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1767 BANOEI, M. M.; MIRSAEIDI, M. S.; HOUSHMAND, M.; TABARSI, P.; EBRAHIMI, G.; ZARGARI, L.; KASHANI, B. H.; MASJEDI, M. R.; MANSOURI, S. D.; RAMIREZ, J. **Vitamin D receptor homozygote mutant *tt* and *bb* are associated with susceptibility to pulmonary tuberculosis in the Iranian population.** *International Journal of Infectious Diseases* (2010) **14** (1) e84-e85 Oxford, UK; Elsevier Ltd [En, 11 ref.] National Institute of Genetic Engineering and Biotechnology, Tehran, Iran. Email: m0mirs01@louisville.edu

In this study, 60 unrelated patients of Iranian ancestry with confirmed pulmonary tuberculosis (PTB) were evaluated for vitamin D receptor polymorphisms to confirm their suggested association with TB susceptibility. All these patients were enrolled from Massih Daneshvari Hospital during February-August 2005. A control group of 62 healthy subjects selected randomly from blood donor centres close to the reported residences of the 60 cases was also evaluated. For each patient, 10 ml of blood was drawn and stored. VDR genotyping of the *FokI*, *BsmI*, and *TaqI* polymorphisms was carried out by PCR amplification using the genomic DNA of the patients and normal subjects and specific primers. All data were statistically analysed with SPSS version 15.0. Mean age of the TB group was 45.8 ± 11 years and that of the control group was 41 ± 9 years ($p=0.74$); 30 patients (50%) in the TB group and 36 (58%) in the control group were male ($p=0.38$). Results showed that: (1) the *FokI* locus of the VDR gene is not associated with either susceptibility or resistance to TB in the

studied population; (2) genotypes *BB* from the *BsmI* locus and *IT* from the *TaqI* locus occur at a significantly lower frequency in TB patients; and (3) genotypes *bb* from the *BsmI* locus and *tt* from the *TaqI* locus occur at a much higher frequency in TB patients. No direct association was observed between the VDR *FokI* polymorphism and the propensity to develop active TB. In summary, significant differences in the frequency of *BsmI* and *TaqI* haplogroups of the VDR are noted between the PTB patients and the healthy control population, which support the link between vitamin D receptor alteration and susceptibility to TB.

1768 SINSIMER, D.; FALLOWS, D.; PEIXOTO, B.; KRAHENBUHL, J.; KAPLAN, G.; MANCA, C. ***Mycobacterium leprae* actively modulates the cytokine response in naïve human monocytes.** *Infection and Immunity* (2010) **78** (1) 293-300 Washington, USA; American Society for Microbiology (ASM) [En, 45 ref.] Laboratory of Mycobacterial Immunity and Pathogenesis, Public Health Research Institute Center, University of Medicine and Dentistry of New Jersey, 225 Warren Street, Newark, NJ 07103, USA. Email: kaplangi@umdnj.edu

Leprosy is a chronic but treatable infectious disease caused by the intracellular pathogen *Mycobacterium leprae*. Host immunity to *M. leprae* determines the diversity of clinical manifestations seen in patients, from tuberculoid leprosy with robust production of Th1-type cytokines to lepromatous disease, characterized by elevated levels of Th2-type cytokines and a suboptimal proinflammatory response. Previous

reports have indicated that *M. leprae* is a poor activator of macrophages and dendritic cells in vitro. To understand whether *M. leprae* fails to elicit an optimal Th1 immune response or actively interferes with its induction, we have examined the early interactions between *M. leprae* and monocytes from healthy human donors. We found that, in naïve monocytes, *M. leprae* induced high levels of the negative regulatory molecules MCP-1 and interleukin-1 (IL-1) receptor antagonist (IL-1Ra), while suppressing IL-6 production through phosphoinositide-3 kinase (PI3K)-dependent mechanisms. In addition, low levels of proinflammatory cytokines were observed in association with reduced activation of nuclear factor- κ B (NF- κ B) and delayed activation of IL-1 β -converting enzyme, ICE (caspase-1), in monocytes stimulated with *M. leprae* compared with *Mycobacterium bovis* BCG stimulation. Interestingly, although in itself a weak stimulator of cytokines, *M. leprae* primed the cells for increased production of tumor necrosis factor alpha and IL-10 in response to a strongly inducing secondary stimulus. Taken together, our results suggest that *M. leprae* plays an active role to control the release of cytokines from monocytes by providing both positive and negative regulatory signals via multiple signaling pathways involving PI3K, NF- κ B, and caspase-1.

1769 AL-ZAROUNI, M.; DASH, N.; AL-ALI, M.; AL-SHEHHI, F.; PANIGRAHI, D. **Tuberculosis and MDR-TB in the Northern Emirates of United Arab Emirates: a 5-year study.** *Southeast Asian Journal of Tropical Medicine and Public Health* (2010) **41** (1) 163-168 Bangkok, Thailand; SEAMEO Regional Tropical Medicine and Public Health Network [En, 30 ref.] Department of Laboratory Sciences, Al-Qassimi Hospital, Ministry of Health, Sharjah, United Arab Emirates. Email: ndash@sharjah.ac.ae

In this study, we describe the prevalence of TB and occurrence of multidrug-resistance tuberculosis (MDR-TB) in a major referral hospital belonging to the Ministry of Health in Sharjah, United Arab Emirates (UAE). A retrospective

review of the clinical and laboratory records of 1,810 suspected cases of TB was carried out between January 2004 and September 2008. The antimicrobial susceptibility patterns of each *Mycobacterium tuberculosis* isolate were analyzed. During the study period, 312 *M. tuberculosis* culture confirmed cases were recorded; 230 were males and 82 were females. The majority of TB cases (36%) were seen among expatriates from South and Southeast Asian countries. Fifty-one active TB cases (16%) were reported in native people (Emaratis) of the country. The peak age group was between 16 and 45 years. Among first-line antituberculosis drugs, resistance to isoniazid was the most common (21%), followed by streptomycin (14%). MDRTB was found in 15 cases (4.8%). Although the prevalence of TB in UAE is fairly low, an increasing number of cultures confirmed TB and MDR-TB among native and expatriate patients, necessitating improved vigilance in case detection, effective management and prevention of MDR and XDR-TB emergence in the country.

1770 GREEN, E.; OBI, C. L.; NCHABELENG, M.; VILLIERS, B. E. DE; SEIN, P. P.; LETSOALO, T.; HOOSEN, A. A.; BESSONG, P. O.; NDIP, R. N. **Drug-susceptibility patterns of *Mycobacterium tuberculosis* in Mpumalanga Province, South Africa: possible guiding design of retreatment regimen.** *Journal of Health, Population and Nutrition* (2010) **28** (1) 7-13 Dhaka, Bangladesh; International Centre for Diarrhoeal Disease Research [En, 35 ref.] AIDS Virus Research Laboratory, Department of Microbiology, University of Venda, South Africa. Email: rndip@ufh.ac.za, ndip3@yahoo.com

Multidrug-resistant tuberculosis (MDR-TB) has been a cause of concern in both developed and developing countries. The prevalence of drug resistance in *Mycobacterium tuberculosis* (MTB) isolates (n=692) from Mpumalanga province was assessed. In total, 692 (64%) MTB strains from cases with pulmonary TB were tested for susceptibility against rifampicin, isoniazid, ethambutol, and streptomycin using the MGIT

960 instrument. Two hundred and nine (30.2%) strains were resistant to one or more drugs. Resistance to one drug ranged from 1.4% for ethambutol to 17.7% for rifampicin. The prevalence of MDR-TB ranged from 6.7% for three drugs to 34% for four drugs, with significant predictors being patients' age-groups of 25-54 years ($p=0.0012$) and >55 years ($p=0.007$). The result showed a high level (58.4%) of MDR-TB from cases in Mpumalanga province. To achieve a higher cure rate in this province, drug-susceptibility tests must be done for every case.

1771 AYÉ, R.; WYSS, K.; ABDUALIMOVA, H.; SAIDALIEV, S. **Household costs of illness during different phases of tuberculosis treatment in Central Asia: a patient survey in Tajikistan.** *BMC Public Health* (2010) **10** (18) (18 January 2010) London, UK; BioMed Central Ltd (En, 41 ref.) Swiss Tropical Institute, Swiss Centre for International Health, Socinstr. 57, 4002 Basel, Switzerland. Email: raffael.aye@unibus.ch

Background: Illness-related costs incurred by patients constitute a severe economic burden for households especially in low-income countries. High household costs of illness lead to impoverishment; they impair affordability and equitable access to health care and consequently hamper tuberculosis (TB) control. So far, no study has investigated patient costs of TB in the former Soviet Union. Methods: All adult new pulmonary TB cases enrolled into the DOTS program in 12 study districts during the study period were enrolled. Medical and non-medical expenditure as well as loss of income were quantified in two interviews covering separate time periods. Costs of different items were summed up to calculate total costs. For missing values, multiple imputation was applied. Results: A cohort of 204 patients under DOTS, 114 men and 90 women, participated in the questionnaire survey. Total illness costs of a TB episode averaged \$1053 (c. \$4900 purchasing power parity, PPP), of which \$292, \$338 and \$422 were encountered before the start of treatment during intensive phase and in continuation phase respectively. Costs per

month were highest before the start of treatment (\$145) and during intensive phase (\$153) and lower during continuation phase (\$95). These differences were highly significant (paired t-test, $p<0.0005$ for both comparisons). Conclusions: The illness-related costs of an episode of TB exceed the per capita GDP of \$1600 PPP about two-and-a-half times. Hence, these costs are catastrophic for concerned households and suggest a high risk for impoverishment. Costs are not equally spread over time, but peak in early stages of treatment, exacerbating the problem of affordability. Mitigation strategies are needed in order to control TB in Tajikistan and may include social support to the patients as well as changes in the management of TB cases. These mitigation strategies should be timed early in treatment when the cost burden is highest.

1772 KUMARASAMY, N.; VENKATESH, K. K.; BELLA DEVALEENOL; POONGULALI, S.; TOKUGHA YEPHTHOMI; PRADEEP, A.; SUNEETA SAGHAYAM; FLANIGAN, T.; MAYER, K. H.; SUNITI SOLOMON **Factors associated with mortality among HIV-infected patients in the era of highly active antiretroviral therapy in southern India.** *International Journal of Infectious Diseases* (2010) **14** (2) e127-e131 Oxford, UK; Elsevier Ltd [En] YRG Centre for AIDS Research and Education, Voluntary Health Services, Taramani, Chennai 600 113, India. Email: kumarasamy@yrgcare.org

Objective: To describe the causes of mortality among the HIV-infected in southern India in the era of highly active antiretroviral therapy (HAART). Methods: Analyses of this patient cohort were conducted using the YRG Centre for AIDS Research and Education HIV Natural History Observational Database. Causes of death were then individually confirmed by patient chart review. Results: Sixty-nine deaths occurred within the inpatient unit; 25% were female and the median age of the 69 patients was 34 years. Over half of the patients (55%) died within three months of initiating HAART. At the time of enrollment into clinical care, the median CD4 cell count was 64 cells/ μ l (interquartile range (IQR)

37-134). At the time of initiating HAART, the median CD4 cell count was 58 cells/ μ l (IQR 31-67) for patients who died within 3 months of initiating HAART and 110 cells/ μ l (IQR 77-189) for patients who died more than 3 months after initiating HAART. Close to three-fourths of patients (70%) died from an AIDS-defining illness (ADI). The major ADI causes of death included *Pneumocystis firoveci* pneumonia (22%), extrapulmonary tuberculosis (19%), CNS toxoplasmosis (12%), and pulmonary tuberculosis (10%). A tenth of patients died from cerebrovascular infarcts. Three patients (4%) died from non-Hodgkin lymphoma. Conclusions : AIDS-related events continue to be the major source of mortality among the HIV-infected in southern India in the era of HAART. This mortality pattern justifies increased proactive efforts to identify HIV-infected patients and initiate HAART earlier, before patients present to care with advanced immunodeficiency.

1773 FADER, T.; PARKS, J.; KHAN, N. U.; MANNING, R.; STOKES, S.; NASIR, N. A. **Extrapulmonary tuberculosis in Kabul, Afghanistan: a hospital-based retrospective review.** *International Journal of Infectious Diseases* (2010) **14** (2) e102-e110 Oxford, UK; Elsevier Ltd [En] CURE International Hospital, PO Box 621, Darulaman Rd, near King's Palace, Karte-Se, Kabul, Afghanistan. Email: jtp27@georgetown.edu, johnticeparks@gmail.com

Objectives : The purpose of this study is to amplify the knowledge base of the epidemiology, symptoms, and signs of extrapulmonary tuberculosis (EPTB) in Afghanistan. Methods : This is a retrospective review of EPTB diagnosed at CURE International Hospital and CURE Family Health Center (FHC) in Kabul, Afghanistan during a recent 20-month period. Results—One hundred eighteen cases were identified from patients presenting to the hospital and FHC. This group represents the spectrum of EPTB seen at a single referral center in Kabul. The ratio of females to males was 2.03:1. Lymph node tuberculosis comprised the greatest number of EPTB cases (37.3%, $n=44$). The central

nervous system was the next most frequent site of EPTB involvement (20.3%, $n=24$), followed in descending order by skeletal, pleural, abdominal, cutaneous, genitourinary, pericardial, miliary, and breast tuberculosis. Conclusions : The 2:1 ratio of female to male EPTB cases coincides with the unusual epidemiologic pattern seen in smear-positive pulmonary TB in Afghanistan. As the first epidemiological report of EPTB from Afghanistan, this study illustrates the varied presentations of EPTB that should be brown by healthcare workers throughout the country.

1774 ADDO, K. K.; HOF, S. VAN DEN; MENSAH, G. I.; HESSE, A.; BONSU, C.; KORAM, K. A.; AFUTU, F. K.; BONSU, F. A. **A tuberculin skin test survey among Ghanaian school children.** *BMC Public Health* (2010) **10** (35) (26 January 2010) London, UK; BioMed Central Ltd [En, 20 ref.] Bacteriology Department, Noguchi Memorial Institute for Medical Research, Legon, Ghana. Email: kaddo@noguchi.mimcom.org

Background: Ghana has not conducted a national tuberculin surveyor tuberculosis prevalence survey since the establishment of the National Tuberculosis Control Programme. The primary objective of this study was therefore to determine the prevalence of tuberculin skin sensitivity in Ghanaian school children aged 6-10 years in 8 out of 10 regions of Ghana between 2004 and 2006. Methods: Tuberculin survey was conducted in 179 primary schools from 21 districts in 8 regions. Schools were purposively selected so as to reflect the proportion of affluent private and free tuition public schools as well as the proportion of small and large schools. Results: Of the 24,778 children registered for the survey, 23,600 (95.2%) were tested of which 21,861 (92.6%) were available for reading. The age distribution showed an increase in numbers of children towards older age: 11% of the children were 6 years and 25%, 10 years. Females were 52.5% and males 47.5%. The proportion of girls was higher in all age groups (range 51.4% to 54.0%, $p<0.001$). BCG scar was visible in 89.3% of the children. The percentage of children with a BCG scar differed by district and by

age. The percentage of children with a BCG scar decreased with increasing age in all districts, reflecting increasing BCG vaccination coverage in Ghana in the last ten years. The risk of tuberculosis infection was low in the northern savannah zones compared to the southern coastal zones. Using a cut-off of 15 mm, the prevalence of infection ranged from 0.0% to 5.4% and the Annual Risks of Tuberculosis Infection 0.0% to 0.6%. There was an increase in the proportion of infected children after the age of 7 years. Children attending low and middle-class schools had a higher risk of infection than children attending upper-class schools. Conclusion: Tuberculosis infection is still a public health problem in Ghana and to monitor the trend, the survey needs to be repeated at 5 years interval.

1775 ZHANG FUREN; CHEN SHUMIN; SUN YIPING; CHU TONGSHENG. **Healthcare seeking behaviour and delay in diagnosis of leprosy in a low endemic area of China.** *Leprosy Review* (2009) **80** (4) 416-423 Colchester, UK; LEPRO [En, 22 ref.] Shandong Provincial Institute of Dermatology, 57 Jiyuan Lu, Jinan, Shandong, 250 022, China. Email: chenshm@public.jn.sd.cn

Delay in diagnosis of leprosy can increase the risk of nerve function impairments and promote the transmission of the infection in a community. In order to understand the factors associated with the delays in diagnosis of leprosy, a questionnaire-based interview was conducted to collect information on the delays among 88 newly diagnosed leprosy patients. The results showed that delay was common and associated with the high rate of disability in the study population. The total mean delay was 50.18 months (median 36 months). The mean patient delay was 24.4 months (median 9.5 months) and the mean health service delay was 25.7 months (median 12 months). Patients with leprosy reported a variety of symptoms/signs at an early stage of the disease, particularly numbness and tingling. Ignorance of the illness was reported to be the main reason for the patient's delay. Health seeking actions ranged from 1 to 50 with a mean

of 7.2 after becoming aware of the first symptom/sign. The effectiveness of early diagnosis of leprosy through health promotion in the population needs to be validated and continuous training on leprosy among healthcare providers is needed.

1776 HATTA, M.; MAKINO, M.; RATNAWATI; MASHUDI; YADI, SABIR, M.; TANDIROGANG, N.; RUSYATI, L. M. M.; KAI, M.; FUKUTOMI, Y.; MIYAMOTO, Y.; MUKAI, T.; MAEDA, Y. **Detection of serum antibodies to *M. leprae* Major Membrane Protein-II in leprosy patients from Indonesia.** *Leprosy Review* (2009) **80** (4) 402-409 Colchester, UK; LEPRO [En, 17 ref.] Department of Microbiology, Faculty of Medicine, Molecular Biology and Immunology Laboratory, Hasanuddin University, Km. 10, Kampus Tamalanrea, Makassar, Indonesia. Email: yumi@nih.go.jp

Background: Sero-diagnostic methods are the easiest way of diagnosing an infectious disease in developing countries. In leprosy, phenolic glycolipid-1 (PGL-I) based methods for the detection of leprosy are currently available, but the use of these methods has been hindered due to the inherent problems of sensitivity. We previously showed that antibodies to Major Membrane Protein-II (MMP-II) derived from *Mycobacterium leprae* could be used to diagnose leprosy in Japan. Methods: Sera from patients and healthy individuals were collected with informed consent and the anti-MMP-II antibody levels of the sera were measured by enzyme-linked immunosorbent assay. The study was conducted at South Sulawesi and Bali, in Indonesia. The study population included 40 each of multi-bacillary leprosy and paucibacillary leprosy patients, 30 tuberculosis and 16 patients with typhoid. Results: We evaluated the anti-MMP-II antibody levels in Indonesian individuals. The cut-off value was determined from receiver operator characteristic curve as 0-124 using the O.D. titers for patients with multi-bacillary leprosy, so that the sensitivity of the test was 97-5% and the specificity taking healthy individuals as controls was 98.4%. Using the determined cut-off values,

98% of multibacillary (MB) leprosy and 48% of paucibacillary (PB) leprosy patients had positive levels of anti-MMP-II antibodies, 13% of patients with typhoid and 22% of the household contacts of MB leprosy had positive levels of anti-MMP-II antibodies. Conclusions: Our results suggest that measuring anti-MMP-II antibody levels could facilitate the detection of leprosy in endemic countries.

1777 VEEN, N. H. J. VAN; LOCKWOOD, D. N. J.; BRAKEL, W. H. VAN; RAMIREZ, J., JR.; RICHARDUS, J. H. **Interventions for erythema nodosum leprosum. A Cochrane review.** *Leprosy Review* (2009) **80** (4) 355-372 Colchester, UK; LEPRO [En, 24 ref.] Department of Public Health, Erasmus MC, University Medical Center Rotterdam, 3000 CA, Netherlands. Email: j.richardus@erasmusmc.nl

Introduction: Treatment for erythema nodosum leprosum (ENL), an immunological complication of leprosy, is diverse. We undertook a systematic review as it was not clear which treatments were most beneficial. Methods: We did a systematic search to identify randomised controlled trials (RCTs) comparing treatment with placebo, no treatment or another therapy. Two authors assessed quality and checked data. Results: We included 13 studies involving 445 participants. These trials assessed: betamethasone, thalidomide, pentoxifylline, clofazimine, indomethacin and levamisole. The quality of the trials was generally poor and no results could be pooled due to the treatments being so heterogeneous. Treatment with thalidomide showed a significant benefit compared to aspirin (RR 2.43; 95% CI 1.28 to 4.59). Clofazimine treatment was superior to prednisolone (more treatment successes; RR 3.67; 95% CI 1.36 to 9.91) and thalidomide (fewer recurrences; RR 0.08; 95% CI 0.01, 0.56). Minor adverse events were significantly lower in participants on a low dose thalidomide regimen compared to a high dose thalidomide regimen (RR 0.46; 95% CI 0.23 to 0.93). Significantly more minor adverse events were reported in participants taking clofazimine

compared with prednisolone (RR 1.92; 95% CI 1.10 to 3.35). None of the studies assessed quality of life or economic outcomes. Conclusion: There is some evidence of benefit for thalidomide and clofazimine, but generally we did not find clear benefits for interventions in the management of ENL. This does not mean they do not work because the studies were small and poorly reported. Larger studies using clear definitions and internationally recognised scales are urgently required.

1778 SLIM, F. J.; FABER, W. R.; MAAS, M. **The role of radiology in nerve function impairment and its musculoskeletal complications in leprosy.** *Leprosy Review* (2009) **80** (4) 373-387 Colchester, UK; LEPRO [En, 81 ref.] Department of Rehabilitation, Academic Medical Center, Meibergdreef 9, 1100 DD Amsterdam, PO Box 22660, Netherlands. Email: f.j.slim@amc.uva.nl

Conventional techniques, such as plain radiography and bonescintigraphy, were used in the past to evaluate skeletal changes in patients with leprosy. More recent publications focus on radiological imaging of affected nerves, and involve advanced modalities such as Computed Tomography (CT-scan), Ultrasonography (US), and Magnetic Resonance Imaging (MRI). US and MRI can play an especially important role in the evaluation of nerve involvement in newly diagnosed patients, and also during leprosy reactions. This is important, because when nerve involvement is diagnosed in time, it may be reversible with adequate treatment. Radiological modalities can also play an important role during the follow-up of patients with leprosy with nerve function impairment. Skeletal and soft-tissue abnormalities occur, even after treatment. The so-called neuropathic foot is a well known consequence. Because of nerve function impairment, there is a constant risk of developing ulcers and subsequent osteomyelitis, or neuro-osteopathy (Charcot foot or tarsal disintegration), which can lead to the amputation of the affected limb. Different radiological modalities can be used during the evaluation and follow-up of

patients with leprosy with a neuropathic foot. With this up-to-date review, we highlight the importance and potential role of radiological imaging techniques in leprosy.

1779 LIU DAOZHONG; LI GANG; HUANG WEI; GAO JUN; YUE CHUNMIN; XIAO QIN. **Analysis of newly detected Leprosy cases and misdiagnosis in Wuhan (1990-2004).** *Leprosy Review* (2009) **80** (4) 410-415 Colchester, UK; LEPRO [En, 9 ref.] Wuhan Institute of Dermatology and Venereology, Hubei Province, 430030, China. Email: liu-dao-zhong@163.com

Objective: To analyse the leprosy epidemiological trends and the diagnostic delay in newly detected cases between 1990 and 2004 in Wuhan. Methods: We reviewed the clinical records of all 80 leprosy patients who were referred to the Wuhan Institute of Dermatology and Venereology (WHIDV) during 1990 and 2004, and the clinical information of diagnosis-delayed cases was analysed. Results: Patients were determined as lepromatous leprosy (LL, 24, 30%), borderline lepromatous leprosy (BL, 15, 18.75%), borderline leprosy (BB, 9, 11.25%), borderline tuberculoid leprosy (BT, 12, 15%), and tuberculoid leprosy (TT, 20, 25%), respectively. The patients were more likely to present with multibacillary (MB, 48 cases) rather than with paucibacillary (PB, 32 cases). Among the 80 newly detected patients, 53 cases (66.25%) had been misdiagnosed (51 cases in general hospitals, two cases in WHIDV), 23 cases were treated with hospitalisation in department of dermatology of general hospitals. Up to 20 kinds of dermatological conditions involved in case misdiagnosis. Conclusions: Misdiagnosis of dermatological conditions and ignorance of the disease among general practitioners and hospital dermatologists were the main causes of diagnostic delay in Wuhan, which is leading to incorrect treatment for patients suffering with a variety of damage due to leprosy.

1780 DAVOODIAN, P.; DADVAND, H.; RAZNAHAN, M.; BAGHESTANI, S.; MAHBUBI, A.; BAGERI, A. **Case finding survey for leprosy in**

Iran: Bandar Abbas and Minab. *Leprosy Review* (2009) **80** (4) 441-444 Colchester, UK; LEPRO [En, 11 ref.] Department of infectious Disease, Hormozgan University of Medical Sciences, Bandar Abbas, Iran. Email: sw_f@yahoo.com

In a descriptive cross-sectional study, medical records of 145 leprosy patients referred to Bandar Abbas Leprosy Centre (Iran) between 1972 and 2004 were reviewed. Family members and neighbours of known patients were the screening population. Family members were examined and the neighbours were educated about manifestations of leprosy. The study was conducted on an initial population of 145 cases (60 females and 85 males) referred with a diagnosis of leprosy. In follow-up visits in 2004, out of 145 patients, 43 (29.7%) were dead and 11 (7.6%) had migrated to another place; finally 91 (62.7%) were available from which 41 were female and 50 were male. Some 461 family members were examined; 1400 neighbours received health education and 48 came for examination. 509 people were examined, 20 of whom were suspected of having leprosy and were referred to the dermatology centre. In the centre, 15 people had biopsies taken from lesions, and 3 people were confirmed as having leprosy. One of them was from a family with a case detection rate of 21.7 in 10000, and 2 of them were neighbours of cases with a case detection rate of 14.3 in 10000. All the detected cases lived in endemic areas. One of them was the grandson of a confirmed case of leprosy, but 2 of them had no close contact with leprosy patients. No disability was present in these newly detected cases.

1781 JONG, B. C. DE; HAMMOND, A.; OTU, J. K.; ANTONIO, M.; ADEGBOLA, R. A.; OTA, M. O. **Immunogenicity of antigens from the TbD1 region present in *M. africanum* and missing from "modern" *M. tuberculosis*: a cross-sectional study.** *BMC Infectious Diseases* (2010) **10** (11) (19 January 2010) London, UK; BioMed Central Ltd [En, 12 ref.] Bacterial Diseases Programme, MRC Laboratories, POB 273, Banjul, Gambia. Email: bdejong@mrc.gm

Background: Currently available tools cannot be used to distinguish between sub-species of the *M. tuberculosis* complex causing latent tuberculosis (TB) infection. *M. africanum* causes up to half of TB in West-Africa and its relatively lower progression to disease suggests the presence of a large reservoir of latent infection relative to *M. tuberculosis*. Methods: We assessed the immunogenicity of the TbD1 region, present in *M. africanum* and absent from "modern" *M. tuberculosis*, in an ELISPOT assay using cells from confirmed *M. africanum* or *M. tuberculosis* infected TB patients without HIV infection in the Gambia. Results: Antigens from the TbD1 region induced IFN γ responses in only 35% patients and did not discriminate between patients infected with *M. africanum* vs. *M. tuberculosis*, while PPD induced universally high responses. Conclusions: Further studies will need to assess other antigens unique to *M. africanum* that may induce discriminatory immune responses.

1782 PARADA, M. T.; ALBA, A.; SEPÚLVEDA, C. **Early and late infections in lung transplantation patients.** In *Proceedings from the Joint Congress of the 10th Latin American Caribbean Society of Transplantation and the 2nd Congress of the Chilean Transplantation Societies. Transplantation Proceedings* (2010) **42** (1) 333-335 New York, USA; Elsevier [En, 11 ref.] Lung Transplant Program, Clinica Las Condes, Santiago, Chile. Email: mtparada@clc.cl

Infections are an important cause of morbidity and mortality among transplanted patients. Their pathophysiology is associated with anatomic factors, immunosuppression, and pretransplant viral exposure. The aim of this investigation was to characterize infections following lung transplantation. We retrospectively analyzed the charts of 51 lung transplant recipients, who were transplanted between 1999 and 2008. Infections were classified according to their origin, etiology, occurrence time, and risk factors. The patient mean age was 55 years (range 13-71), 65% were male, and pulmonary fibrosis was the lung disease etiology in 59% of cases. Seventy-one

episodes of infection were reported in the 51 patients, including (75%) during the first year after transplantation and 30 within the first 3 months (42%). Between the 4th and 11th months the number of infections decreased to 23 (32%), and afterwards there were 18 additional cases. The original site of infection was pulmonary in 43 episodes (60%), and the etiology was bacterial in 34 (48%), with *Pseudomonas* in 12 instances (35% of bacterial infections). Viruses were involved in 25 episodes, especially cytomegalovirus (CMV) in seronegative patients. The nine infections of fungal etiology (13%) were all caused by *Aspergillus* and always associated with either an acute rejection episode or suture damage. Three cases of tuberculosis were diagnosed, including two in the late post-transplant period. Three patients died of early infections. Conclusions. The critical period for infections in lung transplantation patients is the first 3 months, especially for those of bacterial etiology. CMV diseases were more common in seronegative patients and fungal infections in airway injury cases.

2142 FAIRALL, L.; BACHMANN, M. O.; ZWARENSTEIN, M.; BATEMAN, E. D.; NIESSEN, L. W.; LOMBARD, C.; MAJARA, B.; ENGLISH, R.; BHEEKIE, A.; RENSBURG, D. VAN; MAYERS, P.; PETERS, A.; CHAPMAN, R. **Cost-effectiveness of educational outreach to primary care nurses to increase tuberculosis case detection and improve respiratory care: economic evaluation alongside a randomised trial.** *Tropical Medicine and International Health* (2010) **15** (3) 277-286 Oxford, UK; Blackwell Publishing Ltd [En, 36 ref.] Knowledge Translation Unit, University of Cape Town Lung Institute, Cape Town, South Africa. Email: m.bachmann@uea.ac.uk

OBJECTIVE: To evaluate the cost-effectiveness of an educational outreach intervention to improve primary respiratory care by South African nurses. METHODS: Cost-effectiveness analysis alongside a pragmatic cluster randomised controlled trial, with individual patient data. The intervention, the Practical Approach to Lung Health in South Africa (PALSA), comprised educational outreach based

on syndromic clinical practice guidelines for tuberculosis, asthma, chronic obstructive pulmonary disease, pneumonia and other respiratory diseases. The study included 1999 patients aged 15 or over with cough or difficult breathing, attending 40 primary care clinics staffed by nurses in the Free State province. They were interviewed at first presentation, and 1856 (93%) were interviewed 3 months later. RESULTS: The intervention increased the tuberculosis case detection rate by 2.2% and increased the proportion of patients appropriately managed (that is, diagnosed with tuberculosis or prescribed an inhaled corticosteroid for asthma or referred with indicators of severe disease) by 10%. It costs the health service \$68 more for each extra patient diagnosed with tuberculosis and \$15 more for every extra patient appropriately managed. Analyses were most sensitive to assumptions about how long training was effective for and to inclusion of household and tuberculosis treatment costs. CONCLUSION: This educational outreach method was more effective and more costly than usual training in improving tuberculosis, asthma and urgent respiratory care. The extra cost of increasing tuberculosis case detection was comparable to current costs of passive case detection. The syndromic approach increased cost-effectiveness by also improving care of other conditions. This educational intervention was sustainable, reaching thousands of health workers and hundreds of clinics since the trial.

2143 MUPERE, E.; ZALWANGO, S.; CHIUNDA, A.; OKWERA, A.; MUGERWA, R.; WHALEN, C. **Body composition among HIV-seropositive and HIV-seronegative adult patients with pulmonary tuberculosis in Uganda.** *Annals of Epidemiology* (2010) **20** (3) 210-216 New York, USA; Elsevier [En, 40 ref.] Department of Paediatrics and Child Health, School of Medicine, Makerere University, Kampala, Uganda. Email: ccwhalen@uga.edu

PURPOSE: We determined whether human immunodeficiency virus (HIV) infection affects body cell mass and fat mass wasting among adults

with pulmonary tuberculosis (PTB). METHODS: We screened 967 Ugandan adults for PTB and HIV infection in a cross-sectional study. We compared anthropometric and bioelectric impedance analysis (BIA) body composition parameters among HIV-seropositive and HIV-seronegative men and women with or without PTB by using a non-parametric test. RESULTS: We found that poor nutritional status associated with TB differed among men and women. Anthropometric and BIA body composition did not differ between HIV-seropositive and HIV-seronegative patients regardless of gender. Average weight group difference in men consisted of body cell mass and fat mass in equal proportions of 43%. In women, average weight group difference consisted predominantly of fat mass of 73% and body cell mass of 13%. Compared to individuals without TB, patients with TB had lower body mass index, weight, body cell mass, and fat mass regardless of gender and HIV status. CONCLUSIONS: Gender, but not HIV status, was associated with body composition changes in TB. TB appears to be the dominant factor driving the wasting process among co-infected patients.

2144 COULIBALY, B.; COULIBALY-N'GOLO, M. D. G.; EKAZA, E.; AKA, N.; N'GUESSAN, K. R.; BAUDRYARD, A.; ASSANDÉ, J. M.; TRÉBISSOU, N.; GUÉDÉ-GUINA, F.; DOSSO, M. **[Implementation of in vitro culture of *Mycobacterium ulcerans* from clinical samples versus detection of acid-fast bacilli and bacterial genome in Abidjan, Côte d'Ivoire.]** Mise en place de la culture in vitro de *Mycobacterium ulcerans* à partir d'échantillons cliniques versus recherche de BAAR et détection du génome bactérien à Abidjan, Côte d'Ivoire. *Bulletin de la Société de Pathologie Exotique* (2010) **103** (1) 2-7 Paris, France; Springer-Verlag France [Fr, en, 17 ref.] Unité des mycobactéries tuberculeuses et atypiques, département de bactériologie-virologie, institut Pasteur de Côte-d'Ivoire, BP 490, Abidjan 01, Côte d'Ivoire. Email: ekazae@yahoo.fr

Mycobacterium ulcerans infections are a public health problem in Côte d'Ivoire. The etiological

diagnosis of this disease made by culture remains a big concern due to the slowness and difficulties encountered. This detection by culture of *M. ulcerans* represents a big interest as it allows obtaining the circulating strains for research. The purpose of this study was to determine on a routine basis in a poorly equipped laboratory, in vitro culture of *M. ulcerans* from exudates of skin ulcerations and from biopsy of patients with suspected Buruli ulcer. A particular attention was paid to the conditioning of the sample forwarded to the laboratory and inoculation in Lowenstein-Jensen medium supplemented with glycerol. The results of the three methods for the analysis showed 26.7, 57.4 and 17.8% positive rate respectively in the microscopy examination by nested PCR and by culture. In all the analysis the positive rate from biopsy is higher than that obtained from exudates. The overall contamination rate by invasion of the three tubes of culture by fungi is 15.8 with 14.3 and 19.4% respectively, from exudates and biopsies. All positive samples in Ziehl-Neelsen staining and in culture were also positive by nested PCR. The nested PCR confirmed the positive strains found in culture, which were responsible for skin ulcerations. After culture, which only one strain was nPCR negative. This strain was identified as *Mycobacterium gordonae*. Our culture conditions showed that *M. ulcerans* was not the only identified and that other strains were present in the culture. We can conclude that other strain culture of *M. ulcerans*, in spite of the growth difficulties of the bacterium can be performed in laboratory in developing countries despite the lack of reagent and consumables. The implementation of this culture is the only way to determine sensitivity tests in vitro and in vivo in order to treat patients with Buruli ulcer.

2145 GAVIRIA, M. B.; HENAO, H. M.; MARTÍNEZ, T.; BERNAL, E. **[The role of health care providers in the late diagnosis of pulmonary tuberculosis among adults in Medellin, Colombia.]** Papel del personal de salud en el diagnóstico tardío de la tuberculosis pulmonar en

adultos de Medellín. Colombia. *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* (2010) **27** (2) 83-92 Washington, USA; Pan American Health Organization [Es, en. 30 ref.] Facultad Nacional de Salud Pública, Universidad de Antioquia, calle 62 No. 52-59. piso 2. Medellín, Colombia. Email: mgaviria@guajiros.udea.edu.co

Objective. To describe the role of health care providers in the delayed diagnosis of pulmonary tuberculosis (PTB) among the adult population in a city in Colombia. **Methods.** A case study of PTB diagnosis among adults in the city of Medellín, Colombia in 2007. Quantitative and qualitative data were collected through indepth interviews with 19 patients (11 with early diagnosis and 8 with late diagnosis), from medical records, and by a survey of PTB related knowledge and practices among 89 doctors and nurses at health care clinics. A research workshop was held with patients to share to results and validate new categories. **Results.** A lack of PTB knowledge and patient stereotyping were found to lead to misinterpretation of symptoms and the use of symptomatic treatments. The lack of knowledge regarding risk factors and clinical protocols made diagnosis difficult when the patient did not match the stereotype or presented with a more well-known illness. Misinformation on PTB transmission and inappropriate measures led to discriminatory practices and social isolation and only reinforced stereotypes and stigma, which in turn discouraged the quest for medical attention. **Conclusions:** Health care providers played a large part in the late diagnosis of PTB in the adults studied. Beliefs regarding social stigma and a lack of knowledge about the disease - shared by providers and patients - contributed to stereotyping of the illness and the disease-carrier, and limited the probability of an early diagnosis of PTB.

2146 ROCCA, S.; CUBEDDU, T; NIEDDU, A. M.; PIRINO, S.; APPINO, S.; ANTUOFERMO, E.; TANDA, F.; VERIN, R.; SECHI, L. A.; TACCINI, E.; LEONI, A. **Detection of *Mycobacterium avium* spp. paratuberculosis (Map) in samples of sheep**

paratuberculosis (John's disease or JD) and human Crohn's disease (CD) using liquid phase RT-PCR, in situ RT-PCR and immunohistochemistry. In *Proceedings of the 18th SIPAOC Congress, Trezzo sull'Adda, Milan, Italy, 17-20 September 2008*. [Edited by Carta, A.; Garippa, G.; Moniello, G.]. *Small Ruminant Research* (2010) **88** (2/3) 126-134 New York, USA; Elsevier Inc. [En, 32 ref.] Department of Pathology and Veterinary Clinic, Faculty of Veterinary Medicine, University of Sassari, via Vienna 2, 07100 Sassari, Italy. Email: rocca@uniss.it

The association between the human Crohn's disease (CD) and *Mycobacterium avium* ssp. *paratuberculosis* (Map), the etiological agent of the sheep paratuberculosis (John's disease or JD), has been controversial because of technical limits to detection of the microorganism. Intestinal samples from 10 sheep naturally affected with JD (5 paucibacillary and 5 multibacillary infections), 8 humans with CD and 1 sheep experimentally infected with a reference strain (ATCC 43015) of Map isolated from a patient with CD were collected. A procedure for the extraction of RNA from formalin-fixed, paraffin embedded tissues was optimized. Archived tissue samples from cases of JD and CD were examined by light microscopy using Haematoxyline and Eosin and Ziehl-Neelsen stains. Liquid phase RT-PCR and immunohistochemistry were also performed on the same samples. In situ RT-PCR targets were the IS900 sequence and the gene locus F57. The effectiveness of the primer-probes was demonstrated using Dot-Blot testing. A diffuse granulomatous enteritis was present in samples from all sheep with JD; lesions were categorized as subtypes 3b and 3c (Perez classification). Human CD samples appeared very similar to the lymphocytic paucimicrobial form of JD (subtype 3c) and the experimentally infected sheep had an enteritis with lesions compatible with Perez type 2. Liquid phase RT-PCR and Dot-Blot test were positive for Map in all sheep with JD and negative in all samples from CD patients as well as the experimentally infected sheep. In situ RT-PCR was

positive for the presence of Map both in JD and CD infected samples. Immunohistochemistry confirmed the in situ RT-PCR results in all JD and CD samples, with the exception of the experimentally infected sheep, which resulted negative. This study demonstrated the effectiveness of the in situ RT-PCR technique in the contribution to establish Map as the etiological agent of CD.

2147 RANDREMANANA, R. V.; RICHARD, V.; RAKOTOMANANA, F.; SABATIER, P.; BICOUT, D. J. **Bayesian mapping of pulmonary tuberculosis in Antananarivo, Madagascar.** *BMC Infectious Diseases* (2010) **10** (21) (5 February 2010) London, UK; BioMed Central Ltd [En, 27 ref.] Unité Epidémiologie, Institut Pasteur de Madagascar, BP 1274. Antananarivo (101). Madagascar. Email: rrandrem@pasteur.mg

Background: Tuberculosis (TB), an infectious disease caused by the *Mycobacterium tuberculosis* is endemic in Madagascar. The capital, Antananarivo is the most seriously affected area. TB had a non-random spatial distribution in this setting, with clustering in the poorer areas. The aim of this study was to explore this pattern further by a Bayesian approach, and to measure the associations between the spatial variation of TB risk and national control program indicators for all neighbourhoods. Methods: Combination of a Bayesian approach and a generalized linear mixed model (GLMM) was developed to produce smooth risk maps of TB and to model relationships between TB new cases and national TB control program indicators. The TB new cases were collected from records of the 16 Tuberculosis Diagnostic and Treatment Centres (DTC) of the city from 2004-2006. And five TB indicators were considered in the analysis: number of cases undergoing retreatment, number of patients with treatment failure and those suffering relapse after the completion of treatment, number of households with more than one case, number of patients lost to follow-up, and proximity to a DTC. Results: In Antananarivo, 43.23% of the neighbourhoods had a standard-

ized incidence ratio (SIR) above 1, of which 19.28% with a TB risk significantly higher than the average. Identified high TB risk areas were clustered and the distribution of TB was found to be associated mainly with the number of patients lost to follow-up (SIR: 1.10, CI 95%: 1.02-1.19) and the number of households with more than one case (SIR: 1.13, CI 95%: 1.03-1.24). Conclusion: The spatial pattern of TB in Antananarivo and the contribution of national control program indicators to this pattern highlight the importance of the data recorded in the TB registry and the use of spatial approaches for assessing the epidemiological situation for TB. Including these variables into the model increases the reproducibility, as these data are already available for individual DTCs. These findings may also be useful for guiding decisions related to disease control strategies.

2148 AI XIANQIN; MEN KE; GUO LIUJIA; ZHANG TIANHUA; ZHAO YAN; SUN XIAOLU; ZHANG HONGWEI; HE GUANGXUE; WERF, M. J. VAN DER; HOF, S. VAN DEN **Factors associated with low cure rate of tuberculosis in remote poor areas of Shaanxi Province, China: a case control study.** *BMC Public Health* (2010) **10** (112) (7 March 2010) London, UK; BioMed Central Ltd [En, 20 ref.] Shaanxi Provincial Institute for TB Control and Prevention, Xi'an, Shaanxi Province, China. Email: menke@foxmail.com

Background: The directly observed therapy-short course (DOTS) strategy was introduced in Shaanxi province, China to improve tuberculosis (TB) control by means of improved case detection (target: $\geq 70\%$) and treatment success rates (target: $\geq 85\%$) in new smear positive (SS+) TB patients. At a provincial level the targets were both reached in 2005. However in 30 (28%) out of 107 counties of Shaanxi province the cure rate was below 85%. This study aimed to investigate patient and treatment characteristics associated with non-cure after tuberculosis (TB) treatment in these counties. Methods: In this case-control study, new smear positive TB cases in 30 counties with a cure rate $< 85\%$ were included. Cured

patients were compared to non-cured patients using logistic regression analysis to assess determinants for non-cure. Results: Of the 659 patients included, 153 (23.2%) did not have cure as treatment outcome. Interruption of treatment was most strongly associated with non-cure (OR=8.7, 95% CI 3.9-18.4). Other independent risk factors were co-morbidity, low education level, lack of appetite as an initial symptom of TB disease, diagnosis of TB outside of the government TB control institutes, missing sputum re-examinations during treatment, and not having a treatment observer. Twenty-six percent of patients did not have a treatment observer. The non-cure rate was better for those with a doctor (odds ratio (OR) 0.38, 95% confidence interval (CI) 0.17-0.88) as treatment observer than for those with a family member (OR 0.62, 95% CI 0.37-1.03). The main reason for interrupted treatment mentioned by patients was presence of adverse effects during treatment (46.5%). Conclusions: Interruption of treatment was most strongly associated with non-cure. Although treatment observation by medical staff is preferred, in order to diminish the proportion of patients who do not have a treatment observer and thereby reduce the proportion of patients who interrupt treatment, we suggest making it possible for family members, after sufficient training, to be treatment observers in remote areas where it is logistically difficult to have village doctors observe treatment for all patients.

2149 LUO TAO; ZHAO MING; LI XIA; XU PENG; GUI XIAOHONG; PICKERILL, S.; DERIEMER, K.; MEI JIAN; GAO QIAN **Selection of mutations to detect multidrug-resistant *Mycobacterium tuberculosis* strains in Shanghai, China.** *Antimicrobial Agents and Chemotherapy* (2010) **54** (3) 1075-1081 Washington, USA; American Society for Microbiology (ASM) [En, 44 ref.] Key laboratory of Medical Molecular Virology, Institute of Biomedical Sciences and Institute of Medical Microbiology, Fudan University, Shanghai 200032, China. Email: qgao99@yahoo.com

Novel tools are urgently needed for the rapid, reliable detection of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains of *Mycobacterium tuberculosis*. To develop such tools, we need information about the frequency and distribution of the Mycobacterial mutations and genotypes that are associated with phenotypic drug resistance. In a population-based study, we sequenced specific genes of *M. tuberculosis* that were associated with resistance to rifampin and isoniazid in 242 phenotypically MDR isolates and 50 phenotypically pan-susceptible isolates from tuberculosis (TB) cases in Shanghai, China. We estimated the sensitivity and specificity of the mutations, using the results of conventional, culture-based phenotypic drug susceptibility testing as the standard. We detected mutations within the 81-bp core region of *rpoB* in 96.3% of phenotypically MDR isolates. Mutations in two structural genes (*katG* and *inhA*) and two regulatory regions (the promoter of *mabA-inhA* and the intergenic region of *oxyR-ahpC*) were found in 89.3% of the MDR isolates. In total, 88.0% (213/242 strains) of the phenotypic MDR strains were confirmed by mutations in the sequenced regions. Mutations in *emhB306* were also considered a marker for MDR and significantly increased the sensitivity of the approach. Based on our findings, an approach that prospectively screens for mutations in 11 sites of the *M. tuberculosis* genome (*rpoB531*, *rpoB526*, *rpoB516*, *rpoB533*, and *rpoB513*. *katG315*, *inhA-15*, *ahpC-10*, *ahpC-6*, and *ahpC-12*, and *embB306*) could detect 86.8% of MDR strains in Shanghai. This study lays the foundation for the development of a rapid, reliable molecular genetic test to detect MDR strains of *M. tuberculosis* in China.

2150 REYN, C. F. VON; MTEI, L.; ARBEIT, R. D.; WADDELL, R.; COLE, B.; MACKENZIE, T.; MATEE, M.; BAKARI, M.; TVAROHA, S.; ADAMS, L. V.; HORSBURGH, C. R.; PALLANGYO, K.; DARDAR STUDY GROUP **Prevention or tuberculosis in Bacille Calmette-Guerin-primed, HIV-infected adults boosted with an inactivated whole-cell**

mycobacterial vaccine. AIDS (2010) 24 (5) 675-685 Hagerstown, USA; Lippincott Williams & Wilkins. Inc., [En, 57 ref.] Infectious Disease and International Health, Dartmouth Medical School, Hanover. New Hampshire, USA. Email: fvr@hitchcock.org

Objective: To determine whether a multiple-dose series of an inactivated whole cell mycobacterial vaccine, *Mycobacterium vaccae*, can prevent HIV-associated tuberculosis. Design and methods: The DarDar trial was a randomized, placebo-controlled, double-blind trial. The study was carried in an outpatient facility in Dar es Salaam, Tanzania. HIV-infected patients with CD4 cell counts of at least 200 cells/ μ l and a Bacille Calmette-Guérin scar were chosen for the study. The intervention was carried out by random 1:1 assignment to five intradermal doses of *M. Vaccae* or placebo. Tuberculin skin tests were performed, and patients with reactions of at least 5 mm were administered isoniazid for 6 months. The main outcome measures were disseminated (primary endpoint), definite, and probable tuberculosis (secondary endpoints). Results: Two thousand thirteen individuals were randomized (1006 to *M. Vaccae*, 1007 to placebo) and followed every 3 months for a median of 3.3 years. The trial was terminated early because of slow accrual of cases of disseminated tuberculosis and significant protection against definite tuberculosis. Hazard ratios were disseminated tuberculosis 0.52 (95% confidence interval 0.21-1.34; seven cases in *M. Vaccae*, 13 cases in placebo; log-rank $P=0.16$), definite tuberculosis 0.61 (95% confidence interval 0.39-0.96; 33 cases in *M. vaccae*, 52 cases in placebo; $P=0.03$), and probable tuberculosis 1.17 (95% confidence interval 0.76-1.80; 48 cases in *M. vaccae*, 40 cases in placebo; $P=0.46$). Immunization was well tolerated, with no adverse effect on CD4 cell count or HIV viral load, and no increase in the rate of serious adverse events. Conclusion: Administration of a multiple-dose series of *M. vaccae* to HIV-infected adults with childhood Bacille Calmette-Guérin immuni-

zation is safe and is associated with significant protection against definite tuberculosis. These results provide evidence that immunization with a whole cell mycobacterial vaccine is a viable strategy for the prevention of HIV-associated tuberculosis.

2151 MESFIN, M. M.; NEWELL, J. N.; MADELEY, R. J.; MIRZOEV, T. N.; TAREKE, I. G.; KIFLE, Y. T.; GESSESSEW, A.; WALLEY, J. D. **Cost implications of delays to tuberculosis diagnosis among pulmonary tuberculosis patients in Ethiopia.** *BMC Public Health* (2010) **10** (173) (30 March 2010) London, UK; BioMed Central Ltd [En, 19 ref.] Nuffield Centre for International Health and Development, Institute of Health Sciences, University of Leeds, Leeds, UK. Email: M.melese@leeds.ac.uk, J.N.Newell@leeds.ac.uk, richard.madeley@btinternet.com, t.mirzoev@leeds.ac.uk, itareke@yahoo.com, kaluway@yahoo.com, kalkidus@yahoo.com, J.D. Walley@leeds.ac.uk

Background: Delays seeking care worsen the burden of tuberculosis and cost of care for patients, families and the public health system. This study investigates costs of tuberculosis diagnosis incurred by patients, escorts and the public health system in 10 districts of Ethiopia. Methods: New pulmonary tuberculosis patients ≥ 15 years old were interviewed regarding their health care seeking behaviour at the time of diagnosis. Using a structured questionnaire patients were interviewed about the duration of delay at alternative care providers and the public health system prior to diagnosis. Costs incurred by patients, escorts and the public health system were quantified through patient interview and review of medical records. Results: Interviews were held with 537 (58%) smear positive patients and 387 (42%) smear negative pulmonary patients. Of these, 413 (45%) were female; 451 (49%) were rural residents; and the median age was 34 years. The mean (median) days elapsed for consultation at alternative care providers and public health facilities prior to tuberculosis diagnosis was 5 days (0 days) and 3 (3 days)

respectively. The total median cost incurred from first consultation to diagnosis was \$27 per patient (mean=\$59). The median costs per patient incurred by patient, escort and the public health system were \$16 (mean=\$29), \$3 (mean=\$23) and \$3 (mean=\$7) respectively. The total cost per patient diagnosed was higher for women, rural residents; those who received government food for work support, patients with smear negative pulmonary tuberculosis and patients who were not screened for TB in at least one district diagnostic centers. Conclusions: The costs of tuberculosis diagnosis incurred by patients and escorts represent a significant portion of their monthly income. The costs arising from time lost in seeking care comprised a major portion of the total cost of diagnosis, and may worsen the economic position of patients and their families. Getting treatment from alternative sources and low index of suspicion public health providers were key problems contributing to increased cost of tuberculosis diagnosis. Thus, the institution of effective systems of referral, ensuring screening of suspects across the district public health system and the involvement of alternative care providers in district tuberculosis control can reduce delays and the financial burden to patients and escorts.

2152 WAISBORD, S. **Participatory communication for tuberculosis control in prisons in Bolivia, Ecuador, and Paraguay.** *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* (2010) **27** (3) 168-174 Washington, USA; Pan American Health Organization [En, es. 33 ref.] School of Media and Public Affairs, George Washington University, 805 21st Street NW, Suite 400, Washington, DC 20052, USA. Email: waisbord@gwu.edu

Objectives: To assess the challenges in reducing tuberculosis (TB) in prisons in Bolivia, Ecuador, and Paraguay and propose ways to address them through communication interventions. Methods: Challenges to two central goals of TB control—early diagnosis of positive cases and successful application of the directly observed treatment,

short course (DOTS) strategy - were examined. Data were gathered (through in-depth, structured interviews) and focus groups were conducted in the prisons that housed the largest number of male inmates in each country. Interviewees and focus group participants included program directors, administrative personnel, correctional health and security staff, and incarcerated people who were or had been under treatment for TB and had participated as "peers" in health services. Results: The findings showed a range of entrenched obstacles for adequate TB control, Stigmatizing attitudes and low knowledge about TB among inmates and key prison personnel discouraged people living in prisons from seeking diagnosis and treatment. Systemic problems in prison health services, along with squalid living conditions, lack of coordination between national TB programs and prison health systems, and insufficient allocation of resources to health prevented the provision of adequate TB prevention and care. Conclusion. In addressing the barriers to effective TB control in prison systems in Bolivia, Ecuador, and Paraguay, a participatory approach to communication is necessary.

2153 LIN, H. C.; LIN, H. C.; CHEN, S. F. **Increased risk of low birthweight and small for gestational age infants among women with tuberculosis.** *BJOG: An International Journal of Obstetrics and Gynaecology* (2010) **117** (5) 585-590 Oxford, UK; Blackwell Publishing Ltd [En. 24 ref.] School of Health Care Administration, Taipei Medical University, Taipei, Taiwan. Email: jane2@tmu.edu.tw

Objective: As the relationship between tuberculosis (TB) and fetal outcomes remains unclear, this study used a 3-year nationwide population-based data set to determine the risk of adverse pregnancy outcomes [low birth weight (LBW), preterm birth and small for gestational age (SGA) infants] among women with TB. Design: A cross-sectional retrospective study. Setting: Taiwan. Sample: Linking the Taiwan birth certificate registry and the Taiwan National

Health Insurance Research Dataset, we identified 761 women who gave birth from 2001 to 2003 and who had received medication treatment for TB during their pregnancy, together with 3805 unaffected women matched in terms of age and year of delivery. Methods: Conditional logistic regression analyses were performed to compare the risk of LBW, preterm birth and SGA for mothers with TB and unaffected mothers. Main outcome measures: The risk of LBW, preterm birth and SGA. Results: Mothers diagnosed with TB had significantly higher percentages of LBW (8.5 versus 6.4%, $P=0.033$) and SGA (19.7 versus 16.7%, $P=0.048$) infants than unaffected mothers. However, there was no significant difference in preterm birth (8.0 versus 8.0%, $P=0.961$) between these two groups. The adjusted odds ratios of having LBW and SGA infants for mothers with TB were 1.35 (95% CI=1.01-1.81) and 1.22 (95% CI=1.00-1.49), respectively, compared with unaffected mothers. Conclusions: We concluded that women diagnosed with TB during pregnancy are at increased risk for having LBW and SGA babies, compared with unaffected mothers. We suggest that clinicians should make women with TB aware of the potential risks before planning a child.

2154 POKHREL, A. K.; BATES, M. N.; VERMA, S. C.; JOSHI, H. S.; SREERAMAREDDY, C. T.; SMITH, K. R. **Tuberculosis and indoor biomass and kerosene use in Nepal: a case-control study.** *Environmental Health Perspectives* (2010) **118** (4) 558-564 Research Triangle Park, USA; Public Health Service, U.S. Department of Health and Human Services [En, 40 ref.] School of Public Health, 50 University Hall, University of California-Berkeley, Berkeley, CA 94720-7360, USA. Email: krksmith@berkeley.edu

Background: In Nepal, tuberculosis (TB) is a major problem. Worldwide, six previous epidemiologic studies have investigated whether indoor cooking with biomass fuel such as wood or agricultural wastes is associated with TB with inconsistent results. Objectives: Using detailed information on potential confounders, we investigated the associations between TB and the use of biomass

and kerosene fuels. Methods: A hospital-based case-control study was conducted in Pokhara, Nepal. Cases ($n=125$) were women, 20-65 years old, with a confirmed diagnosis of TB. Age-matched controls ($n=250$) were female patients without TB. Detailed exposure histories were collected with a standardized questionnaire. Results: Compared with using a clean-burning fuel stove (liquefied petroleum gas, biogas), the adjusted odds ratio (OR) for using a biomass-fuel stove was 1.21 [95% confidence interval (CI), 0.48-3.05], whereas use of a kerosene-fuel stove had an OR of 3.36 (95% CI, 1.01-11.22). The OR for use of biomass fuel for heating was 3.45 (95% CI, 1.44-8.27) and for use of kerosene lamps for lighting was 9.43 (95% CI, 1.45-61.32). Conclusions: This study provides evidence that the use of indoor biomass fuel, particularly as a source of heating, is associated with TB in women. It also provides the first evidence that using kerosene stoves and wick lamps is associated with TB. These associations require confirmation in other studies. If using kerosene lamps is a risk factor for TB, it would provide strong justification for promoting clean lighting sources, such as solar lamps.

2155 FOX, M. P.; BRENNAN, A.; MASKEW, M.; MACPHAIL, P.; SANNE, I. **Using vital registration data to update mortality among patients lost to follow-up from ART programmes: evidence from the Themba Lethu Clinic, South Africa.** *Tropical Medicine and International Health* (2010) **15** (4) 405-413 Oxford, UK; Blackwell Publishing Ltd [En, 25 ref.] Center for Global Health and Development, Boston University, Crosstown Center, 3rd Floor, 801 Massachusetts Ave, Boston, MA 02118, USA. Email: mfox@bu.edu

OBJECTIVE: To estimate the rates of mortality in patients lost to follow-up (LTFU) from a large urban public sector HIV clinic in South Africa. METHODS: We compared vital status using the clinic's database to vital status verified against the Vital Registration system at the South African Department of Home Affairs. We compared rates of mortality before and after updating mortality

data. Predictors of mortality were estimated using Kaplan-Meier curves and proportional hazard regression. RESULTS: Of the 7097 total patients who initiated highly active antiretroviral therapy at Themba Lethu Clinic by October 1st, 2008 and had an ID number, 6205 were included, 2453 patients (21%) were LTFU, of whom 1037 (42.3%) could be included in the analysis. After matching to the vital registration system, mortality more than doubled from 4.2% (258/6205) to 10.9% (676/6205). Overall 37% of those LTFU died by life-table analysis the probability of survival amongst those LTFU was 69% (95% CI: 66-72%), 64% (95% CI: 61-67%) and 59% (95% CI: 55-62%) by years 1, 2 and 3 since being lost, respectively. Those at highest risk of death after being lost were patients with a history of tuberculosis, CD4 count <100 cells/ μ l, BMI <17.5 , haemoglobin <10 and on <6 months of treatment. CONCLUSION: Mortality was substantially underestimated among patients lost from a South African HIV treatment programme despite limited active tracing. Linking to vital registration systems can provide more accurate assessments of programme effectiveness and target lost patients most at risk for mortality.

2156 LEE CHANGHOON; HWANG JIYOUNG; OH DAEKYU; KEE MEEKYUNG; OH EUNJUNG; AN JUNGWOOK; KIM JINHYUN; DO HEONSOOK; KIM HEEJIN; KIM SUNGSOON; KIM HWAHYUN; NAM JEONGGU **The burden and characteristics of tuberculosis/human immunodeficiency virus (TB/HIV) in South Korea: a study from a population database and a survey.** *BMC Infectious Diseases* (2010) **10** (66) (12 March 2010) London, UK; BioMed Central Ltd [En, 35 ref.] Division of HIV and TB Control, Korea Centers for Disease Control and Prevention, 194 Tongillo, Eunpyung-gu, Seoul, 122-701, Korea Republic. Email: jeonggu@nih.go.kr

Background: Although, in South Korea, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) keeps increasing and tuberculosis (TB) burden is still significant, there have been few reports on TB/HIV cases. In

this study, we investigated the burden and characteristics of TB/HIV patients in South Korea, an area with intermediate burden of TB and a low prevalent area with HIV/AIDS. Methods: We identified patients with TB and cases with HIV between January 1 2001 and December 31 2005, from nationwide reporting system (TBnet and HIV/AIDS registry) through an electronic record linkage method. A questionnaire survey was also conducted and determined the rate of diagnosis of HIV among TB cases in public health units in 2005. Results: The number of cases with both HIV and TB was 137 (0.07% among 197,562 TB cases) and the newly detected TB/HIV cases per 100,000 population was increasing annually: 2001, 0.025; 2002, 0.031; 2003, 0.025; 2004, 0.071; 2005, 0.095. Males between 20 and 59 years of age accounted for 87.6% of TB/HIV patients. Compared with patients with TB alone, those with TB/HIV had a higher percentage of extrapulmonary TB (8.0% vs 19.0%; $p < 0.0001$). The standardized prevalence ratio (SPR) of HIV among patients with TB was 18.46 (95% CI, 15.50-21.83), SPR of HIV among male TB patients aged 20-59 and extrapulmonary TB cases was 39.64 (95% CI, 32.87-47.40) and 43.21 (95% CI, 28.22-63.31) respectively. Through a questionnaire survey of public health units, six patients (0.08%) were confirmed as having HIV among 7,871 TB patients in public health centers in 2005, which is similar to the result from the study through nationwide reporting systems. Conclusions: The prevalence rate of TB/HIV patients is still low but increasing in South Korea. Physicians should consider performing HIV tests among TB patients, especially in higher-risk groups, such as young males with extrapulmonary TB in South Korea.

2157 PEPPER, D. J.; MARAIS, S.; WILKINSON, R. J.; BHAIJEE, F.; MAARTENS, G.; MCILLERON, H.; AZEVEDO, V. DE; COX, H.; MCDERMID, C.; SOKHELA, S.; JANISHA PATEL; MEINTJES, G. **Clinical deterioration during anti-tuberculosis treatment in Africa: incidence, causes and risk factors.** *BMC Infectious Diseases* (2010) **10** (83) (30 March 2010) London, UK; BioMed Central Ltd

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Background: HIV-1 and *Mycobacterium tuberculosis* cause substantial morbidity and mortality. Despite the availability of antiretroviral and antituberculosis treatment in Africa, clinical deterioration during antituberculosis treatment remains a frequent reason for hospital admission. We therefore determined the incidence, causes and risk factors for clinical deterioration. Method: Prospective cohort study of 292 adults who initiated antituberculosis treatment during a 3-month period. We evaluated those with clinical deterioration over the following 24 weeks of treatment. Results: Seventy-one percent (209/292) of patients were HIV-1 infected (median CD4+: 129 cells/ μ litre, IQR: 62-277). At tuberculosis diagnosis, 23% (34/145) of HIV-1 infected patients qualifying for antiretroviral treatment (ART) were receiving ART; 6 months later, 75% (109/145) had received ART. Within 24 weeks of initiating antituberculosis treatment, 40% (117/292) of patients experienced clinical deterioration due to co-morbid illness ($n=70$), tuberculosis related illness ($n=47$), non AIDS-defining HIV-1 related infection ($n=25$) and AIDS-defining illness ($n=21$). Using HIV-1 uninfected patients as the referent group, HIV-1 infected patients had an increasing risk of clinical deterioration as CD4+ counts decreased [CD4+ >350 cells/ μ litre: RR=1.4, 95% CI=0.7-2.9; CD4+: 200-350 cells/ μ litre: RR=2.0, 95% CI=1.1-3.6; CD4+ <200 cells/ μ litre: RR=3.0, 95% CI=1.9-4.7]. During followup, 26% (30/117) of patients with clinical deterioration required hospital admission and 15% (17/117) died. Fifteen deaths were in HIV-1 infected patients with a CD4+ <200

cells/ μ litre. Conclusions: In multivariate analysis, HIV-1 infection and a low CD4+ count at tuberculosis diagnosis were significant risk factors for clinical deterioration and death. The initiation of ART at a CD4+ count of <350 cells/ μ litre will likely reduce the high burden of clinical deterioration.

2158 VASCONCELLOS, S. E. G.; HUARD, R. C.; NIEMANN, S.; KREMER, K.; SANTOS, A. R.; SUFFYS, P. N.; HO, J. L. **Distinct genotypic profiles of the two major clades of *Mycobacterium africanum***. *BMC Infectious Diseases* (2010) **10** (80) (29 March 2010) London, UK; BioMed Central Ltd [En, 57 ref.] Laboratory of Molecular Biology Applied to Mycobacteria, Oswaldo Cruz Institute, Oswaldo Cruz Foundation, Avenida Brasil 4365, Manguinhos 21040-900, Rio de Janeiro, Brazil. Email: ezidiogoncalves@yahoo.com, rchuard@nyp.org, stniemann@yahoo.de, kristin.kremer@rivm.nl, adalbertorezende@yahoo.com.br, psuffys@ioc.fiocruz.br, millennium.john@gmail.com

Background: *Mycobacterium tuberculosis* is the principal etiologic agent of human tuberculosis (TB) and a member of the *M. tuberculosis* complex (MTC). Additional MTC species that cause TB in humans and other mammals include *Mycobacterium africanum* and *Mycobacterium bovis*. One result of studies interrogating recently identified MTC phylogenetic markers has been the recognition of at least two distinct lineages of *M. africanum*, known as West African-1 and West African-2. Methods: We screened a blinded non-random set of MTC strains isolated from TB patients in Ghana (=47) for known chromosomal region-of-difference (RD) loci and single nucleotide polymorphisms (SNPs). A MTC PCR-typing panel, single-target standard PCR, multi-primer PCR, PCR-restriction fragment analysis, and sequence analysis of amplified products were among the methods utilized for the comparative evaluation of targets and identification systems. The MTC distributions of novel SNPs were characterized in the both the Ghana collection and two other diverse collections of MTC strains

($n=175$ in total). Results: The utility of various polymorphisms as species, lineage-, and sublineage-defining phylogenetic markers for *M. africanum* was determined. Novel SNPs were also identified and found to be specific to either *M. africanum* West African-1 (*Rv1332*⁵²³; $n=32$) or *M. africanum* West African-2 (*nat*⁷⁵¹; $n=27$). In the final analysis, a strain identification approach that combined multi-primer PCR targeting of the RD loci RD9, RD10, and RD702 was the most simple, straight-forward, and definitive means of distinguishing the two clades of *M. africanum* from one another and from other MTC species. Conclusion: With this study, we have organized a series of consistent phylogenetically-relevant markers for each of the distinct MTC lineages that share the *M. africanum* designation. A differential distribution of each *M. africanum* clade in Western Africa is described.

2159 MENGISTU LEGESSE; GOBENA AMENI; GEZAHEGNE MAMO; GIRMAY MEDHIN; SHAWEL, D.; BJUNE, G.; ABEBE, F. **Knowledge and perception of pulmonary tuberculosis in pastoral communities in the middle and Lower Awash Valley of Afar region, Ethiopia**. *BMC Public Health* (2010) **10** (187) (12 April 2010) London, UK; BioMed Central Ltd [En, 31 ref.] Aklilu Lemma Institute of Pathobiology, Addis Ababa University, Addis Ababa, Ethiopia. Email: dlegessem@yahoo.com, gobenachimdi2009@yahoo.co.uk, gezahegnemamo@yahoo.com, gtmedhin@yahoo.com, shawelus@yahoo.com, g.a.bjune@medisin.uio.no, fekadu.abebe@medisin.uio.no

Background: Afar pastoralists live in the northeast of Ethiopia, confined to the most arid part of the country, where there is least access to educational, health and other social services. Tuberculosis (TB) is one of the major public health problems in Afar region. Lack of knowledge about TB could affect the health-seeking behaviour of patients and sustain the transmission of the disease within the community. In this study, we assessed the knowledge and perception of apparently healthy individuals about pulmonary

tuberculosis (PTB) in pastoral communities of Afar. Methods: Between March and May 2009, a community-based cross-sectional questionnaire survey involving 818 randomly selected healthy individuals was conducted in pastoral communities of Afar region. Moreover, two focus group discussions (FGDs), one with men and one with women, were conducted in each of the study area to supplement the quantitative study. Results: The majority (95.6%) of the interviewees reported that they have heard about PTB (known locally as “Labadore”). However, the participant associated the cause of PTB with exposure to cold air (45.9%), starvation (38%), dust (21.8%) or smoking/chewing Khat (*Catha edulis*) (16.4%). The discussants also suggested these same factors as the cause of PTB. All the discussants and the majority (74.3%) of the interviewees reported that persistent cough as the main symptom of PTB. About 87.7% of the interviewees and all the

discussants suggested that PTB is treatable with modern drugs. All the discussants and the majority (95%) of the interviewees mentioned that the disease can be transmitted from a patient to another person. Socio-cultural practices, e.g. sharing cups (87.6%), and house type (59.8%) were suggested as risk factors for exposure to PTS in the study areas, while shortage of food (69.7%) and chewing khat (53.8%) were mentioned as factors favouring disease development. Almost all discussants and a considerable number (20.4%) of the interviewees thought that men were the highest risk group to get PTB as well as playing a major role in the epidemiology of the disease. Conclusion: The findings indicate that pastoral communities had basic awareness about the disease. Nevertheless, health education to transform their traditional beliefs and perceptions about the disease to biomedical knowledge is crucial.