45 patients were discharged from hospital, of whom 26 (58%) had achieved sputum culture conversion and 19 (42%) had failed treatment. Median survival of patients who had failed treatment from time of discharge was 19.84 months (IQR 4.16-26.04). Clustering of cases and transmission within families containing a patient who had failed treatment and been discharged were shown with genotypic methods. Net sputum culture conversion occurred in 22 patients (21%) and median time to net culture conversion was 8.7 months (IQR 5.6-26.4). Independent predictors of probability of net culture conversion were no history of multidrug-resistant tuberculosis ($p=0.0007$) and use of clofazamine ($p=0.0069$). Independent overall predictors of survival were net culture conversion ($p<0.0001$) and treatment with clofazamine ($p=0.021$). Antiretroviral therapy was also a predictor of survival in patients with HIV ($p=0.003$). INTERPRETATION: In South Africa, long-term outcomes in patients with XDR tuberculosis are poor, irrespective of HIV status. Because appropriate long-stay or palliative care facilities are scarce, substantial numbers of

patients with XDR tuberculosis who have failed treatment and have positive sputum cultures are being discharged from hospital and are likely to transmit disease into the wider community. Testing of new combined regimens is needed urgently and policy makers should implement interventions to minimise disease spread by patients who fail treatment.

2574 MARTINEZ, A. N.; TALHARI, C.; MORAES, M. O.; TALHARI, S. **PCR-based techniques for leprosy diagnosis: from the laboratory to the clinic.** *PLoS Neglected Tropical Diseases* (2014) **8** (4) e2655 San Francisco, USA; Public Library of Sciences (PLOS) [En, 100 ref.] Laboratório de Hanseníase, Instituto Oswald Cruz - Fiocruz, Rio de Janeiro, Rio de Janeiro, Brazil. Email: mmoraes@fiocruz.br

In leprosy, classic diagnostic tools based on bacillary counts and histopathology have been facing hurdles, especially in distinguishing latent infection from active disease and diagnosing paucibacillary clinical forms. Serological tests and IFN-gamma releasing assays (IGRA) that employ humoral and cellular immune parameters, respectively, are also being used, but recent results indicate that quantitative PCR (qPCR) is a key technique due to its higher sensitivity and specificity. In fact, advances concerning the structure and function of the *Mycobacterium leprae* genome led to the development of specific PCR-based gene amplification assays for leprosy diagnosis and monitoring of household contacts. Also, based on the validation of point-of-care technologies for *M. tuberculosis* DNA detection, it is clear that the same advantages of rapid DNA detection could be observed in respect to leprosy. So far, PCR has proven useful in the determination of transmission routes, *M. leprae* viability, and drug resistance in leprosy. However, PCR has

been ascertained to be especially valuable in diagnosing difficult cases like pure neural leprosy (PNL), paucibacillary (PB), and patients with atypical clinical presentation and histopathological features compatible with leprosy. Also, the detection of *M. leprae* DNA in different samples of the household contacts of leprosy patients is very promising. Although a positive PCR result is not sufficient to establish a causal relationship with disease outcome, quantitation provided by qPCR is clearly capable of indicating increased risk of developing the disease and could alert clinicians to follow these contacts more closely or even define rules for chemoprophylaxis.

2575 BOBOSHA, K.; WILSON, L.; MEIJGAARDEN, K. E. VAN; YONAS BEKELE; ZEWDIE, M.; PLOEG-VAN SCRIP, J. J. VAN DER; MARKOS ABEBE; JEMAL HUSSEIN; SARASWOTI KHADGE; NEUPANE, K. D.; HAGGE, D. A.; JORDANOVA, E. S.; ABRAHAM ASEFFA; OTTEN-HOFF, T. H. M.; GELUK, A. **T-cell regulation in lepromatous leprosy.** *PLoS Neglected Tropical Diseases* (2014) **8** (4) e2773 San Francisco, USA; Public Library of Sciences (PLOS) [En, 51 ref.] The Dept. of Infectious Diseases, Leiden University Medical Center, Leiden, Netherlands. Email: kbobosha@gmail.com

Regulatory T (T_{reg}) cells are known for their role in maintaining self-tolerance and balancing immune reactions in autoimmune diseases and chronic infections. However, regulatory mechanisms can also lead to prolonged survival of pathogens in chronic infections like leprosy and tuberculosis (TB). Despite high humoral responses against *Mycobacterium leprae* (*M. leprae*), lepromatous leprosy (LL) patients have the characteristic inability to generate T helper 1 (Th1) responses against the bacterium.

In this study, we investigated the unresponsiveness to *M. leprae* in peripheral blood mononuclear cells (PBMC) of LL patients by analysis of IFN- γ responses to *M. leprae* before and after depletion of CD25+ cells, by cell subsets analysis of PBMC and by immunohistochemistry of patients' skin lesions. Depletion of CD25+ cells from total PBMC identified two groups of LL patients: 7/18 (38.8%) gained in vitro responsiveness towards *M. leprae* after depletion of CD25+ cells, which was reversed to *M. leprae*-specific T-cell unresponsiveness by addition of autologous CD25+ cells. In contrast, 11/18 (61.1%) remained anergic in the absence of CD25+ T-cells. For both groups mitogen induced IFN- γ was, however, not affected by depletion of CD25+ cells. In *M. leprae* responding healthy controls, treated lepromatous leprosy (LL) and borderline tuberculoid leprosy (BT) patients, depletion of CD25+ cells only slightly increased the IFN- γ response. Furthermore, cell subset analysis showed significantly higher ($p=0.02$) numbers of FoxP3+ CD8+CD25+ T-cells in LL compared to BT patients, whereas confocal microscopy of skin biopsies revealed increased numbers of CD68+CD163+ as well as FoxP3+ cells in lesions of LL compared to tuberculoid and border-line tuberculoid leprosy (TT/BT) lesions. Thus, these data show that CD25+ T cells play a role in *M. leprae*-Th1 unresponsiveness in LL.

2576 PARK HEEJIN; SHIN JUNGAR; KIM HYUNGGJUNG; AHN CHULMIN; CHANG YOONSOO
Whole blood interferon- γ release assay is insufficient for the diagnosis of sputum smear negative pulmonary tuberculosis. *Yonsei Medical Journal* (2014) **55** (3) 725-731 Seoul, Korea Republic; Yonsei University College of Medicine [En, 22 ref.] Department of Internal Medicine, Yonsei University College of Medicine, 211 Eonju-

ro, Gangnamgu, Seoul 135-720, Korea Republic. Email:yschang@yuhs.ac

PURPOSE: We investigated the value of an interferon- γ release assay (IGRA) for the diagnosis of active pulmonary tuberculosis (PTB) among sputum smear negative PTB suspects in an environment with intermediate burden of PTB and high Bacillus Calmette-Guerin (BCG) vaccination rate. **MATERIALS AND METHODS:** We retrospectively reviewed IGRA, medical records, chest PA and CT scan of PTB suspects seen at Gangnam Severance Hospital, Seoul, Korea from Oct. 2007 to Apr. 2013. "Active PTB" was diagnosed when (1) *M. tuberculosis* culture positive, (2) confirmation by pathologic examination; or (3) clinical findings compatible with TB. **RESULTS:** Of 224 sputum smear negative PTB suspects, 94 were confirmed as having active PTB. There were no statistically significant differences in the diagnostic yield of IGRA between immune-compromised and immune-competent sputum smear negative PTB suspects. IGRA did show superior sensitivity 181.9%, 95% confidence interval (CI); 74.13-89.70% in the diagnosis of sputum smear negative PTB when compared with chest high-resolution computed tomography (HRCT), tuberculin skin test (TST), and chest X-ray ($p<0.001$). Also, IGRA showed highest negative predictive value (82.7%, 95% CI; 75.16-90.1.5%) when compared with HRCT, TST and chest X-ray ($p=0.023$). However, combining the results of IGRA with those of HRCT, TST, or both did not increase any diagnostic parameters. **Conclusion:** Failure to increase diagnostic yields by combination with other diagnostic modalities suggests that additional enforcement with IGRA may be insufficient to exclude other diagnoses in sputum smear negative PTB suspects and to

screen active PTB in an environment with intermediate TB prevalence and a high BCG vaccination rate.

We investigated the value of an interferon- γ release assay (IGRA) for the diagnosis of active pulmonary tuberculosis (PTB) among sputum smear negative PTB suspects in an environment with intermediate burden of PTB and high Bacillus Calmette-Guerin (BCG) vaccination rate. **MATERIALS AND METHODS:** We retrospectively reviewed IGRA, medical records, chest PA and CT scan of PTB suspects seen at Gangnam Severance Hospital, Seoul, Korea from Oct. 2007 to Apr. 2013. "Active PTB" was diagnosed when (1) M. tuberculosis culture positive, (2) confirmation by pathologic examination; or (3) clinical findings compatible with TB. **RESULTS:** Of 224 sputum smear negative PTB suspects, 94 were con-firmed as having active PTB. There were no statistically significant differences in the diagnostic yield of IGRA between immune-compromised and immune-competent sputum smear negative PTB suspects. IGR A did show superior sensitivity 181.9%, 95% confidence interval (CI); 74.13-89.70% in the diagnosis of sputum smear negative PTB when compared with chest high-resolution computed tomography (HRCT), tuberculin skin test (TST), and chest X-ray ($p < 0.001$). Also, IGRA showed highest negative predictive value (82.7%, 95% CI; 75.16-90.1.5%) when compared with HRCT, TST and chest X-ray ($p = 0.023$). However, combining the results of IGRA with those of HRCT, TST, or both did not increase any diagnostic parameters. **CONCLUSION:** Failure to increase diagnostic yields by combination with other diagnostic modalities suggests that additional enforcement with IGRA may be insufficient to exclude other diagnoses in sputum smear negative PTB suspects

and to screen active PTB in an environment with intermediate TB prevalence and a high BCG vaccination rate.

2577 PORE, S. M.; SHINDE, K. **Risk factors for drug induced hepatitis with first-line antituberculosis drugs in hospitalized patients of pulmonary tuberculosis.** *Journal of Postgraduate Medicine* (2014) **60** (1) 90-92 Mumbai, India; Medknow Publications [En, 8 ref.] Department of Pharmacology, Government Medical College, Miraj, India. This article reports on the identified risk factors for hepatitis induced by treatment with first-line antituberculosis drugs among pulmonary tuberculosis (PTB) patients ($n = 893$) admitted to the tuberculosis ward of a hospital in India between January 2005 and December 2009. The study shows that drug-induced hepatitis (DIH) is fairly common in hospitalized PTB patients, and alcohol abuse and female gender are independent risk factors for developing DIH.

2949 MIDDELKOOP, K.; BEKKER, L. G.; MORROW, C.; LEE NAMEE; WOOD, R. **Decreasing household contribution to TB transmission with age: a retrospective geographic analysis of young people in a South African township.** *BMC Infectious Diseases* (2014) **14** (221) (23 April 2014) London, UK; BioMed Central Ltd [En, 23 ref.] Desmond Tutu HIV Centre, Institute of Infectious Disease & Molecular Medicine, University of Cape Town, Cape Town, South Africa. Email: keren.middelkoop@hivresearch.org.za

BACKGROUND: Tuberculosis (TB) transmission rates are exceptionally high in endemic TB settings. Adolescence represents a period of increasing TB infection and disease but little is known as to where adolescents acquire TB infection. We explored the relationship between residential exposure to adult TB cases and infection in children and adolescents in a South

African community with high burdens of TB and HIV. **METHODS:** TB infection data were obtained from community, school-based tuberculin skin test (TST) surveys performed in 2006, 2007 and 2009. A subset of 200/ participants received a repeat TST in 2009, among, which incident TB infections were identified. Using residential address, all adult TB cases notified by the community clinic between 1996 and 2009 were cross-referenced with childhood and adolescent TST results. Demographic and clinic data including 111V status were abstracted for TB cases. Multivariate logistic regression models examined the association of adult TB exposure with childhood and adolescent prevalent and incident TB infection. **RESULTS:** Of 1,100 children and adolescents included in the prevalent TB infection analysis, 480 (44%) were TST positive and 651 (59%) were exposed to an adult TB case on their residential plot. Prevalent TB infection in children aged 5-9 and 10-14 years was positively associated with residential exposure to an adult TB case (odds ratio [OR]:2.0; 95% confidence interval [CI]: 1.1-3.6 and OR:1.5; 95% CI: 1.0-2.3 respectively), but no association was found in adolescents years (OR:1.4; 95% CI: 0.9-2.0). HIV status of adult TB cases was not associated with TB infection ($p=0.62$). Of 67 previously TST negative children, 16 (24%) converted to a positive TST in 2009. These incident infections were not associated with residential exposure to an adult TB case (OR: 1.9; 95% CI: 0.5-7.3). **CONCLUSIONS:** TB infection among young children was strongly associated with residential exposure to an adult TB case, but prevalent and incident TB infection in adolescents was not associated with residential exposure. The HIV-status of adult TB cases was not a risk factor for transmission. The high rates of TB infection and

disease among adolescents underscore the importance of identifying where infection occurs in this age group.

2950 ROMERO, M. M.; BASILE, J. I.; LOPEZ, B.; RITACCO, V.; BARRERA, L.; SASIAIN, M. DEL C.; ALEMAN, M. **Outbreaks of *Mycobacterium tuberculosis* MDR strains differentially induce neutrophil respiratory burst involving lipid rafts, p38 MAPK and Syk.** *BMC Infectious Diseases* (2014) **14** (262) (16 May 2014) London, UK; BioMed Central Ltd [En, 57 ref.] *Inmunologia de Enfermedades Respiratorias*, IMEX-CONTICET-ANM, Buenos Aires, Argentina. Email: mer_romero64@hotmail.com, juan.basile@gmail.com, bealopez@anlis.gov.ar, vri-tacco@anlis.gov.ar, lbarrera@anlis.gov.ar, mariadelcarmensasiain@hotmail.com, melealeman@hotmail.com

BACKGROUND: Neutrophils (PMN) are the first cells to infiltrate the lung after infection, and they play a significant protective role in the elimination of pathogen, by releasing preformed oxidants and proteolytic enzymes from granules and generating ROS, thus limiting inflammation by succumbing to apoptosis. In a previous study, we found marked differences in ROS-induced apoptosis between two *Mycobacterium tuberculosis* (Mtb) strains, M and Ra, representative of widespread Mtb families in South America, i.e. Haarlem and Latin-American Mediterranean (LAM), being strain M able to generate further drug resistance and to disseminate aggressively. **METHODS:** In this study we evaluate the nature of bacteria-PMN interaction by assessing ROS production, apoptosis, lipid raft coalescence, and phagocytosis induced by Mtb strains. **RESULTS:** Dectin-1 and TLR2 participate in Mtb-induced ROS generation and apoptosis in PMN involving p38

MAPK and Syk activation with the participation of a TLR2-dependent coalescence of lipid rafts. Further, ROS production occurs during the phagocytosis of nonopsonized bacteria and involves alpha-glucans on the capsule. In contrast, strain M lacks the ability to induce ROS because of: (1) a reduced phagocytosis and (2) a failure in coalescence of lipid raft. CONCLUSIONS: The differences in wall composition could explain the success of some strains which stay unnoticed by the host through inhibition of apoptosis and ROS but making possible its replication inside PMN as a potential evasion mechanism. Innate immune responses elicited by Mtb strain-to-strain variations need to be considered in TB vaccine development.

2951 O'BRIEN, D. P.; COMTE, E.; SERAHNI, M.; EHOUNOU, G.; ANTIERENS, A.; VUAGNAT, H.; CHRISTINET, V.; HAMANI, M. D.; CROS, P. DU **The urgent need for clinical, diagnostic, and operational research for management of Buruli ulcer in Africa.** *Lancet Infectious Diseases* (2014) **14** (5) 435-440 Oxford, UK; Elsevier Ltd [En, 59 ref.] Manson Unit, Medecins Sans Frontieres, Saffron Hill, London EC1N 8QX, UK. Email: daniel.obrien@amsterdam.msf.org

Despite great advances in the diagnosis and treatment of Buruli ulcer, it is one of the least studied major neglected tropical diseases. In Africa, major constraints in the management of Buruli ulcer relate to diagnosis and treatment, and accessibility, feasibility, and delivery of services. In this personal view, we outline key areas for clinical, diagnostic and operational research on this disease in Africa and propose a research agenda that aims to advance the management of buruli ulcer in Africa. A model of care is needed to increase early case detection, to diagnose the disease accurately, to y and improve

treatment, to reduce side-effects of treatment. To deal with populations with HIV and tuberculosis appropriately, to decentralise care, and to scale up coverage in populations at risk. This approach will require commitment and support to strategically implement research by national Buruli ulcer programmes and international technical and donor organisations, combined with adaptations in programme design and advocacy. A critical next step is to build consensus for a research agenda with WHO and relevant groups experienced in Buruli ulcer care or related diseases, and we call on them to help to turn this agenda into reality.

2952 WU YUYAN; GAO YUAN; ZHU BINGOING; ZHOU HAIJIAN; SHI ZHENHUA; WANG JUNSHENG; WANG HAIPO; SHAO ZHUJUN **Antitoxins for diphtheria and tetanus decline more slowly after vaccination with DTwP than with DTaP: a study in a Chinese population.** *Vaccine* (2014) **32** (22) 2570-2573 Oxford, UK; Elsevier Ltd [En, 22 ref.] National Institute for Communicable Disease Control and Prevention, State Key Laboratory for Infectious Disease Prevention and Control, Chinese Center for Disease Control and Prevention, and Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, P.O. Box 5, Changping, Beijing 102206, China. Email: shaozhujun@icdc.cn

OBJECTIVES: DTP vaccines are used for the prevention of pertussis, diphtheria and tetanus. In 2007, in Gaobeidian city, China, the DTwP vaccine was replaced with DTaP. This study described the diphtheria and tetanus sero-epidemiology in subjects vaccinated solely with DTwP or DTaP. METHODS: Blood samples were obtained between October 2012 and June 2013 from 587 healthy subjects aged 2-17 years. Serum IgG antibodies against diphtheria and tetanus

were determined using ELISA. Interrupted time series analyses examined the changes in antitoxin levels over time and analyzed the alterations in diphtheria and tetanus antitoxin levels after the vaccine switch. RESULTS: Mean concentrations of diphtheria antitoxin and tetanus antitoxin were 0.074 IU/ml (95% CI 0.065-0.084) and 0.063 IU/ml (95% CI 0.053-0.076). The protection rates (antitoxins >0.01 IU/ml) for diphtheria and tetanus were 88.25% and 82.11%. Mean antitoxin levels for both diphtheria and tetanus decreased with increasing age, but this decrease was much slower for DTwP than DTaP. CONCLUSIONS: Although the observed protection rates for diphtheria and tetanus were sufficient to prevent an outbreak at present, the mean levels of diphtheria and tetanus antitoxins decreased with increasing age; therefore, booster vaccinations at 7 and 12 years of age would be strengthened in Gaobeidian city, China.

2953 ERSHOVA, J. V.; PODEWILS, L. J.; BRONNER, L. E.; STOCK-WELL, H. G.; DLAMINI, S.; MAMETJA, L. D. **Evaluation of adherence to national treatment guidelines among tuberculosis patients in three provinces of South Africa.** *SAMJ - South African Medical Journal* (2014) **104** (5) 362-368 Pretoria, South Africa; SAMA Health and Medical Publishing Group [En, 16 ref.] Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. Email: jhe3@cdc.gov

BACKGROUND: Standardised tuberculosis (TB) treatment through directly observed therapy (DOT) is available in South Africa, but the level of adherence to standardised TB treatment and its impact on treatment outcomes is unknown. OBJECTIVES: To describe adherence to standardised TB treatment and provision of DOT, and analyse its impact on treatment outcome.

Methods. We utilised data collected for an evaluation of the South African national TB surveillance system. A treatment regimen was considered appropriate if based on national treatment guidelines. Multivariate log-binomial regression was used to evaluate the association between treatment regimens, including DOT provision, and treatment outcome. RESULTS: Of 1 339 TB cases in the parent evaluation, 598 (44.7%) were excluded from analysis owing to missing outcome or treatment information. The majority (697, 94.1%) of the remaining 741 patients received an appropriate TB regimen. Almost all patients (717, 96.8%) received DOT, 443 (59.8%) throughout the treatment course and 274 (37.0%) during the intensive (256, 34.6%) or continuation (18, 2.4%) phase. Independent predictors of poor outcome were partial DOT (adjusted risk ratio (aRR) 3.1, 95% confidence interval (CI) 2.2-4.3) and previous treatment default (aRR 2.3, 95% CI 1.1-4.8). CONCLUSION: Patients who received incomplete DOT or had a history of defaulting from TB treatment had an increased risk of poor outcomes.

2954 VIJAYA BHATT; NEERAJ TIWARI **A spatial scan statistic for survival data base on Weibull distribution.** *Statistics in Medicine* (2014) **33** (11) 1867-1876 Chichester, UK: Wiley-Blackwell [En, 16ref.] Department of Statistics, Kumaun University-S.S.J. Campus, Almora, India. Email: bhatt_vijaya@yahoo.co.in

The spatial scan statistic has been developed as a geographical cluster detection analysis tool for different types of data sets such as Bernoulli, Poisson, ordinal, normal and exponential. We propose a scan statistic for survival data based on Weibull distribution. It may also be used for other survival distributions, such as exponential, gamma, and log normal. The proposed method

is applied on the survival data of tuberculosis patients for the years 2004-2005 in Nainital district of Uttarakhand, India. Simulation studies reveal that the proposed method performs well for different survival distribution functions.

2955 KAWAI, K.; MEYDANI, S. N.; URASSA, W.; WU, D.; MUGUSI, F. M.; SAATHOFF, E.; BOSCH, R. J.; VILLAMOR, E.; SPIEGELMAN, D.; FAWZI, W. W. **Micronutrient supplementation and T cell-mediated immune responses in patients with tuberculosis in Tanzania.** *Epidemiology and Infection* (2014) **142** (7) 1505-1509 Cambridge, UK; Cambridge University Press [En, 13 ref.] Department of Epidemiology, Harvard School of Public Health, 677 Huntington Avenue, Boston MA 02115, USA. Email: kkawai@post.harvard.edu

Limited studies exist regarding whether incorporating micro-nutrient supplements during tuberculosis (TB) treatment may improve cell-mediated immune response. We examined the effect of micronutrient supplementation on lymphocyte proliferation response to mycobacteria or T-cell mitogens in a randomized trial conducted on 423 patients with pulmonary TB. Eligible participants were randomly assigned to receive a daily dose of micronutrients (vitamins A, B-complex, C, E, and selenium) or placebo at the time of initiation of TB treatment. We found no overall effect of micronutrient supplements on lymphocyte proliferative responses to phytohaemagglutinin or purified protein derivatives in HIV-negative and HIV-positive TB patients. Of HIV-negative TB patients, the micronutrient group tended to show higher proliferative responses to concanavalin A than the placebo group, although the clinical relevance of this finding is not readily notable. The role of nutritional intervention in this vulnerable

population remains an important area of future research.

2956 BIGWAN, E. I.; OHAERI, M. C.; OKONKWO, H. I.; UDOSEN, I. S.; MARKUS, G. C.; SHEYIN, Z. **Prevalence of acid-alcohol-fast bacilli among patients with suspected cases of pulmonary tuberculosis in Jos, Nigeria.** *African Journal of Clinical and Experimental Microbiology* (2014) **15** (2) 103-108 Kwara State, Nigeria; African Journal of Clinical and Experimental Microbiology [En, fr, 18 ref.] Department of Medical Laboratory Science, University of Jos, Plateau State, Nigeria. Email: emabigwan@yahoo.com

Mycobacterium tuberculosis is a major public health problem in globally due to its high tendency of person-person transmission, morbidity, and mortality. This study aimed at determining the prevalence of AAFB within the study area. Sputum samples were collected from three hundred and three (303) patients with suspected cases of pulmonary tuberculosis attending Plateau State Specialist. Hospital and Faith Alive Foundation. The samples were examined using Ziehl Neelsen method. Structured questionnaires were administered to obtain some demographic data from patients that consented. Results were tested statistically for significance at $p < 0.05$ using Chi-square test. Out of the samples examined, 29(9.57.0%) were positive for AAFB. The study showed that the prevalence of smear-positive increased with age between 15 and 45 and then decreased from age groups 46 and above. The study also revealed that males had a higher prevalence with 19 (12.34%) than females who had 10 (6.71%). Marital status showed that divorced individuals had the highest prevalence of 2 (12.50%) followed by married, singles and the widowed with 18 (11.76%), 8

(6.34%), and I (5.90%) respectively. Statistically the study reveals that age groups, sex, hospital (location) does not have any effects on the prevalence ($p>0.05$) while marital status showed a significant effect on the prevalence ($p<0.05$). There is need for a more collaborative efforts and political will by the government and non-governmental agencies in order to fast track prevention and control measures aimed at eliminating the infection in the nearest future.

2957 EKUNDAYO, E. O.; ABBEY, S. D.; OKORIE O
Case detection rate of direct sputum smear microscopy for diagnosis of pulmonary tuberculosis in Abia State, Nigeria. *African Journal of Clinical and Experimental Microbiology* (2014) **15** (2) 109-116 Kwara State, Nigeria; African Journal of Clinical and Experimental Microbiology [En, fr, 31 ref.] Department of Microbiology, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. Email: ekundayo.emmanuel@mouau.edu.ng

The accuracy of sputum smear microscopy, the tuberculosis case-finding method in the Abia State TB Control Programme has never been assessed due to lack of culture facilities. To assess the accuracy of sputum smear microscopy in routine control programme conditions in Abia State, sputum samples from patients undergoing investigation for tuberculosis were analyzed using Ziehl-Neelsen staining technique for sputum smear microscopy and culture on Lowenstein-Jensen medium as reference standard. Out of 150 participants tested, 51 were smear-positive for acid fast bacilli (positivity rate, 34.0%, 51/150) while 79 were culture positive for *Mycobacterium tuberculosis* complex and 12 for non-tuberculous mycobacteria (NTM). Thirty-seven of the 79 culture positive for *M. tuberculosis* were smear

positive giving a ratio of smear to culture positivity of 46.84%. Forty-two (42.4%) of the 99 smear negative cases were culture positive for *M. tuberculosis*. The sensitivity of smear microscopy was 50.0% (95%CI=39.0-61.0) and specificity was 92.3% (95% CI=86.4-98.2). The prevalence of HIV/TB coinfection among the study participants was 48% (12/25). Although the case-detection rate of smear microscopy was moderate in this study, the large proportion of TB patients missed by smear microscopy is a cause for concern and requires concerted effort to improve the sensitivity of smear microscopy. Introduction of more sensitive diagnostic methods like culture also need to be considered.

2958 GREGOIRE, A. K.; FLAVIEN, K. H.; RAPHAEL, O.; DEMINE, B.; CHRISTOPHE, M. G.; MARIE, A. K.; HERVE, Y. A. K.; YVES, T.
[Evolution of postoperative issue of pulmonary tuberculosis in seropositive HIV cases.] Evolution post-operatoire des sequelles de tuberculose pulmonaire chez les seropositifs VIH. *Pan African Medical Journal* (2014) **17**, 20 Kampala, Uganda; African Field Epidemiology Network [Fr, 13 ref.] Service des Maladies Cardio-Vasculaires et Thoraciques du CHU de Bouake, Cote d'Ivoire. This study reported the clinical and developmental aspects of tuberculous pulmonary sequelae (SPT) in seropositive HIV cases (HIV+). This is a prospective cross-sectional study conducted between November 2005 and October 2012 involving 20 HIV+ patients who had a history of pulmonary tuberculosis (PTB), were treated and declared cured, and admitted during the study period for surgery for SPT. A serological survey was carried out systematically for HIV during the preoperative assessment. Preoperative factors, mortality, postoperative complications (CPOP), hospital stay, diagnosis,

and monitoring of medium-term STP following surgery were evaluated. Seropositive cases for HTV1+ (n=12, 60%), HIV 1+ and 2+ (n=4, 20%) and HIV2+ (n=4, 20%) were determined. The mean duration of symptoms of PTS was 26.22 ± 21.3 months. STP included empyema or encysted pleurisy (n=16, 80%), destroyed lung (n=2, 10%) and bronchial dilatation (n=2, 10%). HIV+ cases showed no pulmonary aspergilloma. The average hospital stay was 13.1 ± 10.2 days. The total follow-up was 82 patient-years with an average follow-up of 4.2 ± 2.3 years (range 1 to 7 years). The mortality rate in the short and medium term was zero. No immediate postoperative deaths were noted. Immediate CPOP were prolonged in 75% of immunocompromised cases. Late CPOP (n = 3) was composed of restrictive pulmonary syndrome, persistent empyema and restrictive residual pleural thickening. In the short term, the rate of radiological healing was 80% (n=16).

2959 NGAMA, C. K.; MUTEYA, M. M.; LUKUSHA, Y. I. I.; KAPEND, S. M.; TSHAMBA, H. M.; MAKINKO, P. I.; MULUMBA, C. M.; KAPEND A KALALA, L. **[Epidemiological and clinical profile of tuberculosis in the health zone of Lubumbashi (DR Congo).] Profil epiderniologique et clinique de la tuberculose dans la zone de sante de Lubumbashi (RD Congo).** *Pan African Medical Journal* (2014) **17**, 70 Kampala, Uganda; African Field Epidemiology Network [Fr, 13 ref.] Service de medecine interne, Cliniques Universitaires de Lubumbashi, Unilu, BP 1825, Congo.

INTRODUCTION: The aim of this study was to determine the demo-graphic distribution of tuberculosis (TB) patients and the types of tuberculosis based on the location of the disease, and to examine the therapeutic outcome of patients according to different locations. METHODS: A descriptive cross-sectional study

was conducted on patients diagnosed and treated for TB during 1 January 2010 -30 June 2011 in the health area of Lubumbashi, one of 11 health centres of the District of Lubumbashi in Katanga (DR Congo). All Congolese TB patients who consulted at the health area during the study period were included. Age, sex, place of residence, clinical picture at the first consultation and the results of laboratory test of sputum Ziehl-Neelsen staining were the parameters analysed. Results: A total of 708 TB patients were recorded, with a prevalence of 0.5%. Males accounted for 58.78% of cases, compared with 41.25% of females; the sex ration was 1.42 in favour of males. The average age was 33 ± 15 years. The majority of patients were 54.79 and belonged to the age group between 21 and 40 years. Extrapulmonary tuberculosis accounted for 51.8% of cases, against 50.2% of pulmonary tuberculosis, with sweat, positive cases at 31.9%. Death of patients with haecillilorni was 5 times more compared to pulmonary smear positive deaths and other forms of tuberculosis (OR 95% CI: 5.2712.92,9.591; P-0.00). The majority of patients resided in Luhumbashi (41.7%) and Kampemba (23.2%). CONCLUSION: Extra-pulmonary tuberculosis (pleural) rates were high, compared to pulmonary tuberculosis, and it is this latter form of tuberculosis which has led to many more deaths. An improved system of health care in 113 diagnostic procedures, monitoring of bacilliform patients and encouraging of treatment adherence is required.

2960 IBRAHIM, L. M.; OLERIBE, O. O., NGUKU, P.; TONGWONG, G. C.; MATO, L. G.; LONGKYER, M. I.; OGIRI, S.; NSUBUGA, P. **Evaluation of quality of TB control services by private health care providers in Plateau state, Nigeria; 2012.** *Pan African Medical Journal* (2014) **17**, 77 Kampala,

Uganda; African Field Epidemiology Network [En, 12 ref.] Nigeria Field Epidemiology and Laboratory Training Programme, #50 Haile Selassie Street, Asokoro, Abuja, Nigeria.

INTRODUCTION: Tuberculosis (TB) is public health concern in Nigeria. The country uses the Directly Observed Treatment Short course (DOTS) strategy for its control. Plateau state started using the DOTS strategy in 2001 and had the Private health facilities (PHF) as an important stakeholder. We evaluated their contributions to case finding and quality of the services to identify gaps in monitoring and evaluation in the TB control services within the PHF to plan for intervention so as to meet the set target for TB control in the state. **METHODS:** We used the logical framework approach to identify and analyze the problem. We drew up an objective tree and from the objective tree developed a logical framework matrix including evaluation plan. We also conducted desk review to extract data on case findings, case management and outcomes of the treatment. We interviewed TB focal persons and laboratory personnel using structured questionnaire. The data was analyzed using excel spread sheet. **RESULTS:** Of the 127 health facilities with TB patients on treatment 27 (21.3%) were PHF. The PHF reported 54.6% (1494) of TB cases in 2011. The sputum conversion rates, cured rate, treatment success rate, and default rates were 85%, 73%, 81.4% and 6.6% respectively. The discordant rates were 3.1% and 1.2% for the state and private health facilities respectively. **CONCLUSION:** Log frame approach is a useful tool for evaluation of TB control services and helps provide evidence for decision making to improve quality of the TB services in the public and private health facilities in the state.

2961 IBRAHIM, L. M.; HADEJIA, I. S.; NGUKU, P.; DANKOLI, R.; WAZIRI, N. E; AKHIMIEN, M. O.;

OGIRI, S.; OYEMAKINDE, A.; DALHATU, I.; NWANYANWU, O.; NSUBUGA, P. **Factors associated with interruption of treatment among pulmonary tuberculosis patients in Plateau State, Nigeria. 2011. *Pan African Medical Journal* (2014) 17, 78** Kampala, Uganda; African Field Epidemiology Network [En, 21 ref.] Nigeria Field Epidemiology and Laboratory Training Program, #50 Haile Selassie Street, Asokoro, Abuja, Nigeria.

INTRODUCTION: Nigeria has one of the highest tuberculosis (TB) burdens in the world with estimated incidence of 133 per 100,000 populations. Multi-drug resistant TB (MDR-TB) is an emerging threat of the TB control in Nigeria caused mainly by incomplete treatment. This study explored factors that affect adherence to treatment among patients undergoing direct observation of TB treatment in Plateau state, Nigeria. **METHODS:** Between June and July 2011, we reviewed medical records and interviewed randomly selected pulmonary TB patients in their eighth month of treatment. Information on patients' clinical, socio-demographic and behavioral characteristics was collected using checklist and structured questionnaire for knowledge of treatment duration and reasons for interruption of treatment. We conducted focus group discussions with patients about barriers to treatment adherence. Data were analyzed with Epi Info software. **RESULTS:** Of 378 records reviewed, 229 (61%) patients were male; mean age 37.6±13.5 years and 71 (19%) interrupted their treatment. Interruption of treatment was associated with living >5 km from TB treatment site (AOR: 1.3; 05%: 5.7-22.2), lack of knowledge of duration of treatment (AOR: 1.1; CI 95%: 2.8-13.2) and cigarette smoking (AOR: 3.4; CI 05%: 1.5-8.0). Major reasons for the interruption were lack of transport fare (40%) and feeling well

(25%). Focused group discussions revealed unfriendly attitudes of health care workers as barriers to adherence to treatment. **CONCLUSION:** This study revealed knowledge of the patients on the duration of treatment, distance and health workers attitude as the major determinants of adherence to TB treatment. Training for health care workers on patient education was conducted during routine supportive supervision.

2962 ABID, H.; CHAABOUNI, S.; FRIKHA, F.; TOUMI, N.; SOUISSI, B.; LAHIANI, D.; BAHLOUL, Z.; MAHFOUDH, K. B. **[Contribution of imaging in the diagnosis of infectious sacroiliitis: about 19 cases.] Apport de l'imagerie dans le diagnostic des sacroiliites infectieuses: a propos de 19 cas.** *Pan African Medical Journal* (2014) **17**, 171 Kampala, Uganda; African Field Epidemiology Network [Fr, 24 ref.] Service de Radiologie, CHU Habib Bourguiba, 3029 Sfax, Tunisia. Infectious sacroiliitis deserves to be known better. Its diagnosis is often delayed because of misleading symptoms and difficulties in the exploration of the sacroiliac joint. Our study was based on a retrospective study of infectious sacroiliitis cases, collected between 1997 and 2008, from our university centre in Sfax, Tunisia. The diagnosis of sacroiliitis was held in the presence of clinical and radiological findings of sacroiliac involvement. We report 19 cases of infectious sacroiliitis (10 men and 9 women) with a mean age of 32 years. All cases were unilateral sacroiliitis. Standard radiographs were suggestive in 14 cases and normal in all other cases. Computed tomography was performed in 13 cases, which showed soft tissue abscess in 8 cases and osseous sequestration in 2 cases. Magnetic resonance imaging was performed in 8 cases, showing soft tissue infiltration in all cases and abscess in 3 cases. The organism was identified in 9 cases

(3 cases of tuberculosis, 3 cases of brucellosis, 2 cases of pyogenic sacroiliac iliitis and one case of candidiasis). This identification was made by biopsy in 3 cases, blood culture in 2 cases, sampling at admission in one case, and serology in 3 cases. For other cases, pyogenic origin was chosen on clinical and biological arguments. Imaging plays a crucial role in the early diagnosis and aetiological orientation of infectious sacroiliitis.

2963 ZIDA, S.; TARNAGDA, Z.; KABORE, A.; ZINGUE, D.; HIEN, H.; SANOU, A.; GOMGNIMBOU, K. M.; NOUCTARA, M.; OUEDRAOGO, M.; OUEDRAOGO, O.; GODRELTIL, S.; MEDA, N. **[Current state of atypical mycobacteriosis in Burkina Faso: results of a regional survey.] Etat des lieux des mycobacterioses atypiques au Burkina Faso: resultats d'une enquete regionale.** *Pan African Medical Journal* (2014) **17**, 188 Kampala, Uganda; African Field Epidemiology Network [Fr, 15 ref.] Centre MURAZ, Bobo Dioulasso, Burkina Faso.

A cross-sectional study was conducted to determine the frequency of isolation of atypical mycobacteria in microscopy-positive pulmonary tuberculosis (MPT) patients in Burkina Faso, during March 2011-February 2012. MPT patients aged over 15 years from diagnostic and treatment centres in High-Basins Region were included in the study. Mycobacterial culture and biochemical identification were performed on samples from the patients, and HIV serology was performed by rapid tests. A frequency of 11% (8/73) of atypical mycobacteria and 89.0% (65/73) of *Mycobacterium tuberculosis* complex were identified in 73 MPT patients. The 20-40 years age group was the most affected by mycobacteriosis in general and constituted 48% of the sample. There were 12.2% (8/66) HIV-positive patients,

83.3% (55/66) HIV-negative patients, and 4.5% (3/66) of patients had unknown HIV status. This study highlights the involvement of atypical mycobacteria in the pathogenesis of some MPT patients. The role of atypical mycobacteria in pulmonary infections is probably underestimated and should be examined in more detail and on a larger sample.

2964 MEDA, Z. C.; HUANG, C. C.; SOMME, I.; KONATE, L.; SOMDA, P. K; DJIBOUGOU, A. D.; SANOU, **M. Tuberculosis in developing countries: conditions for successful use of a decentralized approach in a rural health district.** *Pan African Medical Journal* (2014) **17**, 198 Kampala, Uganda; African Field Epidemiology Network [En, 26 ref.] Ministry of Health, Burkina Faso, 09 BP 450 Ouagadougou 09, Burkina Faso.

INTRODUCTION: This article reports the results and the lessons learned from implementing the decentralized approach to tuberculosis (TB) detection and treatment, embedded with Human Immunodeficiency Virus (HIV) co-infection in health district. The objective was to increase the TB screening indicators in the district using the common ways for offering care to patients in health district. METHODS: Conducted from August 2006 to July 2007, this large-scale intervention using Non-experimental study Designs has implemented a decentralized approach for fighting against TB in Orodara Health District (OHD), Burkina Faso. Pretest-posttest design has been used for quantitative part using indicators in one hand and posttests-only design for the qualitative part in other hand. In the pretest-posttest design, the TB indicators from years before 2006 (from 2002 to 2005) were used as earlier measurement observations allowing examining changes over time. The decentralized approach was incorporated into the annual

planning of the OHD. For the quantitative study design, indicators used were those from National TB Program in Burkina Faso: TB detection rate, incidence density of TB per 100,000 inhabitants per year, and HIV prevalence in incident TB cases with positive smears. Data entry and analysis employed Microsoft Access and Excel software. For the qualitative, in-depth interview was used in which a total of 16 persons have been interviewed. Discussions were tape-recorded and transcribed verbatim for analysis using the computer-based qualitative software program named QSR NVIVO. RESULTS: There were a total of 99,259 outpatient visits during the study period: the 7,345 patients (7.43%) presented with cough. Of the 7,345 patient having cough, 503 cases (6.8%) were declared chronic coughing. These 503 patients were screened for TB, including 35.59% whose coughing had lasted 10 to 15 days. We observed an increase in a measured variable was observed. The TB detection rate and incidence-density rate based on positive smears were 16.11% (11.00% in 2005) and 10.42 per 100,000 inhabitants per year (6.88 per 100,000 inhabitants in 2005), respectively. There were 29 patients positive for TB: 41.37% of these had cough lasting 10 to 15 days, 10.34% were also positive for HIV, and 68.97% were from rural areas. Health workers and patients reported satisfaction with the intervention. It was found that implementing a decentralized approach to TB prevention in rural areas is plausible and effective under some conditions: considering that health district system is functional; carefully designing the intervention for TB case management; setting up and implementing of decentralized approach including strong monitoring; and taking into account the all financing, community and

volunteer involvement, evaluation of the cost savings from integrating specific donor funding, and being supported by regional and central levels including National TB program. Conclusion: The study has shown that TB detection rate can be increased by implementing a decentralized approach to primary care. When carefully implemented, a decentralized approach is a suitable approach to TB and HIV prevention in rural and inaccessible settings.

2965 EKUKWE, N. C.; BAIN, L. E.; JINGI, A. M.; SYLVIA, K.; MINTOM, P.; MENANGA, A. **Bilateral pulmonary embolism in a patient with pulmonary tuberculosis: a rare association in Yaounde, Cameroon.** *Pan African Medical Journal* (2014) **17**, 262 Kampala, Uganda; African Field Epidemiology Network [En, 10 ref.] Faculty of Medicine and Biomedical Sciences, Department of Internal Medicine, Yaounde, Cameroon. Pulmonary embolism is a complication of pulmonary tuberculosis that has received little emphasis in the literature. We describe a 52 year old male, with no risk factors for thromboembolic disease referred to our service for an in depth clinical review for cardiomegaly and dyspnea on exertion. Echocardiography and CT scans revealed dilated heart cavities and bilateral proximal pulmonary emboli respectively and a cavitation in the apical lobe of the right lung. Bronchial aspirate and culture revealed the presence of *Mycobacterium tuberculosis*. There was no evidence of malignancy. Elsewhere, a clinical review and a lower limb ultrasound showed no evidence of deep venous thrombosis. Clinical course on anti-tuberculosis and anti-coagulant therapies was remarkably favourable. Clinicians need to be conscious of the risk of developing thromboembolic disease in patients treated for tuberculosis, in especially high prevalence settings like ours.

2966 SEUNG, K. J.; BECERRA, M. C.; ATWOOD, S. S.; ALCANTARA, F.; BONILLA, C. A.; MITNICK, C. D. **Salvage therapy for multidrug-resistant tuberculosis.** *Clinical Microbiology and Infection* (2014) **20** (5) 441-446 Oxford, UK; Wiley-Blackwell [En, 31 ref.] Division of Global Health Equity, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA. Email: kjseung@pih.org

Treatment of multidrug-resistant tuberculosis (MDR-TB), defined as *Mycobacterium tuberculosis* resistant to both isoniazid and rifampicin, is challenging under the best of circumstances, and particularly in resource-limited settings. For patients who remain persistently sputum-culture-positive despite therapy with second-line TB drugs, treatment options are limited, especially if disease is too advanced for resective surgery. Salvage therapy refers to the design of a regimen combining new and previously used drugs in a final effort to attain sputum conversion before declaring treatment to have failed. We retrospectively evaluated the outcomes of salvage therapy in 213 Peruvian patients. Salvage regimens included a median of two new drugs (range 1-6) and nine (range 5-43) total (new plus previously used) drugs. The most frequently used new drug was moxifloxacin, followed by capreomycin, amoxicillin-clavulanate, kanamycin and clarithromycin. Culture conversion occurred in 65 (30.5%) patients. Salvage regimens that included moxifloxacin were significantly more likely to be followed by culture conversion (OR 2.2; p 0.02). Later-generation fluoroquinolones such as moxifloxacin should be used in salvage therapy but also in the initial treatment of MDR-TB, if the best clinical strategy is to use the most effective drugs when the patient has the best chance for

cure. New TB drugs are most likely to be initially used in salvage patients, in conditions similar to those described here. Close bacteriological monitoring of these patients will be essential, as useful information about the best way to use these new drugs can be gained from analysis of salvage therapy cohorts.

2967 YADAV, R. P.; NISHIKIORI, N.; SATHA, P.; EANG, M. T.; LUBELL, Y. **Cost-effectiveness of a tuberculosis active case finding program targeting household and neighborhood contacts in Cambodia.** *American Journal of Tropical Medicine and Hygiene* (2014) **90** (5) 866-872 Deerfield, USA; American Society of Tropical Medicine and Hygiene [En, 26 ref.] World Health Organization, Representative Office in Cambodia, Phnom Penh, Cambodia. Email: yadavr@wpro.who.int, nobu.nishikiori@gmail.com, peousatha@yahoo.com, mao@online.com.kh, yoel@tropmedres.ac

In many high-risk populations, access to tuberculosis (TB) diagnosis and treatment is limited and pockets of high prevalence persist. We estimated the cost-effectiveness of an extensive active case finding program in areas of Cambodia where TB notifications and household poverty rates are highest and access to care is restricted. Thirty operational health districts with high TB incidence and household poverty were randomized into intervention and control groups. In intervention operational health districts, all household and symptomatic neighborhood contacts of registered TB patients of the past two years were encouraged to attend screening at mobile centers. In control districts, routine passive case finding activities continued. The program screened more than 35,000 household and neighborhood contacts and identified 810 bacteriologically confirmed cases. The cost-

effectiveness analysis estimated that in these cases the reduction in mortality from 14% to 2% would result in a cost per daily adjusted life year averted of \$330, suggesting that active case finding was highly cost-effective.

3315 MONTEIRO, L. D.; ALENCAR, C. H.; BARBOSA, J. C.; NOVAES, C. C. B. S.; SILVA, R. DE C. P. DA; HEUKELBACH, J. **Limited activity and social participation after hospital discharge from leprosy treatment in a hyperendemic area in north Brazil.** *Rvista Brasileira de Epidemiologia* (2014) **17** (1) 91-104 Rio de Janeiro, Brazil; Associacao Brasileira de Pos-Graduacao em Saude coletiva [En, Pt, 30 ref.] Departamento de Saude Comunitaria da Faculdade de Medicina da Universidade Federal do Ceara, Fortaleza, CE, Brazil. Email: heukelhach@web.de

INTRODUCTION: Neural damages are among the main factors that contribute to physical disability in leprosy. Systematic monitoring using a broad physical, psychological and social approach is necessary. OBJECTIVE: The objective of this study was to characterize the limitation of activity and social participation and its correlation with disabilities and/or impairment in individuals after being discharged from a multidrug leprosy therapy. METHOD: A cross-sectional study conducted in Araguaina, state of Tocantins, which is a leprosy hyperendemic municipality. We included cases of patients who were discharged from treatment considered as cured from January 2004 to December 2009. We performed dermatological examination and applied the Screening Activity Limitation and Safety Awareness (SALSA) and social participation scales. RESULTS: We included 282 individuals (mean age: 45.8 years old). The paucibacillary operational classification was more common (170; 60.3%). The eye-hand-foot score ranged

from 0 to 12 (mean: 0.7). A total of 84 (29.8%) individuals presented limited activity. A slight restriction in social participation occurred in 18 (6.3%) cases. There was a statistically significant correlation between activity limitation, age ($r=0.40$; $p<0.0001$) and degree of functional limitation ($r=0.54$; $p<0.0001$), as well as of restricted social participation, activity limitation ($r=0.56$, $p<0.0001$) and functional limitations ($r=0.54$, $p<0.0001$). **CONCLUSION:** Functional limitation due to leprosy had an impact on the conduct of activities and social participation after the discharge from a leprosy treatment. The association between Screening of Activity Limitation and Safety Awareness and participation scales will assist in designing evidence-based assistance measures.

3316 GRINSZTEJN, B.; CASTRO, N. DE; ARNOLD, V.; VELOSO, V. G.; MORGADO, M.; PILOTTO, J. H.; BRITES, C.; MADRUGA, J. V.; BARCELLOS, N. T.; SANTOS, B. R.; VORSATZ, C.; FAGARD, C.; SAN-TINI-OLIVEIRA, M.; PATEY, O.; DELAUGERRE, C.; CHENE, G.; MOLINA, J. M. **Raltegravir for the treatment of patients co-infected with HIV and tuberculosis (ANRS 12 180 reflate TB): a multicentre, phase 2, non-comparative, openlabel, randomised trial.** *Lancet Infectious Diseases* (2014) **14** (6) 459-467 Oxford, UK; Elsevier Ltd [En, 23 ref.] STD/AIDS Clinical Research Laboratory-Evandro Chagas Clinical Research Institute-Fiocruz, Hopital Saint-Louis, Assistance Publique Hopitaux de Paris, France. Email: gbeatriz@ipecc.fiocruz.br

BACKGROUND: Concurrent treatment of HIV and tuberculosis is complicated by drug interactions. We explored the safety and efficacy of raltegravir as an alternative to efavirenz for patients co-infected with HIV and tuberculosis. **METHODS:** We did a multicentre, phase 2, non-comparative,

open-label, randomised trial at eight sites in Brazil and France. Using a computer-generated randomisation sequence, we randomly allocated antiretroviral-naive adult patients with HIV-1 and tuberculosis (aged 18 years with a plasma HIV RNA concentration of >1000 copies per mL) to receive raltegravir 400 mg twice a day, raltegravir 800 mg twice daily, or efavirenz 600 mg once daily plus tenofovir and lamivudine (1:1:1; stratified by country). Patients began study treatment after the start of tuberculosis treatment. The primary endpoint was virological suppression at 24 weeks (HIV RNA <50 copies per mL) in all patients who received at least one dose of study drug (modified intention-to-treat analysis). We recorded death, study drug discontinuation, and loss to follow-up as failures to achieve the primary endpoint. We assessed safety in all patients who received study drugs. This study is registered in ClinicalTrials.gov, number NCT00822315. **FINDINGS:** Between July 3, 2009, and June 6, 2011, we enrolled and randomly assigned treatment to 155 individuals; 153 (51 in each group) received at least one dose of the study drug and were included in the primary analysis. 133 patients (87%) completed follow-up at week 48. At week 24, virological suppression was achieved in 39 patients (76%, 95% CI 65-88) in the raltegravir 400 mg group, 40 patients (78%, 67-90) in the raltegravir 800 mg group, and 32 patients (63%, 49-76) in the efavirenz group. The adverse-event profile was much the same across the three groups. Three (6%) patients allocated to efavirenz and three (6%) patients allocated to raltegravir 800 mg twice daily discontinued the study drugs due to adverse events. Seven patients died during the study (one in the raltegravir 400 mg group, four in the raltegravir 800 mg group, and two in the efavirenz group): none of the deaths was deemed related to study treatment.

INTERPRETATION: Raltegravir 400 mg twice daily might be an alternative to efavirenz for the treatment of patients co-infected with HIV and tuberculosis.

3317 HUANG KHAILIN [HUANG, K. L. G] JOHNSON, P. **Epidemiology and management of Buruli ulcer.** *Expert Review of Anti-infective Therapy* (2014) **12** (7) 855-865 London, UK; Informa UK Ltd [En] Department of Infectious Diseases, Austin Hospital, Victoria 3084, Australia. Email: paul.johnson@austin.org.au

Buruli ulcer (*Mycobacterium ulcerans* infection) is a neglected tropical disease of skin and subcutaneous tissue that can result in long-term cosmetic and functional disability. It is a geographically restricted infection but transmission has been reported in endemic areas in more than 30 countries worldwide. The heaviest burden of disease lies in West and Sub-Saharan Africa where it affects children and adults in subsistence agricultural communities. *Mycobacterium ulcerans* infection is probably acquired via inoculation of the skin either directly from the environment or indirectly via insect bites. The environmental reservoir and exact route of transmission are not completely understood. It may be that the mode of acquisition varies in different parts of the world. Because of this uncertainty it has been nicknamed the 'mysterious disease'. The therapeutic approach has evolved in the past decade from aggressive surgical resection alone, to a greater focus on antibiotic therapy combined with adjunctive surgery.

3318 KENYI, L. J.; MARTIN, T.; OHISA, G.; MATTHEW, D.; MACHARIA, S.; JOSEPH, L. **Knowledge, attitude and practice (KAP) of tuberculosis patients enrolled on treatment in Juba city, South Sudan 2010: a pilot study.** *South*

Sudan Medical Journal (2014) **7** (2) 28-32 Juba, South Sudan; South Sudan Doctors Association [En, 4 ref.] Deputy Head of Unit, National Tuberculosis, Leprosy and Buruli Ulcer Control Program (NTLBP), Ministry of Health (MoH), Republic of South Sudan, P.O.BOX. 80, Juba, Sudan. Email: lou.joseph16@gmail.com

STUDY SETTING: Juba Teaching Hospital, Juba city, Republic of South Sudan, 2010. OBJECTIVE: To examine, knowledge, attitude and practices of tuberculosis (TB) patients enrolled on tuberculosis treatment, Juba, South Sudan. DESIGN: Descriptive study. RESULTS: Knowledge in TB: Of the 102 patients interviewed; up to 80.4% were not knowledgeable on cause of TB, 52% did not know correct signs and symptoms of TB, 39.2% did not know overall treatment duration, 54.9% did not know the importance of strict adherence to treatment. Knowledge on correct diagnosis was 87.3% and on correct means of TB transmission was 79.4%. PRACTICES AND ATTITUDES: On practices; 94.1% respondents were able to perform at least one task to stop spread of disease, access to free TB test occurred in 100% of cases and for free drugs in 99% cases. Health care workers correctly suspected TB on first contact in 95.1% of cases. Patients were offered health education on drug side effects in 93.1% of cases, on HIV testing and counselling in 74.5% of cases. Disclosure of TB diagnosis by patient to family or community did not occur in 91.2% cases. Family, community and employers offered support to patients in 92.2%, 95.1% and 98% of cases respectively. CONCLUSION: We found key knowledge gaps among Juba TB patients enrolled on treatment. These knowledge gaps are probably responsible for the high treatment defaulter rates reported in Juba, South Sudan. Tuberculosis patients are still

not interested to freely reveal disease diagnosis to members of the family and community at large.

3319 WERNGREN, J.; WIKANDER, M.; PERSKVIST, N.; BALASUBRAMANIAN, V.; SAMBANDAMURTHY, V. K.; RODRIGUES, C.; HOFFNER, S. **In vitro activity of AZD5847 against geographically diverse clinical isolates of *Mycobacterium tuberculosis*. *Antimicrobial Agents and Chemotherapy* (2014) 58 (7) 4222-4223** Washington, USA; American Society for Microbiology (ASM) [En, 17 ref.] The Public Health Agency of Sweden, Department of Microbiology, Unit of Highly Pathogenic Bacteria, Solna, Sweden. Email: jim.wergren@folkhalsomyndigheten.se, dr_crodrigues@hindujahospital.com

The MIC of the novel antituberculosis (anti-TB) drug AZD5847 was determined against 146 clinical isolates from diverse geographical regions, including eastern Europe, North America, Africa, and Asia, using the automated Bactec Mycobacterial Growth Indicator Tube (MGIT) 960 system. These isolates originated from specimen sources such as sputum, bronchial alveolar lavage fluid, pleural fluid, abscess material, lung biopsies, and feces. The overall MIC, was 1.0 mg/liter (range, 0.125 to 4 mg/liter). The MICs of AZD5847 for isolates of *Mycobacterium tuberculosis* were similar among drug-sensitive strains, multidrug-resistant strains. The good in vitro activity of AZD5847 against *M. tuberculosis* and the lack of cross-resistance make this agent a promising anti-TB drug candidate.

3320 XIA YINYIN, GOEL, S.; HARRIES, A. D.; ZHANG ZHIGUO, GAO TIEJIE; WANG LIXIA; CHENG SHIMING; LIN YAN, DU XIN **Prevalence of extended treatment in pulmonary tuberculosis patients receiving first-line therapy and its**

association with recurrent tuberculosis in Beijing, China. *Transactions of the Royal Society of Tropical Medicine and Hygiene* (2014) 108 (7) 402-407 Oxford, UK; Oxford University Press [En, 18 ref.] Chinese Center for Disease Control and Prevention, 155 Changbai Road, ChangPing District, Beijing, China. Email: stat@chinatb.org

BACKGROUND: In China, it is known that extended treatment is given to patients with pulmonary TB after they have successfully completed 6 months of first-line treatment. This practice is not officially reported to the National Tuberculosis Control Programme, so there are no data on its prevalence, its possible benefits in terms of preventing recurrent disease or the costs. This study aimed to provide information, from a single TB dispensary in Beijing, China, on the prevalence of extended anti-TB treatment and its relationship with recurrent TB. METHODS: Retrospective cohort study using the electronic national TB information system and dispensary medical records. RESULTS: Of 935 patients with pulmonary TB who completed 6-7 months of first-line drug treatment, 399 (43%) were given extended treatment. This was more common in patients with smear-positive disease, and those with lung cavities and more extensive radiographic lobar involvement at the time of diagnosis. Over 3-4 years follow-up, recurrent disease was not significantly different in patients who received extended treatment (2.8%, 11/399) as compared to those who received the standard 6-month treatment (3.7%, 20/534). The median length of extended treatment was 89 days at a median cost of US\$111 for drugs and US\$32 for laboratory examinations. CONCLUSIONS: This study shows that extended treatment is common in one TB dispensary in Beijing. Further studies are needed to determine

the countrywide prevalence of this practice and ascertain more conclusively the apparent lack of benefit.

3321 UKWAJA, K. N.; OSHI, D. C.; OSHI, S. N.; ALOBU, I. **Profile and treatment outcome of smear-positive TB patients who failed to smear convert after 2 months of treatment in Nigeria.** *Transactions of the Royal Society of Tropical Medicine and Hygiene* (2014) **108** (7) 431-438 Oxford, UK; Oxford University Press [En, 30 ref.] Department of Internal Medicine, Federal Teaching Hospital, Abakaliki, Ebonyi State, Nigeria. Email: ukwajakingsley@yahoo.co.uk

BACKGROUND: In Nigeria little is known about the profile and treatment outcomes of smear-positive pulmonary TB (SPPTB) patients with persistent smear positivity after 2 months of treatment. METHODS: A retrospective cohort study was carried out to determine the characteristics and treatment outcomes of patients with persistent smear positivity after 2 months of treatment among adults with SPPTB between 2011 and 2012 in two large health facilities in Nigeria. Findings were compared with SPPTB patients who had a negative smear conversion in the same period. RESULTS: Of 929 eligible patients, 187 (20.1%) had persistent smear positivity after 2 months of treatment. Independent predictors for persistent smear positivity were older age ($p < 0.001$) and care at a public facility ($p < 0.001$). Patients with persistent smear positivity had a higher proportion of unsuccessful treatment outcomes compared with those with a negative smear conversion (21.9% vs 12.4%; $p < 0.001$), mainly due to treatment failure ($p < 0.001$). Across treatment category (new versus previously treated cases), age group and residence category (urban versus rural), rates of unsuccessful outcomes were

significantly higher among patients with persistent smear positivity. CONCLUSION: Treatment outcomes of SPPTB patients with persistent smear positivity were inferior to those who smear converted, with treatment failure being a major problem. This needs to be urgently addressed by the National Tuberculosis Control Programme.

3322 WEISS, P.; CHEN WENJIA; COOK, V. J.; JOHNSTON, J. C. **Treatment outcomes from community-based drug resistant tuberculosis treatment programs: a systematic review and meta-analysis.** *BMC Infectious Diseases* (2014) **14** (333) (17 June 2014) London, UK; BioMed Central Ltd [En, 34 ref.] School of Humanitarian Studies, Royal Roads University, 2005 Sooke Rd, Victoria, British Columbia, Canada. james.johnston@bccdc.ca

BACKGROUND: There is increasing evidence that community-based treatment of drug resistant tuberculosis (DRTB) is a feasible and cost-effective alternative to centralized, hospital-based care. Although several large programs have reported favourable out-comes from community-based treatment, to date there has been no systematic assessment of community-based DRTB treatment program outcomes. The objective of this study was to synthesize available evidence on treatment outcomes from community based multi-drug resistant (MDRTB) and extensively drug resistant tuberculosis (XDRTB) treatment programs. METHODS: We performed a systematic review and meta-analysis of the published literature to examine treatment outcomes from community-based MDRTB and XDRTB treatment programs. Studies reporting outcomes from programs using community-based treatment strategies and reporting outcomes consistent with WHO guidelines were

included for analysis. Treatment outcomes, including treatment success, default, failure, and death were pooled for analysis. Meta-regression was performed to examine for associations between treatment outcomes and program or patient factors. RESULTS: Over-all 10 studies reporting outcomes on 1288 DRTB patients were included for analysis. Of this population, 65% [95% CI 59-71%] of patients had a successful outcome, 15% [95% CI 12-19%] defaulted, 13% [95% CI 9-18%] died, and 6% [95% CI 3-11%] failed treatment for a total of 35% [95% CI 29-41%] with unsuccessful treatment outcome. Meta-regression failed to identify any factors associated with treatment success, including study year, age of participants, HIV prevalence, XDRTB prevalence, treatment regimen, directly observed therapy (DOT) location or DOT provider. CONCLUSIONS: Outcomes of community-based MDRTB and XDRTB treatment outcomes appear similar to overall treatment outcomes published in three systematic reviews on MDRTB therapy. Work is needed to delineate program characteristics associated with improved treatment outcomes.

3323 AHMAD KHAN, F.; VERKUUL, S.; PARRISH, A.; CHIKWAVA, F.; NTUMY, R.; EL-SADR, W.; HOWARD, A. A. **Performance of symptom-based tuberculosis screening among people living with HIV: not as great as hoped.** *AIDS* (2014) **28** (10) 1463-1472 Hagerstown, USA; Lippincott Williams & Wilkins, Inc. [En, 29 ref.] ICAP Columbia University, Mailman School of Public Health, 722 West 168 St., New York, NY 10032, USA. Email: aah2138@columbia.edu

OBJECTIVE: The objective of the present study was to determine the diagnostic performance of the symptom-based tuberculosis (TB) screening questionnaire recommended by WHO for

people living with HIV (PLWH) in resource-limited settings, among adults off and on antiretroviral therapy (ART). DESIGN: Cross-sectional study at two HIV clinics in South Africa. METHODS: A total of 825 PLWH completed the screening questionnaire and underwent investigations [chest radiography (CXR) and microbiologic testing of sputa]. A positive screen was defined as presence of cough, fever, night sweats, or weight loss. Pulmonary tuberculosis (PTB) was defined as sputum smear positive for acid-fast bacilli or growth of *Mycobacterium tuberculosis*. RESULTS: Of 737 participants with at least one diagnostic sputum specimen, PTB was diagnosed in 31 of 522 (5.9%) on ART, and 34 of 215 (15.8%) not on ART. The questionnaire missed 15 of 31 (48.4%) PTB cases on ART, and three of 34 (8.8%) not on ART. Among participants on ART, post-test probability of PTB diagnosis (95% confidence interval) was 6.8% (4.0-10.9%) if screening positive, and 5.2% (2.9-8.4%) if screening negative, whereas among participants not on ART, post-test probabilities were 20.3% (14.2-27.5%) and 4.8% (1.0-13.5%), respectively. Among participants diagnosed with PTB, those on ART were significantly less likely to screen positive (adjusted odds ratio 0.04, 95% confidence interval: 0.01-0.39). In both groups (ART and no ART), screening was more sensitive when CXR was incorporated. CONCLUSION: For case detection and exclusion of PTB, the WHO-recommended questionnaire performed adequately among PLWH not on ART, and poorly among those on ART. Further research is needed to identify feasible and effective TB screening strategies for PLWH in resource-limited settings.

3698 DOVONOU, C. A.; ZOUNTCHEME, E. U.; ADOUKONOU, T.; ZANNOU, D. M.; HOUNGB, E. F.; AKPONA, S. **[Morbidity and mortality in the**

Internal Medicine Service of CHDB over a period of three years (2009-2011).] Morbidity et mortalite dans le service de medecine interne du Centre Hospitalier Departemental du Borgou sur une periode de trois ans (2009-2011). *Medecine d'Afrique Noire* (2014) **61** (2) 111-118 La Seyne sur Mer, France; API DPM [Fr, en]

The objective of this study was to survey the morbidity and mortality in the internal medicine department of a teaching hospital in Borgou, Benin during the period 1 January 2009-31 December 2011. The medical records of all patients admitted to the hospital during the study period were retrospectively analysed. A total of 918 patients were included. The average age of patients was 40.5 ± 17.6 years. Majority (85.94%) of patients were aged 15-60 years. The sex ratio was 1.03. Infectious and parasitic diseases accounted for 53% of all admissions, followed by digestive diseases (11.22%), cardiovascular diseases (11%), and pulmonary diseases (9.6%). The 5 causes of death were human immunodeficiency virus (HIV) infection (31.40%), liver cirrhosis (20.30%), non-tuberculosis infections (7.60%), tuberculosis (6.80%), and malignant tumours (5.9%). The most lethal diseases were liver cirrhosis (39.2%), malignant tumours (30.43%), and HIV-related opportunistic infections (29.27%). Results showed that infectious diseases were the main diseases at the internal medicine department but liver cirrhosis and tumours had high mortality. This study points out the importance of appropriate and timely clinical management of diseases to prevent mortality.

3699 CABALAR, M.; YAYLA, V.; ULUTAS, S. SENAIAM, S.; OKTAR, A. C. **The clinical & neurophysiological study of leprosy.** *Pakistan Journal of Medical Sciences* (2014) **30** (3)

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OBJECTIVES: The aim of this study was to evaluate neurological and neurophysiological features of leprosy. **METHODS:** Seventy seven hospitalized leprosy patients (52 male, 25 female) were examined neurological and neurophysiologically between 2010 and 2012. Standard procedures were performed for evaluating sensory and motor conduction studies to all patients. Motor studies were carried out on median, ulnar, tibial and common peroneal nerves. Sensory studies were carried out on median, ulnar and sural nerves. Sympathetic skin response (SSR) recordings on both hands and feet, and the heart rate (R-R) interval variation (RRIV) recordings on precordial region were done in order to evaluate the autonomic dysfunction. **RESULTS:** The mean age was 59.11 ± 14.95 years ranging between 17 and 80 years. The mean duration of disease was 35.58 ± 18.30 years. Clinically, the patients had severe deformity and disability. In neurophysiological examinations, sensory, motor conduction studies of the lower extremities were found to be more severely affected than upper, and sensory impairment predominated over motor. Abnormal SSRs were recorded in 63 (81.8%) cases of leprosy. Abnormal RRIVs were recorded in 41 (53.2%) cases and abnormal RRIVs with hyperventilation were recorded in 55 (71.4%) cases of leprosy. Significant differences were found between SSR and sensory conduction parameters of median, ulnar nerves as well as motor conduction parameters of median, ulnar and peroneal nerves ($p < 0.05$). **CONCLUSION:** Peripheral nervous system dysfunction is

accompanied by autonomic nervous system dysfunction in leprosy patients. Sympathetic involvement may predominate over parasympathetic involvement.

3700 MUHAMMAD ATIF; SYED AZHAR, S. S.; ASRUL AKMAL SHAME; ALI, I.; ASIF, M.; ZAHEER-UDDIN BABAR **Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia.** *BMC Infectious Diseases* (2014) **14** (399) (19 July 2014) London, UK; BioMed Central Ltd [En, 33 ref.] Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia. Email: pharmacist_atif@yahoo.com

BACKGROUND: According to the World Health Organization's recent report, in Malaysia, tuberculosis (TB) treatment success rate for new smear positive pulmonary tuberculosis (PTB) patients is still below the global success target of 85%. In this study, we evaluated TB treatment outcome among new smear positive PTB patients, and identified the predictors of unsuccessful treatment outcome and longer duration of treatment (i.e., >6 months). METHODS: The population in this study consisted of all new smear positive PTB patients who were diagnosed at the chest clinic of Penang General Hospital between March 2010 and February 2011. During the study period, a standardized data collection form was used to obtain socio-demographic, clinical and treatment related data of the patients from their medical charts and TB notification forms (Tuberculosis Information System; TBIS). These data sources were reviewed at the time of the diagnosis of the patients and then at the subsequent follow-up visits until their final treatment outcomes were available. The treatment outcomes of the patients were reported in line with six outcome

categories recommended by World Health Organization. Multiple logistic regression analysis was used to find the independent risk factors for unsuccessful treatment outcome and longer treatment duration. Data were analyzed using the PASW (Predictive Analysis Soft-Ware, version 19.0. Armonk, NY: IBM Corp). RESULTS: Among the 336 PTB patients (236 male and 100 female) notified during the study period, the treatment success rate was 67.26% (n=226). Out of 110 patients in unsuccessful outcome category, 30 defaulted from the treatment, 59 died and 21 were transferred to other health care facilities. The mean duration of TB treatment was 8.19. (SD 1.65) months. In multiple logistic regression analysis, risk factors for unsuccessful treatment outcome were foreign nationality, male gender and being illiterate. Similarly, risk factors for mortality due to TB included high-grade sputum and presence of lung cavities at the start of treatment, being alcoholic and elderly. Likewise, con-current diabetes, presence of lung cavities at the start of the treatment and being a smoker were the significant predictors of longer treatment duration. CONCLUSION: Our findings indicated that the treatment success rate among the new smear positive PTB patients was less than the success target set by World Health Organization. The proportion of patients in the successful outcome category may be increased by closely monitoring the treatment progress of the patients with aforementioned high risk characteristics. Similarly, more aggressive follow-up of the treatment defaulters and transferred out patients could also improve the TB treatment success rate.

3701 ZETOLA, N. M.; MACESIC, N.; MODONGO, C.; SHIN, S. H.; NCUBE, R.; COLLMAN, R. G. **Longer hospital stay is associated with**

higher rates of tuberculosis-related morbidity and mortality within 12 months after discharge in a referral hospital in sub-Saharan Africa. *BMC Infectious Diseases* (2014) **14** (409) (22 July 2014) London, UK; BioMed Central Ltd [En, 39 ref.] Division of Infectious Disease, University of Pennsylvania, Philadelphia, Pennsylvania, USA. Email: nzetola@hotmail.com, nenadmacesic@yahoo.com.au, ntungwana@yahoo.co.uk, sanghy-ukshin@mednet.ucla.edu, rncube@gmail.com, collmanr@rmail.med.upenn.edu

BACKGROUND: Nosocomial transmission of pulmonary tuberculosis (PTB) is a problem in resource-limited settings. However, the degree of TB exposure and the intermediate- and long-term morbidity and mortality of hospital-associated TB is unclear. In this study we determined: (1) the nature, patterns and intensity of TB exposure occurring in the context of current TB cohorting practices in medical centre with a high prevalence of TB and HIV; (2) the one-year TB incidence after discharge; and (3) one-year TB-related mortality after hospital discharge. **METHODS:** Factors leading to nosocomial TB exposure were collected daily over a 3-month period. Patients were followed for 1-year after discharge. TB incidence and mortality were calculated and logistic regression was used to determine the factors associated with TB incidence and mortality during follow up. Results 1,094 patients were admitted to the medical wards between May 01 and July 31, 2010. HIV was confirmed in 690/1,094 (63.1%) of them. A total of 215/1,094 (19.7%) patients were diagnosed with PTB and 178/1,094 (16.3%) patients died during the course of their hospitalization; 12/178 (6.7%) patients died from TB-related complications. Eventually, 916 (83.7%) patients were discharged and followed for one year after it. Of these, 51

(5.6%) were diagnosed with PTB during the year of follow up (annual TB rate of 3,712 cases per 100,000 person per year). Overall, 57/916 (6.2%) patients died during the follow up period, of whom 26/57 (45.6%) died from confirmed TB. One-year TB incidence rate and TB-associated mortality were associated with the number of days that the patient remained hospitalized, the number of days spent in the cohorting bay (regardless of whether the patient was eventually diagnosed with TB or not), and the number and proximity to TB index cases. There was no difference in the performance of each of these 3 measurements of nosocomial TB exposure for the prediction of one-year TB incidence. **CONCLUSION:** Substantial TB exposure, particularly among HIV-infected patients, occurs in nosocomial settings despite implementation of cohorting measures. Nosocomial TB exposure is strongly associated with one-year TB incidence and TB-related mortality. Further studies are needed to identify strategies to reduce such exposure among susceptible patients.

3702 YOUSEF, B. A.; KHALIL, E. A.; HAMID, N. H.; WIDATALLA, S. E. **TNF- α and IL-10 levels: possible risk markers for latent *M. tuberculosis* infections among Sudanese.** *International Journal of Tropical Medicine* (2014) **9** (1) 1-6 Faisalabad, Pakistan; Medwell Online [En, 34 ref.] Department of Pharmacology, Faculty of Pharmacy, University of Khartoum, P.O. Box 1996, Khartoum, Sudan.

Factors responsible for the control of *M. tuberculosis* infection includes T cells, macrophages and cytokines. The incidence and prevalence of latent tuberculosis in Sudan have not yet been reported and latent tuberculosis infection is regarded as a significant risk factor for active pulmonary tuberculosis. This study

aimed to understand the role of immune responses particularly the cytokines profile (levels of TNF- α and IL-10) as risk factors of infection in patients with active and latent *M. tuberculosis* infections. A case control study was conducted in various hospitals in Greater Khartoum, a total of 48 patients and volunteers were enrolled (17 active pulmonary TB patients, 17 latent TB patients and 14 apparently healthy individuals). Whole blood culture with PPD, PHA and LPS stimulation and TNF- α and IL-10, measurement by ELISA were conducted. The results have shown TNF- α and IL-10 significantly higher in active TB patients compared to latent TB patients and healthy individuals ($p < 0.001$). On the other hand, patients with latent TB infection had significantly higher levels of TNF- α and IL-10 compared to healthy individuals ($p < 0.001$). Therefore, the differences in the TNF- α and IL-10 levels probably indicate pivotal roles in the pathogenesis of *M. tuberculosis* infection. Furthermore, TNF- α and IL-10 levels can provide a useful marker for the development of overt and latent TB infections.

3703 TREN TINI, M. M.; OLIVEIRA, F. M. DE; GAETI, M. P. N.; BATISTA, A. C.; LIMA, E. M.; KIPNIS, A.; JUNQUEIRA-KIPNIS, A. P. **Microstructured liposome subunit vaccines reduce lung inflammation and bacterial load after *Mycobacterium tuberculosis* infection.** *Vaccine* (2014) **32** (34) 4324-4332 Oxford, UK; Elsevier Ltd [En, 60 ref.] Laboratorio de Imunopatologia das Doencas Infecciosas, Instituto de Patologia Tropical e Saude Universidade Federal de Goias, Setor Universitario, Goiania - Goias, CEP 74605-050, Brazil. Email: apkipnis@gmail.com, ana_kipnis@ufg.br

BACKGROUND: Tuberculosis is a disease affecting millions of people throughout the world. One of

the main problems in controlling the disease is the low efficacy of the Bacillus Calmette-Guerin (13CG) vaccine in protecting young adults. The development of new vaccines that induce a long-lasting immune response or that stimulate the immunity induced by BCG may improve the control of tuberculosis. METHODS: The use of microstructured liposomes containing HspX, with or without MPL or CpG DNA adjuvants, as vaccines for tuberculosis was evaluated. The HspX-specific humoral and cellular immune responses to the different vaccine formulations were compared. RESULTS: All vaccines containing liposome microparticles and HspX were immunogenic. Vaccines formulated with CpG DNA and HspX induced the strongest humoral and cellular immune responses, mainly by inducing interferon- γ and tumor necrosis factor- α expression by both CD4+ and CD8+ T cells. HspX and MPL mainly induced CD8+ T-cell activation and specific humoral responses. When evaluated the protective efficacy of the formulations against *Mycobacterium tuberculosis* challenge, the microstructured liposome containing L-HspX and L-HspX-CPG DNA reduced both lung inflammatory lesions and the bacterial load. CONCLUSION: We have thus demonstrated, for the first time, the use of microstructured liposomes as an adjuvant and delivery system for a vaccine formulation against tuberculosis.

3704 LIU HAICAN; JIANG YI; LI MACHAO; ZHAO XIUQIN; WAN KANGLIN **[Polymorphisms of human T and B cell epitopes in pstS1 of *Mycobacterium tuberculosis* complex strains in China.]** *Disease Surveillance* (2014) **29** (4) 260-265 Beijing, China; Editorial Board of Disease Surveillance [Ch, en, 19 ref.] State Key Laboratory for Communicable Disease Prevention and Control, Institute for Communicable Disease

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OBJECTIVE: To study the polymorphisms in *pstSI* and its human T and B cell epitopes of *Mycobacterium tuberculosis* complex (MTBC) strains in China. **METHODS:** The *pstS1* sequences of the 180 clinical MTBC isolates and 11 BCG strains were obtained by PCR and first generation sequencing, and together with the published data of one *Mycobacterium bovis* and 3 BCG strains, the sequences were compared with the human T and B cell epitope sequences from Immune Epitope Database (IEDB). The dN and dS values were calculated with Mega 5 software.

RESULTS: Two kinds of insertion and 4 single nucleotide polymorphism (SNP) mutations were found in *pstSI* gene of the studied samples, which affected 79.17% (19/24) of B cell epitopes and 65.22% (15/23) of T cell epitopes area. The dN value of whole *pstSI* gene was 0.000 14, those of T epitopes and non-T epitopes areas were 0.000 17 and 0.000 05 respectively and those of B cell epitopes and non-B epitopes areas were 0.000 23 and zero. The dS value of all sequence types were zero as there was no synonymous mutation. **CONCLUSION:** The polymorphisms exist in the *pstSI* and its human T and B cell epitopes of the MTBC strains selected in China, and the T and B epitope regions have relatively high levels of mutation.