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# The International Journal of Tuberculosis and Lung Disease

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## **ABSTRACT BOOK**

**35th World Conference  
on Lung Health of the  
International Union Against  
Tuberculosis and Lung Disease**

**PARIS • FRANCE  
28 OCTOBER–1 NOVEMBER 2004**

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# Awards of the International Union Against Tuberculosis and Lung Disease

At each **Annual Union World Conference** the following awards are presented:

Two prizes of US \$2000.00:

- A **Scientific Prize** is awarded to a young researcher (under 45 years of age) for his/her work on tuberculosis or non-tuberculous lung disease published in the last 2 years. One copy of the publication should be sent to the Union Secretariat with the candidate's application.
- A **Public Health Prize (The Karel Styblo Prize)** is awarded to a health worker (physician or lay person) for his/her contribution to tuberculosis control or non-tuberculous lung disease. Applicants should include a well-documented description of his/her work, together with the comments of the manager of the association or programme.

Applications, including a full curriculum vitae, should be sent by the candidates to the Union Secretariat in Paris 3 months before the World Conference (i.e., 1 July 2005).

The title of **Honorary Member of the Union** is granted to a person who has distinguished him/herself in active participation in the Union's activities and fulfilment of its goals. UNION Constituent Members can nominate likely candidates 3 months before the World Conference (i.e., 1 July 2005).

**The Union Medal** is awarded to those members who have made an outstanding contribution to the control of tuberculosis or non-tuberculous lung disease, by their scientific work and/or actions in the field.

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### 11<sup>TH</sup> Conference of the Union Latin America Region

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# The International Journal of Tuberculosis and Lung Disease

SUPPLEMENT

VOLUME 8 NUMBER 11

NOVEMBER 2004

## SECTION 1:

### S1 PLENARY SESSIONS

## SECTION 2: SYMPOSIA

### SATURDAY, 30 OCTOBER 2004

- S2 HIV/TB lung disease: turning the tide to reach the child MDGs by 2015
- S3 Tuberculosis in prisons or closed institutions
- S5 Impact of new mechanisms to increase access to high quality anti-tuberculosis drugs
- S6 Drug resistance: is it worth measuring?
- S7 Emergency and continuing care in asthma
- S9 CREATE, a response to TB/HIV
- S11 Ensuring quality of care in DOTS implementation/ integrating laboratory, NTPs and organisation
- S13 Tuberculosis prevalence surveys
- S14 Drug resistance and treatment of MDR-TB
- S15 Loopholes in national legislations: need for international regulations—the FCTC
- S16 Can you get tuberculosis from your food?

### SUNDAY, 31 OCTOBER 2004

- S17 HIV/TB: scaling up the use of ARVs—links to TB control
- S18 Advances in the development of new diagnostic tests for tuberculosis
- S20 Improvement of indoor and ambient air quality in developing countries
- S20 Women, tobacco, lung health and the economic consequences
- S20 Enhancing case finding: report on FIDELIS projects in China
- S22 Tuberculosis management in children: obstacles to reaching the millennium development goals
- S23 Incentives for DOTS performance: enabling or corrupting?
- S24 TB in mobile populations and in persons with undocumented residence status
- S26 Operational research to improve National Tuberculosis Programmes
- S28 Bacterial virulence of tubercle bacilli and genetic susceptibility in humans
- S29 New TB drug development

### MONDAY, 1 NOVEMBER 2004

- S30 TB treatment adherence in resource-poor settings
- S31 Human resource development for TB control
- S33 Harm reduction and funding by tobacco transnationals
- S34 Microscopy and culture
- S37 Contact investigation and active case finding in high incidence countries
- S37 HIV/TB: two diseases, one patient
- S39 Scaling up public-private mix for DOTS: how can it contribute to achieving MDGs?

## SECTION 3: POSTER SESSIONS

### SATURDAY, 30 OCTOBER 2004

#### Thematic slide presentations (TS)

- S42 Clinical trials and tuberculosis basic science

#### Poster discussion sessions (PC)

- S44 DOTS expansion
- S48 Clinical trials and tuberculosis basic science
- S51 Policy and programme implementation: TB and HIV
- S55 Clinical research and smear examination

#### Poster display sessions (PS)

- S58 Clinical trials and drug development
- S65 Drug resistance/MDR-TB management–1
- S70 Tuberculosis and HIV
- S76 Tuberculosis in high-burden countries–1
- S83 Epidemiology of TB: special populations and institutions (migrants, hospitals, prisons)–1
- S88 Tuberculosis and poverty
- S95 DOTS: public-private mix
- S100 Tobacco and air pollution–1

### SUNDAY, 31 OCTOBER 2004

#### Thematic slide presentations (TS)

- S105 Progress in TB control

#### Poster discussion sessions (PC)

- S107 Epidemiology of tuberculosis and tobacco
- S111 Drug resistance/MDR-TB management
- S115 Training, human resources and community participation
- S118 Diagnostic methods and drug susceptibility

#### Poster display sessions (PS)

- S121 Bacteriology and immunology
- S129 Clinical tuberculosis
- S134 Drug resistance/MDR-TB management–2
- S140 Tuberculosis and lung disease in children
- S146 Practical Approach to Lung Health (PAL) and asthma
- S154 Tuberculosis in high-burden countries–2
- S161 Patient treatment adherence/management–1
- S166 Policy and programme implementation: TB control in special populations and institutions

### MONDAY, 1 NOVEMBER 2004

#### Thematic slide presentations (TS)

- S173 Education, advocacy and social issues

#### Poster discussion sessions (PC)

- S176 Epidemiology of tuberculosis
- S179 Clinical research and treatment of lung disease
- S182 Tuberculosis and society/poverty
- S184 Management innovations to improve the quality of DOTS

#### Poster display sessions (PS)

- S187 Tuberculosis diagnosis
- S194 Tuberculosis in low-burden countries
- S200 Epidemiology of TB: special populations and institutions (migrants, hospitals, prisons)–2
- S205 DOTS expansion
- S212 Tuberculosis education and training
- S219 Drug resistance/MDR-TB management–3
- S224 Patient treatment adherence/management–2
- S230 Tobacco and air pollution–2

- S235 INDEX

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Journal of Tuberculosis  
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# 35th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease Paris, France, 28 October–1 November 2004

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## SECTION 1: PLENARY SESSIONS SATURDAY 30 OCTOBER 2004

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### Poverty, inequality and tobacco

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Tobacco increases poverty, both in smokers and workers in the tobacco industry. Smoking prevalence is usually high among poor or uneducated men. Among the poor in low-income countries, daily spending on tobacco means daily spending on scant family resources, resulting in malnutrition among family members. In Bangladesh, 10.5 million go hungry. Male smokers' daily spending on cigarettes is enough to purchase nearly 3000 calories of rice, and 300 children die every day because money is diverted from food to tobacco.

In developing countries, expenditure on tobacco erodes expenditure on important basic needs such as education and health. This causes large impact on the prospects of children. In Vietnam, annual household expenditure on tobacco is respectively 1.7 and 1.5 times higher than expenditure on education and health.

Workers in the tobacco industry in low-income countries are generally poor. Tobacco farmers are illiterate due to a lack of opportunity to attend school, and are generally in poor health. In Kenya's one tobacco growing district, 52% of children are malnourished. They are prone to illness from exposure to green tobacco while picking the leaves. Most suffer multi-generational poverty, despite the long period of growing tobacco, due to the high cost of investments, and when crops fail or auction prices are low they incur debt.

Workers in manufacturing tobacco products are also generally poor due to low wages, e.g., 30 cents/day to roll bids in India and 6 cents/5 hours in one site in Bangladesh. They also suffer health risks: bidi workers have to remain in inhumane postures for hours.

There is inequality due to tobacco among countries worldwide. Approximately 30% of smokers globally live in low- and middle-income countries. If the current trend continues to the year 2030, these countries will have 7 million smoking-attributable deaths yearly, 70% of the world total. Cessation rates in low- and middle-income countries are lower than in high-income countries, approximately 30% of men, compared to only 2% of men in China, 5% in India, and 10% in Vietnam. Inequality within countries is apparent: the rate of smoking among poor or uneducated men is higher than in men with higher income or education.

### Nursing and Millennium Development Goals

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The Millennium Development Goals (MDGs), adopted by the international community in 2000, include three that are directly related to health. It has been recognised that these will not be achieved unless good quality health services and interventions are accessible, particularly to the most vulnerable populations. Human resources for health, which include nursing and midwifery cadres, are increasingly recognised as one of the crucial elements in attaining the MDGs. In many countries in the African Region, nursing personnel comprise 50–70% of the health workforce. If utilised properly they could provide a platform for scaling up effective interventions to contribute to the attainment of the MDGs. This session will examine ways of mobilising the nursing workforce.

## SECTION 2: SYMPOSIA SATURDAY 30 OCTOBER 2004

### HIV/TB LUNG DISEASE: TURNING THE TIDE TO REACH THE CHILD MDGS BY 2015

#### TB in HIV-infected children

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There is limited information on the global burden of paediatric TB with and without concomitant HIV infection. Global surveillance presently focuses on reporting of smear-positive cases, and small children rarely produce sputum. Instead, the diagnosis of child TB is commonly based on a combination of epidemiological information and non-specific signs and symptoms. It is evident that the increase in adult TB, linked to the HIV epidemic, also affects the paediatric population. As in adults, concomitant HIV incurs significant risk for the child to develop clinical TB and has an impact on diagnosis, treatment and outcome. BCG given at birth seems to provide less or no protection to the HIV infected child. Dually infected children are at increased risk of over- as well as under-diagnosis of TB. The predictive value of major diagnostic tools like TST and chest radiography is lower and other HIV related infections like PCP, LIP or recurrent bacterial infections may present with clinical findings similar to those of pulmonary TB. Standard TB drugs are generally well tolerated, and ethambutol could safely replace thiacetazone in HIV-positive children. Although HIV infection is a strong predictor of a fatal outcome in a mixed TB population, treatment success rates of over 50% may be achieved in a high-endemic, low-income country within a decentralized DOTS programme. There is as yet little experience of combining HIV and TB treatment. Childhood TB is an increasing cause of childhood morbidity and mortality. It is the result of present transmission and thus an indicator of insufficient control efforts. Better diagnostic tools, including a uniform case definition, are urgently needed if the surveillance of paediatric TB is to be improved. All children with TB should be screened for HIV infection. Children living in the same household as an adult with smear-positive TB should receive medical TB prophylaxis.

### Reducing pneumonia-related mortality in low-resource, HIV-endemic country: Malawi CLH project

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Over 10 million children below the age of 5 years die annually from preventable causes. Of the deaths occurring in 2000, 41% were in Sub-Saharan Africa with a further 34% in South Asia. In sub-Saharan Africa the distribution of deaths was as follows: diarrhoea (20%), pneumonia (21%), malaria (22%), AIDS (8%) and neonatal causes (25%). Pneumonia and diarrhoea account for a large proportion of child deaths in all countries within this region. Underweight children are at higher risk of dying from infectious diseases with approximately 53% of all deaths being attributed to this factor. Of these, 35% can be attributed to the underweight status on diarrhoea, pneumonia, measles and malaria.

Cost-effective intervention strategies to address these illnesses are available. Sufficient evidence exists that shows that when these interventions are adopted (e.g., antibiotics for pneumonia) that there is a reduction in the cause-specific mortality in children less than 5 years of age in low-income countries. These interventions are judged feasible for high levels of implementation (99% population coverage) in low-income countries. If such levels of coverage could be attained it is estimated that over 66% of deaths could be prevented by these interventions that are feasible and available today. But these interventions are not reaching the children who need them. There is a need to tailor intervention packages to the local needs. Malaria, pneumonia, diarrhoea and HIV/AIDS interventions must be central in the hyperendemic areas.

The struggle of child survival will continue being a failure if governments, international agencies and NGO's overlook the priority needed to be given to delivering such tailored packages such as that of the Child Lung Health Project in Malawi.

The purpose of the Child Lung Health (CLH) Project is to improve the survival and wellbeing of children in a low-income country in sub-Saharan Africa where HIV infection is highly endemic. The project is designed to establish a sustainable and reproducible system for the surveillance, diagnosis, and management of the respiratory diseases that afflict children, including acute respiratory infection, mainly pneumonia, HIV related lung diseases, tuberculosis and asthma, in communities throughout African countries. The project applied the UNION Model for successful health and public health services for tuberculosis to the problem of respiratory diseases of the children in such countries. Implementation was a step-wise approach, monitored and evaluated, emphasizing sustainability, reproducibility, efficiency and sustainability.

The CLH Project has been adopted by the Malawi Ministry of Health and Population, and has been incorporated into the Preventive Services Division and is being managed through the ARI/IMCI Programme based in the Community Health Sciences Unit (CHSU). Implementation of the Project began in January 2000 with the first 5 district hospital health workers receiving training in September 2000. At the beginning of 2004, the fifth and final year of the Project, there are 25 districts out of a total of 26, with government hospitals, implementing the Project.

Implementation was done in a step-wise approach with four, five or six districts included each year. Lessons learnt from the previous districts implementing the project assisted the Ministry of Health and Population and the CLH Project Managers in implementing the project in the remaining districts.

Since the CLH Project was implemented in October 2000 up to December 2003 24 735 children 5 years of age have been admitted with pneumonia. Analysis of the routine data collected on these children will be presented and will show for example that the CFR for pneumonia has been reduced from 20% to in some districts 8% and treatment completed has risen from 50% to about 80%.

It will be demonstrated that a well planned, implemented and well assessed public health project focusing on a few diseases can make a difference.

## TUBERCULOSIS IN PRISONS OR CLOSED INSTITUTIONS

### Nursing care for tuberculosis patients in Thai prisons: challenges and limitations

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**Background:** Through strong collaboration between the National Tuberculosis (TB) Program and the Department of Corrections, Ministry of Justice, the DOTS strategy has been implemented in every prison since 2001. Nurses perform key functions necessary for the successful DOTS implementation.

**Nursing care:** At prisons, nurses: 1) establish political commitments from the prison authorities which the commitments allow them to separate infectious patients from other prisoners and to coordinate with local health services; 2) identify and manage TB suspects by following established DOTS protocols; 3) collaborate with physicians at local hospitals for diagnosis and standard regimens and provide the DOT in prisons; 4) negotiate with the Provincial Health Offices for pharmacological agents and other essential supplies; and 5) register patients in TB prison register and perform cohort reports.

**Challenges:** Thai nurses have a plethora of challenges. First, prisoner-nurse ratios are high. However, teaching prison staff about their roles to provide the DOT can be a solution to the malady. Second, delay in diagnosis is common according to passive case-finding. Prison staff can also help nurses screen TB suspects inside the cells. Finally, many TB patients are transferred out during the treatment. Strengthening collaboration between prisons and local health services is essential to trace the transferred patients.

**Limitations:** High proportions of TB patients who are infected with HIV create complex approaches to care. Advanced care for these patients is very limited and the dual diagnoses may cause high death rates. Lack of laboratory capacity within the prisons is also limited nurses to perform active case-finding.

**Conclusion:** Nurses provide essential health services for TB patients in Thai prisons. Although challenges and limitations exist, solutions are proposed to help these nurses to work effectively and to assure that prisoners have access to humane and quality health care.

### Case finding strategies for prisons: rethinking approaches

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**Background:** WHO recommends special attention for case detection among high-risk groups such as people in institutions.

**Objectives:** To assess the respective benefits of the different methods of case finding in prisons of the Southern Caucasus.

**Design:** 1) Monitoring of case detection through review of record data; 2) longitudinal prospective study of TB suspects identified through clinical questionnaire and mass miniature radiography.

**Methods:** 1) Screening (active case finding) through clinical questionnaire and MMR (mass miniature radiography) is used to identify TB suspects who are confirmed by sputum smear microscopy and/or culture. Passive case finding is done solely by clinical questionnaire. 2) 1227 detainees were screened through clinical questionnaire and 1194 through MMR with culture as gold standard for TB diagnosis confirmation.

**Main results:** 1) In three prison settings, the clinical questionnaire yielded between 14% and 30% of TB suspects. 8.6% were positive on smear and/or culture. The national medical staff diagnosed only 2.1% of TB cases. 2) In our study, the clinical questionnaire yielded 14.2% of TB suspects, of whom 7.5% had TB. MMR identified 2.8% of TB suspects, of whom 17.6% had TB. Only 1% of the screened population was suspect by both methods. The positive predictive value of the questionnaire and MMR are respectively 7.5% and 17.6%. Sensitivity is respectively 52% and

24%, whereas specificity is similar (86.6% for the questionnaire and 84% for MMR).

**Conclusions:** The positive predictive value in a prison setting of a clinical questionnaire and MMR was low. The questionnaire was twice as sensitive as MMR. The clinical questionnaire presented in our study had the advantage of identifying more true cases of tuberculosis. For MMR to detect as many TB cases as the clinical questionnaire, the prison population should have been screened twice (1372 extra X-rays would have been necessary, which represents the total prison population envisaged by the study).

### Establishing a national prison IEC program: the Honduras experience

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Health communication campaigns have made considerable contributions to tuberculosis control programs throughout the world. Besides providing factual knowledge about tuberculosis, educational interventions have been credited with raising community members understanding of beneficial treatment outcomes, increasing medication adherence, improving treatment completion and decreasing default rates—demonstrating that informed communities are in a better position to participate in their health care and maximize the therapeutic benefits of available medical treatment. This is particularly important since behavioral factors play a significant role in the development of multi-drug resistant tuberculosis and disease transmission.

Prison community culture varies from region to region. However hierarchical power structures are universally found and create a myriad of challenges that can undermine tuberculosis control efforts. Educational campaigns can be as effective within these communities as those targeting the civilian community. Moreover educational interventions have the capacity to engage programmatic support from influential prisoners, leading to enhanced program outcomes.

To facilitate implementation and prisoner acceptance of the WHO DOTS strategy in Honduran prisons, emphasis was placed on educational initiatives. From 2001–2003, prison medical and administrative staff employed five educational themes: tuberculosis etiology, risk, and transmission; seek medical attention for cough lasting more than 15 days; diagnosis accomplished through sputum microscopy; availability of a cure; and avoid relapse through adherence.

Both qualitative and quantitative evaluations of program effectiveness demonstrate the positive impact of these initiatives. (Qualitative assessment: focus groups conducted in 5 prisons. Quantitative evaluation: survey of 194 prisoners and staff from 9 prisons, biannual assessments of case detection, cure rates,

and default rates) Factors contributing to program success include: staff collaboration with prisoners to develop educational activities and messages, education provided to entire prison community, regularly updating messages, and disseminating creative ideas and materials throughout the system. This program and its success factors will be discussed in greater detail.

### Continuity of TB care following release from prison: Monitoring Committees in Kazakhstan

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In 2003, the TB notification rate in Kazakh prisons was 1936.7 per 100 000 population, 12 times higher than in the civil community.

Since 2001, the KNCV Tuberculosis Foundation, together with Penal Reform International and Kazakhstan Central Prison Authorities is working on the project "Human Rights in prison management. Alternatives to imprisonment. Tuberculosis treatment in Kazakh prisons" in four Oblasts: Pavlodar, Eastern Kazakhstan, Akmola and Karaganda.

In 1999 DOTS strategy was implemented simultaneously in both civil and prison health care system. However the interaction between the civil health system and the prison health system is still poor. One of the problems is follow up of TB patients who need to finish treatment after release. In 2001 and 2002 in the four pilot oblasts on average 25% out of new and re-treatment cases were released before completion of treatment. Of those 27% had positive sputum smear results at the beginning of treatment and were released before the end of intensive phase. About 70–75% out of all TB patients who have been released while still on treatment didn't register at civil TB dispensaries to continue their treatment and could be source of TB in the community.

The KNCV supported project assisted the establishment of four Monitoring Committees. The Monitoring Committees in Pavlodar, Eastern Kazakhstan and Karaganda started work since March 2003. The Monitoring Committee in Akmola was established in October 2003.

The Monitoring Committees consist of volunteers from civil society with different backgrounds (TB doctors, human rights lawyers, psychologists, teachers and journalists).

The objectives of the Monitoring Committees are:

- To strengthen link between prisons and civil society
- To assist in strengthening cooperation between prison and civil health care services to improve TB control in the region
- To involve civil society in support for prisoners

The main activities of the Monitoring Committees are:

- Regular visits to the prisons for monitoring of Human Rights records and anti-tuberculosis activities.



- Follow up of released TB patients needed to complete treatment.
- Preparation of prisoners for release and support (assistance in social support, counseling, providing information about civil services, etc.).

As a result, interaction between prison and civil health care services is improved and defaulter rate after release has decreased to 40–45% in 2003. Thus, involvement of local NGOs in supervision of prisons and support of prisoners contribute to strengthening link between prisons and community and integration of TB control in prisons and community.

### **The emerging HIV/TB epidemic in prisons of Central Asia**

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Eastern Europe and the Central Asian Republics (CAR) are experiencing the world's fastest growing HIV/AIDS epidemic. Official estimates 300 000 injecting drug users in the CAR out of a population of 55 million. Between 71–85% of cases of HIV are found in this group. The total number of officially registered HIV+ cases varies from 170 to 4174 between the Tajikistan, Kyrgyzstan, Uzbekistan and Kazakhstan; the real figure is probably much higher. Tuberculosis (TB) in the penitentiary systems in the CAR remains widespread, uncontrolled and a leading cause of mortality among inmates.

Despite differences among the CAR penitentiary systems, all share the common problem that the conditions for inmates promote widespread transmission of HIV and TB.

Injecting drugs is common in the CAR penitentiary systems. Due to a lack of harm reduction projects and syringe exchange programs in prisons, inmates are engaging in high risk behaviours, including the sharing of injection equipment. According to official prison statistics, at the beginning of 2004, there were 52–600 HIV-positive prisoners. In CAR prisons, TB is the main opportunistic disease among people living with AIDS. The high prevalence of TB, coupled with the high incidence rate of HIV in prisons, points to a dramatic rise in TB-HIV co-infection.

Epidemiological reports underestimate the rate of HIV/AIDS in CAR prisons. Yet given the poor health conditions and high rates of injecting drug use in prisons, experts assume that the HIV and TB rates in prisons exceed the rates in society and point to a high interaction of the two infections. At this stage there are no formalised co-ordinated TB/HIV control programmes. Medical services within the penitentiary systems are committed to implementing WHO guidelines.

Strong grounds exist for the analysis of opportunities and the creation of joint TB/HIV control programmes within the framework of national health-care systems.

### **IMPACT OF NEW MECHANISMS TO INCREASE ACCESS TO HIGH QUALITY ANTI-TUBERCULOSIS DRUGS**

#### **Introduction de la quadruple association en RD Congo par le Global TB Drug Facility : leçons apprises**

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**Problèmes :** Avant l'introduction de Global Drug Facility (GDF), l'approvisionnement en médicaments antituberculeux était couvert par les Organisations non gouvernementales (ONG). Cependant, ces ONG n'étaient pas à mesure de couvrir les besoins de tout le pays. La RD Congo a alors soumis une proposition au GDF en 2001 parce que le pays manquait de stock de sécurité et n'avait pas assez de médicaments pour traiter tous les malades. Certaines coordinations n'avaient pas des médicaments. LE gouvernement ne pouvait pas acheter les médicaments antituberculeux face aux troubles dans le pays et du fait de la situation économique précaire. Aussi, compte tenu du besoin d'avoir un système de gestion simplifié et de simplifier la prise des médicaments par les patients, le PNT a demandé la quadruple association au GDF.

**Objectifs :** L'appui de GDF en RD Congo a permis :

- 1 le renforcement du partenariat dans le pays et la mise en place d'un Comité de gestion des médicaments.
- 2 le renforcement de la gestion des médicaments par la publication d'un guide technique de gestion des médicaments et
- 3 la simplification de la gestion des médicaments par la quadruple association.
- 4 la construction d'un dépôt des médicaments au niveau de l'unité centrale

La présentation examinera ces 3 points en détails.

#### **How the GDF is increasing uptake of new products for TB control (GDF patient kits/blisters/FDCs)**

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The GDF has found that one of the best ways to improve drug selection, needs estimation, procurement, distribution and rational use, is by promoting fixed-dose combination (FDC) drugs in blister packs and Patient Kits.

New formulations have been developed that allow first-line TB treatment to include only two products, the 4-drug FDC for the intensive phase and the 2-drug FDC for the continuation phase. According to WHO treatment guidelines, this regimen can be used for patients diagnosed as either Category I or III. For the Category II patient, the regimen with three prod-

ucts may be used: the 4-drug FDC and streptomycin for the intensive phase and the 3-drug FDC for the continuation phase. Overall, the advantages of FDCs are the following: reduce number of tablets a patient must swallow each day; simplify dose calculations for practitioners since all drugs are included in a single tablet; prevent use of drug regimens other than those proposed by the TB programme; reduce risk of drug resistance since monotherapy is avoided; follows WHO guidelines for TB control.

Further simplification of TB drug treatment is promoted by the use of Patient Kits, where all drugs needed for a full course of treatment are included in a single package. The Kit, called the Stop TB Patient Kit, exclusively uses FDC drugs in blister packs, and, as a result, all the drug selection advantages cited above come into play. Additional advantages of using these types of products include: facilitation of stock management, which promotes availability of adequate drug supplies; demonstration to the patient that a full course of treatment is available when needed; facilitation of monitoring of prescribing habits to determine if DOT is being followed.

The purpose of innovative products and packaging is to promote DOTS and DOTS expansion to help countries meet the global TB control targets. These products are not intended to replace the directly observed component of the DOTS scheme.

## DRUG RESISTANCE: IS IT WORTH MEASURING?

### PT among SRL: results of the last five rounds

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From 1999 to 2004, one round of external quality assessment of susceptibility testing (DST) has been organised annually by the coordinating laboratory, located at the Institute of Tropical Medicine in Antwerp, Belgium. Identical panels of *Mycobacterium tuberculosis* strains were sent out to all Supra-national Reference Laboratories (SRL). To reach better statistical significance, the number of strains was raised from ten strains sent in duplicate to 20, half of them in duplicate, during the last two rounds. Constitution of the panels aimed at 50% proportions of resistant strains for each of the four main drugs tested (isoniazid, rifampicin, ethambutol and streptomycin), in different combinations. Also since the last two rounds, a 50% resistant subset of the panel had to be devoid of multidrug resistant strains. For all these reasons, strains with rather exceptional patterns of resistance had to be included repeatedly, and a con-

siderable proportion of those turned out to be borderline resistant strains. For all five of the rounds, borderline strains had to be excluded from final analysis for one drug or the other, when concordance between the SRL didn't reach 80%. For rifampicin, this was the case for respectively 2, 1, 3, 2, and 1 strain of rounds 6, 7, 8, 9 and 10. Since DST results of such strains are uninterpretable with the current system based on a judicial result, phenotypic as well as genotypic pre-testing was done for the last two rounds to exclude such strains, but these efforts were not entirely successful. Other measures are now being implemented as well. The overall lesson learned from these rounds is that variation of results of panel tests among proficient labs depends mainly on the constitution of the panels and much less on details of the method used.

### Second-line drug susceptibility testing: where are we and where are we going?

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Wide use of rifampicin containing regimens for the treatment of tuberculosis (TB) often leads to a steady increase in multidrug resistant tuberculosis (MDR-TB) among both treatment failure cases and new cases in many parts of the world. Vigorous creation and transmission as the result of the programmatic errors have increased MDR-TB to a serious level in some parts of the world. MDR-TB demands far more costs and efforts for the marginal reduction that can be achieved theoretically by blocking the influx of new MDR-TB into the pool through efficient management of new cases and also by reducing the pool with an effective MDR treatment programme. Now increasing numbers of programmes in many areas implement MDR-TB control programmes such as DOTS-Plus, using second-line anti-tuberculosis drugs (SLD). This situation, in turn, has increased the demand of SLD susceptibility testing (SLDST).

The SLDST results, however, are often disappointing mainly due to 1) poor correlation with clinical response, 2) poor reproducibility due to technical fragility to the physicochemical test environment, and 3) poor standardization of the test procedures. This is where we are now with regard to SLDST.

Clinical irrelevance of the test results partly stems from poorly defined in vitro criteria of SLD resistance. Many of the conventional and newly appeared test systems for SLD have been poorly (or not) calibrated with the representative samples of well defined probably resistant (PR) and susceptible (PS) clinical isolates of *Mycobacterium tuberculosis*. Therefore it is urgent to collect representative PR samples of clinical isolates from patients, who continuously expectorate live *M. tuberculosis* in spite of more than 6 months of treatment with a regimen containing the

concerned drug; their susceptibility levels should then be compared with those of the representative sample of *M. tuberculosis* isolates from patients who have never been treated with anti-tuberculosis drugs to determine the clinically relevant criteria of resistance.

Once the clinically relevant in vitro criteria of resistance have been determined, the test procedure should be carefully standardized and simplified to be able to yield reproducible results. Minimum procedural input at the routine work station can increase reproducibility of test results.

As regards the technical complexity and fragility, it is desirable to centralize SLDST performance as much as possible without sacrificing timely provision of services to all MDR-TB cases in the country.

To provide reliable SLDST results, it is essential to perform SLDST under systematic external quality control built into the national and international laboratory network with a well balanced panel of PR and PS strains.

In conclusion, SLDST is now mostly used for individual MDR-TB treatment, but it could be harmful rather than beneficial unless it is improved through the collective efforts mentioned above.

### DST of atypical mycobacteria

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Antimicrobial susceptibility testing (DST) of *M. tuberculosis* plays an important role in the patient management, especially in case of chronic disease or where drug resistance is highly prevalent. However, role of DST of mycobacteria other than *M. tuberculosis* or atypical mycobacteria is uncertain and its clinical relevance is debatable. There are several factors involved in effectiveness of DST information and these factors should be taken into consideration before undertaking DST of atypical mycobacteria.

First, following the established guidelines it should be ascertained that the isolated atypical mycobacteria are not environmental contaminants or because of colonization, but actually are causing the disease. It is also important to establish what species is causing the infection. Reliability and clinical relevance of DST results vary depending on species of mycobacteria. For example *M. kansasii* does respond to various anti TB drugs and DST is useful, while in vitro DST and in vivo response do not correlate well in case of *M. avium* and some rapid growers. Type of media used for DST is critical, as solid media in general do not yield good results while liquid media give more susceptible results. Procedure for DST also may be different from the one used for *M. tuberculosis* and some of these procedures have been published. NCCLS has also given some guidelines for DST for atypical mycobacteria. These issues will be covered in detail in the talk.

*M. avium* infection, especially in immunocompromised patients is of main interest. Our research indicated that DST, using liquid media, in such cases might be of some use. However, some other factors are important to consider. Poor absorption of drug in such cases may influence the effectiveness of those drugs to which isolates are found susceptible. Another study indicated possibility of emergence of resistance much faster than what has been seen with *M. tuberculosis*. This rapid emergence of resistance seen in vitro may explain why these mycobacteria cannot be completely eliminated in-vivo irrespective of giving effective therapy.

Lastly, importance of carrying out DST depends upon prevalence of atypical mycobacterial infection and availability of resources. In low-resource countries where infection due to *M. tuberculosis* is the main burden, atypical infection is not that common and due to limited available resources DST of atypical mycobacteria is of less value. DST of atypical mycobacteria may be tried only if it is critical for the patient management, resources are available and one has a well-established laboratory with technologists experienced in DST.

### EMERGENCY AND CONTINUING CARE IN ASTHMA

#### Emergency and continuing care for asthma in North America: a prospective evaluation of asthma management in Vancouver

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**Background:** Previous evaluations of asthma management have shown significant care gaps in the management of acute asthma. As part of a prospective Global Survey of Asthma Practice (GASP) we prospectively evaluated a cohort of asthma patients who attended a University affiliated hospital emergency department (ED).

**Methods:** Patients attending the ED with acute asthma were prospectively evaluated with a standardized assessment tool. Baseline characteristics, pre admission asthma management, investigations done in the ED as well as discharge medications were all documented.

**Results:** A total of 96 patient visits were evaluated, 49 (51%) were male, mean age 41 ( $\pm 15.7$ ), mean pulse 96 ( $\pm 15.1$ ), and mean respirations 22 ( $\pm 9.61$ ) per minute. Six subjects were seen in the ED at least twice and 4 at least three times. Peak expiratory flow rate was measured in 87 subjects pre salbutamol (252

L/min  $\pm$  131.3) and in 87.2 hours post bronchodilator (329 L/min  $\pm$  134.12). Seventy three per cent of subjects had previously been to an Emergency Department with their asthma. A total of 34 subjects had previously been admitted to hospital with acute asthma. At baseline 39 (41%) of subjects reported not taking inhaled corticosteroids. A total of 25 (25%) of subjects took a long acting beta agonist. Interestingly 20 (21%) of subjects reported taking no short acting beta agonist but 28 (29%) of subjects were taking more than 1 canister per month. In the previous year 38% of subjects took at least one course of oral prednisone. The predominant mode of treatment in the ED was nebulised beta agonist 67 (71.3%) of subjects, with a further 51 (54%) of subjects receiving MDI therapy. Ipratropium bromide was prescribed in 74 (77.9%) of subjects. Systemic steroids were given to 59 (62%) of subjects. Only 2 subjects received intravenous magnesium and no patients received theophylline or adrenaline. One subject received IV salbutamol. In total 17 subjects received oxygen at an FIO<sub>2</sub> of 28% or less. Seven subjects received a sedative. Twelve patients were admitted to hospital. One patient died during their hospitalization. Peak flow rates at the time of discharge were a mean of 341 L/min. At discharge 34 (36%) were discharged with no systematic prednisone. Fourteen subjects were discharged on an antibiotic. Twenty three subjects were discharged on inhaled corticosteroids. A minority of subjects received a prescription for an anti cholinergic at the time of discharge.

**Conclusions:** In this study we have shown that patients coming to the ED have an excessive use of rescue medication with a history of frequent prior ED visits and hospitalizations with acute asthma. Overall there was a high utilization of objective measurements of airflow obstruction and use of bronchodilator therapy although with a relatively high use of nebulizers. There was an under utilization of systemic corticosteroids and a low proportion of subjects received oral or inhaled corticosteroids at discharge. Only two patients received intravenous magnesium despite its documented benefits in severe acute asthma. These data suggest there continues to be a significant care gap both in the community and in the Emergency Department in terms of the optimal management of acute asthma.

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### Asthma in emergency departments in the Middle East

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Asthma is a common medical emergency faced by emergency departments (ED) and intensive care spe-

cialists. In 2003, we carried out a study in Ramallah Hospital in Palestine, which is the main governmental hospital in Ramallah district in the West Bank of Palestine. The aim of this baseline survey was to identify patients who were not being treated according to guidelines, and their careers, so as to be able to identify an intervention to remedy this. Data of 121 patients with a final diagnosis of asthma at the ER, with or without further complications, were collected using a questionnaire. Data showed that symptoms varied widely among patients, of whom 62% were using at least six types of oral medications and 53% used at least four types of inhaled medications, which gives a total use of at least 10 types of medications by 41% of the patients. Most of asthma oral medications were used by at least 92% of the patients, except short acting  $\beta$ -agonist (84%) and anti-leukotriens (19%). At discharge, 78% were prescribed steroids or theophylline, but only 22% had these in their medications, and 54% were prescribed ant histamine but 44% already had it in their medications. For inhaled medications, steroids, anti-cholinergic, and short acting  $\beta$ -agonist were frequently prescribed, but not long-acting  $\beta$ -agonist or cromoglycate. At discharge, 76% were prescribed steroids, 80% short-acting  $\beta$ -agonist, 44% cromoglycate, 41% anticholinergic, and 12% were prescribed long-acting  $\beta$ -agonist. This study showed the patients visiting ER rooms had high number of prescribed medications and were mainly insured patients. We conclude that there is a need to devise and assess an audit tool for use in emergency rooms that will inform the local health services on the need for improving asthma management and identify the targets for improvement.

### Ensuring an appropriate supply of medication in asthma: the Union's role

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Management of asthma is a new public health problem in most middle-income countries, and the prevalence of asthma is increasing in low- and middle-income countries. For these reasons, the Union published an Asthma guide in 1996 and updated it in 2004. The Union Asthma guide recommends essential standardised measures for asthma management that can be applied in all countries in the world, including developing countries. The components of the intervention proposed include a technical package for management and an information system for continuous evaluation. The technical package recommends standardised diagnosis, treatment, and health education. Long-term treatment is stepwise, using only two cost-effective drugs (inhaled salbutamol 100  $\mu$ g and inhaled beclomethasone 250  $\mu$ g). No other costly new drugs or association of drugs are recommended.

The feasibility and the efficacy of this intervention were demonstrated in several pilot projects in developing countries, and its cost-efficacy was demonstrated in a limited study in Mexico. The reduction in health costs by the implementation of long-term management was linked to the dramatic decrease in the number of hospitalisations and emergency room visits. The Global Asthma Survey of Practice conducted in several countries confirmed that the majority of asthmatics in emergency rooms did not receive regular long-term treatment with inhaled steroids.

Several barriers are identified for the implementation of long-term asthma management in developing countries. One of the main obstacles is the affordability for patients of essential asthma drugs and particularly inhaled steroids. Studies conducted in several countries showed large differences in price for the same drug, and that it was possible to buy this drug at lower prices in a general tender on condition that large numbers of inhalers are purchased.

Reducing the cost of essential drugs will be a challenge, to increase drug coverage and the possibility to implement asthma management in countries other than the industrialised world, which represent less than 15% of the world's population. International NGOs should work together as a task force for asthma management by creating a global Asthma Drug Facility (ADF), as recently proposed by the Union. This type of structure may enable interested countries to purchase essential drugs for asthma at lower prices. This structure could be modelled on the Global Drug Facility (GDF) implemented by the Stop TB Partnership for anti-tuberculosis drugs. Pooled procurement of TB drugs in the last 10 years has led to the reduction in the price of the anti-tuberculosis drugs and to rapid expansion of the DOTS strategy in most high-burden countries. An ADF may be a solution, by coordinating and pooling procurement of essential asthma drugs for several developing countries, and providing, as for tuberculosis programmes, technical assistance in asthma management and distribution of good quality essential asthma drugs. These countries could buy the essential asthma drugs needed for their patients to ADF at lower prices. Nevertheless, the creation of an ADF is a big challenge and will need financial support by donors at the beginning. All partners, including the pharmaceutical industry, will need to become involved for the success of this project.

### **The future of the Global Asthma Survey of Practice**

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Asthma is a growing problem in middle-income countries that is likely to increase. Traditional health care systems, which have been developed to deal with acute problems such as infections and trauma, are not

well designed to deliver health care for chronic conditions, which require continuity of care. Continuity of care over prolonged periods, though not generally over a life time, has, however, been a characteristic of TB services.

GASP was developed by the IUATLD to investigate and document the need for continuous care and to provide a monitoring tool for the quality of the local services. It is based in emergency departments and assesses the acute cases of asthma that are seen in these clinics and the past treatment of their condition. It is the first phase of a development programme.

The initial GASP surveys pointed out major deficiencies in the current management of asthma both in and out of emergency departments, and these were found even in areas with dedicated staff with an interest in asthma. There were, however, inconsistencies in the data and it has been decided to attempt a more rigorous assessment before entering the full programme.

This presentation will focus on the past results and further plans of the UNION and the overall structure of the main programme.

## **CREATE, A RESPONSE TO TB/HIV**

### **Introduction to CREATE**

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The incidence of HIV-related tuberculosis is increasing dramatically, accounting for at least one third of all AIDS deaths. The principal public health intervention for TB control worldwide is DOTS, but this is failing to control TB rates in populations with a high prevalence of HIV. Despite high expectations, the introduction of antiretroviral therapy may have limited impact on TB incidence. Control of TB in the setting of the HIV pandemic requires novel strategies and new paradigms of public health. Even with existing tools, HIV-related TB incidence and mortality can be lowered. Selective intervention at critical points in the TB life-cycle, with TB preventive therapy, improved treatment and active case-finding may reduce TB incidence in populations with high rates of HIV infection. With this in mind, the Consortium to Respond Effectively to the AIDS-TB Epidemic (CREATE) was established in 2002, and expanded substantially in 2004.

CREATE is an international consortium of experienced researchers and public health officials that has designed a portfolio of studies at a population level that will validate strategies of novel and complementary interventions to control tuberculosis in settings with a high burden of HIV. During a year-long first phase of support from the Bill and Melinda Gates

Foundation, we used a process of data and literature synthesis, mathematical modeling and consultation with global experts in TB, HIV, public health and population level clinical research to identify specific interventions that are most likely to be effective in substantially reducing TB incidence in areas with high HIV prevalence. We have now been funded to conduct three population level trials that will evaluate novel TB control strategies in high burden settings. By developing, defining and evaluating new paradigms of TB control in communities currently heavily afflicted with HIV infection, CREATE will contribute a rigorous evidence base upon which new and effective global policies for TB/HIV control can be advocated.

### **The ZAMSTAR study: community and household-level interventions to enhance case-finding and treatment of TB & HIV in Zambia and South Africa**

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Key obstacles to the control of the combined epidemics of tuberculosis and HIV in much of sub-Saharan Africa are the inadequacy of existing health systems to find and cure infectious cases; failure of existing approaches to deliver sufficient preventive therapy to make a public health impact; and the continuing stigma, despair and denial that surround HIV.

Clinical, epidemiological, anthropological and operational research on the interactions between HIV and tuberculosis in Zambia and South Africa over the past decade suggest that two interventions that go beyond current tuberculosis control policies could substantially reduce the burden of tuberculosis and HIV.

- 1 Improved case finding—By allowing individuals direct access to diagnostic services and empowering and encouraging communities to seek care, we will bypass the health system barriers, reduce diagnostic delay and thus reduce the number of people who are spreading infection.
- 2 Integrated TB/HIV care delivered through the household—By harnessing the capacity of households and the community we will reduce the burden on the health system, increase the coverage and efficiency of preventive and curative tuberculosis services and break down the barriers of stigma and denial.

The ZAMSTAR study will evaluate these interventions at the community level by means of a community randomised trial.

The primary outcome will be the prevalence of culture positive tuberculosis among a randomly selected population of adults in each arm of the trial, measured after 3 years of the interventions. Secondary

outcomes include indicators of tuberculosis and HIV programme performance and changes in HIV incidence and stigma at the household level. This study will determine the effectiveness of these interventions across two different countries and urban and rural settings, so the results should be of broad relevance to policy makers.

### **Treatment for latent TB infection for HIV-infected population with access to HAART in Rio de Janeiro, Brazil**

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Potential medical and public health strategies to reduce the incidence of HIV-related TB in developing countries include the use of INH preventive therapy (IPT) and provision of antiretroviral (ARV) therapy to patients with advanced HIV disease. Available data demonstrate that ARVs dramatically reduce the risk of TB in HIV-infected patients, but rates of TB remain unacceptably high despite this intervention. Additionally, many people develop TB before they are eligible to receive ARV treatment. The impact of combined ARV and IPT programs is not known, but together these strategies could potentially reduce TB risk to extremely low levels.

Tuberculosis remains a major public health problem in Brazil. Approximately 35% of HIV-infected adults in Rio de Janeiro are co-infected with latent TB. The Brazilian policies for the provision of treatment to HIV-infected people are among the most progressive in the world. Brazil provides combination antiretroviral therapy free of charge to all patients who meet clinical criteria and maintains an extensive clinic and laboratory system for the appropriate prescription and monitoring of therapy. The use of IPT, however, has been very limited and TB remains a prominent disease in AIDS patients.

We propose a cluster randomized trial (CRT) to determine if the routine detection of latent TB in HIV-infected patients identified at HIV clinics in Rio de Janeiro, followed by treatment with isoniazid, will reduce TB incidence in this population. The CRT will take a phased-implementation approach to ensure that all clinics will eventually have full coverage. The study population will be comprised of HIV-infected individuals who attend 29 government HIV clinics in Rio de Janeiro. We expect that IPT use in addition to ARVs will result in a 40–60% reduction in TB incidence, and that approximately 50% of the prevented TB cases will be in patients not yet eligible for HAART.

## **The Gates Foundation: challenges in TB & HIV**

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Many of the world's greatest health problems such as HIV and TB can be alleviated greatly and many of the problems associated with these diseases are solvable. With increasing globalization, disparities in health that lead to these diseases can no longer be ignored and must be addressed. Both HIV and TB are priority areas for the Bill and Melinda Gates Foundation. The approach to TB is composed of three strategies. The first is to prevent incident disease through the development of a vaccine and new drugs that prevent reactivation of latent TB. The second is reduction of prevalent disease through the development and deployment of TB diagnostics that detect TB more quickly and reliably and development of new drugs that decrease the complexity and duration of TB treatment. The third area of focus is the appropriate management of TB in regions with high HIV prevalence. With regard to HIV efforts are aimed at prevention of HIV infections through the development of a safe, affordable vaccine against HIV and effective microbicides. Additional efforts are aimed at adaptation of current tools and development of new tools for decreasing HIV transmission. Innovative models are being formulated for prevention of HIV in areas where there are emerging epidemics and tools are being developed to optimize access to antiretroviral therapy.

## **ENSURING QUALITY OF CARE IN DOTS IMPLEMENTATION/INTEGRATING LABORATORY, NTPS AND ORGANISATION**

### **Developing a conceptual framework for evaluating DOT focusing on the performance of the care provider**

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This study deals with DOT performance, focusing on the care process and considering aspects of the interface between users and health professionals with a view to tuberculosis control (TB).

One of the theoretical-methodological approaches used for evaluating TB control strategies is the Health Service System Components Evaluation: Structure-Process-Outcome, which are interdependent and inter-related. Each Health Service possesses a structure that

allows for service delivery; a process that covers both the care provided by professionals and the care received by the patient and/or the community; an outcome that reflects various aspects of health status. These components interact with individual behavior and are influenced by sociocultural, political and economic aspects of the environment where health actions are developed.

DOT performance evaluation can be carried out through the construction of indices related to the structure, process and result components.

These indices can be constructed in a simple way (DOT activities: amount of activities carried out per supervision) or by relating variables within and among the components. The structure/process relation identifies the existing resources and the production of actions (performance agility: availability [hours/month] of transport-driver/amount of home visits carried out in DOT), while the process/result relation identifies to what extent the result is related to the production of actions (Monitoring of medication intake [MI]: amount of supervisions observing MI/total amount of supervisions carried out).

We consider that this approach allows for DOT performance evaluation, thus supporting the implementation and organization of TB control activities.

### **Developing a tool to evaluate the appropriateness and relevance of TB services**

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The recent resurgence of tuberculosis in many industrialised countries is characterised by a concentration of disease in specific subgroups of the urban population. Rates of tuberculosis are often now highest among those who have poorest access to services and substantial unmet health and social care needs. In London, these groups include recent entrants from countries with a high prevalence of tuberculosis, homeless people, prisoners and persons who abuse drugs and alcohol.

Epidemiological transition results in new challenges to disease control. Tuberculosis services must actively seek to adapt to the changing needs of those groups at highest risk of infection and active disease. In response, the London TB Nurses Network developed a methodology and survey tool to profile the needs and social characteristics of all tuberculosis patients on treatment. Data from this study have enabled providers to better describe and communicate how social characteristics affect risk of disease, poor adherence, drug resistance and relapse. Patient profiling can capture non-routine surveillance data to inform tuberculosis service development and be used to

evaluate the impact of specific initiatives and interventions. The approach is adaptable to a wide variety of international settings.

### **Implementing patient-centred interventions in the context of DOT: feasibility in a South African setting**

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A patient-centred approach (PCA) is seen as an essential element of any chronic care programme. The concept can be applied in a variety of ways, but evidence suggests that a PCA enhances patient satisfaction and can improve adherence to treatment. Some available tuberculosis (TB) treatment guidelines mention patient-centredness, but seldom translate this concept into practical interventions. It is unclear how a PCA may be applied and received within the context of Directly Observed Treatment (DOT), particularly in low- and middle-income countries where the burden of TB is greatest.

The study presented explored the feasibility of implementing a PCA in the context of DOT for TB patients in a South African setting. An innovative multi-faceted intervention was developed to enhance the quality of provider-patient interactions. These interventions included communication training for health providers, a hand-held photo novella for patients and a prepackaged medication system. The implementation process involved four urban primary health care clinics. Facility-based TB staff and managers participated together with other facility staff, lay health workers and TB patients.

A team of social scientists and health systems researchers used largely qualitative methods to describe the sequence of action cycles around the research question. Data sources included field notes, participant observation, audio and video recordings of interactions between the research team, managers, staff and patients. These interactions incorporated meetings, focus group discussions, training sessions and consultations. Quantitative data included structured client interviews and TB outcome data.

This paper presents the findings of this process evaluation, which indicated that implementation of these patient-centred interventions was limited. The study narrative highlights the dynamics that challenge and facilitate these types of quality improvement initiatives in these settings. The paper offers potential lessons for quality improvement leaders, public health researchers, managers and policy makers with an interest in improving caring within TB control programmes.

### **Quality of and communication between laboratories in Hong Kong**

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In Hong Kong, the Department of Health provides clinical care for all TB patients seen in the public sector, and carries out all requisite clinical investigations and treatment. The TB Reference laboratory (TRL) processes all government chest clinic specimens for microscopy, culture and drug susceptibility testing (DST), so that >80% of all positive clinical mycobacterial isolates are processed.

In 2003, out of a total of 8799 specimen cultures for identification of *M. tuberculosis*, 4035 (45.9%), 4500 (51.1%), and 264 (3.0%) were from hospital in-patients, chest clinic out-patients, and other services respectively. Based on this centralized TB Laboratory service, a quality assurance (QA) system that utilizes blinded rechecking of all AFB smear microscopy slides is in place. A territory wide QA program is run so that a panel of unknown slides are distributed quarterly to participating laboratories. Percentage of slides returned ranged from 92.4% to 98.4%. Averaged concordance rates for positive and negative smears were 98.5% and 98.3% respectively.

These QA programs serve as basis for an on-going dialogue between central and peripheral laboratories, and also sets the mechanism for continuous quality improvement. The TRL is also an important part of the TB notification registry by supplying information on all culture-positive cases that are detected in the TRL, and this is essential for effective contact tracing. Through this mechanism, gaps and deficiencies have been identified and led to improvements in the overall TB case registration and detection.

Improving on the quality of TB laboratories, and the training of high quality staff, can substantially improve TB control and will influence treatment outcomes as well as contribute to the implementation of DOTS in NTPs.

### **Integration found in laboratory assessments in high-burden countries**

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The level of integration of TB laboratory services into the National Tuberculosis Programme (NTP) is highly variable. Although overall it parallels the degree of integration of the NTP into the general health services, especially in less developed countries laboratory services are often weak and under-funded, so that direct interventions by the NTP remain necessary to assure a permanent service and to attain the necessary quality. In practice, reliable AFB-microscopy



would often not be possible without help by the NTP for procurement of quality microscopes, sputum pots and slides. Laboratory quality assurance systems may be poorly developed or non-functional, and the NTP often has to set up a system under its direct control. The same is true for national guidelines regarding smear-microscopy, without involvement of the NTP uniformity of practice is the exception, resulting in serious problems. While these and other interventions may at times be resented, and occasionally lead to disputes about policy and guidelines from the side of the Directorate of Laboratory Services, they probably remain indispensable in all high-burden countries. Only with advanced economical development, or special support to the Laboratory Services, can labs be expected to meet the conditions needed for TB control with only minimal help from the NTP. Even then, its intervention may be needed to guarantee largely free diagnosis, with access also for the poor. An example will be given where the AFB-microscopy network had completely collapsed when the NTP left its organisation and management to the Laboratory Directorate, resulting in severe under-detection with TB escaping control.

## TUBERCULOSIS PREVALENCE SURVEYS

### Reassessment of TB burden in Cambodia

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The National Tuberculosis Programme of Cambodia has successfully conducted series of TB surveys since year 2000, including the 1st national TB disease prevalence survey in 2002. These surveys have provided a rich body of information that will be important for TB control in Cambodia.

The crude prevalence rate of smear-positive TB was 270/100 000. This is only half the WHO estimate, which was derived from older and less-reliable surveys. The prevalence in males (387/100 000) was 2.5 times higher than the prevalence in females (163), despite the fact that the male/female ratio in case notifications was 1.1:1. Prevalence increased with age, reaching a maximum in the oldest age group, rather than in young adults. Smear-positive prevalence was lower in villages that are nearer to DOTS service centres. The prevalence of all bacteriologically-positive TB was high at 902/100 000, and no multidrug-resistant TB was identified. The annual risk of infection (ARI) was calculated from the results of a tuberculin skin-test survey, either by choosing a cut-off point at 10 mm induration, or by using the mirror method assuming a mode of 16 mm. The variable results for

different age groups of children were 1–4 yr: cut-off 0.99%/yr, mirror 0.46%/yr; 5–9 yr: 2.10%, 1.00%; 10–14 yr: 3.21%, 1.62%.

We interpret these findings as follows. Eight years of effort to control TB especially in a recent decentralised DOTS program have probably reduced prevalence by shortening the delay to treatment, without generating MDR-TB. The reduction in smear-positive prevalence should have reduced transmission, and the estimated ARI appears to be low and falling in comparison with the measured prevalence. However, control may not yet have had a significant impact on incidence, as cases continue to arise from a huge pool of latent infections. The smear-positive incidence rate could still be higher than 200/100 000/yr, but no precise estimate has been made. TB-HIV co-infection accounts for 10–15% of new cases, and the incidence of culture-positive (but smear-negative) disease might be higher than is generally appreciated. Further analysis and studies will be essential to provide a full understanding of TB epidemiology under the strict DOTS program that has been implemented in Cambodia.

### The impact of TB control in China

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**Background:** China has 1.5 million new TB cases each year, the highest incidence of any country except India. A new TB control project based on short-course chemotherapy was introduced in half the country in 1991, following a national survey of TB prevalence in 1990. Another survey was done in 2000 to re-evaluate the national TB burden, and to assess the impact of the control project after nearly a decade of implementation.

**Methods:** The 2000 survey identified 375 599 eligible individuals at 257 investigation points chosen from all 30 provinces by stratified random sampling. Children (0–14 years) became TB suspects if they had an induration  $\geq 10$  mm following a tuberculin skin test and an abnormal fluorograph. Adult TB suspects were those with prolonged cough and/or abnormal fluorograph. Diagnosis among suspects was by chest X-ray, sputum smear microscopy and culture.

**Findings:** A total of 365 097 persons were examined among those eligible (97%). The prevalences of pulmonary, culture-positive and smear-positive TB in 2000 were 367, 160 and 122 per 100 000 population. The prevalence of culture-positive TB in the project area was 150/100 000 in 2000 compared with 177/100 000 in other areas. Between 1990 and 2000, the prevalence of culture-positive TB fell by 37% (95%CL  $\pm 16\%$ ) more in project than non-project areas, and smear-positive disease by  $38 \pm 18\%$ . The impact of the project was larger, though not signifi-

cantly larger, in urban areas, in the middle and west of the country, and among men.

**Interpretation:** Short-course chemotherapy following WHO guidelines significantly reduced TB prevalence between 1991 and 2000, eliminating a third of a million culture-positive TB cases from a population of more than half a billion children and adults.

### **The impact of HIV on TB prevalence in Southern Africa**

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HIV infection is a strong risk factor for incident tuberculosis (TB) disease. During the last two decades TB case-notification rates have greatly increased in Southern Africa, mainly because of the severe regional HIV epidemic. The impact of HIV on the point prevalence of TB disease has not, however, been directly investigated until recently. The results of two cross-sectional prevalence surveys for HIV infection and TB disease in Southern Africans will be discussed. These were prompted by the observation that the point prevalence of TB disease in South African gold miners appeared to have been relatively stable during a period of rapidly rising HIV prevalence and TB incidence rates. Both surveys, one in South African gold miners (HIV prevalence 26%) and one in employees of 22 different companies in Harare, Zimbabwe (HIV prevalence 19%), included a period of follow-up for incident TB. In both studies the strength of association between prevalent undiagnosed TB disease and HIV infection (prevalence rate ratio) was much lower than for incident TB disease (incidence rate ratio). The low ratio of prevalent to incident TB disease in HIV-positive participants implies that the mean interval between the onset of HIV-associated TB disease and diagnosis was relatively brief, which may reflect an intrinsically fast rate of TB disease progression and presentation in immunosuppressed patients. Our findings from both sites suggest that the HIV epidemic may have had relatively little impact on the point prevalence of undiagnosed TB disease, and that the majority of infectious prevalent TB cases may be HIV-negative, even in high HIV prevalence settings. Both study populations had ready access to TB diagnosis through company clinics, however, so that further HIV and TB disease surveys will be needed before these conclusions can be generalized to populations with less optimal health care provision.

### **TB prevalence surveys can be used to assess progress towards the Millennium Development Goals**

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One of the Millennium Development Goals is to reverse global tuberculosis incidence by the year 2015. Indicators to measure progress towards achieving this goal are tuberculosis prevalence and death rates (indicator 23) and the proportion of cases detected and cured under DOTS (indicator 24). For the latter indicator, the World Health Organization (WHO) has formulated the following targets: a case detection rate of 70% and a cure rate of 85%. The case detection rate is measured as the number of notified cases per 100 000 population per year divided by the estimated incidence rate per 100 000 population per year. Unfortunately, tuberculosis incidence is uncertain and is not measured, but estimated indirectly. Consequently, the case detection rate is uncertain as well. This uncertainty is largest in countries heavily affected by the HIV epidemic in sub-Saharan Africa.

This presentation proposes a new indicator to assess case detection: the patient diagnostic rate (PDR). PDR is the rate at which prevalent cases are detected by control programs and can be measured as the number of notified cases per 100 000 population per year divided by the prevalence per 100 000. Prevalence can be measured directly through national prevalence surveys. Conducting prevalence surveys at 5 to 10 year intervals would allow high-burden countries to measure progress towards achieving the Millennium Development Goals by providing information on tuberculosis prevalence and on case detection performance using PDR.

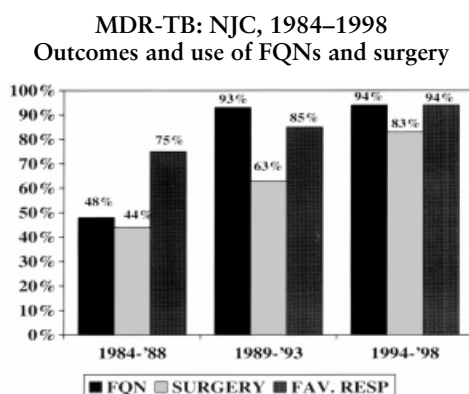
### **DRUG RESISTANCE AND TREATMENT OF MDR-TB**

#### **Important variables in the management of a large cohort of MDR-TB cases**

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205 patients with advanced MDR-TB were treated at the National Jewish Hospital between 1984–1998. The TB strains were resistant on average to 6 drugs, generally including all of the 1st line agents. The median age of the patients was 40 years; 58% were males; 53% were foreign born. Because these patients were very similar in terms of drug-resistance and extent of disease to a prior cohort reported from our institution (Goble, NEJM, 1993), we compared treatment outcomes focusing on the two new elements of

management, fluoroquinolone [FQN] antibiotics and resectional surgery [RS]. The results were divided into 5 year periods, 1984–1988, 1989–1993, 1994–1998. Over time, we employed both modalities, FQNs and RS more aggressively. As seen in this figure, successful outcomes increased as we utilized FQNs and RS more aggressively:



In the multiple predictor model, the use of RS was most significantly associated with favorable outcomes. The contribution of FQN therapy was probably lessened due to the use of less potent agents (cipro- and ofloxacin) rather than levofloxacin or moxifloxacin.

## LOOPHOLES IN NATIONAL LEGISLATIONS: NEED FOR INTERNATIONAL REGULATIONS—THE FCTC

### Watch-dogs and work-horses: civil society support for international tobacco control standards

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The Framework Convention on Tobacco Control (FCTC) is the world's first global treaty for public health, negotiated under the auspices of the World Health Organization (WHO) and adopted by the World Health Assembly in May 2003. The treaty will come into force after 40 countries ratify it, which means agreeing to implement a prescribed range of effective tobacco control measures at national level and cooperating internationally on those measures that require cross-border action. The treaty also requires countries to assist each other to meet their obligations through resource-sharing and technical assistance.

Although it is governments who have the power to ratify the treaty, in most cases it is non governmental organisations (NGOs) who have driven the process. Substantial NGO pressure during the years of negoti-

ations resulted in a strong treaty text. The role of NGOs is now formally recognised throughout the FCTC—in helping to plan and implement measures at national level, in assisting with monitoring and reporting, and in participating as observers in the Conference of the Parties (COP) which will be the body that oversees the treaty when it comes into force. Apart from this formal role, NGOs will have an ongoing advocacy role. Many of the measures in the treaty represent the minimum level of activity necessary to make an impact—to realise the full potential of the treaty, NGOs will have to continue to press governments to do more than the minimum.

The FCTC presents a real opportunity for effective global action on tobacco, but it also presents NGOs with a substantial challenge: that of being ready to play their part in its implementation. NGOs' own strategic and operational planning must include a response to the FCTC opportunity, and in many cases this may require NGOs to undertake some internal capacity building. Assistance with this is available from NGO coalitions such as INGCAT (the International Non Governmental Coalition Against Tobacco) and FCA (Framework Convention Alliance).

### Even when there is an advertising ban, they advertise: current activities in France and ways to counter them

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Promoting and advertising tobacco products is designed to recruit new and young smokers, to increase the number of smokers and to keep existing smokers preventing them from quitting.

France adopted a complete ban on tobacco advertising and promotion in 1991. The ban included in the Tobacco Act better known as Loi Evin has been in force for over 10 years.

The French Cancer League (LNCC) and the Comité National Contre le Tabagisme (CNCT) with the financial support of the health ministry has recently conducted an analysis to review the situation concerning the enforcement of the ban.

Using tobacco industry internal documents, verdicts of past litigation, and concrete examples of new forms of promotion, the study demonstrates that although, traditional advertising has almost disappeared (billboards, TV etc.), the tobacco industry and others continue to heavily promote tobacco products as they adapt to new situations, use and abuse loopholes in the legislation, exploit the lack of enforcement mechanisms, the lack of dissuasive penalties and the feeble means of a NGOs in charge of the monitoring and surveillance.

The experiences, lessons learned, recommenda-

tions, current projects and tools to improve the legal text and move towards a better and stringent enforcement of the ban will be presented.

## CAN YOU GET TUBERCULOSIS FROM YOUR FOOD?

### Bovine TB in Argentina and other Latin American countries, current situation

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Twenty three Latin American and Caribbean countries adhered to a PAHO/WHO survey in 1999–2001. In most of these countries compulsory notification of bovine TB is followed. Control activities are based on tuberculin testing and veterinary inspection in official abattoirs. In certain cases microbiological and histopathological confirmation of lesions suspected of TB is performed. In 21 out of these 23 countries, herds either suspected or confirmed as TB infected should be submitted to tuberculin testing. Sixteen of those 21 countries have reported to follow so far a test-slaughter policy on bovine cattle found positive to the tuberculin test. Nevertheless, in practice, most countries in the Region find it difficult to comply with this policy.

Out of the 53.5 million bovine population in Argentina, approximately 3 million are dairy cattle. From 1969 to 2002, in nearly 10 million bovines slaughtered annually, the percentage of carcasses condemned for TB decreased from 6.7% to 1.3%. In 1999 a compulsory TB program has been implemented based on test-and-cull strategies. Since then, 3500 farms holding 1.2 million head have been officially declared free of the disease. Ninety percent of these tuberculosis-free animals are held in dairy herds. The number of herds officially declared free of TB increased from 44 in 1995 to 3455 in 2003. Between 1969 and 2002, in 1.5 to 1.7 million swine carcasses inspected annually at slaughterhouses; condemnations for TB decreased from 8.4% to 0.7%.

Human infection attributable to *Mycobacterium bovis* fluctuates around 0.5% of all cases of TB diagnosed by culture throughout the country, ranging from nil to 2% according to the area. The highest rates are observed in the provinces where cattle industry is held. Human TB of bovine origin in Argentina is mainly an occupational disease acquired from cattle by aerosol and affecting middle-aged males not infected with HIV.

### *Mycobacterium bovis* isolates from zebu carcasses confiscated from the main slaughterhouse in N'Djamena, Chad

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Bovine tuberculosis was among the main causes of meat confiscation in the main slaughterhouse of N'Djaména, Chad. During a prospective slaughterhouse study of 2 months (July–August 2002), the meat inspectors have confiscated 727 cattle carcasses due to bovine tuberculosis. The microbiological examination of 201 tubercle lesions deriving from 75 zebu Mbororo and 124 zebu Arab carcasses has demonstrated for the first time the presence of *Mycobacterium bovis* in Chad. Total confiscation of the objected carcasses was significantly higher for Mbororo (33%, 56 partial confiscation and 19 total) than for Arab zebus (9%, 113 and 11) ( $P = 0.002$ ). *M. bovis* was more often cultured from specimens of Mbororo cattle than of Arab cattle ( $P = 0.004$ ). Spoligotyping of 56 *M. bovis* isolates showed that they lacked the direct repeat (DR) 30 as has been described for Cameroon isolates. In contrast to Cameroon isolates, almost of Chadian isolates did not show DR 15. This study showed a 50% clustering of *M. bovis* strains coming from a sample with a bovine tuberculosis and slaughterhouse prevalence of 7%.

### Veterinary surveillance of TB in meat and milk production: methods of assessment and control

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Transmission of *M. bovis* infection to man occurs by direct and indirect contact with infected animals. The risk of transmission by meat consumption mainly depends on the stage of the disease. In EU slaughtered bovines must be inspected by an official veterinarian, including palpation and incision of organs and lymph nodes. In case of generalized tuberculosis or multiple lesions, the carcass must be destroyed.

Concerning milk and dairy products the risk due to the consumption of raw milk is controlled excluding the milk from infected herds, hence the importance of applying a reliable diagnosis protocol.

In vita diagnosis is based mainly on the cellular mediated immunity detection by the skin test and the gamma interferon test. Post mortem diagnosis is based on a panel of different investigations:

- anatomo-pathological examination
- histological examination;
- bacteriological examination;
- bio-molecular techniques.

Positive results are communicated to the veterinary authorities responsible for supervision of the herd.

Where the infection persists, all the bovines are tested yearly: positive bovines must be slaughtered.

The presentation shows possibilities, costs and effectiveness of different strategies of risk identification and control, on the basis of a twenty years eradication program performed in a highly infected area.

### **Cattle and pig tuberculosis; role of meat inspection in human health protection in Central European countries**

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Among the countries of the Central Europe (Czech Republic, Croatia, Poland, Slovakia, Slovenia, Hungary etc.) bovine tuberculosis was put under control between the years 1960 and 1980. In the subsequent post-elimination period, reduction in the number of new cases of bovine tuberculosis was recorded and the last case of bovine tuberculosis in cattle was registered in 1990s in the Czech Republic, Slovenia, and Slovakia. A similar trend of incidence of bovine tuberculosis incidence in other domestic and wild animals was recorded. However, *Mycobacterium tuberculosis* may also participate in the occurrence of tuberculous lesions and was isolated from animals originating from the Czech Republic, Slovakia, Croatia and Poland (dogs, cattle, pigs, and different wild animals reared in zoological gardens). After control of bovine tuberculosis in Central Europe, the most significant causes of mycobacterial infections producing tuberculous lesions in the lymph nodes of domestic animals (particularly cattle and pigs) became *Mycobacterium avium* complex. Among IS1245 RFLP types of 250 pig, human, and environmental isolates identical RFLP types obtained from pigs and environment were identified, which confirmed the hypothesis, that different part of environment contaminated with mycobacteria represents a significant source of mycobacterial infection for pigs. In the years 1990 to 2002 *M. tuberculosis* was bacteriologically confirmed in a total of 14 891 patients (relative number of bacteriologically confirmed cases decreased from 14.9 to 7.8 per 100 000 inhabitants). In the same period *M. avium* complex isolates were bacteriologically confirmed in a total of 689 patients (relative number of bacteriologically confirmed cases ranged between 0.28 and 0.95 per 100 000 inhabitants). More than 77% of patients were older than 50 years and during the last 6 year increasing incidence from 0.28 to 0.95 per 100 000 inhabitants was documented.

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## **SUNDAY 31 OCTOBER 2004**

### **HIV/TB: SCALING UP THE USE OF ARVS—LINKS TO TB CONTROL**

#### **Integration of HIV and TB: from policy to practice**

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There is an overwhelming need to scale up highly active antiretroviral therapy (HAART) in Africa, where the AIDS epidemic is taking an appalling toll. Large numbers of AIDS patients will be difficult to reach in resource-poor environments using a medicalised model, which is demanding of expertise and technology. Anti-tuberculosis treatment, administered through DOTS, has been used successfully for treating TB patients in poor countries, and scaling up HAART has much to learn from TB service delivery. Malawi, a small and impoverished country in Southern Africa, serves as an example.

In the same way as for DOTS, a framework has been developed for delivery of HAART consisting of a goal, specific objectives, a strategy, a policy package, key operations and indicators.

The diagnosis of TB depends on simple technology such as smear microscopy, recognizing the fact that mycobacterial culture is not feasible in peripheral units. Similarly, simple criteria for assessing eligibility to HAART have been developed which do not need high technology. Malawi is scaling up HAART to over 50 sites by offering the first line ARV regimen only, an approach borrowed from the TB programme, which has not invested in expensive and toxic second line drugs. For both anti-TB treatment and HAART, guardian based supervision is used to improve drug adherence. The TB programme regularly reports on cases and treatment outcome using a variety of monitoring tools. Similar tools have been adapted for monitoring HAART, which allows regular reporting of cases and treatment outcome, which in turn will help with realistic drug procurement orders.

DOTS has a good track record for TB control in poor areas of the world, and if the same model can be made to work for the delivery of HAART, many lives can be saved and the risk of drug resistance kept low.

### **Delivering HIV care to persons co-infected with TB and HIV: the Khayelitsha experience**

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In many countries including South Africa the increasing HIV and TB epidemics are impacting significantly on already weakened public sector services. Khayelitsha is a township of Cape Town with 450 000 inhabitants, where the HIV sero-prevalence in pregnant mothers at ante-natal services was 25% in 2002. The annual TB case detection rate was 1152 per 100 000 population in 2002. Early in 2003 the HIV and TB services at Site B primary care clinic in Khayelitsha, where antiretroviral therapy (ART) is provided, were integrated, following a review of the scope, process and performance of each of the services. The results of the review conducted before and after the pilot integration project are presented.

The scope, process and performance of the services were assessed through observations of the service and individual and group interviews with key persons and by examining the reports from the health information system and clinical data.

In 2001 the HIV status of 26% of TB patients was known whereas the status of 39% of patients was known in 2003. More patients co-infected with TB and HIV are now on cotrimoxazole prophylaxis. In 2001 less than 5% of HIV-infected patients received Isoniazid prophylaxis. This increased to 11% in 2003. A larger proportion of patients with smear negative TB were on treatment in 2003. Even though there is a 63% reduction in TB incidence in patients on antiretroviral therapy, 13% of these patients still acquire TB each year indicating that even with ART there is still a large group of co-infected patients. There is a dissonance between the directly observed approach to TB treatment and patient-centred supportive approach to ART treatment. There is less duplication with a common information system and single set of records and less waiting time for patients.

The pilot project suggests that there are benefits to integrating HIV and TB services. Constraints to this process are discussed.

### **HIV and TB activities within the Gates Foundation**

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Many of the world's greatest health problems such HIV and TB can be alleviated greatly and many of the problems associated with these diseases are solvable. With increasing globalization, disparities in health that lead to these diseases can no longer be ignored and must be addressed. Both HIV and TB are priority

areas for the Bill and Melinda Gates Foundation. The approach to TB is composed of three strategies. The first is to prevent incident disease through the development of a vaccine and new drugs that prevent reactivation of latent TB. The second is reduction of prevalent disease through the development and deployment of TB diagnostics that detect TB more quickly and reliably and development of new drugs that decrease the complexity and duration of TB treatment. The third area of focus is the appropriate management of TB in regions with high HIV prevalence. With regard to HIV efforts are aimed at prevention of HIV infections through the development of a safe, affordable vaccine against HIV and effective microbicides. Additional efforts are aimed at adaptation of current tools and development of new tools for decreasing HIV transmission. Innovative models are being formulated for prevention of HIV in areas where there are emerging epidemics and tools are being developed to optimize access to antiretroviral therapy.

### **ADVANCES IN THE DEVELOPMENT OF NEW DIAGNOSTIC TESTS FOR TUBERCULOSIS**

#### **FIND, an innovative approach to addressing a critical need for tuberculosis control**

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The biotechnology revolution of the past few decades has not benefited most tuberculosis patients who are trying to discover the cause of their illness. No simple point-of-care diagnostic tests have yet proven superior to microscopy, and more complex technologies that are superior to microscopy have not been implemented widely in disease-endemic settings. Recognizing that this situation will not improve without a focused effort, the Bill and Melinda Gates Foundation has created FIND (the Foundation for Innovative New Diagnostics), an independent, not-for-profit entity which is dedicated to providing technology solutions to meet diagnostic needs in the developing world. With an initial focus on tuberculosis, FIND will address the critical need for new diagnostics by developing entirely new tests, optimizing existing tests or proving their performance in disease-endemic settings, and demonstrating the utility and impact of new technologies on national TB control programs.

FIND is unique as the only non-profit organization dedicated wholly to the development of diagnostic tests for infectious diseases, and was created to overcome the obstacles that have blocked academic, government and corporate entities from moving promising ideas through a developmental pipeline and ensuring

their implementation by public health systems to decrease global health inequities. By harvesting the best biotechnologies available and developing and proving new tests for patient management, disease control, and surveillance, FIND aims to create a model for public action that addresses the current failure of market forces to provide diagnostics for neglected diseases. FIND works in close collaboration with the World Health Organization and its Special Programme for Research and Training in Tropical Diseases (TDR), with which it shares a joint workplan in the area of tuberculosis diagnostics.

### **The market for TB diagnostic tests**

TO BE ANNOUNCED

Despite recent philanthropic initiatives that prioritize TB and the creation of private-public partnerships, diagnostic tool developers consistently report a struggle to attract public and private investment for new diagnostic tools research and development (R&D). Knowledge of the global market size for TB diagnostics and credible estimates of potential financial and social returns on investment is critically important to potential investors and has, until now, been largely unknown. This presentation will provide an accurate assessment of the current and future global TB diagnostics market, an overview of TB laboratory services around the world and physician diagnostic practices in key markets.

### **WHO/TDR activities in support of new TB diagnostics**

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In 1996, WHO reviewed the status of efforts to develop new diagnostics for tuberculosis and noted that recent progress in basic research had made possible the creation of a range of new tests. However, these tests were generally not appropriate for use in low-income countries. WHO determined that additional emphasis was needed to accelerate the development of the new products for use in low-income countries. A strategy of stimulating and facilitating industry to adapt available technologies for new diagnostics rather than the direct funding of competitive product development was developed and the TB Diagnostics Initiative (TBDI) was formulated to implement this strategy in 1997. In 1998, tuberculosis was added to TDR's portfolio and it soon thereafter became the home of a 10 million USD Bill and Melinda Gates Foundation grant to support the TBDI. Over the past several years TDR has made a significant contribution to the promotion of new diagnostics for tubercu-

losis through funding research into novel diagnostic methods and improved methods for smear microscopy; establishment of a TB Specimen Bank and Strain Bank, operational research coupled with mathematical modeling to predict the impact of new technologies in National Programs, a report on the global TB diagnostics market and through a network of clinical trial sites. TDR's efforts culminated in May 2003, when the Foundation for Innovative New Diagnostics (FIND) was launched. The major highlights and key achievements of past activities and future plans for TB diagnostic development in collaboration with FIND will be presented.

### **Perils and pitfalls in clinical trials of new TB diagnostics**

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There are presently no internationally accepted standards for the clinical evaluation of diagnostic tests for tuberculosis. Moreover, many developing countries do not regulate the marketing of diagnostic tests. As a consequence there are a number of TB diagnostics on the market in developing countries that have been shown to perform poorly when assessed in independent studies. Development and promulgation of GLP and GCP standards for assessing new diagnostic tests for TB are necessary to provide data to those regulatory authorities that do approve such tests for marketing, to international technical bodies such as WHO and the IUATLD who may issue guidelines on the use of these tests, and to NTP managers and donor agencies who may consider purchasing these tests for programmatic use. Problems that have been identified in past assessments of TB diagnostics include the failure to assess the tests in the intended patient population (e.g., a new test for case detection should be evaluated in patients being evaluated for TB disease), insufficient sample size to draw statistically valid conclusions about test performance, failure to include culture-negative TB cases with a resultant decrease in specificity of a new test, and problems in performance of the comparator 'gold standard' diagnostic test (e.g., the accepted test for diagnosing latent TB infection, the PPD skin test, lacks sensitivity and specificity). In addition, relatively few studies have closely examined cost data other data related to test performance that are required for an informed decision about recommending and implementing new tests in control programs. This presentation will outline a standardized approach to the laboratory and clinical assessment of new case detection tools, new tests for the diagnosis of drug resistance, and new tests for the diagnosis of latent TB infection. Examples from studies that are being undertaken by FIND and WHO/TDR will be presented.

## IMPROVEMENT OF INDOOR AND AMBIENT AIR QUALITY IN DEVELOPING COUNTRIES

### Effets sanitaires de la pollution atmosphérique urbaine en Afrique du nord : cas de la ville d'Alger

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**Contexte :** La pollution atmosphérique dans la zone d'Alger est principalement d'origine automobile et les différentes mesures effectuées ont montré des niveaux de pollution très élevés pour de nombreux polluants.

#### Objectifs :

- Mettre en place un système de recueil de données sur la pollution atmosphérique,
- Mettre en place un système de recueil de la morbidité respiratoire en consultation ambulatoire,
- Evaluer l'impact sanitaire de la pollution atmosphérique urbaine par les poussières (PM<sub>10</sub>) à Alger.

**Méthodologie :** C'est une étude descriptive permettant d'évaluer l'impact sanitaire de la pollution atmosphérique par les poussières en population générale. Un capteur de poussières (PM<sub>10</sub>) installé a permis un suivi permanent et continu des niveaux du polluant. Le recueil de la morbidité respiratoire en consultation ambulatoire a porté sur les motifs de consultations. Notre analyse pour apprécier l'effet attribuable à la pollution, s'est basée sur les résultats de l'étude de S.HAJAT menée à Londres en prenant comme référence la relation dose—réponse trouvée dans ce travail.

**Résultats :** Pour l'indicateur d'exposition, le niveau moyen journalier est 61 µg/m<sup>3</sup> [29–93] et la saison hivernale est caractérisée par un taux élevé (DS < 10<sup>-6</sup>). Les données de morbidité extra-hospitalière montrent que le nombre moyen quotidien de consultations pour affections respiratoires est de 25,29 [14,67–37,91]. Cette moyenne est élevée en période hivernale (DS, *p* < 10<sup>-6</sup>).

**Conclusion :** Cette démarche d'évaluation de l'impact sanitaire a permis de déterminer le nombre de consultations attribuables à la pollution atmosphérique par les PM<sub>10</sub>. Elle devrait être étendue à de plus vastes territoires englobant d'autres villes et impliquant plusieurs structures sanitaires pour déterminer la fonction exposition—risque spécifique par la mise sur pied d'étude de type écologique temporelle.

## WOMEN, TOBACCO, LUNG HEALTH AND THE ECONOMIC CONSEQUENCES

### Meeting the challenge of female smoking in the new century: developing country perspective

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Although we may not have the exact statistics from developing countries, the trend in women smoking is alarming—as smoking rates for males are going down, those for females are catching up. WHY? Any little attempt at analyzing this has revealed the folly of using the same rationale and intervention strategies for males as for females. Female smoking is not a simple habit that can be easily modified. It is not only determined by social and psychological factors, but by the fact that it presents benefits and performs functions for both individual women and the societies in which they exist. Ignoring this results in ineffective and wasteful programming which could even be counter productive. Therefore there is a need for women-specific strategies of cessation which will take into account subtleties of women's lives and how they perceive the value of their own lives and behavior. In addition a few elements to be considered are:

- a Examining and assessing real knowledge gaps
- b Learning from the individual woman why she is smoking, and why and how she would give it up i.e, her total participation
- c Looking at her more positively—banking on her achievements and assertiveness
- d Emotional appeal because of her role in the family and society as a caregiver and a source of life
- e Need to bring the analysis of women's smoking out of limited health and medicinal effects to a more comprehensive interdisciplinary analysis
- f Considering her as a decision maker for her own behavior.

## ENHANCING CASE FINDING: REPORT ON FIDELIS PROJECTS IN CHINA

### Increasing case-detection in poverty and remote areas of Gansu Province, China: collection of sputum at village level

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**Background:** According to WHO, China had a case-detection rate of 36% and a DOTS detection rate of 33% for new smear-positive cases in 2000. In the 2000 National TB Prevalence Survey, 43% of the prevalent TB cases actually had not been diagnosed.



**Objectives:** To increase case finding rate through improving access to TB control services of the patients in poor and remote areas.

**Methods:** The components of the project include the following: 1) Development of the system to collect sputa from TB suspects at the village level, transport them to the township hospital/clinic, make sputum smears at the township level, and transport the smears to the county level for reading; 2) Design and produce a standard set of materials/registries for the sputum referral and active suspect recruitment; 3) Training village doctors to collect good quality sputum, and training township doctors to make good quality smears; 4) Supervision and monitoring visits to the township and village level conducted by county TB staffs on a regular basis; 5) Follow-up on all patients with positive smears to ensure that they are started on treatment.

**Results:** The period of the project is from Oct. 2003 to Sep. 2004. The period of result analyzed is only 8 months which is from Oct. 2003 to May 2004. In general, the project progressed well and the cumulative case detection achieved the planned target of case detection. The number of new smear positive cases found is 3.3 times than same period of last year. Among of them, patient with limited access to health care is 80%, 57.6% of new smear positive cases found is from sputum smear examination in township level. The sputum negative conversion rate is 95% for the new smear positive cases at the end of 2nd month after treatment.

**Conclusion:** Using the collection of sputa at village level to increasing case-detection in poverty and remote areas is available, advantageous, and extend to other poverty and remote areas.

### **Strengthening the referral of TB cases and suspects from the hospital system to the TB dispensary in Hunan province, China**

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**Background:** 2000 NPS showed, only 12% of prevalent TB cases found were diagnosed at the TB dispensaries while the community health providers diagnosed 88% of them. Sadly, only 13% of the prevalent cases diagnosed with TB by the community health care providers were referred to the TB dispensaries.

**Objectives:** To increase case detection rate through strengthened referral system of TB cases and suspects from the hospital system to the TB dispensary.

**Methods:** 1) Design a comprehensive case-referral program based on national best practices. 2) Meeting with health officials to get commitment. 3) Design and produce a standard case referral materials/registries. 4) Trainings for township and county hospital staffs to implement the referral program and utilize the re-

ferral materials. 5) Supervision and monitoring visits to the county and township hospitals conducted by county TB staffs on monthly basis. 6) Quarterly meeting with hospital staffs to discuss progress and solve problems. 7) Monitor completeness of referral and the extent to which referred patients actually come to the TB dispensary. 8) Follow-up on all referral defaulters, including home visits, by health care workers.

**Results:** The duration of the project is from Oct. 2003 to Sep. 2004. In general, the project progressed well. The number of new smear positive detected in 8 months (Oct. 2003–May 2004) is 1.3 times than whole number of last year. Among them, patient with limited access to health care is 87%, 45% is referred by general hospitals; The 2nd month sputum negative conversion rate is 95%.

**Conclusion:** Through this project, a mechanism of referral system has been developed; it is available and sustainable in China, especially in poor and remote area.

### **Newer models of hospital-public health collaboration in DOTS implementation in Hubei Province—also called public-public mix DOTS (PPM-DOTS)**

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**Background:** Most TB patients in China initially seek care in the hospital system when they become ill. Three-quarters of these patients are never reported and referred to the TB dispensary system. Little hospitals were involved in DOTS implementation.

**Objectives:** To increase case detection through improving collaboration between TB dispensary and general hospitals.

**Methods:** The strategy is that general hospitals were involved in DOTS implementation by enhancing hospital sputum smear laboratory diagnosis. Main activities included a) designing the program whereby the TB suspects are examined at the county general hospital using sputum microscopy; b) training the microscopists of the county general hospital on sputum microscopy and re-train townships and county hospitals to refer TB patients to TB dispensary; c) conducting quality assurance of sputum microscopy in the general hospital by the prefecture and county TB dispensary; d) conducting quarterly meeting to discuss progress and solve problems; e) regular monitoring and supervision; and f) follow-up of on all referral defaulters.

**Results:** The period of the project is from Oct. 2003 to Sep. 2004. The period of result analyzed is only 8 months which is from Oct. 2003 to May 2004. In general, the project progressed well. The number of new smear positive cases found is 1.8 times than

same period of last year. Among them, patients with limited access to health care comprise 63.4%. The sputum negative conversion rate is 97.2% for the new smear positive cases at the end of the 2nd month after treatment.

**Conclusion:** Case detection can be increased through involving more health facilities in DOTS Implementation.

### Social mobilization in Hebei, China

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**Background:** FIDELIS project in Hebei province covers 45 counties with the population of 19 million.

**Objective:** To implement the innovative TB Health Promotion Strategy to further increase the case-detection rate in Hebei Province.

**Methods:** To randomly select 45 counties in Hebei province and carry out multiple innovative health promotion activities including training, writing slogan on the wall in every village, sticking government notice and poster, sending sheet by students, carrying out different kinds of recreation on TB, disseminating TB related-information through mass media, referring TB suspects to TB unit by village doctor and village leaders, informing TB policy and knowledge by county governor and village leader through broadcasting or TV.

**Results:** The period of the project if from Jun. 2004 to Dec. 2004, in first half year of 2004, 26 094 TB suspects were identified which has achieved 75.3% of the project goal (total: 34 655) and 4402 new SS+ cases were detected in the project area which has achieved 57.2% of project goal (total: 7701 cases). The number of new SS+ cases detected is more than twice of the baseline. 3500(79.5%) of the 4402 are with limited access to health service which has exceeded the expected total number of 3247.

**Conclusion:** The implemented health promotion strategy has greatly increased the case-detection rate in project area which prove the effectiveness of different health promotion activities especially slogans on the wall, mass media, and government notice.

## TUBERCULOSIS MANAGEMENT IN CHILDREN: OBSTACLES TO REACHING THE MILLENNIUM DEVELOPEMENT GOALS

### Treatment of TB in the HIV area

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The management of childhood TB is particularly difficult in regions where childhood HIV infection is also endemic. It is well established that HIV-infected children do not respond as well to treatment for tuberculosis as HIV-uninfected children. One important reason for this, especially in the low-resource setting where pulmonary TB is rarely confirmed, is that the child does not have TB but rather another cause of HIV-related lung disease. However, even in children with confirmed TB, treatment response is worse and mortality is significantly higher in those that have HIV co-infection. The main reasons for this poorer response have not been clearly defined, but possible HIV-related risk factors include: degree of immunosuppression; malabsorption of anti-TB drugs; greater likelihood of mixed infections; poorer compliance as greater social dislocation and less supervision in families living with HIV/AIDS; and more adverse drug reactions. In HIV endemic regions, thiacetazone has been replaced by ethambutol in many HIV-endemic regions, including for infants and young children. Dosages for anti-TB drugs have been mainly extrapolated from pharmacokinetic data in adults and so studies are needed in children to determine whether currently recommended dosages are satisfactory in the context of HIV and severe malnutrition. Similarly, regimens have been uniformly adapted without evidence of relative efficacy in children (e.g., continuation phase of 6EH vs. 4RH). Finally, HIV status is often unknown in children with suspected TB because testing is not routine. The importance and value of an HIV test in this clinical circumstance needs to be emphasised. Aside from considering other diagnoses in the HIV-infected child who presents with suspected TB, and considering additional treatment options (e.g., cotrimoxazole prophylaxis, ARVT), it avoids the not unusual scenario of the HIV-uninfected child with TB being erroneously diagnosed as HIV/AIDS on clinical grounds alone.

### Multidrug resistant (MDR) TB treatment and prophylaxis in children

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Children mainly develop new MDR-TB. MDR-TB is as infectious as drug-susceptible TB and causes dis-

ease. Diagnosis is confirmed by culture and susceptibility testing (DST), but should be suspected if a) an adult index case has MDR-TB, b) a child is a treatment failure despite compliant therapy, or c) an adult index case with unknown DST is a treatment failure or a retreatment case.

In the absence of the child's culture and DST, the adult index case's DST should be used to determine the treatment regimen. Three or more drugs should be used to which the strain is susceptible or naive. Treatment duration depends on the extent of disease; usually 12 to 18 months. Drugs used in MDR-TB regimens are generally more toxic than first-line drugs and some drugs are not recommended for use in children, and therefore MDR cases are best managed at specialised units. With correct dosing, few long-term adverse events are seen with drugs such as ethionamide, ethambutol and the fluoroquinolones. Early diagnosis and individualised treatment is effective in the management of MDR-TB in children. Appropriate chemoprophylaxis with drugs to which the index case's strain is susceptible could be effective in preventing MDR-TB.

### The place of new diagnostics in childhood TB

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Childhood tuberculosis often presents non-specifically and is a common differential diagnosis in high prevalence areas. Current diagnostic tools have poor sensitivity and cannot reliably exclude tuberculosis, so overdiagnosis is common. HIV co-infection exacerbates this problem and accounts for an increasing proportion of paediatric tuberculosis globally. Improved diagnostic evaluation of children with suspected tuberculosis and children with latent tuberculosis infection is a priority.

A rapid T cell-based blood test for *M. tuberculosis* infection, the enzyme-linked immunospot (ELISPOT) assay, recently received regulatory approval in Europe. The assay enumerates individual T cells specific for antigens expressed by *M. tuberculosis* but absent from BCG. The clinical utility of this new diagnostic in childhood tuberculosis was prospectively assessed in parallel with the tuberculin skin test in 1881 children. Children at risk of latent tuberculosis infection were studied in 3 settings: teenagers in a point-source secondary school outbreak in England ( $n = 535$ ); neonates exposed to multidrug-resistant tuberculosis on an Italian maternity unit ( $n = 41$ ) and child household contacts of smear-positive pulmonary tuberculosis cases in Istanbul ( $n = 1012$ ). In addition, African children with suspected active tuberculosis were studied in routine clinical practice in kwazulu-Natal ( $n = 293$ ), a region of high HIV prevalence. All children had full clinical and radiological assessment and

test results were compared with final clinical and microbiological diagnoses after unblinding.

All evidence to date indicates that ELISPOT is more sensitive and specific than the tuberculin skin test for a) diagnosis of latent tuberculosis infection in asymptomatic children and b) for rapid detection of tuberculosis infection in children with active tuberculosis. In contrast to the skin test, ELISPOT is not confounded by prior BCG vaccination and its sensitivity is not significantly adversely affected by HIV coinfection, young age or malnutrition. The talk will focus on diagnosis of active tuberculosis in resource-poor settings and implications for improving clinical practice.

### INCENTIVES FOR DOTS PERFORMANCE: ENABLING OR CORRUPTING?

#### Evaluating enabler and incentive schemes: what are we learning?

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Incentives have emerged over the last two years as a topic of relevance to DOTS scale-up and to all new strategies meant to extend DOTS to reach more patients. The 'mainstreaming' of this issue is promising but needs to be accompanied by more thorough research and evaluation. Since 2001, a joint work programme of MSH/RPM Plus, the World Bank and WHO/Stop TB has been working to build the evidence base on the impact of incentives and enablers (I&E) on TB programme performance. The presentation describes the conceptual framework and hypotheses regarding the role of I&E in TB control, and the principal activities of the joint work programme, which have taken place in Africa, Asia, Europe and Latin America. Evidence gathered so far from these activities is presented, with an emphasis on quality of evidence available, current gaps in evidence, and challenges faced in implementing and managing incentives schemes. The presentation concludes by cataloging the available evidence for the enabling contributions for I&E and examples of corrupting effects that have been encountered.

The evidence to date suggests that even though there are many examples of I&E schemes being used by TB programmes in many different contexts, most of these have not been explicitly piloted or evaluated, so their impact on programme performance is difficult to assess. In addition, not enough qualitative research has been done to assess the enabling or corrupting influences these schemes may have on individuals. However, in only a few cases have unintended effects undermined the incentive scheme, and in other cases, unwanted effects were identified and eliminated by

the programme. Anticipating and controlling for unintended perverse effects is an important part of designing an effective I&E scheme, and requires pre-implementation planning and strong management of the scheme.

### **Reducing defaulter rates in Russia requires support for providers and patients**

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Social support of TB patients was provided within seven WHO TB control pilot projects in Russia to ensure DOT and to decrease a number of interruptions and defaults. Different frameworks were used: programmes conducted by regional branches of Russian Red Cross, local medical institutions or social affairs departments. The results were analyzed in cooperation with CDC.

To strengthen patients' adherence to treatment free transportation to the sites of treatment, milk and juice supplies for medicines intake, monthly and daily food kits, hygienic kits, clothing or food at the cost of 15–20 USD upon treatment completion were provided.

Social support was provided to TB patients selected out of socially vulnerable groups: 50.7% were unemployed, 45% ex-prisoners, 12.5% homeless and 65% alcohol abusers.

Result-oriented quarterly salary incentives for medical workers were provided to increase commitment.

The most extensive experience of implementing the programme in Russia was obtained in Ivanovo. Before the WHO TB control project started in 1996 more than 30% of TB patients defaulted treatment. Owing to the introduced system of TB patients' management, the number of defaulters decreased to 15% by 1999. After a programme of patient incentives started in 2000 the number of defaulters in the region remains no more than 5%. Before starting the social support programme, the project couldn't exceed a 60% treatment success rate in new smear-positive TB patients, but in 2001, soon after the programme started, the rate increased to 70.4% and continues to grow.

Arrangement of incentives for patients seems to be an important tool for enhancing the effectiveness of TB control programmes. Incentives for medical workers were criticized. This approach needs to be consulted with partners, MoH and further revised. Results should be further analyzed and an operational research should be designed to prepare recommendations by an appropriate Thematic Working Group.

### **Performance-based support for DOTS innovations: the FIDELIS approach**

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FIDELIS is a global fund hosted by the Union and currently being funded by CIDA that specifically aims at cure of new sputum positive (NSP) cases prioritizing those with limited access to health services. FIDELIS aims to serve as a stimulus for, and promoter of, cost-effective and sustainable innovative ideas that are capable of demonstrating independently verifiable results.

Since the focus of FIDELIS is on the performance outcome one of the core eligibility criteria is a cost of less than USD 80 to FIDELIS per Additional Weighted Treatment Success (AWTS).

Contract negotiations are focussed on the technical and operational aspects of the project in formulating structured work plan which facilitates achievement of the desired results.

For process monitoring of the project performance, NSP case detection rate and sputum conversion are monitored on monthly basis and form basis of subsequent release of funds to the projects.

At the time of preparation of abstract there have been three funding rounds of FIDELIS in which out of 63 proposals received for consideration, 17 projects covering a population of 140 million in Bangladesh, China, Indonesia, Kenya, Pakistan, Sudan, Tajikistan and Tanzania, have been approved. Through these 17 projects it is expected that more than 85 000 NSP cases would be detected, and at least 70 000 are likely to be cured, as a result of which, nearly a million new infections shall be prevented and more than 10 000 deaths averted. Request for Proposals for the fourth round closes on 1st June 2004.

The innovations in these projects include strategies like strengthening existing facilities including improvement in diagnosis, improvement of referrals, community based DOTS, intensifying IEC and involvement of Private Health Care providers. Some of the interventions involve payment of performance based incentives to peripheral health care workers to compensate for the increased work load and direct and indirect costs to these workers for provision of DOTS services.

### **TB IN MOBILE POPULATIONS AND IN PERSONS WITH UNDOCUMENTED RESIDENCE STATUS**

#### **Tuberculosis in persons with illegal residence status in low-prevalence countries: size of the problem and possible solutions**

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During the last decades an increasing number of persons have come to reside in high-income areas of the

world, but the immigration pattern has varied between countries and changed over time. In Western Europe main trends have been planned economic migration in the 1960s and 1970s, political asylum seekers in the 1970s and 1980s, with a more mixed picture since the 1990s, when criteria for giving asylum were made stricter in most countries and the Schengen agreement strengthened enforcement. The number of persons with undocumented residence status has therefore increased.

As tuberculosis has declined in the indigenous population in high-income countries, the proportion of tuberculosis cases in foreign-born persons has increased. Tuberculosis in persons with undocumented residence status is of special importance because many come from countries with high incidence of tuberculosis, and some from settings with high levels of multidrug resistant tuberculosis and/or HIV infection. The conditions before and during travel to the high-income countries may have increased the risk of tuberculosis infection and disease further.

Tuberculosis control is based upon early detection and effective treatment of infectious cases without creating resistant strains. From a public health perspective, persons with undocumented residence status therefore need easy access to health services for tuberculosis diagnosis and a well organised system for treatment delivery. Usually services not linked to the authorities are best fitted to provide health services to this group. In some cases completion of treatment can be planned with the health authorities in the country of origin, but this is often difficult because of political, ethnic or other problems such as drug abuse and/or HIV infection. The best solution would be to offer temporary legal stay as long as treatment lasts for all tuberculosis patients, as this will also encourage all persons with symptoms to come forward for diagnosis.

#### **Experience from The Netherlands, where the policy for several years has been to allow persons with illegal residence status to remain in the country until treatment is finished**

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Several developments regarding the number of persons without a legal permit to stay have taken place in the Netherlands during the last decennium: a growing number of asylum seekers, as a response to this a tendency to restrict the possibilities to apply for asylum, introduction of legal impediments to limit the use of public services by persons without a legal permit to stay and a new more restrictive Immigration Act (2000).

Partners in the Netherlands TB control network have taken several steps to ascertain accessible case finding and treatment facilities for persons with TB without a residence permit:

- establishment of the Board Of Tuberculosis control in Asylum seekers and illegal persons (BOTA) with all stake holders involved (including representatives of relevant ministries)
- creation of a national Fund to pay medical costs to health care providers in case provide medical care (investigations, drugs) to illegal persons (not only for TB)
- continuation in the new Immigration Act of the already existing rule that foreigners with tuberculosis can get a temporary permit to stay during the treatment for TB
- legislation that illegal persons with TB can use facilities meant for asylumseekers ('bed, bread, bath')

In the presentation the actual impact of this policy and the threats for the future will be presented.

#### **TB prevalence among immigration applicants from high prevalence countries: experience of the International Organisation for Migration in the Balkans**

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The South-Eastern region of Europe, the Balkans was historically well known as hot bed of TB. The territory of the former Federal Republic of Yugoslavia since the beginning of the last decade of the past century (1990) has been exposed continuously to bloody armed conflicts, which resulted in serious destruction of health services/the national health system.

Although with the end of the Kosovo crisis in 1999 the open armed conflicts have been terminated, the presence of international peace keeping forces is still needed in BiH and Kosovo. As a consequence of the very slow political and economical restoration process, both internal and cross border mobility is still high. There are hundreds of thousands internally displaced people in the region and tens of thousands are intending to immigrate into Western countries.

Due to a number of factors including mass migration, life in collective centers, physical and psychological stress, lack of food and proper nutrition, damaged health facilities, shortages of drugs, equipment and materials, disrupted economies the general health of the population was significantly compromised. This may result in a rapid spread in some infectious diseases, those that are known as 're-emerging' worldwide, such as Tuberculosis.

Since the beginning of the consolidation (1999) no TB epidemiology survey has been launched in the region for controlling/supporting the recent official yearly reports (75–90/100 000 new TB cases/year) with generally high figures, but still surprisingly lower than those in the health statistics of these provinces in the last year of the former Yugoslavia. (1989: BiH: 95.7/100 000; Pristina: 185/100 000 new cases).

International Organization for Migration (IOM) upon the request of the relevant Embassies is performing the health assessment of immigration applicants to Australia, Canada, New Zealand and USA. Among the 1086 Kosovar applicants there were five (460/100 000) active cases while in the Republic of Macedonia there were four active cases among the 3192 applicants (125/100 000). Here the ratio of inactive cases was as high as 1.69%. The high likelihood of being exposed to TB in the region is underlined by a recent Tuberculin skin test survey of more than 4000 primary school pupils conducted by IOM within the frame of a joint TB and HIV/AIDS prevention program. The ratio of hyper-reactors was found higher than 2%.

IOM data suggests that the spread of TB in this 'sending' region is much higher than it is officially reported.

#### **Experience of allowing persons with undocumented residence status with TB to remain in the country**

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According to the 2000 US census, 36% (2.8 million) of the New York City (NYC) population were born outside the United States, the majority from countries of high TB incidence. One of the most significant trends in the recent history of tuberculosis control in NYC has been the rapid decline in active tuberculosis cases among U.S.-born persons (from 3132 in 1992 to 353 in 2003) while cases among non-U.S.-born persons increased slightly (from 676 in 1992 to 776 in 2003). One of the barriers that prevents persons from seeking care for tuberculosis is the fear of deportation because of undocumented status.

US law allows undocumented immigrants to receive emergency treatment but has no provision for non-emergent care. Tuberculosis rarely falls into the emergent care category. Undocumented immigrants do not have public assistance entitlements such as food stamps and medical insurance coverage. One-third of immigrants in the US and almost two-thirds (63%) of those in New York City do not have health coverage. Some state and city laws ensure provision of tuberculosis treatment free of charge to patients regardless of their residency status. However, some TB patients go to great lengths to hide their immigration status, including trading identities or frequently changing their names. This creates a great challenge for effective case identification, management and contact investigation. Due to the lack of legal backing to assure treatment until completion for TB patients with undocumented status, this issue is dealt with on a case-by-case basis through tailored social services support.

In recognition of this problem, the federal Advisory Council for the Elimination of Tuberculosis recommended the formation of an inter-agency policy group to create a collaborative interaction between the Departments of Health and Human Services and Justice to improve screening, reporting and treatment of tuberculosis.

#### **OPERATIONAL RESEARCH TO IMPROVE NATIONAL TUBERCULOSIS PROGRAMMES**

##### **A case-control study of risk factors for tuberculosis (TB) relapse in 2 provinces: Thua Thien-Hue and Quang Tri, Vietnam, 2001**

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**Introduction:** In Vietnam, the TB relapse rate is high, approximately 10%. In this setting, risk factors for relapse are poorly understood.

**Methods:** Collecting data from the first episode of all relapse TB patients with acid fast bacilli (AFB)-positive smears registered in 2001 (cases), and previously cured new TB patients from 1999, who had not relapsed with TB in 2001 (controls). Two controls per case were randomly selected.

**Results:** Analysis based on 55 cases and 122 controls revealed that cases were significantly more likely to have had a detection delay (OR 3.2; 95% CI: 1.1–9.6). Those  $\geq 55$  years were significantly more likely to relapse than those  $< 55$  years (OR 2.4; 95% CI: 1.1–5.6). Other variables significantly associated with relapse were treatment interruption in the intensive phase (OR 20.6; 95% CI 2.5–458.7), discontinuing treatment in the continuation phase (OR 2.6; 95% CI 1.1–6.0), and being an outpatient vs. in-patient in the intensive phase (OR 2.7; 95% CI 1.3–5.7). Finally, the cases were 2.2 times more likely to have had poor knowledge (95% CI 1.1–4.7).

**Conclusions:** The risk of relapse from TB increases with delayed detection, older age, and poor adherence during the primary TB episode, and poor knowledge.

##### **Reasons for delayed diagnosis of TB in Bolivia, 2002**

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**Setting:** 31 health centers, 1st and 2nd level in the departments of Santa Cruz and Cochabamba, Bolivia.

**Objective:** To determine the factors of delay in the diagnosis of new smear positive cases of Pulmonary Tuberculosis.

**Design:** Case-control survey to 122 controls (time

between the beginning of cough and diagnosis  $\leq 3$  months) and 161 cases (time between the beginning of cough and diagnosis 3 months) with interviews to measure access to health centers, general aspects of patients, delay between the beginning of cough, first consultation, diagnosis and treatment initiation and interviews to health providers.

**Results:** The diagnosis delay was associated with the incapacity of health services for not giving the diagnosis of first consultation (OR 3.6; IC 2.0–6.3) and the department of Santa Cruz respect to Cochabamba (OR 2.6; IC 1.5–4.5), in ones who applied for the second consultation, the delay was similarly related to the incapacity of health services for not giving the diagnosis (OR 3.0; IC 1.6–5.9) and the department of Santa Cruz (OR 2.7; IC 1.4–5.1), with a deficient application of technical guidelines on behalf of health providers. The comparative analysis from the beginning time of cough–first consultation and the beginning of cough–treatment showed a median of 3.5 times higher than the controls. The length of time between the first consultation to the diagnosis and from diagnosis to treatment presented the same median for cases and controls (2 and 1 day respectably) but with averages from 2 to 5 times higher in the cases. The general analysis of times showed that over 90% of delay concerned to patient time (the beginning of cough–first consultation) in the cases and controls.

**Conclusion:** There are very long times between the beginning of cough and beginning of treatment linked to inherent aspects to health services and sick patients. These results will help the National Program to take steps for a better control.

### Postura del personal de salud ante la búsqueda de casos de tuberculosis

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**Background:** The tuberculosis (TB) problem, is vulnerable if doctors and nurses develop or modify their attitude toward the search for TB new cases, procuring the induction to predict health personnel behavior. Still with very elaborated attitude scales, it is in great part inaccessible for measurement. An alternative is proposed: the notion of attitude as a result of a reflexive and deliberate effort for a construction of an own point of view, highly selective and firmly sustained.

**Objective:** To know the attitude of the health personnel involved with the TB Action Program before the search of tuberculosis cases.

**Hypothesis:** There is scarce development of attitude toward the case search of TB patients in the health personnel, which flow out in an irreflexive task.

**Methodology:** Double aseveration sets were designed (two opposed statements, mutually exclusive, referred to one same aspect). The possible outcomes

are defined as a consequence that may be favourable or disfavourable, and by this means is traducted in attitude. (consequence means: acceptance of one aseveration and rejection of the other that form the particular set). The inconsequence may be: by indiscriminate agreement or disagreement, i.e., that opposed or polar sets are accepted, or that both are rejected. This is translated into the no formation of an attitude.

**Sample selection criteria:** For convenience 12 Mexican states were selected with high pulmonary TB morbidity rates (6 that registered the highest rates and 6 that had the lowest); the health units of local level (10%), were selected randomly, using the SPSS statistical program.

**Design:** Observational, transversal, comparative. The development of an attitude means do and construct, understand and interpret, select and generate, discriminate and propose, which has a personal means and social transcendence.

### To determine the effect of the implementation of pulmonary tuberculosis (PTB) score sheets and cough reminders on the detection of pulmonary TB in patients visiting Primary Health Care (PHC) services and Community Health Centers (CHC) in the Free State Province in South Africa

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**Aim:** To determine the effect of the implementation of Pulmonary Tuberculosis (PTB) score sheets and cough reminders on the detection of pulmonary TB in patients visiting Primary Health Care (PHC) services and Community Health Centers (CHC) in the Free State

**Methods:** The study is an experimental study. An experimental group of 40 PHC clinics/CHC where the PTB score sheets were implemented, 40 PHC clinics where the cough reminder were implemented and a control group of 40 PHC clinics/CHCs were selected by randomized selection of the local areas. PTB score sheets/cough reminders were attached to all clinic patient cards in the experimental group. The effects of the implementation of the PTB score sheet on case detection are measured after two quarters of implementation, by comparing the clinic specific quarterly statistics.

**Outcome:** The preliminary results suggest an improvement of PTB case findings of 20%. The results will be presented.

## BACTERIAL VIRULENCE OF TUBERCLE BACILLI AND GENETIC SUSCEPTIBILITY IN HUMANS

### Transmission of resistant *Mycobacterium tuberculosis* strains

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The worldwide resurgence of tuberculosis has been accompanied by rising drug resistance.

In the Netherlands a nation wide surveillance in the past decade (8334 cases) facilitated to investigate transmission of resistant variants of *Mycobacterium tuberculosis*. Transmission of multidrug resistance (MDR) was limited to a few single-case events, except for transmission of a MDR strain in 2004 from an immigrant to six other persons. The respective strain exhibited an exceptional combination of drug resistance mutations.

In general, INH resistance proved a negative risk factor for transmission (OR 0.69; 95%CI 0.54–0.89). However, INH resistant strains with mutations at amino acid (AA) position 315 of the catalase gene were transmitted at the same rate as susceptible strains. Moreover, AA 315 mutants were more often MDR ( $P < 0.002$ ) and associated with pulmonary TB ( $P < 0.02$ ).

Several studies reported associations between the genetically conserved Beijing genotype lineage of *M. tuberculosis* and (MD) resistance. In Vietnam, the significant correlation between the Beijing genotype and relapses of tuberculosis after curative treatment recently confirmed this picture. In the Archangel Oblast, Russia, in the period of 1998–2000, 30/119 isolates (25.2%) were MDR. Twelve out of 30 MDR cases were defined as new, suggesting transmission of MDR plays an important role in this area. Of the Beijing genotype isolates, 43.4% were MDR vs 10.6% of the other genotypes.

To investigate the accurate (trends in) prevalence of the Beijing strains and its association with drug resistance a worldwide survey was recently finalized using a standard strain definition. Data sets from 41 studies, representing 27 440 tuberculosis patients from 31 countries, were included. There appeared to be four distinct patterns to Beijing strain tuberculosis: 1) endemic with no association with drug resistance (in East Asia); 2) epidemic and associated with resistance (USA, Cuba, former USSR, Western Europe); 3) epidemic and drug sensitive (Malawi, Argentina, Gran Canaria); 4) very low prevalence or absent (parts of Europe, Africa).

### Genetic dissection of immunity to infection: the human model

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Humans are exposed to a variety of poorly virulent micro-organisms. Only a minority of infected individuals develop clinical disease. The interindividual variability of clinical outcome is thought to result in part from variability in the human genes that control host defense. In this well-defined microbiological and clinical context, the principles of mouse immunology and the methods of human genetics can be combined to facilitate the genetic dissection of immunity to infection in humans. The natural infections are unique to the human model, not being found in any of the animal models of experimental infection. We will review current genetic knowledge concerning the simple and complex inheritance of predisposition to infectious diseases in humans. Rare patients with Mendelian disorders have been found to be vulnerable to environmental microbes. Most cases of presumed Mendelian susceptibility to these remain unexplained. In the general population, common infectious diseases have been shown to be associated with certain human genetic polymorphisms and linked to certain chromosomal regions. However, the causal vulnerability genes themselves have yet to be identified and their pathogenic alleles biologically validated. The studies carried out to date have been fruitful, initiating the genetic dissection of protective immunity against a variety of microbial species in natural conditions of infection. The human model may well become a model of choice for the investigation of immunity to infectious agents.

### Immunotherapy of tuberculosis: rethinking a paradox

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Granulomas, the hallmark of human infection with *M. tuberculosis*, contain intracellular infections that cannot otherwise be eradicated by host defenses. The sequential recruitment of cells of increasing specificity to the site of TB infection forms a physical barrier to mycobacterial dissemination, creating a hostile microenvironment in which oxygen tension, pH, and micronutrient supply are all reduced. Faced with this environment, mycobacteria undergo profound alterations in metabolism, biosynthesis, and replication. The deleterious impact of impaired granuloma formation and maintenance on TB immunity is most apparent in AIDS, which not only increases the overall risk of progression to active tuberculosis, but also accelerates this progression and increases the risk of its extrapulmonary spread. It is therefore fitting that



AIDS treatment provides the clearest example that immunotherapy (i.e., restoration of TB-specific immune function by anti-retroviral therapy) reduces TB risk: three studies performed in TB-endemic regions clearly demonstrate that ART reduces TB risk in individuals with low CD4 counts by approximately 80%, a level of protection substantially superior to preventive chemotherapy in this population.

In the context of chemotherapy of active tuberculosis, however, the role of the granuloma is reversed: protecting the mycobacterium rather than the host, by creating a microenvironment in which drug penetration is reduced and the molecular targets of these drugs are not well expressed. AIDS/TB patients who experience Immune Reconstitution Syndrome, or patients to whom IL-2 is administered to augment immunity, serve to illustrate this concept, as these increase TB relapse risk or otherwise delay the response to chemotherapy. In contrast, controlled prospective studies of anti-TNF therapies indicate beneficial effects on the microbiologic response to TB chemotherapy. We may therefore find that intentional disruption of granulomas during TB treatment may help eradicate the population of latent bacilli we currently cannot readily sterilize.

## NEW TB DRUG DEVELOPMENT

### Results with moxifloxacin in the murine model of TB

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The new 8-methoxyfluoroquinolone moxifloxacin has potent activity against both actively multiplying and non-actively multiplying tubercle bacilli. In the murine model, it has demonstrated bactericidal activity that is greater than that of older fluoroquinolones and similar to that of isoniazid. More recently, moxifloxacin has been shown to have additive sterilizing activity when combined with rifampin and pyrazinamide that may permit shortening the duration of chemotherapy for tuberculosis (TB) by as much as 2 months. Additional studies in the murine model suggest moxifloxacin can shorten the duration of treatment of multidrug-resistant TB and contribute to more efficacious intermittent regimens for treatment of both active and latent TB infection.

### Eradication of *Mycobacterium tuberculosis* infection in 2 months with LL-3858: a preclinical study

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Tuberculosis is a chronic respiratory disease, caused by *Mycobacterium tuberculosis*, continues to present as a major global health problem with approximately 8 million new cases and close to 3 million deaths each year. In recent years there has been a worldwide upsurge in incidence of tuberculosis especially those caused by multidrug resistant strains of *M. tuberculosis* and the association of the disease with AIDS patients. Currently, more than 15 antimycobacterial drugs are available for tuberculosis patients which are given in combination. These combination drugs together are effective in treatment against sensitive *M. tuberculosis* infection in 4–6 months time, but is not effective against MDR strains. In past 30 years very little efforts have been made to develop new drug to treat tuberculosis caused by MDR strains and latent tuberculosis. Thus, there is an urgent need to develop new drug against tuberculosis that is safe, effective and reduces the total treatment time when given alone or in combination. We have synthesized ~500 novel compounds, several of these compounds have shown antimycobacterial activity one such compound; LL3858, was found to be the most active ( $MIC_{50}$  0.12 and  $MIC_{90}$  0.25  $\mu$ g/ml) against sensitive and resistant strains. LL3858 is mycobactericidal and has synergy with Rifampicin. Mono therapy of *M. tuberculosis* infected mice with LL3858 (12.5 mg/kg) significantly reduced the tubercle bacilli load after one month treatment, and demonstrated a complete absence of growth in organs of 33% of animals after 3 months. Combination of LL3858 with first line anti TB drugs i.e. isoniazid Rifampicin, and Pyrazinamide i.e. LL4858 (LIRZ) induced complete eradication of mycobacterial load from the target organs of animals infected with sensitive or resistant strains of *M. tuberculosis* after 2 months treatment with once daily dose. Furthermore, LL4858 also prevented relapse in mice upto two months post treatment, indicating that the present combination LL4858 is superior then the existing combinations of anti TB drugs. Further, the combination is bioavailable and has better half life,  $C_{max}$ , the combination is non-genotoxic and has an  $LD_{50}$  2500mg/kg in mice. The combination also did not show any adverse effect on the nervous, cardiovascular respiratory and autonomic systems in rodent and non rodents.

The results of our study suggest that LL4858 is a novel combination consisting of a novel antimycobacterial compound (LL3858) that is safe, nontoxic and provides effective cure against tuberculosis in 2 months in our Preclinical studies.

### Surrogate marker studies in TB

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Surrogate markers of relapse are measures that are correlated with the definitive end-point, relapse, in assessing the activity of anti-tuberculosis drugs. They can be obtained earlier or more easily than estimating relapse, which has to be measured on large numbers of patients with a follow-up of at least one year after a full course of treatment. Furthermore, in assessing sterilizing drugs that might shorten treatment, it is usually unethical to try out a shortened regimen incorporating the test drug without evidence that the drug is likely to shorten treatment. Surrogate markers include in vitro tests of sterilizing activity and also long term mouse experiments. However, I will be considering direct tests of the sterilizing activity of a drug in patients with pulmonary tuberculosis by measuring the speed with which it kills persisting bacilli in sputum. Such surrogate markers are (1) the ratio between bactericidal activity of the drug during the first 2 days and from 2 days onwards in studies of early bactericidal activity extended to for at least 5 days. Studies during the initial phase of treatment: (2) the proportion of patients with negative sputum cultures at 8 weeks; (3) estimation of the regression coefficients in serial sputum cfu counts (SSCC); (4) survival analysis of the time to sputum conversion, using Kaplan-Meier graphs and the log rank test. Further important measures that correlate with relapse are estimates of the bacillary tolerance of pretreatment strains, and the Wallis whole blood assay. It is envisaged that such tests will become standard procedures in the development of new sterilizing drugs.

**Methods:** A case-control study compared the characteristics of defaulters (patients who left treatment before therapy was complete) to patients who completed treatment in California from 1996–1997. Reasons for defaulting, smear and culture status at the time of default, and attempts to return patients to treatment were enumerated.

**Results:** 69 defaulters and 401 treatment completers were identified. Median time to default was 125 days (range 3–777 days) from TB treatment initiation. Compared to treatment completers, defaulters were more likely to previously have had TB (AOR 2.3; 95% CI 1.1–5.08), be of Hispanic ethnicity and Mexican-born (AOR 2.5; 95% CI 1.2–5.0) and lack possession of a Social Security number (AOR 2.3; 95% CI 1.2–4.4); or had been homeless (AOR 3.0; 95% CI 1.2–7.4), changed residences (AOR 2.1; 95% CI 1.1–3.9), received no DOT although determined to be 'high-priority for DOT' (AOR 2.6; 95% CI 1.4–5.0) and had diabetes (AOR 2.6; 95% CI 1.2–3.9). Documented reasons for default included patient non-adherence (46%), inadequate management or coordination by the treating health department or provider (28%), and movement out of the US before finishing treatment (23%). Thirty-three (47.8%) patients with pulmonary TB were culture-positive at the time of default, and up to 19% defaulted while AFB smear-positive. Sixteen defaulters (23%) had an interim default, were returned to therapy and ultimately left treatment. The health department made attempts to locate and/or contact the patient in 90% of all defaults.

**Conclusions:** Interventions are needed to improve DOT provision to high-risk and smear-positive patients, the continuity of TB care, including treatment referral processes with Mexico, and health department case management and oversight practices.

## MONDAY 1 NOVEMBER 2004

### TB TREATMENT ADHERENCE IN RESOURCE-POOR SETTINGS

#### Characteristics of patients defaulting from treatment in California: attempts to return patients to therapy

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**Background:** Persons who default from therapy are at higher risk for relapse of disease or acquisition of drug resistance, and represent a risk for continued transmission within the community. Local health departments can expend substantial resources to prevent default or return non-adherent patients to treatment.

#### Risk factors for MDR TB treatment non-adherence, South Africa, 1999–2001

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**Background:** Every year approximately 6000 people are registered with multidrug-resistant tuberculosis (MDR TB) in South Africa. Of those who start treatment, approximately 15%–20% default despite the use of the WHO DOTS control strategy.

**Methods:** Using registries and a standardized questionnaire, a case-control study [ratio 1:2] was conducted in four provinces to determine risk factors for treatment non-adherence. Cases were defined as patients who began MDR TB treatment between October 1, 1999 and September 30, 2001 and defaulted from therapy for more than 2 months; controls were defined as patients who began therapy during the same time and were cured, completed or failed.

**Results:** We identified 242 cases and 420 controls. Of these, 25 (3.8%) were incorrectly classified as completers and 30 (4.5%) were incorrectly classified as defaulters. After reclassification, we found that 111 defaulters had died (54/247, or 22%) and thus excluded. We located, consented, and interviewed 91 cases (38% response rate) and 282 controls (67% response). Among all interviewees, 61% were male; the median age was 38 years (range 16–68 years). Reasons for defaulting included feeling better and thinking treatment was no longer necessary (28.5%), drug side effects (23.1%), not believing that they had MDR TB (12.1%), cost of transport to clinics (11.0%), and feeling poorly treated by health care staff (11.0%). Compared to controls, cases were more likely to report being dissatisfied with health care staff attitudes (OR [odds ratio] 10.5, 95% CI [confidence interval] 3.0–40.0), lacking support from friends and family (OR 2.4, 95% CI 1.1–5.0), having drug side effects (OR 2.0, 95% CI 1.02–4.2), renting versus owning a house (OR 1.7, 95% CI 1.01–2.8), and feeling ashamed about having TB (OR 1.7, 95% CI 1.01–2.8).

**Conclusions:** In South Africa, risk factors for treatment non-adherence include the quality of the patient-provider relationship, lack of information about MDR TB treatment, lack of social and economic support, and side effects from treatment.

## HUMAN RESOURCE DEVELOPMENT FOR TB CONTROL

### Overview of HRD for TB control

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HRH related issues have emerged as the major challenges for reaching and sustaining TB control targets. Inadequate HR e.g., lack of skilled and/or motivated staff; inadequate distribution of staff; poor retention; deficiencies of staff at all levels following decentralization and staff with inadequate qualifications/competencies rank first within the top five constraints to achieving global TB control targets. Traditionally HRD for TB control has been the organization of training courses. However, HRD needs to be understood more broadly and building capacity in HR management and planning is required at all levels. HRD capacity must be strengthened through collaboration and co-ordination with other HR departments, programmes and institutions at global and national level to ensure that at national level HR development capacity for DOTS expansion is developed and maintained. This represent a paradigm shift in the approach to HR for TB control. HRD for TB control is divided into two parts—the quality of exist-

ing staff at all levels and the need for additional staff. Quality is the direct responsibility of the NTP while issues related to the quantity and the general health system is the responsibility of departments for human resources within the MOH. NTPs must know their staffing needs and gaps and have a clear definition of tasks to be performed at different levels of the health system to implement the DOTS strategy, assigned these tasks to specific categories of health workers; know the time needed to implement those tasks particularly at the peripheral level where changes in the number of cases diagnosed and treated have the biggest impact on the workload; know how many staff of the respective categories needed to maintain the service delivery level necessary to reach and maintain the disease control targets; know how many are available at any point in time. Subsequently the NTP need to work with HRH departments to fill gaps and develop the long term strategy.

### Encouraging best practices in TB control

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Tuberculosis (TB) has been a serious health problem. A decade ago the World Health Organization (WHO) declared TB a global emergency, warning that with the advent of HIV/AIDS the situation had potential to worsen considerably as regards increased incidence, morbidity and mortality. Doomed predictions of doubling incidence rates within a short time span have materialized, particularly in sub-Saharan Africa, where HIV infection rates are very high. TB is the main opportunistic infection, responsible for one third of all AIDS-related deaths.

The DOTS strategy has been aggressively promoted by Union/WHO and country programs actively supported. Nevertheless, progress in terms of both DOTS coverage and improved treatment outcomes has remained elusive. The HIV epidemic has reversed TB control gains in countries with previously good TB control. Efforts to integrate with the HIV/AIDS program have yet to make an impact.

TB control is extremely difficult to achieve in an environment of low socio-economic development and extreme poverty. Health sector reform in poor countries leading to an integrated and comprehensive approach to primary health care offers as many opportunities as serious threats for the once vertical TB program. Staff in the TB field requires sophisticated skills development to successfully advocate and ensure enough resources are invested in TB control.

Under the DOTS strategy much has been done in terms of staff training for TB control, but the human resource (HR) development framework has been simplistic in its approach. Training efforts have focused

on technical medical skills for diagnosis and treatment of cases and on mechanical completion of forms and registers. Capacity development efforts have not been able to address the requirements to effectively negotiate the complexities of improving TB control in an environment of limited resources and competing needs.

Information systems in particular are conceived with an up-ward ("star-gazing") flow of data in mind. Its design is determined by higher level needs, is not flexible to add local relevant indicators and does not give speedy access to facility reports and listings helpful for local action, lacking the detail which could inspire and empower staff at lower levels, where change has to take place to make a difference.

7 years experience of trying to bring about TB control in Cape Town (incidence rate >600/100 000, population 3.1 million) is described, identifying the problems encountered and ways to effect change, with a focus on the human resources (HR) and capacity development and skills required to improve the situation. The HR development lessons learnt are proving applicable and just as relevant to other areas of health, particularly to the expansion of HIV/AIDS care programs and ARVs rollout.

**Survey on tuberculosis teaching at Brazilian nursing schools, 2004: A Multicentric Study/ University of Sao Paulo/Latin American Nursing and Allied Professional Network on Tuberculosis Control/International Union Against Tuberculosis Lung Disease (Union)/ São Paulo Research Foundation (FAPESP)**

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UNION meetings highlighted the need to identify how Nursing Education Institutions approach TB teaching in their curricula. This study is a collaborative project between the University of São Paulo (a WHO Collaborating Center for Nursing Development), the Brazilian Control TB programme (TCP) and UNION. **Objectives:** To identify the approach to tuberculosis adopted in the undergraduate curricula of Nursing Schools in Brazil and to estimate the time dedicated to tuberculosis teaching, verifying the theoretical content and training in health institutions, involving operational and epidemiological aspects of TCP through a questionnaire. **Methods:** Survey in 2004; Study population: 347 Nursing Schools, distributed throughout the Brazilian regions: 4.9% North, 13.8% Northeast, 20.5% South, 56.2% Southeast, 4.6% Central-West; 25.9% of which were public

schools and 74.1% private. **Results:** The 32% questionnaires that were answered were analyzed in a database (Excel) and summarized by means of the Statistical Package for Social Sciences (SPSS). 26.7% of the schools are public and 73.3% private; 33.3% are Schools and 66.7% Universities. 100% of the schools dedicate time to TB teaching; the theoretical hour load ranges from 4 to 8h in 40% of the schools and 10 to 20h of practical training in 36%, in the framework of primary and predominantly secondary care levels. Practical TB teaching with respect to treatment type was: 66.7% self-administered treatment (SAT), 70% supervised treatment (ST), at the following treatment places: (25%) home, (56.7%) Health Unit, (46.7%) Family Health Program, (30%) clinics, (25%) hospitals, 13.3% no attention to this issue.

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**Regional human resource development (HRD) workshops for high-burden countries**

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Competent health care workers are critical to the successful expansion and strengthening of the DOTS strategy and, ultimately, for global TB control. A series of workshops have been organized for focal points for training within national tuberculosis programs by the Task Force Training (TFT) of the Tuberculosis Coalition for Technical Assistance. The goal of the workshops was to determine training needs, resources, and barriers to DOTS implementation in high burden countries, as well to enhance participants' skills in needs assessment and human resource development (HRD). This presentation will describe the workshops, follow-up, and outcomes to date.

**Human resource development in low-income/ high-burden countries**

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The alarming deterioration of the health systems has been noted as a major stumbling block for developing countries to address the burden of disease and human suffering. One major contributor is the severe shortage of health workers as well as the geographic maldistribution of health workers. Abundant evidence shows that human force drives health system performance. This presentation will focus on challenges and opportunities, and possible actions and strategies that should be employed to ensure that health workers are mobilised to combat this health crisis.

## HARM REDUCTION AND FUNDING BY TOBACCO TRANSNATIONALS

### Harm reduction: pro

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Most smokers want to stop smoking (or say so), and regret to have started. The problem in practice is that only some of them really try to stop and the majority of smokers who stop will relapse. Obtaining smoking cessation should be the aim of any intervention towards smokers, and is sometimes urgent for those with smoking-related diseases.

The paradox is that the smokers most in danger of suffering from tobacco-related disease are those with the lowest rate of success. Hard-core smokers do not want, do not intend, and do not attempt to quit. One third of them even do not consider that smoking currently affect their health or will affect it in the future. So we fail to help the smokers who need it most, particularly depressive patients, patients with COPD, women and young smokers. What can be done to decrease the risk of disease among smokers unwilling to stop?

Any reduction of the exposition to noxious substances should be regarded as a progress towards better health. Among the solutions proposed, smoking light cigarettes is the attitude most frequently adopted spontaneously by smokers, under the influence of the tobacco industry, but is a gross illusion. Using less dangerous products like *snus* may be a solution but is currently forbidden by law in most countries. Smoking less, with or without long-term use of nicotine replacement, is appealing to many smokers and is well accepted, but its efficacy has been questioned. Finally, any procedure or attitude increasing the motivation to stop smoking is welcome.

Up to now, there is no convincing demonstration of a decrease in mortality among smokers reducing their tobacco consumption. It may be that the markers for the benefits of reduction are not the pertinent ones. The demonstrated benefits of smoking reduction are:

- 1 A decrease of symptoms
- 2 An increase in the quality of life
- 3 A decrease of inflammation in the airways
- 4 A reduction of some risk factors for cardiovascular disease
- 5 A reduction of adverse effects during pregnancy
- 6 An increase in the motivation to quit

Smoking reduction should not be regarded as a sustainable target but as a transitional period. Among other benefits, it maintains the contact between the physician and the smokers and may prevent depression (for both of them!)

### Harm reduction: con

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A lot of so called 'harm reduction' methods are considered for smoking:

- 1 Shift towards so called 'light' cigarettes: low yields of toxins in smoking machines induce smoking compensation (occlusion of filter-vents and more intensive smoking).
- 2 Shift towards cigars: lower risks but nevertheless larger than non smoking.
- 3 Unassisted reduction of CPD: mostly of short duration, induces smoking compensation and has no significant long-term health effects. A 50% reduction of CPD in pregnant women does not increase significantly the birth weight with an initial CPD higher than five. Similar RR of hospital admission for COPD and of all-cause mortality after 15 year are observed in heavy smokers and reducers.
- 4 NRT assisted continuous reduction: uncommon, short lived, with 2 year success rates of 6.3% (gum) and 9.5% or 7.5% (inhaler). E-CO decreases less than CPD. No hard data about health effects of intermittent, NRT assisted, 'temporary abstinence', probably useful seen the rapid withdrawal after smoking interruption.
- 5 Increased rates of bupropion assisted smoking reduction are not persistent at 12 month.
- 6 'Potential reduced exposure products' (PREPs) are currently not available and need independent monitoring before consideration (Eclipse, Accord, nitrosamine free cigarettes, . . .).
- 7 Less dangerous than smoking, smokeless tobacco has nevertheless numerous health drawbacks.

For those unwilling or unable to abstain from nicotine, permanent indefinite NRT should be preferred to 'snus' as the best approach to harm reduction.

Disadvantages of a harm reduction policy include the following:

- Carcinogenicity is much more influenced by duration of smoking period than by number of CPD;
- Smoking reduction could deter smokers from complete cessation and maintain smoking as a 'normal' societal behaviour, favouring initiation; can represent a perturbing health message where individual potential benefit is counterbalanced by a possible public health nuisance.

### Funding of the scientific world by tobacco transnationals: l'Affaire Rylander

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In March 2001, two smoking-prevention associations of Geneva (Switzerland), CIPRET-Genève and Oxy-Genève, denounced in a press conference an infiltration of the University of Geneva by the tobacco industry. The agent of the infiltration was a reputed

Swedish professor, whose main affiliation was with the University of Gothenburg. His name: Ragnar Rylander. He had been 'secretly employed by Philip Morris' for 30 years. He was 'one of [their] most highly paid consultants.' He supervised the operations of INBIFO, the ultra-secret biological laboratory of Philip Morris in Germany. For years, he received research reports on the studies conducted at INBIFO, which demonstrated in particular the high toxicity of sidestream smoke. He channeled the reports to Philip Morris, at the private house of one of their executives, where they would be read, acted upon and then destroyed. In spite of his firsthand and exclusive knowledge about the acute toxicity of sidestream smoke, not only Rylander has concealed it, but he has dedicated an important part of his career denying that ETS is harmful. To that end, he organized symposia on behalf of the tobacco industry and published studies paid by Philip Morris without disclosing his source of funding and concealing his conflict of interest. Following the revelations by CIPRET-Genève and OxyGenève, Rylander sued Jean-Charles Rielle, the physician-in-charge of CIPRET and Pascal Diethelm, the president of OxyGenève, accusing them of defamation. The trial that ensued has exposed the affair to the public in its full dimension and has unearthed more evidence, all highly damaging for the tobacco industry. The trial, which required five judgments by four different courts, came to its final verdict in December 2003. The Swiss judges concluded that Diethelm and Rielle 'did not exaggerate in using the term "scientific fraud" to qualify this double role: that of professor in the field of environmental medicine and independent researcher, a role Rylander attributed to himself, and, at the same time, the role of collaborator at the service of an industry that has always positioned itself against public health'. They observed that 'Geneva has indeed been the centre of an unprecedented scientific fraud in so far as Ragnar Rylander, acting in his capacity of associate professor at the University, took advantage of its influence and reputation, not hesitating to put science at the service of money and not heeding the mission entrusted to this public institution, a mission which consists in particular in disseminating a culture founded on scientific knowledge and raising public awareness of the responsibilities that teachers assume towards society.' Diethelm and Rielle were fully acquitted. The trial, and its landmark judgment, has had an eye-opening effect on the practices of the tobacco industry among public health authorities, in the media and the public at large. It has also offered an example of the need to introduce more rigorous ethical rules and be wary about potential conflicts of interest. Finally, it provided a good illustration of the dangers confronting scientists and academic research institution when accepting money from the tobacco industry.

All the quotations in the above text are from the final judgment of 15 December 2003 by the Geneva Court of Justice.

## MICROSCOPY AND CULTURE

### Are current programme guidelines for the use of AFB microscopy appropriate?

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Sputum smear microscopy for acid-fast bacilli (AFB) is the recommended diagnostic and treatment monitoring tool for TB control programs in high-prevalence situations, but it is often resented because of a perceived low sensitivity and tediousness. While sensitivity is more difficult to influence, tediousness for laboratories as well as patients may be reduced, simply by critical evaluation of current standard guidelines with streamlining of the procedures whenever possible. The diagnostic strategy of examining three sputa, spot-morning-spot, is less effective and wasteful. The often poor spot-specimens may lead to a missed diagnosis based on a first negative spot and poor examination of the other specimens, while the last spot brings almost no additional cases if two others were properly examined. Two successive morning specimens delivered to the lab together might be most efficient strategy. The definition of a smear-positive case based on two AFB-positive samples cannot be justified based on technical characteristics of smear-microscopy compared to culture or chest X-Ray. Treatment based on a single positive smear would improve interruption of TB transmission, for very few false diagnoses, especially when effective AFB-smear quality assurance exists. The result 1-9 AFB (scanty) causes a lot of confusion and wrong practices. A threshold of 1 or few AFB per 100 fields, correlates better with culture as well as results of further smears, and might be more appropriate for well-managed microscopy networks. AFB-smears for treatment monitoring suffer more from reduced specificity, since they most often indicate dead bacilli only. Routinely examining two sputa at each follow-up may thus not be justified, the more so since two contradictory results (not rare with these predominantly paucibacillary specimens) will often cause confusion. One good morning control specimen is sufficient, but declaration of failure should sometimes wait for confirmation by a second specimen at a few weeks distance.

### AFB smear microscopy diagnostic services in Bolivia: management and assessment

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Bolivia, a South American country, has a high incidence of tuberculosis disease, 125/100 000 population. The National TBC Control Program in recent

years has improved its strategies and the laboratory network is working with supplementation of materials, reagents, and budget to make supervision, trainings, an evaluation, to provide quality bacteriological diagnosis rapidly.

The coverage of the AFB smear microscopy diagnostic services in Bolivia is around 15 000 habitants for one microscopy diagnostic service. Distribution is in relation to accessibility and population density. In this structure there are microscopy services and laboratory services; in the first case some services are in the health post, without laboratory and the other services have a laboratory environment. The services have regular supplies in the form of reagents, slides, registers, and forms to provide reports on results, quality control of smear, supervision and evaluation.

All of the technical and administrative procedures are standardized and are available in the Laboratory Network handbook.

The Laboratory network in Bolivia has 489 smear microscopy diagnostic services that use the Ziehl Neelsen method and 6 laboratories that perform culture on Löwenstein Jensen and Stonebrink Medium using the Petroff decontamination method, and drug sensitivity testing according to the proportion method. Quality assessment AFB is ongoing; all laboratories send slides to the Department Laboratory for quality control of each slide according to the Quality Control Guide. At National level all the information is analyzed.

For 2000 to 2002, the following information is available. In 2000 total number of AFB slides was 158 015; this increased in 2001 to 205 451 and 231 600 in 2002. In each regional laboratory they received 37% of all slides in 2000, 44.7% in 2001 and 40% in 2002. Check up was 65% in 2000, 45.5% in 2001 and 50% in 2002.

	2000	2001	2002
Positive predictive value	98.3%	96.9%	98.7%
Negative predictive value	99.9%	99.4%	99.7%
Specificity	99.7%	99.3%	99.8%
Sensitivity	99.7%	97.6%	97.7%
Discordance	0.3%	1%	0.3%
Concordance	99.7%	99%	99.7%

The report of Regional Laboratories the continuous change of Human resources is a big threat to diagnostic of tuberculosis in smear microscopy diagnostic services in Bolivia, also the quality of microscope because in tropical area the humidity and the low quality of environment damage the immersion lens of microscope. The challenge is to improve the diagnostic through the supervision and training for new resources in each regional.

Now we can say is very important to do the assessment and quality control of AFB smear microscopy, to support the National TB Control Program.

## Improvements in AFB smear microscopy: challenges and suggestions

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The three main challenges addressed are: the acceptability of presently used sputum specimen collection systems for TB suspects and of presently used smear microscopy technology systems for the lab technicians; the 'specificity' of AFB sputum smear microscopy (all mycobacteria are AFB) and its 'sensitivity' (high numbers of AFB in the specimen required for their detection).

As for the TB suspect, the present standard sputum collection system—spot/early morning/spot—(by no means employed everywhere) was introduced in 1959 in a specific setting, which may not be prevalent in today's HBC situations. In fact, it is questionable if a universally valid norm is possible at all. An outstanding challenge concerns also sputum smear monitoring of chemotherapy (Int J Tuberc Lung Dis 2004; 8: 114–116). From the lab's point of view, technicians often detest the investigation of sputum specimens for AFB.

Based on data from quite different settings, including those with high HIV infection prevalence, the 'specificity' of sputum smear results positive for AFB is high ( $\geq 80\%$ ) for the *M. tuberculosis*-complex.

The 'sensitivity' of sputum smear examination for AFB is relatively low (approx 45–80% of culture+PTB). Suggestions for improvement generally include an 'enrichment' produced by liquefaction & sedimentation (centrifuge or other means) of the sputum. The general use of NaOCl (household bleach) has recently been advocated. Certainly, this technology should be subject to appropriate multicenter studies (Int J Tuberc Lung Dis 2004, 8: 609–613) also because, among others, it improves the acceptability of sputum smear microscopy by the laboratory technicians.

The 1.4 million Sm+ PTB notified by DOTS programs in 2002 represent 37% of the estimated incidence, just over half way to the 70% target (WHO/HTM/TB/2004.331). Thus, there is no spare time for any high tech experiments.

## From AFB smear microscopy to culture-based diagnosis

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Le diagnostic de certitude de la tuberculose repose sur la mise en évidence du bacille *M. tuberculosis* dans les prélèvements. Plusieurs techniques peuvent conduire à cet objectif :

- 1 L'examen au microscope des frottis permet de voir des bacilles acido alcool-résistants. Dans un contexte épidémiologique précis et devant un tableau clinique évocateur de tuberculose évolutive, l'examen microscopique constitue une technique simple, facile, peu coûteuse et dont le rapport coût-efficacité

est très élevé dans les pays à faible revenu et à taux d'endémicité élevé.

Mais, le rendement de l'examen microscopique dans le diagnostic de la tuberculose reste faible, il ne permet de reconnaître que les cas cracheurs de grande quantité de bacilles (plus de 10 000 bacilles par ml de crachats), qui sont certes les plus contagieux, mais les cas moins riches sont également des sources potentielles de maladie. La rupture de la chaîne de transmission de la tuberculose dans la communauté passe par la détection précoce des cas contagieux potentiels et leur mise au traitement avant l'apparition des bacilles au microscope. Ces cas sont susceptibles d'être diagnostiqués par des techniques capables de mettre en évidence les bacilles de la tuberculose même quand ils sont en faible quantité dans les prélèvements. La culture est une de ces techniques.

- 2 Décider d'introduire la technique de diagnostic par la culture doit être motivé par le besoin de renforcement du dépistage et du traitement des cas dans le cadre du Programme National de lutte contre la tuberculose : diagnostiquer les cas de tuberculose pulmonaire à microscopie négative, confirmer les cas de tuberculose extra-pulmonaires peuvent être les objectifs d'un renforcement du réseau de laboratoires.
- 3 Les techniques d'isolement en culture sont multiples et le choix varie en fonction des moyens matériels et financiers disponibles. Renforcer le diagnostic par l'introduction de la culture signifie qu'un réseau de dépistage par les techniques plus simples et moins coûteuses comme la microscopie est déjà bien organisé, bien contrôlé et que tous les cas à microscopie positive sont diagnostiqués et mis sous traitement jusqu'à leur guérison. Les structures de santé impliqués dans la lutte contre la tuberculose doivent être accessibles à la majorité des patients pour le diagnostic, le contrôle de l'efficacité du traitement et la déclaration de la guérison.

Les conditions d'introduction de la culture pour le diagnostic de la tuberculose dans les pays à haute prévalence et à faible revenu sont passées en revue, les avantages et les inconvénients ainsi que les résultats attendus sont présentés.

### Is DST needed in NTPs in low- and middle-income countries?

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The third report of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance (DRS) has indicated that the burden of multidrug-resistant tuberculosis (MDR-TB) can be described in terms of prevalence, but also in terms of the absolute number of cases and, most importantly, the capacity of the coun-

try to address the problem. In countries with low numbers of TB cases, high MDR prevalence may not reflect high absolute numbers of cases. Conversely, a low prevalence of MDR of even 1–3% in high-burden countries, such as India, Indonesia or China, could reflect a considerable number of MDR cases that the respective national TB programmes must treat and cure.

Applying the estimated proportion of MDR-TB cases among new cases globally, the WHO SEA Region accounts for the highest estimated MDR burden, of about 39% of all MDR cases, in terms of absolute numbers, followed by the Africa Region, with about 29% of MDR cases, and the Western Pacific Region, with around 18% cases. The majority of the low- and middle-income countries are situated in these three WHO regions and together contribute almost 87% of such cases. The three other regions contribute to the remaining 13% of all MDR cases.

It is also observed that retreatment cases contribute significantly to the prevalence of MDR cases. Also, the proportion of re-treatment cases in most low- and middle-income countries has still not come down making it necessary to perform drug susceptibility testing (DST) for these patients. However, very few countries in these regions have internationally/nationally accredited laboratories performing DST.

The situation now needs to be reviewed and indications for DST, methods of DST, levels of laboratory network that should undertake this task and the type of support needed to sustain the laboratories for considerable number of years have to be defined.

An exercise was undertaken by the Government of India to address this problem, and the knowledge gained in this exercise is utilized in this presentation. Although there are international guidelines for establishing National Reference Laboratories (NRLs) and Intermediate Reference Laboratories (IRLs) for the purposes of routine specimen testing and DRS, the indications for DST in these countries are still not properly understood. One of the important indications for DST in low- and middle-income countries could be failure to respond to retreatment regimens under DOTS.

One or more NRLs could be developed with international assistance in each country and one or more IRLs in each province/state. Rapid but simple methods of DST for H and R must be standardised for the purposes of routine identification of MDR cases, particularly direct tests in egg-based media. The currently recommended indirect method of proportion susceptibility testing (PST) may continue to be encouraged for DRS in all these laboratories.

One of the neglected areas is infrastructure in terms of manpower, equipment and resources for sustaining the effort over time. These need to be addressed on a priority basis by all governments and international bodies.



## CONTACT INVESTIGATION AND ACTIVE CASE FINDING IN HIGH INCIDENCE COUNTRIES

### Incorporating active case finding in the household into the TB control program in Sudan

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**Objectives:** The objectives of this study was, to develop a method of active case finding in the household and administer preventive therapy, to child household contacts of tuberculosis (TB) patients; in the National TB control programme in Sudan and describe outcomes of TB contact investigations, factors correlated with those outcomes, and current successes and ways to improve TB contact investigations.

**Methods:** All the new cases (patients; aged more than 15 years old; and were diagnosed as pulmonary, sputum-smear (+) (who did not, receive treatment or on treatment for less than 2 weeks) during routine registration in TB centers were invited to participate in the study. 10 338 were pulmonary, sputum-smear (+) TB patients were reported in the Sudan during year 2002, of them 3586 are from Khartoum State; were entered in the study from January 2002 through December 2002 from different centers.

**Results:** 83.7% (3000) were index cases for family contacts. Total contacts with a mean family size of 4 persons were 9000. Of which 42.6% (3834) were children below 15 years, 15 % (575) were of eligible (not vaccinated and with age less than 15 years old) contacts, received tuberculin skin tests (TSTs). 34% (196) were TST (+).

### Yield of active finding in Malawi: results of a pilot project

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**Background:** National TB Control Programmes (including Malawi) recommend investigation and management of childhood contacts of index cases with smear-positive PTB. It rarely happens. Previous work from Malawi found that active finding among contacts yielded a much higher number of TB cases than passive case finding, that only about 20% of well child contacts received preventive therapy and that the perceived need for a CXR as part of contact investigation was an obstacle to effective management (Zachariah R, et al. Int J Tuberc Lung Dis 2003; 7: 1033–39). A recent study from Botswana identified certain characteristics among index cases that were associated with increased risk for infection of childhood contacts that might better direct contact man-

agement (Kenyon TA, et al. Int J Tuberc Lung Dis 2002; 6: 843–50).

**Objectives:** We are conducting an operational study of child contacts of cases with smear-positive PTB to 1) identify risk factors among index cases associated with risk of infection (i.e., positive Mantoux); and 2) to determine the yield of TB cases among children using a clinical algorithm.

**Methods:** All children who are household contacts of cases of smear-positive PTB admitted to Queen Elizabeth Central Hospital, Blantyre, Malawi are being assessed using a clinical algorithm, Mantoux test, CXR and HIV test.

**Results:** Preliminary results are not available now but will be presented at the symposium.

## HIV/TB: TWO DISEASES, ONE PATIENT

### Isoniazid preventive therapy for HIV-infected patients

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Human immunodeficiency virus (HIV) infection is the most powerful known risk factor for progression from latent infection with *Mycobacterium tuberculosis* to active tuberculosis (TB) disease. Multiple clinical trials of the efficacy of isoniazid preventive therapy (IPT) for six to 12 months in tuberculin skin test (TST)-positive HIV-infected persons living in settings with a high prevalence of TB have found that the short term the risk of developing TB disease was reduced by about 60% with IPT. Where TST is not feasible, WHO recommends that the following HIV-infected persons be considered for IPT: those living in populations with a high (>30%) prevalence of TB infection, including health care workers; household contacts of TB patients; prisoners; and miners. Preliminary data have shown that secondary prophylaxis with IPT after treatment of TB disease reduces the recurrence rate by half. Despite its efficacy in reducing TB disease rates among HIV-infected persons, the feasibility of providing IPT in resource-limited settings is not clear. Multiple steps are required to establish and maintain a quality IPT program: identifying HIV-infected persons; screening to exclude active TB; determining who is likely to have TB infection, with TST or by history; maintaining a supply of isoniazid; and supervising patients for toxicity and adherence during therapy. As HIV counseling and testing services expand more people will be eligible for treatment of latent TB infection. The necessary step of screening to identify undiagnosed TB disease (intensified TB case finding) will also reduce TB morbidity and mortality in HIV-infected persons. IPT should be

part of a package of care for persons living with HIV infection. In addition, community and home-based HIV care programs should provide IPT to children living with TB cases. Collaboration between TB and HIV/AIDS programs can reduce the burden of TB in persons living with HIV/AIDS.

### **Use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking HAART: a review of current CDC guidelines**

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Complex pharmacologic interactions can result when patients are treated with protease inhibitors or non-nucleoside reverse transcriptase inhibitors (NNRTIs) for HIV infection together with rifamycins for tuberculosis. The principal locus of these drug-drug interactions is the cytochrome P450 (CYP) system in the intestinal wall and liver, specifically the isoenzyme CYP3A4. Rifamycins are antituberculosis agents that induce the activity of CYP3A4 and may thereby substantially decrease serum concentrations of protease inhibitors and NNRTIs. The available rifamycins differ in potency as CYP3A4 inducers, with rifampin being the most potent, rifapentine being intermediate, and rifabutin being the least potent inducer. Unlike rifampin and rifapentine, however, rifabutin is also a substrate for CYP3A4; thus, its serum concentration is affected by the degree to which CYP3A4 is inhibited or induced by protease inhibitors and NNRTIs. Rifapentine, a long-acting rifamycin, is not recommended for the treatment of TB in HIV-infected persons because of its association with acquired rifamycin resistance in such patients. Among the available antiretroviral agents, ritonavir has the highest potency in inhibiting CYP3A4, a quality that increases the serum concentrations of other coadministered protease inhibitors, though it can also increase concentrations of rifabutin and a rifabutin metabolite to toxic levels. This presentation will review pharmacokinetic and clinical data pertaining to interactions between these agents, as well as the most recent Centers for Disease Control and Prevention recommendations for their use.

### **TB/HIV operational research agenda**

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The TB/HIV working group of the Stop TB partnership recommended the scaling up of joint TB and HIV activities<sup>1</sup> with special emphasis on ART for TB patients. The implementation of joint TB/HIV activities has increased in urgency and importance the need for an operational research agenda. This is in recognition

of the fact that optimised control for TB would of necessity be dependent on improved HIV case detection and treatment especially among dually infected individuals. A set of priority TB/HIV research areas has been identified by the TB/HIV working group. These areas range from operational, biomedical to epidemiology and economic analysis of TB/HIV research priorities. Finalization of these research priorities is needed in order to guide national programmes in the implementation of joint TB/HIV activities.

1 Interim policy on collaborative TB/HIV activities. WHO/HTM/2004.330

### **Collaborative TB/HIV activities increasing accesses to HIV testing and counseling and care and support services for people living with HIV/AIDS in Malawi: the only sure way to reduce the dual burden of TB and HIV**

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**Introduction:** Malawi has one of the highest levels of HIV infection in the world. In 2003, an estimated 14.4% HIV sero-prevalence rate was reported. Every year, more than 80 000 people die from AIDS. 110 000 new infections occur annually, most of these among young people. The HIV epidemic has fuelled an equally severe tuberculosis (TB) epidemic. TB notifications have risen by a factor of 500% between 1985 and 2003. In 2000 there was a 77% HIV sero-prevalence rate in TB patients. One of the serious adverse consequences of the joint HIV-TB epidemic has been an increasing case fatality rate in TB patients, which in those with smear positive pulmonary TB is about 20% and those with smear negative PTB and EPTB is higher at 30%.

**Rationale:** As a result of the high burden of TB and HIV/AIDS, Malawi developed a 3-year plan in 2002 to implement collaborative TB/HIV activities in phased a manner. Deliverable objectives include a) the provision of VCT and cotrimoxazole to TB patients, b) provision of antiretroviral therapy to eligible TB patients.

**Results:** Implementation of planned activities began in January 2003. The first activity was a countrywide situation analysis of HIV/AIDS and joint TB-HIV services. A package of VCT and cotrimoxazole to TB patients is currently being offered in 15 hospitals. From July to December 2003, 4122 TB patients were registered in these hospitals of whom 2825 (69%) accepted HIV testing. Of those who were tested 1899 (67%) were HIV positive and 1853 (98%) received cotrimoxazole. Of those placed on cotrimoxazole 1597 (86%) started this intervention within a week of TB registration

**Conclusion:** Collaborative TB-HIV activities in Malawi have increased the access to VCT services by TB pa-

tients and the general public thereby offering them the opportunity to access care packages like cotrimoxazole and ART

## SCALING UP PUBLIC-PRIVATE MIX FOR DOTS: HOW CAN IT CONTRIBUTE TO ACHIEVING MDGS?

### Public-private mix DOTS and the Millennium Development Goals

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Two MDGs relate closely to TB. The first is to halve, between 1990 and 2015, the proportion of people whose income is less than one dollar a day. The second is to have halted by 2015, and begun to reverse, the incidence of malaria and other major diseases. The indicators associated with this target are the prevalence and death rates associated with TB and the proportion of TB cases detected and cured under DOTS.

TB control can help to meet the goal for reducing poverty in a number of ways and PPM DOTS can enhance these effects. It can reduce the time from diagnosis to treatment. It can also reduce the direct and indirect costs of treatment to patients.

The MDG of reducing deaths from TB can be met if TB control comes as close as possible to meeting the global goals for case detection and cure rates. Increasing case detection will depend on involving the private sector to a much greater extent in TB control. Countries in which the private sector is active should aim to increase case detection by 20 to 30% through working with this sector. Cure rates in the private sector can also be improved through a PPM DOTS approach.

A number of steps can be taken to enhance PPM DOTS and contribute more to the global realization of the MDGs. These include: paying greater attention to the medium- and long-run achievement of the MDGs, engaging more with local medical societies, and strengthening country PPM cells. It will also require creating better linkages with HIV and with the global 3 by 5 program, paying greater attention to reducing the social constraints to TB control, and speeding the development and use of new diagnostics, drugs, and vaccines.

### Scaling up PPM DOTS: a global outlook

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Over 40 Public-Private Mix DOTS (PPM DOTS) projects have been launched in since 1995 in 10 coun-

tries in Asia and Africa. 24 PPM DOTS projects have been evaluated and 13 journal articles on PPM DOTS evaluations have been published. The available evidence indicates that PPM DOTS is feasible and effective in increasing case detection and maintaining high success rates in a variety of settings when implemented under proper conditions. Treatment outcome has been evaluated and reported for over 20 000 TB patients treated by private providers in 15 PPM DOTS projects. Treatment success rate was close to or above the global target in most projects that provided drugs free of charge to patients. The impact on case detection has been evaluated in eight PPM DOTS projects. All these projects showed increased case detection. An economic evaluation of two PPM DOTS projects indicated that the approach is cost-effective.

PPM DOTS has moved from small size pilots to medium size initiatives involving up to several hundred private providers treating several thousands of TB patients. Some initiatives have continued and expanded over periods of 7–9 years, indicating that the approach is sustainable and can go to scale. However, the real test of sustainability and feasibility comes with initiatives of nationwide PPM DOTS scale-up which are taking place in several high burden countries at present. Existing recording and reporting systems currently used in national TB control programs have been adapted to enable monitoring and evaluation of the processes and outcomes of these initiatives.

In order for PPM DOTS to effectively contribute to the process of reaching the Millennium Development Goals PPM DOTS also need to make TB services accessible to the poor, reduce the financial burden for poor patients and decrease the diagnostic delay. Studies aimed to address these issues are currently under way.

### Experiences from the first year of the scaling up of the Public-Private Mix (PPM) DOTS initiative in India

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The DOTS programme in India currently covers 82% of the population and is planned to cover the entire country by 2005. Despite rapid expansion, people living in bigger cities have relatively poor access to DOTS services, leading to low case detection in such areas. Earlier PPM models in India have shown that PPM can increase case detection without compromising the quality of DOTS.

In August 2003, the Government of India launched a pilot project to scale up PPM in 14 major cities. WHO consultants and additional field supervisors were recruited to the project. For reporting purposes, health providers were classified into six categories: government health department facilities, government

facilities outside health department, medical colleges, corporate sector, private providers and non-governmental organisations.

After a situational analysis, the district authorities listed and prioritised the providers. Advocacy meetings, sensitisation and training programmes were then conducted. The programme schemes for involvement of private practitioners and NGOs have been followed. Microscopy centres and DOT centres are being opened in the different sectors based on requirement and capacity of the respective providers. The national TB programme provides free drugs, laboratory consumables, printed material and training to the key staff of the involved facility. The existing surveillance system has been modified to capture disaggregated data on the contribution to case detection by the different provider categories.

Initial results show that the PPM scaling up in the pilot sites has resulted in a substantial proportion of additional cases coming from the different provider categories. This suggests that scaling up of PPM in a planned and systematic manner, based on the lessons learnt from previous successful PPM models, and implementation of a strict mechanism to ensure quality of services, could result in improved case detection and better access to DOTS services in urban areas.

#### **PPMD: impact on case detection and outcomes in the Philippines**

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In the past year, the Philippines has seen an increase in the number of public-private mix DOTS centers which are of 2 types: publicly initiated and privately initiated. Twenty-two have been certified nationwide. From an original 5 pilot sites from the CDC-PhilCAT models, which has recently gone through an external evaluation, the Global Fund for TB PPM project, implemented by PhilCAT, has just finished its one year of evaluation and has established the National PPMD Coordinating committee, 5 regional PPMD Coordinating committees and 7 PPM DOTS Centers (4 in the private and 3 in the public).. The Phil. TB Initiatives in the private sector, on the other hand, has finished the second situational analysis involving 4 of the original CDC-PhilCAT, and has started scaling up by setting up 20 PPM DOTS centers in 17 cities throughout the Philippines. Master TB Educator Grants have been given to 10 leading Philippine medical schools, covering 70% of all students, and all medical schools are required to either link up with DOTS Centers or established their own quality DOTS Centers.

We previously reported that publicly initiated PPMD could increase case detection rate to as much

as 10–20% in early data from Dumalag in Capiz, a small publicly initiated PPMD in the Visayas Region. Data from De La Sale University PPM DOTS Center show that a single PPM DOTS Center could contribute to as much as 12% incrementally and 15% additionally in the community's total case detection rate and up to 5% of the province. This data does not include referrals by private physicians to the RHUs. Outcomes were comparable to the local community's success rates.

While most of the PPMD centers have been in operation for less than a year, the potential impact on improving case detection rates to reach the 2005 targets cannot be overlooked. Latest NTP data show 61% CDR for 2003. Added to this are marshalling of other resources including other stakeholders, such as the social mobilization project under GFATM being implemented by World Vision, the Rotary 3830 District in the Philippines to contribute 5000 new cases by mobilizing its clubs in Makati and nearby communities and the LEAD project of MSH, which concentrates on local government, the Philippine NTP with its partners is hopefully on its way to achieving global targets through PPM scaled up activities.

#### **Scaling up Public-Private Mix DOTS in Kenya**

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Although Kenya achieved 100% geographic DOTS coverage since 1998 the case detection rate is estimated at only 50–55%. The implementation of DOTS has been a public sector affair even though about half of health care facilities are in the private sector. The private sector TB management practices plus liberalization of anti-TB drug market have been a major cause of concern.

The Kenyan PPMDOTS initiative was the brainchild of the Kenya Association for the Prevention of Tuberculosis and Lung Diseases together with the NLTP. The project rationale was to address the 'perceived' poor TB management practices in the private sector, offer affordable and quality anti-TB drugs in the private sector, retain patients diagnosed in this sector in the same sector thereby decongest the public sector, accelerate DOTS implementation to achieve TB control targets and match available resources to TB control needs.

The initiative started in Nairobi, the capital city, where there is the largest concentration of private health care providers in 2001 but shut down after one year. In March 2002 the initiative was revived and after one year during which about 954 patients were treated with a good treatment outcome in 84% of them the project was rolled out to four other cities. The capacity of KAPTLD to provide the human resource required for training and supervision of

PPMDOTS sites is limited and therefore the NLTP is increasingly taking up this role with KAPTLD providing technical back up. Thus the initiative is being incorporated into routine programme activities. A PPMDOTS manual for TB coordinators has been prepared to facilitate this process. Both NLTP and KAPTLD agree that incorporating PPMDOTS into routine programme activities will enable more providers, including those serving low income groups to be reached and therefore achieve coverage that would impact favorably on TB control in Kenya.

### **Scaling up PPM DOTS through social franchising in Myanmar**

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**Background:** Population Services International (PSI) has been social marketing a range of health products and services in Myanmar since 1995. PSI/Myanmar has developed a franchised network of private General Practitioners, the *Sun Quality Health* (SQH) network, since 2001. In mid-2004 the network had more than 400 active members providing reproductive health services to approximately 70 000 women.

**Social franchising for DOTS:** In March, 2004, PSI began to integrate TB DOTS into the franchised services offered by the SQH network. Selected GPs receive 3 days training in DOTS, refer TB suspects to trained and accredited private laboratories for sputum microscopy, classify the cases and initiate treatment with FDCs. Drugs are provided free of charge by the NTP. PSI developed branded patient treatment kits and has embarked on a range of promotional activities, including television spots and a poster campaign. PSI staff visit participating providers several times per month and collect data for case registration and monitoring. The National TB Programme (NTP) participated in the design of the programme, contributes to the GP training, provides TB drugs free of charge, and performs quality assurance monitoring for the laboratory services.

**Preliminary results:** In the first 2 months of operations, the first group of 26 participating private providers registered 130 new TB cases. By November, 2004, PSI expects to have trained 100 GPs to participate in DOTS. Initial experiences suggest that many participating GPs are highly motivated to engage fully in DOTS, that case retention rates amongst the private providers may be high, and that the 'branded' communications campaign may have contributed to encouraging rates of case detection.

**Lessons and conclusions:** Initial experience in Myanmar suggests great potential for social franchising as a strategy to engage private providers in TB DOTS in a sustained manner and to scale.

## SECTION 3: POSTER SESSIONS SATURDAY 30 OCTOBER 2004

### THEMATIC SLIDE PRESENTATIONS

#### CLINICAL TRIALS AND TUBERCULOSIS BASIC SCIENCE

##### TS-148-182 Endothelin and nitric oxide function in pulmonary tuberculosis in mice

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**Introduction:** Endothelin and nitric oxide (NO) are involved in the normal homeostasis of pulmonary vascular tone. A second role for NO is in antimicrobial activity against *Mycobacterium tuberculosis*. In mice lacking the NO synthase enzyme [iNOS-KO mice] the course of TB infection is characterized by rapid severe necrosis. However, during the first 20 days of the infection these mice show no differences in the bacterial load, suggesting that the necrosis is not due to uncontrolled bacterial growth. We therefore investigated if endothelin activity in iNOS-KO contributed to this event.

**Objective:** To test whether endothelin activity in iNOS-KO promoted the observed severe necrosis.

**Methods:** iNOS-KO and wild type mice were infected by aerosol with *M. tuberculosis* and endothelin function was blocked using specific blockers (BQ-788 or BQ-123) or monoclonal antibody to endothelin.

**Results:** Endothelin blockage in wild-type mice induced higher levels of NO secretion by lung cells, but this did not decrease the bacterial load. iNOSKO infected mice expressed higher mRNA for endothelin than wild type mice. Blockage of endothelin in wild type mice enhanced inflammation in the lungs which was associated with large numbers of neutrophils entering the bronchoalveolar spaces.

**Conclusion:** The data supports the hypothesis that increased endothelin activity in iNOS-KO mice underlies the subsequent inflammation seen in these mice after infection with *M. tuberculosis*.

##### TS-188-232 Utility of mycobacterial interspersed repetitive unit typing to differentiate multidrug-resistant *Mycobacterium tuberculosis* of the Beijing family

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Mycobacterial interspersed repetitive units (MIRUs) typing have been found to allow rapid, reliable, high-throughput genotyping of *Mycobacterium tuberculosis* and may represent a feasible approach to study global *M. tuberculosis* molecular epidemiology. To evaluate the use of MIRU typing in discriminating drug resistant *M. tuberculosis* strains of the Beijing genotype family, 102 multidrug-resistant (MDR) clinical isolates and 253 randomly selected non-MDR resistant isolates collected from 2000 to 2003 in Hong Kong were subjected to 12 loci MIRU typing, spoligotyping, and IS6110 restriction fragment length polymorphism (RFLP) typing. Spoligotyping showed that 241/355 (68%) of the isolates belonged to Beijing family genotype. MIRU typing showed lower discrimination in differentiating between the Beijing family strains (Hunter-Gaston discriminative index (HGI) of 0.9183) when compared with IS6110 RFLP method (HGI = 0.9979). For non-Beijing strains, MIRU typing provided discrimination (HGI = 0.9944) comparable to RFLP method (HGI = 0.9967). There was no remarkable difference in discrimination power between the two methods in differentiating both within or between MDR and non-MDR strains of *M. tuberculosis*. Dendrogram constructed using the MIRU typing data showed a clear segregation between the Beijing and non-Beijing genotype. This supported the potential use of this method to analyse the global genetic diversity of MDR *M. tuberculosis* strains that may be at different levels of evolutionary divergence.

##### TS-526-589 Capreomycin resistance in mycobacteria

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**Objective:** Studies in other bacteria suggest that resistance to the macrocyclic peptide antibiotics viomycin and capreomycin correlate with changes in 16S rRNA or acquisition of antibiotic-modifying enzymes. We investigated the molecular basis of capreomycin resistance in mycobacteria.

**Methods:** Spontaneous and transposon-generated

*Mycobacterium smegmatis* and *M. tuberculosis* capreomycin-resistant mutants were characterized.

**Results:** About 1 in  $5 \times 10^3$  transposon-mutagenized *M. smegmatis* bacteria were capreomycin resistant. The transposons mapped to a gene in the *M. smegmatis* sequence that corresponds to the *tlyA* gene (Rv1694) of *M. tuberculosis*. Complementation of the mutants with plasmids expressing the wild-type *tlyA* gene restored capreomycin susceptibility. Spontaneous capreomycin-resistant *M. smegmatis* or *M. tuberculosis* mutants were recovered at a frequency of about 1 in  $5.5 \times 10^4$  and 1 in  $10^7$  cells, respectively. Nine of the nine *M. smegmatis* mutants and 28 of the 30 *M. tuberculosis* mutants studied had mutations in the *tlyA* gene. Also, four of the four capreomycin-resistant, kanamycin-susceptible clinical *M. tuberculosis* isolates studied contained mutations in the *tlyA* gene. The predicted TlyA protein sequence displays strong homologies with rRNA methyltransferases and RNA binding proteins.

**Conclusions:** Capreomycin resistance can result from the loss of function of a putative methyltransferase. In such mutants, capreomycin susceptibility is dominant to capreomycin resistance.

#### TS-545-604 Evaluation of the single nucleotide polymorphisms (SNPs) in the TNF- $\alpha$ (–238/–308) and IL-10 (–1082/–819/–592) as genetic markers for tuberculosis (TB) outcome in Brazilian subjects

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**Background:** Host genetic factors may play a role in the susceptibility to active tuberculosis (TB), and several polymorphisms in different cytokine coding genes have been described and associated with diseases to date.

**Objectives:** To investigate whether polymorphisms within the promoter region of the TNF- $\alpha$  (–238/–308) and Interleukin-10 (–1082/–819/–592) coding genes are associated to the occurrence of infection and/or active TB.

**Methods:** SNPs within the TNF- $\alpha$  and IL-10 genes were analyzed by PCR-RFLP among two groups of individuals: patients with TB ( $n = 200$ ), and asymptomatic healthy care workers (HCWs) with positive tuberculin skin test (TST) ( $n = 103$ ).

**Results:** In this study, the presence of the –238A allele was associated with susceptibility to infection, disease occurrence and severity. On the contrary, the –308A allele was associated with protection to the occurrence of active TB. Regarding to IL-10, individual analysis of each SNP showed an association of the

mutant homozygous with protection against the occurrence of TB.

**Conclusions:** These results suggest the importance of genetics studies pursuing a better understanding of to key issues on the human pathogenesis of *M. tuberculosis*.

This work was supported by Faperj and Millenium Project.

#### TS-552-620 The –238 TNF- $\alpha$ polymorphism and TB susceptibility in Brazil subjects

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**Background:** TNF- $\alpha$  is a complex cytokine that has a key role in TB immune response. Studies have shown the importance of the single nucleotide polymorphism at the –238 position in the negative regulation of the gene and decrease in the protein production.

**Objectives:** Investigate whether –238 SNP is associated with susceptibility to the infection, disease and severity of TB among Brazilian subjects.

**Methods:** Genotyping of TB patients ( $n = 200$ ) and asymptomatic healthy care workers (HCWs) ( $n = 167$ ) was carried out by PCR-RFLP.

**Results:** A significant increased frequency of the –238A allele was observed in: 1) converters of tuberculin skin test (TST) when compared to the non converters among HCWs ( $P = 0.03$ ; OR = 0.20; IC = 0.03–1.04); 2) active TB patients, when compared to HCWs with positive TST ( $P = 0.03$ ; OR = 2.30; IC = 1.1–5.5); and 3) extrapulmonary and disseminated TB forms in relation to the pulmonary forms ( $P < 0.01$ ; OR = 0.15; IC = 0.06–0.36). These results strongly suggest that the –238A allele may be a susceptibility marker for infection with *M. tuberculosis*, occurrence of active disease and severity TB forms in our population.

Supported by FAPERJ.

#### TS-559-680 Activity of the novel nitroimidazopyran PA-824 (PA) in the murine model of tuberculosis (TB)

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**Setting:** PA has activity in vitro against actively multiplying and non-multiplying *Mycobacterium tuberculosis*.

**First experiment:** After aerosol infection with 3.69 log<sub>10</sub> CFU of *M. tuberculosis* H37Rv, mice were treated for 4 weeks with PA (range: 3.125 to 200 mg/

kg/day) or isoniazid (H) 25 mg/kg/day as positive control. PA in doses  $\geq 12.5$  mg/kg and H prevented gross organ lesions. Bactericidal activity ( $\geq 99\%$  reduction in CFU counts compared to pre-treatment controls) was observed with H and with PA in doses  $\geq 100$  mg/kg.

**Second experiment:** When CFU counts were  $9.79 \pm 0.13$  CFU in lungs and  $5.58 \pm 0.43$  log<sub>10</sub> in spleens, aerosol infected mice were daily treated for 2 mo. with PA 100 mg/kg, H 25 mg/kg, PA+H, or rifampin (R) + H + pyrazinamide (Z) as positive control. After 2-mo of RHZ, mice were shifted to daily treatment for 2- and 4-mo with PA, H, R, or moxifloxacin (M) alone to comparatively assess sterilizing activity. After 2-mo, log<sub>10</sub> CFU counts were 3.72, 6.06, 5.52, and 5.93 in lungs of mice treated with RHZ, PA, H, and PA+H, respectively. Similar results were observed in spleens.

**Conclusions:** PA-824 has bactericidal and, perhaps, sterilizing activity.

#### TS-640-711 Shortening the duration of therapy of murine tuberculosis (TB) with moxifloxacin (M) containing regimens

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**Rationale:** Recently, the substitution of M for isoniazid (H) in the standard regimen (2RHZ/4RH) resulted in a 2 mo. reduction in the time to culture negativity in the experimental murine model of TB. To further assess whether this substitution might permit shortening the duration of therapy for human TB, we determined the relapse rate after treatment of 3, 4, and 5 mos. duration in the murine model.

**Methods:** BALB/c mice were aerosol infected with 3.24 log<sub>10</sub>CFU of *M. tuberculosis* H37Rv. At treatment onset, 21 days later, the CFU counts were 6.92 CFU in lungs and 3.08 log<sub>10</sub> in spleens. The tested regimens were 2RHZ/4RH (positive control), 1RMZ/4RM, 2RMZ/3RM, 5RMZ, all of them given for 3, 4, or 5 mo. After completing therapy, mice were observed for 3 mo., then sacrificed (12 mice per group) to determine relapse rates.

**Results:** Relapse rate: proportion of mice relapsing by regimen and duration of treatment

Regimens	3-month	4-month	5-month
2RHZ/4RH	11/12	5/12	1/12
1RMZ/4RM	4/12*	0/12**	0/12
2RMZ/3RM	2/12*	0/12**	0/12
5RMZ	4/12*	0/12**	0/12

\*  $P < 0.05$  and \*\*  $P < 0.01$  vs standard regimen.

**Conclusions:** The results further support the sterilizing activity of M and its potential for shortening the duration of therapy for TB by as much as 2 months.

## POSTER DISCUSSION SESSIONS

### DOTS EXPANSION

#### PC-168-204 DOTS expansion in collaboration with NSDP-PSTC (NGO) clinics in Dhaka City

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**Introduction:** TB expansion in big cities is complex. More concentration of patients at Chest Diseases Clinics are the general norms.

**Objective:** To establish network and linkages between NTP Chest Clinics and NGO clinics in DOTS management.

**Method:** DOTS expansion and implementation through involvement of NGO clinics in Dhaka city after adequate training, supply of drugs and logistics and follow up by supervision, monitoring and reporting to NTP.

**Results:** During 2nd quarter of 2003 all category of staff of 6 NSDP-PSTC clinics (one-third of total population of Dhaka city) trained on policies and guidelines of NTP. 3 Clinics were established and developed for sputum microscopy and EQA. Implementation of DOTS were in place from 3rd quarter of 2003. Under the ESP services of NGOs TB has been given priority and good network was established by senior service providers, service providers, counsellors, and paramedics. A special link with private practitioners was also established within its area. NTP and NSDP-PSTC clinic staff regularly monitor plan of action and supervision, monitoring and reporting are done on quarterly basis. A total of 330 cases were diagnosed and under treatment until the end of December 2003 and results are yet to be analysed. A detailed analysis of operational and technical aspects will be done in June 2004.

**Conclusion:** Involvement of NGOs in TB Control services is an utmost importance especially in big cities.

#### PC-514-571 The relationship between DOTS population access and TB case detection: experience from the DOTS expansion strategy implementation in Nigeria

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Nigeria has an estimated population of 130m people and ranks 5th among the 22 highest TB burden countries of the world. The country is administratively divided into 36 State and a Federal capital Territory (FCT), which are further sub-divided into 774 Local



government Area councils (LGAs). A National Tuberculosis Control programme has been operational since 1991. WHO estimates 250 000 (275/100 000 population) all forms of TB occurring in Nigeria annually. The TB-HIV co-infection rate rose from 2% in 1992 to 19.1% in 2001. As at June 2002 only 21 out of 36 states in Nigeria and the FCT were implementing the DOTS strategy in 417 LGAs. DOTS expansion commenced in October 2002, with the support of a CIDA grant. By February 2004 all 36 states and FCT have commenced implementation of the DOTS strategy in 493 of 774 LGAs. The rapid expansion of the diagnostic and treatment services network increased the population access to DOTS from about 45% in 2002 to about 65% by end of 2003. The increase in population access to DOTS as a result of DOTS expansion in newly implementing states resulted in a substantial increase in TB Case Detection Rate (CDR) in 2003 over the previous year (CDR 16% in 2002 to 23% in 2003; i.e. equivalent to 44% increase). The 16 DOTS expansion states contributed 32% of total case notification and 31% smear positive case detection, with Lagos State alone contributing a substantial part. In contrast, the CDR in previously supported DOTS maintenance states has remained largely unchanged. This paper attempts to illustrate graphically the impact of the DOTS expansion strategy implementation on the TB case detection in comparison with the trend of routine implementation over the years. The Nigerian experience has demonstrated that increasing population access to DOTS has direct positive influence on TB case detection. It is unclear to what extent inadequate access to DOTS account for the gross difference between the country's CDR and the WHO estimates.

#### PC-557-627 Attempts at refining community based DOTS in South Africa

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**Objective:** Develop a methodology for implementing and evaluating Community Based DOTS (CBD) in Alberton Sub-District, Gauteng Province, South Africa. **Background:** With the extent of the TB and HIV/AIDS epidemic in South Africa, there is a need to work towards more user-friendly monitoring of TB treatment. Development of CBD needs to include strengthening of the TB program so that CBD can absorb some of the pressure on TB clinics. TADSA is a national NGO facilitating introduction and evaluation of CBD in all provinces of South Africa. Alberton Sub-district was selected as a priority intervention district, with a cure rate of 56% and smear conversion rate of 60%.

#### Methods:

- Formative assessment; functional TB control a pre-requisite for introduction of CBD
- Customized intervention developed
- All tiers of CBD personnel trained
- Routine monitoring and quality improvement program introduced

**Results:** 6 clinics had functional TB control; 1 DOT Coordinator and Trainer trained at each clinic; 35 Treatment Supporters recruited and trained; 101 patients receiving treatment in the community. Early indications: the introduction of CBD has been acceptable, smear conversion rates increased by 5% even though case-finding increased by 23%, full results will be presented including perceptions of carers and caregivers.

#### PC-601-673 Tuberculosis status before and after the implementation of DOTS in the western region of Nepal

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**Introduction:** DOTS strategy started in 1996 expanded to all 16 districts of the western region of Nepal by April 2001.

**Objectives:** To show the impact of DOTS in the overall outcome over the years since its implementation as against the unsupervised methodology.

**Methods:** Comparative studies of tuberculosis situation just before and after the implementation of DOTS in the western region of Nepal.

**Results:** With 12 month unsupervised therapy in 1995, the case-finding rate was nearly 30%, treatment success rate 40%, defaulter rate 15% and nearly 45% labelled no result. In 1996 DOTS was implemented with one treatment centre (TC) and two treatment sub-centres (STC) and initial one-year findings were over 90% of treatment success rate and defaulter rate of less than 5%. Gradual expansion with 57 TC and 254 STC has covered 96% of the population in the region that initially started with the coverage of ~ 2% of the population. The case finding rate improved to 70% in 2003. Treatment success rate of nearly 90% has been sustained over the years with the defaulters less than 5%.

**Conclusion:** DOTS strategy has tremendously improved the overall outcome of tuberculosis control programme of western region of Nepal.

**PC-683-756 Implementation and expansion of the DOTS strategy in Myanmar**

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**Introduction:** Myanmar is among 22 TB high-burden countries. DOTS is accepted as the National TB Strategy since 1997 and a Five Year Strategic Plan (2002–2006) was approved by the Ministry of Health. Myanmar is receiving support from WHO, IUATLD, the Global Drug Facility and other partners. The Global Fund to Fight AIDS, TB and Malaria (GFATM) approved a TB proposal in the second round.

**Objective:** To measure progress towards WHO global targets.

**Methods:** Cohort analysis based on the WHO quarterly reports on case-finding and treatment outcomes from townships and NTP annual reports.

**Findings:** DOTS coverage increased from 47% (1997) to 100% (2003). For new smear-positive pulmonary TB patients, case-detection increased from 44% (1994) to 70% (2002) while treatment success remained stable at 82%. Main challenges are sustainability of TB drug supply, poor access to diagnosis and treatment in remote areas, lack of capacity for supervision and laboratory work, TB-HIV and delay in receipt of GFATM funds.

**Conclusion:** With high-level political commitment towards DOTS and external assistance, Myanmar is approaching WHO global targets despite of limited resources. Now that 100% DOTS coverage is achieved, NTP and the partners have to focus on enhancing quality of TB services nationwide.

**PC-735-811 Progress in the revision of the national TB policy and expansion of the revised TB control strategy in the Russian Federation**

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**Introduction:** The National TB control programme was revised and majority of essential DOTS components were introduced. The country adopted international recommendations and issued regulations on chemotherapy, laboratory and monitoring based on cohort analysis. Russia has insufficient resources and capacities for expansion of the revised strategy.

**Objectives:** To review the country plans and needs for the effective expansion of the revised TB control strategy.

**Methods:** Discussions and assessment through the High Level Working Group, Interagency Coordination Committee and the newly established Country Coordination Mechanism.

**Results:** The implementation plan for DOTS expansion

including trainings was prepared. Country needs were preliminary assessed. Additional resources are mobilized (the WB loan project, started from December 2003, and an application to GFATM 4th round). The mechanism for international assistance and implementation is being established. Recommendations for detailed assessment at the regional level were prepared.

**Conclusions:**

- Revision of the national programme must be completed in line with WHO recommendations (TB-HIV, DOTS+, social support)
- Training of national trainers and development of training materials are essential initial steps
- Training, evaluation and TB monitoring require international assistance
- Implementation of new approaches should be performed gradually with the technical assistance from international partners.

**PC-796-869 Ten years of DOTS in Southern Nigeria: the experience of the KfW/GLRA support project**

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**Introduction:** Modern TB control based on DOTS as recommended by the WHO and the Union was introduced in 14 states in southern Nigeria between 1993 and 1994 with the assistance of the German Bank for Reconstruction (KfW) and the German Leprosy and Tuberculosis Relief Association (GLRA).

**Objective:** This presentation will highlight the major milestones in the development of this project from its beginning as a limited hospital-based service to a largely decentralised system with options for ambulatory treatment and describe the principal factors affecting programme performance. Decentralisation and increased geographical coverage should lead to corresponding service access but the experience here was that programme performance, especially with respect to case detection has lagged behind. How does one explain this apparent 'hollow magnification'? We believe the factors include:

- 1 Neglect of the private sector
- 2 Preponderance of poorly-attended PHC centres as service delivery centres
- 3 Undue rigidity with the letter as against the spirit of DOT
- 4 Lack of good governance on the part of the various tiers of government
- 5 Absence of an operational research component
- 6 Absence of a strategic (development) plan with regular programme reviews at predetermined intervals

**Conclusion:** The lessons from here should inform programme planning and implementation in Nigeria's new DOTS states as well as a repositioning of the KfW/GLRA support project.

### PC-873-949 Urban tuberculosis control in Kathmandu metropolitan city

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**Introduction:** The DOTS strategy was introduced in Nepal in 1996. Reinforcement of the DOTS strategy in urban areas was started in Kathmandu in 2000.

**Objectives:** To improve TB situation in Kathmandu through developing an urban DOTS model in Nepal.

**Methods:** Improved access to TB diagnosis and treatment, and mobilization of private sectors and volunteers for late patient tracing.

**Results:** The number of treatment centers increased from 18 to 32 in the past three years. Five private clinics/hospitals and 7 NGOs have been involved and 15 centers have diagnostic facilities. The new smear positive cases increased from 789 to 903, which indicates 3% improvement in case finding rate. The cure rate of new cases was improved from 78 to 81% but the defaulter rate was as high as 8%. The follow-up of the late patients was conducted by volunteers and 259 patients were traced. Thirty-nine per cent of the late cases could return to the treatment, but 23% were lost. Forty-eight per cent of the defaulted cases are expected to be due to migration.

**Conclusion:** The case finding and cure rates were able to be improved in Kathmandu. Interventions to target migrating patients appear crucial in urban TB control of Nepal.

### PC-881-955 Effect of expansion of Nepal DOTS Programme on hospital utilisation for tuberculosis

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**Introduction:** The Nepal Tuberculosis Programme expanded national ambulatory DOTS from 1996 to 2002 using mainly health centers and health posts. Tansen UMN a major Tuberculosis referral hospital in the Western Region, has experienced a drop in TB related activity during the same time.

**Objectives:** To analyse the trends in hospital utilisation for Tuberculosis using routine statistics, and contrast this with NTP activity in the catchment area, to ascertain the possible effects of NTP DOTS on hospital utilisation.

**Methods:** Compare routinely annual statistics from UMN Tansen Hospital (Tuberculosis Total visits, new cases, smear-positive cases, TB follow-up visits from 1993/4 to 2001/2, and also overall out-patient data

compared to case finding data from the National Tuberculosis programme, analysing for trend during same time period, the DOTS expansion Phase of the NTP.

**Results:** There were reductions in total TB visits (71%), follow-up visits (88%), new smear positives (41%) (639 less patients/yr), all new TB cases (30%). This happened during a time of increased hospital in-patient activity. The trend concurs with NTP DOTS expansion (additional 1528 smear positive cases/year in the Western region—including hospital catchment area).

**Conclusion:** The Nationwide DOTs programme expansion has been associated with a significant reduction in TB related hospital workload.

### PC-906-983 Impact de la décentralisation sur la lutte antituberculeuse dans la ville de Conakry

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**Objet :** Déterminer les effets de la décentralisation sur la lutte antituberculeuse (LAT) à Conakry.

**Cadre :** Conakry.

**Méthode :** Une enquête a été réalisée dans les 18 centres de prise en charge de la tuberculose de Conakry du 5 Février au 5 juin 2000. Elle a concerné 10% des malades suivis dans chaque centre soit 180 tuberculeux et a porté sur : la distance entre le centre de traitement et le domicile du malade, le mode de déplacement du malade, les frais de transport, la qualité des soins et les difficultés signalées par les malades, la supervision du traitement, la séance d'éducation sanitaire, les résultats du dépistage et du traitement.

**Résultats :** 90,6% des malades ont leurs domiciles situés à moins d'1 km et à 1 km des centres de traitement. 59,44% des malades vont à pieds dans les centres de traitement pour prendre les médicaments contre 40,55% qui utilisent un moyen de déplacement. La moyenne de frais de transport payé par jour est de 400FG (le minima payé par trajet est de 300FG et le maxima 600FG). La qualité des soins a été jugée bonne par 92% des malades. 14% des malades ont signalé des difficultés (isolement, perte de l'emploi et de l'année scolaire, ressources faibles, souci du VIH) qui ne sont pas liées aux structures sanitaires et au personnel soignant. 93% des malades ont bénéficié régulièrement des séances d'éducation sanitaire. Le traitement est quotidiennement supervisé chez 61,66% des malades pour 62,8% de malades à la phase intensive. 92% des malades savent la durée de leur traitement (8 mois) et 72% le nombre de contrôle de crachats à effectuer. 98,64 des malades dépistés sont faits au CAT-port et au LNR. Le taux de succès du traitement est au dessus de 75%.

**Conclusion :** Les effets bénéfiques de la décentralisation sur la lutte antituberculeuse à Conakry sont évidents. Cependant, si elle est excellente sur les activités

du traitement, celles du dépistage nécessitent d'être améliorées en intégrant de façon objective dans les centres satellites.

## CLINICAL TRIALS AND TUBERCULOSIS BASIC SCIENCE

### PC-342-366 Novel compounds active against multi-resistant strains of *Mycobacterium tuberculosis*

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**Objectives:** During the past two decades the WHO indicated an increasing number of TB patients infected by strains of *M. tuberculosis* resistant to most of the available drugs. In contrast it has been nearly 30 years since the introduction of a novel compound for the treatment of TB. We synthesized series of analogues of our newly discovered class of antimycobacterial compounds based on dialkyldithiocarbamates to enhance in vitro and in vivo activity by structure activity relationship studies.

**Methods:** Molecules were derived by specific methods of classical synthesis. In vitro activity was determined fast growing mycobacteria and drug resistant clinical isolates of *Mycobacterium tuberculosis*. In vivo activity was tested in a murine model of TB infection.

**Results:** While starting compounds were active against Gram-positive bacteria, mycobacteria, fungi and yeasts, in the course of the investigations activity was focused on bacteria and mycobacteria. Various analogues demonstrated high in vitro activity against *M. tuberculosis* including clinical isolates and MDR strains. MIC's of the most advanced compounds for *M. tuberculosis* H37Rv and clinically isolated MDR strains were  $<0.78$ – $<0.063$  µg/ml. The compounds were therapeutically active after oral application in mice infected with *M. tuberculosis* H37Rv with 100% survival rates. The LD50 in mice after oral application was  $>500$  mg/kg for all compounds. Additionally, synthesis of the compounds is efficient and inexpensive.

**Conclusions:** Considering the activity of the novel compounds against MDR strains of *M. tuberculosis*, the mechanism of action must be different to that of the existing therapeutics. Due to the narrow spectrum of activity and the low toxicity this new class of antimycobacterial compounds represents a promising lead candidate for low cost drugs to overcome MDR-TB with reduced side effects.

### PC-483-524 Bioequivalence assessment of rifampicin from a three drug fixed-dose combination (FDC) formulation using an FDC as reference product at the same dose levels

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Bioequivalence assessment of rifampicin containing fixed-dose combinations (FDC) is an integral part of the prequalification program. In practice FDCs are compared with loose combinations at the same dose levels, where selection of reference formulation remains the choice of sponsor. Since bioequivalence is assessed traditionally by comparing the test product with the innovator's product as reference at the same dose levels, an attempt was made in the present study to determine the bioequivalence of rifampicin in a three drug FDC formulation containing the doses of rifampicin, isoniazid and ethambutol hydrochloride (Svizera Labs) recommended by the World Health Organization (WHO) against an FDC (Akurit-3) as reference product. The study was conducted as per the WHO protocol using 20 volunteers with an extended sampling time up to 24 hr. The test formulation was bioequivalent to the reference product with respect to the essential pharmacokinetic parameters ( $AUC_{0-24}$ ,  $46.68 \pm 5.66$  and  $51.64 \pm 8.03$  mg.h/ml,  $C_{max}$ ,  $7.36 \pm 1.24$  and  $7.74 \pm 1.39$  mg/ml,  $T_{max}$ ,  $2.24 \pm 0.62$  and  $2.05 \pm 0.67$  hr, for test and reference formulations, respectively) and values are within the reported normal range. Therefore it was concluded that an FDC could be used as reference product for bioequivalence assessment of rifampicin containing FDCs and both WHO/IUATLD should develop reference product for anti-TB FDCs.

### PC-483-525 Dissolution test as a surrogate for quality evaluation of rifampicin containing fixed-dose combination formulations

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Standard dissolution procedure does not guarantee acceptable bioavailability of rifampicin from fixed-dose combination (FDC) formulations of anti-TB drugs. The present investigation was aimed at developing a dissolution methodology to predict in vivo performance of rifampicin containing FDC products. Six FDC formulations were used in this study (four had passed bioequivalence while two failed). Dissolution studies were conducted at agitation intensity of 30–100 rpm as a measure of hydrodynamic stress and at pH buffers corresponding to gastric and intestinal conditions. Dissolution at 50 rpm was most sensitive

and differentiated the release profiles of rifampicin under various pH conditions. It was possible to predict in vivo performance of rifampicin from FDCs when in vitro rate and extent of release at various pH buffers was correlated with site, pH and concentration dependent absorption of rifampicin along with gastric emptying time. It was also seen that dissolution conditions recommended in USP for different types of FDCs were insensitive for the formulation changes. Based on this comprehensive evaluation, a decision tree is proposed which will act as a guideline for quality evaluation of FDC products and also will provide a fundamental knowledge for optimization of formulations failing in dissolution studies.

**PC-541-602 Characterization of *Trpo* mutations in in vitro-selected rifampicin-resistant mutants of *M. tuberculosis***

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**Introduction:** *M. tuberculosis* adapts to antibiotics by spontaneous mutation. Mutations in a core region of the *rpoB* gene have been demonstrated in around 97% of the clinically rifampicin (Rif.) resistant isolates of *M. tuberculosis*.

**Objective:** To identify and assess the representability of mutations developed in in vitro-selected Rif. resistant mutants of *M. tuberculosis*.

**Method:** We sequenced a region of the *rpoB* gene in 184 Rif. resistant mutants selected from 8 non-related clinical isolates. Eighty-nine mutants were of the Beijing genotype.

**Results:** As reported for clinical isolates we found mutations at codons 531 and 526 to be the most prevalent. Mutations at codon 516 were less frequent among in vitro mutants whereas mutations at codon 522 were more prevalent than among clinical isolates. A total of 13 deletions were detected, of which 4 are not previously described. Furthermore one double, one triple and one not earlier described point mutation were exclusively observed in mutants of the Beijing genotype.

**Conclusions:** Our results indicate that some in vitro-mutations, possibly due to biological cost, are less frequent among clinical isolates. The multiple mutations found in the Beijing mutants could reflect alterations in their DNA repair systems.

**PC-636-706 Does antiretroviral treatment reduce tuberculosis incidence? The Brazil experience, 1995–2001**

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**Introduction:** Approximately 600 000 Brazilians are infected with the human immunodeficiency virus (HIV) and high tuberculosis (TB) rates pose increased risks to this population. Since 1996, Brazil's health policy includes free access to antiretroviral therapy (ART) for HIV-infected patients, and there is evidence that this strategy decreases TB risk in these patients.

**Objectives:** To measure the impact of ART on TB incidence in Brazil.

**Methods:** We conducted a national retrospective cohort study of adults with laboratory-confirmed HIV infection between 1995–2001. Patients were randomly selected in HIV treatment centers chosen by population-proportional-to-size sampling. Concomitant receipt of two nucleoside reverse transcriptase inhibitors (RTI) plus either a protease inhibitor or a non-nucleoside RTI defined highly active ART (HAART).

**Results:** Tuberculosis was diagnosed in 49/317 (16%) patients. At TB diagnosis, 42 (86%) patients were not receiving HAART (non-HAART), 17 (40%) of whom were taking no ART. Only 10% of these patients had received TB preventive therapy (PT). Patients receiving HAART were at significantly less risk of TB disease than non-HAART recipients (RR. 0.13, 95% C.I. = 0.02–0.82), even after adjusting for PT use.

**Conclusion:** Use of HAART by HIV-infected patients in Brazil is associated with a significantly lower risk of TB disease compared to non-HAART recipients.

**PC-645-714 Association study of the +874T/A IFN- $\gamma$  SNP with TB outcome**

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**Background:** Interferon gamma (IFN- $\gamma$ ) is an essential cytokine in the control of *Mycobacterium tuberculosis* infection. Studies have been shown the evaluated of the distribution of the single nucleotide polymor-

phism (SNP) +874 T/A within the IFN- $\gamma$  and its association to tuberculosis (TB).

**Objectives:** To evaluate the possible association of this SNP among TB patients and a group of health care workers (HCWs) with positive or negative tuberculin skin test (TST), with susceptibility, severity or protection to TB.

**Method:** Genotyping of the DNA samples was carried out by Amplification Refractory Mutational System (ARMS-PCR) technique.

**Results:** Ninety-three TB patients and 266 HCWs were included. A significant association with the AA genotype and the +874A allele was observed among TB cases in comparison to HCWs, and the TT genotype occurred more frequently among TST + HCWs with TST + ( $P = 0.01$ ). Analysis according to the gender showed a significant association of the AA genotype with the patients and of the TT genotype with the HCWs among males ( $P = 0.03$  and  $P < 0.01$ ) respectively.

**Conclusion:** The results observed in this study highlight that the genetic defect in the production of IFN- $\gamma$  may contribute to increase the risk of developing tuberculosis.

Financial support: Institutos do Milênio, Cornell University.

#### **PC-761-835 Development and application of tools to study pathogenesis in *Mycobacterium bovis* infected cattle**

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**Introduction:** Pathognomonic marker of tuberculosis is the formation of a tuberculous granuloma. Although a lot of work has been done to study the pathogenesis in humans, very little work has been done to study the pathogenesis in cattle.

**Objectives:** To classify different stages of granulomatous inflammation and identify the cells, cytokines and markers of fibrosis associated with different stages of these granulomas in experimentally infected cows.

**Methods:** Tissues from experimentally infected cows were examined by H&E to identify different stages of granulomas and mRNA and protein expression for cell markers, cytokines and pro-fibrotic markers were studied by immunohistochemistry and in-situ hybridisation.

**Results:** Granulomas were classed into the four granuloma stages on the basis of H&E staining. There was a depletion of lymphocytes and an increase in the number of macrophages and type I procollagen at the sites of lesions with advancement of infection. Our initial results also indicate that these tools can provide information on pathological response on the effectiveness of vaccines.

**Conclusion:** Development of these tools will improve our understanding of the pathogenesis of bovine tuberculosis and help to discriminate between different stages of pathological response.

#### **PC-792-864 Heterogeneity of antibody response to mycobacterial antigens in tuberculosis**

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**Introduction:** Different clinical outcomes of tuberculosis are related to the balance between cell-mediated and humoral immunity.

**Objective:** To analyse humoral immune response to recombinant and native mycobacterial antigens in relation to clinical presentations of pulmonary TB in adults (A) and children (C).

**Methods:** 327 serum samples (215 A, 112 C). Adults: non-cavitary ( $n = 120$ ), cavitary ( $n = 65$ ), caseous pneumonia ( $n = 12$ ), disseminated TB ( $n = 18$ ). Children: 81 primary, 31 postprimary. ELISA detecting IgG, IgA and IgM against antigens: 38 kDa and 16 kDa, 38kDa and lipoarabinomannan, and A-60 were used.

**Results:** Mean IgG level was higher in cavitary TB compared to all other subgroups ( $P < 0.001$ ). IgG production was very low in primary TB compared to postprimary ( $P < 0.0001$ ) and in C group compared to A ( $P < 0.0001$ ). IgM level did not differ between examined groups. IgA level was highest in caseous pneumonia. In all subgroups person-to-person heterogeneity of antigen recognition was observed.

**Conclusions:** Humoral immune response is associated with the phase of TB and is stronger in most advanced forms.

#### **PC-921-996 Description of risk factors for patients and doctors delay of pulmonary smear-positive tuberculosis in Mongolia**

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**Introduction:** Delays in case finding and treatment are common in Mongolia. Both forms of delay have been studied to some extent in other countries. However, little is known about the magnitude of this problem in Mongolia.

**Objectives:** The purpose of the study, therefore, was to investigate factors responsible for delay, both from the onset of symptoms to diagnosis, and from diagnosis to commencement of therapy.

**Methods:** Using a standard questionnaire, all patients with smear positive pulmonary tuberculosis,

newly diagnosed during the seven months from March 2002 to September 2002, were interviewed by doctors at the TB dispensaries. For each patient the following information was gathered: level of education, occupation, initial symptoms of pulmonary tuberculosis, the date of appearance of the initial symptoms, and the date of their first medical consultation. The patient was also asked about the qualification of the doctor who was first consulted by the patient, the results of both smear examination and chest X-rays taken before starting treatment for tuberculosis. A Kruskal-Wallis test was used to determine whether educational level, occupation, age group and any difficulty had any effect on patient delay. Epi-Info 2000 (version 1.1) was used for statistical procedures.

**Results:** There were 111 male (53.1%) and 98 female (46.9%) patients. Sixty-nine patients (33%) were employed, 14 (6.7%) were secondary school children, 12 (5.7%) were students, 14 (6.7%) were retired persons, 5 (2.4%) were classed as disabled, and 95 (45.5%) were unemployed. The median patient delay to seek consultation with a medical provider was 30 days (range of 0–660 days). 29.1% of the patients sought a medical facility within 14 days, and 54.9% within one month of the onset of their symptoms. However, about 17.8% of the patients visited a medical attention for the first time more than 3 months after the onset of symptoms. Of the 209 persons with whom doctor delay could be assessed, the median delay was 20 days (range: 0–358 days). 65.6% of the patients were treated within 30 days, 87.1% within 90 days and 95.7% within 180 days. 1 (0.5%) was initially evaluated by a bag (small village) doctor, 115 (55%) by a family doctor, 11 (5.3%) by a general doctor, 57 (27.3%) by a TB doctor, 8 (3.8%) at a private hospital and 17 (8.1%) in another medical facility.

**Conclusion:** To decrease patient delay, advocacy activities to increase awareness about tuberculosis should be expanded, especially amongst schoolchildren, students and retired groups in the population. The quality of medical training for both family and som (township level) doctors should be improved, in order to increase awareness of tuberculosis and reduce doctor delays.

#### **PC-438-477 Reliable and reproducible evaluation method for cytokines and iNOS mRNA expression in guinea pig lung tissue by RT-PCR using newly designed primer sets**

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**Introduction:** Guinea pigs are often used as an animal model of human tuberculosis (TB). However,

there are few methods available for examining the immunologic processes involved in guinea pig TB.

**Objectives:** To design reverse transcription (RT)-PCR primer sets to examine mRNA expression of cytokines and iNOS in the lung tissues of guinea pig infected with *M. tuberculosis*.

**Methods:** Homology of mRNA sequence among guinea pig, mouse and rat, or the Primer 3, internet primer design programme was used to design RT-PCR primer sets for guinea pig. Total RNA was extracted with TRIzol reagents from *M. tuberculosis* infected guinea pig lung tissues. mRNAs were purified with Oligotex<sup>TM</sup>-dT30<sup>super</sup>mRNA Purification kit (TakaraBio, Japan). b-actin and GAPDH primer sets which had been already published were used as internal positive controls. mRNAs before reverse transcription were used as templates for negative control PCR amplification in each primer set to confirm no genomic DNA contamination.

**Results:** RT-PCR primers for IFN-gamma, TNF-alpha, IL-1beta, IL-2, IL-10, IL-12p40, iNOS, TGF-beta, and GM-CSF were designed. PCR products with expected length were reproducibly obtained using these primer sets.

**Conclusion:** With these primer sets, mRNA expression of cytokines and iNOS can be semi-quantitatively examined by the conventional RT-PCR in guinea pig TB model as performed in mouse model.

## **POLICY AND PROGRAMME IMPLEMENTATION: TB AND HIV**

### **PC-363-389 Clinical and strain associations with recent *M. tuberculosis* infection among HIV-positive patients in the DARDAR TB vaccine trial**

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**Introduction:** Molecular strain typing can be used to identify clustering and recent infection with *Mycobacterium tuberculosis*.

**Objectives:** To identify clustered isolates of *M. tuberculosis* and clinical and genetic correlates of clustering among HIV-positive patients in a TB vaccine trial in Tanzania.

**Methods:** IS6110 typing and spoligotyping were performed on *M. tuberculosis* isolates. Isolates with the same IS6110 patterns were defined as 'clustered' (re-

cent infection); isolates with related IS6110 patterns were defined as a 'family'.

**Results:** 98 isolates were analyzed, including 36 from HIV-positive study patients and 62 concurrent community isolates (HIV-status unknown). Among study patients 10/36 (28%) isolates were clustered as were 15/62 (24%) of community isolates ( $P = 0.8$ ). Clustering was present in 6/18 (33%) with CD4 >200 and 4/18 (22%) with CD4 <200 ( $P = 0.7$ ). Clustering was not associated with baseline tuberculin reactivity or prior tuberculosis. The most common family (designated GD) of isolates comprised 33 isolates representing a genetic lineage previously identified in East Asia; 15 (45%) were clustered vs. 10 (15%) of the remaining 65 isolates ( $P = 0.003$ ). Spoligotyping demonstrated 10 strain families. Additional strain data will be presented.

**Conclusion:** Recent *M. tuberculosis* infection in Tanzania is associated with East Asian strain *M. tuberculosis*, but not with prior tuberculosis, tuberculin reactivity or CD4 count.

#### PC-403-441 Low drug concentrations in acquired rifamycin resistance treatment failure or relapse among patients with HIV-related tuberculosis treated with largely twice-weekly rifabutin and isoniazid

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**Objectives:** To better understand the causes of acquired rifamycin resistance (ARR) in treatment failure or relapse of HIV-related tuberculosis, we performed a pharmacokinetic substudy of patients in a treatment trial receiving twice-weekly rifabutin and isoniazid during continuation-phase therapy.

**Methods:** Of the 169 tuberculosis patients in the study, 102 (60%) agreed to enroll in the pharmacokinetic substudy. This included 7 of the 8 persons who had ARR treatment failure/relapse.

**Results:** Both rifabutin and isoniazid area under the concentration-time curves (AUC) were lower in patients with ARR failure/relapse vs. others (median rifabutin AUC<sub>0-24</sub> 3.3 vs. 5.2 µg\*hour/ml,  $P = 0.06$  exact test; and median isoniazid AUC<sub>0-12</sub> 20.6 vs. 29.0 µg\*hour/ml,  $P = 0.21$ ), but these differences were not statistically significant. However, in a step-wise Proportional Hazards model adjusted for CD4

cell count, lower plasma concentrations of rifabutin were associated with ARR failure/relapse (HR 1.59 [95% CI 1.04–2.44,  $P = 0.03$ ]). Rifabutin was estimated to be detectable in plasma at least 37 hours (median) longer than isoniazid after drug administration.

**Conclusion:** Among patients with HIV-related tuberculosis, lower concentrations of rifabutin were found in patients with ARR failure/relapse. Prolonged plasma concentrations of rifabutin without isoniazid may facilitate development of acquired rifamycin resistance.

#### PC-473-515 Predictors of survival in a cohort of patients receiving treatment for tuberculosis under routine control conditions in Addis Ababa, Ethiopia

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**Introduction:** TB-HIV co-infection affects the outcome of TB treatment. This study provides an evaluation of treatment outcome and survival of TB patients routinely diagnosed and treated in two peripheral facilities in Addis Ababa.

**Methods:** 256 patients registered for TB treatment under routine TB Control Programme conditions, have been evaluated. Baseline data included clinical history, smear for AFB, culture, CXR and HIV parameters. Patients were treated ambulatory with SCC (DOT). Home visits 36–42 months after start of treatment and survival analysis have been carried out.

**Results:** From a total of 252 patients, 67% were pulmonary vs. 33% extrapulmonary TB. 127 (65%) were proven TB. 132 (52%) were HIV-positive. At follow-up, 115 patients were alive (45%), 91 died (36%) and 51 (19%) had another outcome. Mortality among HIV-positive patients was 73% vs. 12% among HIV-negatives. Of all death, 33% occurred before completion of treatment. High death rates were associated with HIV-positivity, absence of bacteriological confirmation, smear-negative and extra-pulmonary forms and male sex.

**Conclusion:** There is an urgent need for collaborative implementation of additional interventions, such as anti-retroviral therapy and co-trimoxazole prophylaxis, for TB-HIV co-infected patients.

#### PC-577-645 Under-diagnosis and reporting of human immunodeficiency virus (HIV) infection and tuberculosis (TB) in the United Kingdom (UK): a case for policy change

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HIV is the most powerful recognised risk factor for developing TB disease and is fuelling the epidemic in



high prevalence populations. Both infections are on the increase in the UK with over 7000 each of new TB infections and HIV diagnoses in 2002. One third of the estimated 50 000 people living with HIV in the UK remain undiagnosed. TB surpassed PCP as the most common initial AIDS defining illness in 2002, accounting for 31% (251/807) of AIDS cases, a rise from <5% (59/1577) in 1992. Heterosexual men and women were more likely to present with TB than men who have sex with men (4% cf 39% in 2002, OR = 16.1 (8.1–2.8)). Only 30% of AIDS cases with an initial TB diagnosis had been reported to the TB surveillance system on matching. Previous co-infection estimates of 3–10% among TB patients are likely to be under-estimates given matching limitations and evidence of under-reporting. TB is now a leading cause of HIV related morbidity. Early diagnosis of HIV and prompt reporting of TB is paramount in the control and prevention of these infections. Routine testing for HIV in patients diagnosed with TB is currently being considered in the UK.

**PC-612-677 Survival analysis of tuberculosis (TB) patients co-infected with human immunodeficiency virus (HIV) and the impact of highly active antiretroviral therapy (HAART) implementation at a University Hospital in Rio de Janeiro, Brazil**

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**Introduction:** The TB-HIV co-infection imposes a worse prognosis to both diseases. After introduction of HAART, the HIV infection evolution changed dramatically. However, the precisely impact of HAART in TB-HIV co-infection still demands cohort analysis. **Objective:** To evaluate short-term survival of active TB among HIV seropositive patients and its association with HAART implementation.

**Methods:** A retrospective cohort study from 1995 to 2000. Clinical charts were systematically reviewed. Kaplan-Meier curves and Cox models were used to determine short-term survival and risk factors associated with prolonged survival.

**Results:** 258 patients were analyzed. The multivariate analysis was adjusted for age, gender, CDC AIDS status, previous use of anti-retroviral therapy or HAART, pneumocystosis prophylaxis, T lymphocyte counts and time to begin HAART after TB diagnosis.

The use of HAART after TB diagnosis was associated with decreased risk of death (hazard ratio 0.13, 95% CI = 0.054–0.33) and early HAART implementation with higher survival (hazard ratio 0.92, 95% CI = 0.86–0.99; per week after TB diagnosis).

**Conclusions:** The implementation of HAART after TB diagnosis was a major factor in decreasing risk of death. The exact time to begin HAART in TB patient needs further studies, but our results suggested that early implementation could determine higher survival.

**PC-616-688 Rifampicin pharmacokinetics in AIDS and tuberculosis (TB) co-infected patients treated with ritonavir and saquinavir**

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To investigate the effects of concomitant use of ritonavir and saquinavir on the pharmacokinetics of rifampicin (R). Time-concentration curve of rifampicin at the steady state was determined after 4 weeks of antituberculosis therapy. Another pharmacokinetics profile of rifampicin was carried out after another 4 weeks with the simultaneous use of ritonavir/saquinavir (RS) therapy. Blood samples were collected before and one, two, three, four, five, six and eight hours after ingestion of fixed-dose isoniazid/rifampicin capsules (400/600 mg). Plasma was analyzed by a colorimetric method. The following pharmacokinetics parameters were evaluated: maximum plasma concentration ( $C_{max}$ ), time to reach  $C_{max}$  ( $T_{max}$ ), area under the concentration vs. time curve ( $AUC_{0-8}$ ) and extrapolated to infinity ( $AUC_{0-inf}$ ) and half-life. Twelve AIDS patients were included. The mean CD4 count was  $148 \pm 114$  cells/mm<sup>3</sup>. The combination of saquinavir/ritonavir and rifampicin was well tolerated and HIV viremia remained under control. The pharmacokinetic parameters of rifampicin are shown in the Table.

**Rifampicin pharmacokinetic parameters**

Parameter	Without RS	With RS
$AUC_{0-8}$ (μgh/ml)	57.608 ± 21.772	64.727 ± 22.027
$AUC_{0-inf}$ (μgh/ml)	78.167 ± 30.644	81.334 ± 34.312
$C_{max}$ (μg/ml)	12.895 ± 5.213	15.138 ± 4.714
$T_{max}$ (h)	2.750 ± 0.622	2.917 ± 0.793
Half-life (h)	3.597 ± 1.738	2.425 ± 0.952
Elimination rate (1/h)	0.225 ± 0.078	0.332 ± 0.134

RS = ritonavir/saquinavir. Mean ± standard deviation.

Our results demonstrated that the association of saquinavir/ritonavir did not interfere with the bioavailability of rifampicin.

### PC-633-705 Poor male involvement in HIV-TB DOTS prevention mother to child transmission programme in Enugu

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**Issues:** HIV and TB are trailed with so many misconceptions in the committees and as such reduce the effectiveness of outreach programmes.

**Description:** Park Lane Hospital is in a high density urban community in Enugu, Nigeria that offers PMTCT services. In 2002 September there was integration of TB Dots in the PMTCT programme do to high incidence of TB infection among the pregnant women. Activities was intensified about the integrated programmes to create awareness to the communities. A year after an outreach evaluation was done to assess the performance of out reach workers, community awareness of the services, identify gaps for improvement. Fifteen FGDs, one to one interviews was used.

**Lessons learnt:** Basic information on TB-HIV/STIs PMTCT existed in most of the groups, and stigmatization/discrimination are common. The older men had very little information about the issues. Poor male involvement brought about low male participation.

**Recommendation:** Continued education and support to the outreach workers enable deal with misconception in the communities. Identification of effective strategy to involve men in the HIV/TB PMTCT services, couple counselling as a key to achieving the above will booster attendance, adherence to ARV/TB DOTS, and partners treatment in STIs.

### PC-752-826 Using TB DOTS infrastructure and strategy to provide antiretroviral drugs in rural Cambodia

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**Objective:** To utilize a community-based DOTS program to deliver AIDS care with antiretrovirals in rural Cambodia.

**Methods:** A DOTS program run by a non-governmental organization, Cambodian Health Committee (CHC), providing home delivery of tuberculosis drugs (Home DOTS) and community education was used to expand care to individuals with AIDS. Beginning in 2004, all patients identified for TB treatment were offered HIV testing and counseling services by DOTS workers trained for this task. Immunosuppressed TB patients and others found to be HIV positive with a CD4 count less than 200/mm<sup>3</sup> were eligible for antiretrovirals. Treatment compliance strategies were adapted from TB drug adherence methods developed by CHC, including extensive education on HIV transmission, prevention, drug therapy and side effects, identifying a

patient supporter, demonstrating compliance with a vitamin regimen, signing a treatment contract and linkage of a microcredit program.

**Results:** Rapid clinical improvement and outstanding compliance were achieved in this pilot program. Outreach provided AIDS education and identified patients eligible for treatment.

**Conclusion:** Well-functioning TB programs and Home DOTS provide important infrastructure to support anti-retroviral delivery. Resource-poor areas should utilize these networks as antiretrovirals become available.

### PC-771-845 The Zambian National TB/HIV Survey

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**Introduction:** With plans for expansion of combined TB and HIV activities, it is important to have a baseline of TB and HIV services that are available in the country.  
**Objective:** To document TB and HIV activities in all 72 districts in Zambia

**Methods:** Questionnaires for district health managers and health facilities conducting TB and HIV activities were developed. Another questionnaire was developed for HIV support groups. Researchers visited every district and health facility conducting these activities in Zambia between January and April 2004. Data were collected on numbers accessing services, staffing, laboratory and drug supplies.

**Results:** Data were collected from 68/72 districts. To date 120 TB diagnostic centres, 110 VCT centres and 31 PMTCT facilities have been visited. TB management was generally found to be good with well-kept registers. VCT services are available in all districts except two but testing facilities are mostly based only in the district hospital. Standardised recording tools for VCT services are lacking. TB-HIV collaborative activities were only present in 2 districts at the time of the survey. HIV support groups are only available in a few districts.

**Conclusions:** Baseline data on TB and HIV services is vital to plan for expansion of TB-HIV collaborative activities.

### PC-833-904 'Satan now has two diseases—TB and HIV': old and new stigmas related to TB in Zambia

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**Background:** Causes and experiences of TB related stigma in high HIV prevalence countries need to be

understood and documented since stigma is increasingly becoming a barrier to effective TB management. **Methods:** Qualitative research, 2002, Zambia, in two high-density urban Lusaka compounds and a rural Chieftaincy, Southern Province. Participatory rapid appraisal methods (free-listing, picture discussions, timelines, 8 participatory workshops with children), 68 key informant interviews, 25 focus group discussions and longitudinal in-depth interviews with 13 TB affected urban households.

**Results:** Old TB stigma-related to dirty environments, certain occupations, 'stubborn' character, family disposition, social and sexual transgressions, and, fear of infection—has deepened and extended with HIV as TB is widely diagnosed as a sign of HIV. This multi-layered stigma means TB patients experience withdrawal and/or reduced care, isolation, public defamation and rejection. They may consequently avoid or hide diagnosis and treatment, feel ashamed and depressed. **Conclusions:** TB stigma has deepened and extended because of the HIV epidemic with serious public health consequences including delayed diagnosis, internalised stigma and perceptions that TB is incurable. Up-to-date community health and anti-stigma education is needed and should include supporting TB patients to better cope with stigma.

## CLINICAL RESEARCH AND SMEAR EXAMINATION

### PC-102-148 Blind rechecking of AFB smear examination in Cebu City

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**Introduction:** A feasibility study of the blind rechecking method for AFB microscopy, recommended in the APHL document, was made in Cebu City. The study was conducted at five (5) microscopy centers in 2003. **Method:** Lot Quality Assurance System was employed to determine sample size for rechecking. Zero acceptance error and 90% sensitivity were chosen as sampling condition. Sample slides were reread blindly. Besides the quality of smear preparation of the sample slides were assessed.

**Results:** 1) The new system reduced sample slides from 5188 (conventional method) to only 676 (new system). This reduction of workload of NTP coordinator and controllers left ample time for monitoring and corrective action for improvement of microscopy service. 2) 7 major errors were found in 1st to 3rd quarters and disappeared in the 4th quarter. This is

considered appropriate and timely corrective action. 3) Around 90% of sample slides were scored as good for the most of assessment points except evenness which were not satisfactory. Retraining on smear preparation particularly evenness was indicated.

**Conclusion:** New EQA was successfully introduced in NTP Cebu City and Philippines. National standard EQA manual has been developed based on the experience of these studies (Cebu Province and Cebu City).

### PC-125-159 An investigation on the quality control of slides by 'blind method' in some provinces

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**Introduction:** Since 1992, National Tuberculosis Programme has carried out the quality control of slide in several provinces in Vietnam. The method fulfilled by the provinces staff: read all positive (+) slides and 10% negative (−) ones which is monthly sent by district staff. In order to estimate the quality control of slides objectively, readers (province staff) need not know about the result readed in district laboratories. This will also examine the professional level of staff in district and provincial laboratories. The National Tuberculosis Programme started the quality control of slides by the 'blind method' on 1 January 2000.

**Objective:** 1) To investigate the quality control of slides by the 'blind method' in 21 province laboratories. 2) Advantages and difficulties.

#### Method:

- Object: 21 laboratories of 21 provinces in Vietnam.
- Reports on quality control of slides was carried out in the 3rd quarter 2000.
- Duration: October 2000–April 2001
- Control the total positive slides and 10% negative slides of the investigated provinces.
- Check the qualities of slides mixture, reading, storing area and period of storage (positive slides: 3 months, negative one: 1 month.)

**Result:** Among provinces investigated, there were 13 provinces used 'Blind Method': in 6804 positive slides there were 0.72% fault positive; in 7233 negative slides there were 0.29% fault negative. 8 provinces didn't used 'Blind Method'.

#### Conclusions:

- Documents and tables must be unified.
- Staff should be trained in the quality control of slides by 'blind method'.
- The negative slides need to be stored sufficiently in 1 month.

### PC-412-451 Feasibility of the 2002 guidelines for external quality assessment for smear microscopy. Experience from Kinshasa, DRC

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**Background:** Although smear microscopy is essential in TB diagnosis, external quality assessment (EQA) is often not prioritized in resource-poor countries.

**Objectives:** Determine feasibility of new smear microscopy EQA guidelines.

**Methods:** EQA was performed in 14 laboratories using the new 2002 guidelines. Activities included on-site evaluation by comprehensive checklist, blinded slide rechecking, and development of a quality improvement plan based on EQA results. Additionally, laboratory technicians received training.

**Results:** On-site evaluation was time consuming and identified similar problems in different laboratories: shortage of materials, absence of laboratory request forms, insufficient safety procedures, lack of supervisory visits feedback and incorrect smear microscopy procedures. Implementation of new slide storage procedures was more complex than anticipated. Slide rechecking at the national reference laboratory demonstrated discordance results in 6% of 438 slides. Recoloration identified another 2% discordances. All laboratories had false negative results, 4 had false positive results. Pre-training, technicians had good theoretical TB knowledge but scored poorly on smear preparation, staining and reading procedures. Scores improved dramatically (+26% average) following a 5-day training course.

**Conclusion:** EQA is essential in improving the quality of smear microscopy and should be linked to feedback, laboratory technicians training and a quality improvement budget.

### PC-734-810 Case finding of sputum smear positive patients in the general health care system (GHC) in Vladimir Region, Russia

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**Introduction:** DOTS was introduced in Vladimir Region in October 2000.

**Objectives:** To evaluate DOTS implementation.

**Methods:** Quarterly and monitoring missions reports.

**Results:** Before DOTS implementation sputum microscopy in GHC facilities was not performed routinely, laboratories lacked capacities; GHC staff did not

demonstrate adequate TB awareness. The programme provided regular trainings, supervision, monitoring, improved case management and strengthened the laboratory system. A system of smear microscopy TB detection in GHC was developed. Internal and external quality control of microscopy was introduced. Before implementation of the programme, microscopy of only one smear was done in more than 90% of referred cases. In 2003 microscopy of three smears was performed in 83% of cases. During 3 years of the programme unsatisfactory collection of sputum reduced from 25% to 8.5%, a number of laboratory mistakes decreased from 15% to 3%. A number of sputum smear (SS)+ cases detected in GHC increased from 0.05% to 70%. The proportion of SS+ pulmonary TB cases increased from 27.8% to 53%. DOTS activities improved detection of SS+ cases in GHC and shortened TB diagnosis time from 2–3 months to 2 days. The methods and results of the programme are recommended for dissemination.

### PC-759-833 Effectiveness of tuberculosis (TB) case detection by microscopy and X-ray methods

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**Background:** The DOTS program in the pilot regions, Dushanbe city and Rudaki rayon, of Tajikistan started in July 2002. These regions house 13% of Tajikistan's population.

**Objective:** To assess the economic effectiveness of microscopy and X-ray methods for pulmonary tuberculosis diagnostics in a retrospective study in Dushanbe.

**Methods:** We included 3802 patients with tuberculosis symptoms, who came to the medical institutes during the period from January till December 2003. They were diagnosed by sputum microscopy. During this same period 37 509 patients were screened for TB by X-ray method.

**Results:** 7.9% (301) of TB smear-positive cases were detected by microscopy method and 0.9% (320) TB cases were found out by X-ray method. Financial expenditures to identify one case detected by microscopy method were \$3.2, while the cost to identify one case detected by X-ray method was \$232.5.

**Conclusion:** Economic effectiveness of microscopy method of TB pulmonary cases showed to be significantly higher than of the X-ray method. However, further research is necessary in future to evaluate the effectiveness of X-ray diagnostic methods in the TB contact groups.

### PC-760-834 Determinants of the quality sputum collection for the diagnosis of tuberculosis in Lusaka

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**Background:** Lusaka district has the highest rate of TB notifications in Zambia (1210/100 000/year). Notifications show a high proportion of smear negative cases and needs further investigation.

**Objectives:** To determine factors associated with collection of quality sputum samples for diagnosis of TB.

**Methods:** Five diagnostic centers were selected. We assessed the perception of 385 TB suspects using a structured questionnaire. A checklist was used to observe laboratory procedures and interaction between patients and staff during consultation. Perception of health workers was assessed using focus group discussion.

**Results:** Median age was 32, 48% were women. 73% were requested to buy sputum container. The correct number of sputum samples was more likely to be collected if instructions were given by nurse compared to clinical officers. 54% of the patients felt that staff members were not helpful in giving them clear instructions. Of all sputum specimens, 44% were not checked for quality, and generally quality was not reported back to the patient.

**Conclusion:** Inadequate health service is given to TB suspects. Containers were not provided to patients and instructions on how to produce sputum were poorly given. Lab staff did not often examine the quality of sputum before performing AFB.

### PC-784-858 External proficiency testing in the SAARC regional network of TB reference laboratories

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**Introduction:** South Asian Association for Regional Cooperation (SAARC) Regional TB Reference Laboratory supports National TB Reference Laboratories by coordinating and conducting many laboratory activities to improve quality assurance. External Proficiency Testing is one of the three methods for quality assessment. It is one of the regional activities of SAARC TB Reference Laboratory.

**Objective:** To evaluate the performance of sputum microscopy in the TB Reference Laboratories in SAARC Region.

**Methods:** A panel of 10 slides stained with Ziehl-Neelsen was prepared and sent to nine National TB Reference Laboratories. Those laboratories were re-

quested to examine the panel of slides by Laboratory Technician. The reports were analyzed after receiving from all nine Reference Laboratories.

**Results:** All the laboratories had 100% consistency to negative and 3+ slides and 83.3%, 75% and 47.2% to 1+, 2+ and 1-9 AFB/100 visual fields, respectively. The result revealed that none of the National TB Reference Laboratories reported errors of any type.

**Conclusion:** It is concluded that the performance of the all the Reference Laboratories was excellent. The result also proved that SAARC Regional TB Reference Laboratory is capable to conduct such type of regional activities.

### PC-900-974 Assessment of the physical conditions and current laboratory practice of health care laboratories carrying out sputum smear microscopy in Northwest Ethiopia

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**Introduction:** Tuberculosis is one of the nosocomial infections. It was found that health care workers have two to ten times' higher risk of infection than that of the general public.

**Objective:** The main objective of the present study was to assess the physical conditions and current laboratory practice of health care laboratories carrying out sputum smear microscopy.

**Methods:** A cross-sectional study was conducted in Northwestern Ethiopia involving 15 health institutes in August 2003. A structured and pre-tested questionnaire was used to collect information on the physical conditions of the laboratories and on the current laboratory practice pertaining to handling sputum specimens.

**Results:** The entire laboratories had an area of less than 25m<sup>2</sup>. None of them had a separate room for sputum smear preparation. Any of these laboratories had no safety cabinet. Only 3 laboratories used face-masks and only 2 of them decontaminate sputum specimen prior to disposal. Incinerator as a means of sputum specimen disposal has been used in only 6 of them.

**Conclusion:** The physical conditions of the laboratories were found below the standard given by WHO/IUATLD recommendations. A large number of sputum specimens continue to be handled despite the poor conditions and procedures in all the health care laboratories. To minimize risk of infection, laboratory safety standards need to be improved.

## POSTER DISPLAY SESSIONS

### CLINICAL TRIALS AND DRUG DEVELOPMENT

#### PS-140-175 Possible causes of persisting cough

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**Objectives:** To reveal possible causes of persisting cough without any pathologic changes in chest X-ray.

**Techniques:** Clinical, laboratory, X-ray studies, polymeric chain reaction to reveal agents of TB, pertussis, mycoplasma infection in sputum or bronchial washing.

**Results:** 32 patients were examined, 19 male and 13 female from 12 to 50. In 4 cases pertussis causative agents was revealed. The course of the disease was atypical, cough was persistent without marked pathology in lungs and hemogram. In 5 patients TB agents were found. After fibrobronchoscopy and computed tomography TB endobronchitis was revealed in 2 cases; chest lymphatic nodes TB in 3 cases. Pneumonic mycoplasma was found in 4 patients. 9 patients had no these agents. Lung pathology was not observed and hemogram was normal. For these patients treatment with inhalant bronchodilator was effective.

**Conclusions:** Pneumonic mycoplasma was found to be the most frequent cause of persisting cough. Patients with persisting cough should be tested for pertussis and TB.

#### PS-149-183 Psychiatric peculiarities in patients with tuberculosis

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**Introduction:** Chemioresistant forms of tuberculosis limits possibilities of chemotherapy, and it makes doctors to look for alternative methods of treatment in order to increase natural resistance, formation of correct attitude of patients regarding their health condition and need of adequate treatment.

**Objectives:** The aim of our investigation was to study the spectrum of psychiatric disorders and attitude to sickness of newly revealed patients with tuberculosis.

**Methods:** Methods of investigation: clinical and psychopathological, psychological, statistical.

**Results:** Results of investigation: 46 newly revealed patients have been examined. The age of patients was at the range from 18 to 53 years old. All of those patients were with widely spread forms of lung tuberculosis. 43% consumed alcohol, 14% showed abnormal behaviour. Almost half of the patients were unemployed. 90% revealed various psychopathological syndromes. 80% of patients had affective and neurosis-like disorders.

Psychopathological alterations appeared mostly during the first 2–4 weeks after the diagnosis confirmation. Social status of the patients and their premorbid features of character played an important role in developing of the psychiatric disorders.

**Conclusion:** Psychiatric disorders unfavourably influenced the course of tuberculosis. Therefore, special rehabilitation programmes for such patients must be created and implemented.

#### PS-192-235 Thoracoplasty in the treatment of spread fibro-cavernous lung tuberculosis

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Thoracoplasty results at spread fibro-cavernous lung tuberculosis were studied in 43 patients aged 20 to 55 years. 25 of them were men, 18 were women. The patients suffered from TB during 2–5 and more years. The preceding continuous chemotherapy was ineffective. One-sided fibro-cavernous tuberculosis with focus dissemination into the opposite lung was diagnosed in 38 patients (88.4%), two sided fibro-cavernous tuberculosis in 5 (11.6%). All 43 patients had sputum smear positive, 18 of them (41.9%) had polyresistant forms. Pre-surgical treatment was done during 2–3 months and included intensive chemotherapy (HREZS) combined with pneumoperitoneum and general care treatment. Right-side operations were done in 15 patients (34.9%), left-side in 28 (65.1%). Upper back-side 6-rib thoracoplasty was conducted in 40 patients (93.0%), 7–8 rib thoracoplasty in 3 (7.0%). After the operation two of the patients (4.6%) had developed pleural empyema, which was healed by therapeutical treatment. Good results were observed in all 43 operated patients. In 2–5 years after the operation 4 patients (9.3%) had developed TB relapses on the operated side. Clinical recovery was observed in 39 patients (90.7%).

**Conclusion:** Upper-back sidethoracoplasty is an effective and safe method of surgical treatment at spread fibro-cavernous lung tuberculosis, and in 90.7% of the time provides full clinical recovery.

#### PS-227-260 Tonsillar tuberculosis associated with pulmonary foci

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Tonsillar tuberculosis is one of the uncommon forms of extrapulmonary tuberculosis. We report a case of tonsillar tuberculosis associated with pulmonary lesions. A 48-year-old male was admitted for evaluation of hoarseness, difficulty in swallowing, weight loss, cough and fever. On admission his posterior pharynx was erythematous and the tonsils were ulcer-

ated and covered by whitish exudation. Chest X ray showed several cavities, and numerous acid-fast bacilli were found in the sputum smear. Culture of the sputum was positive. Clinical and histopathological investigation demonstrated granulomatous inflammation with necrosis containing acid-fast rods in the tissue specimens. Since a histological study revealed tonsillar tuberculosis, anti-tuberculosis agents were administered. He was placed on a fifth antituberculous drug for 3 months daily, followed by a treatment with three drugs for another 9 months. After treatment the pulmonary lesions were improved, and his symptoms were relieved. The present case provides evidence that pharyngeal tuberculosis may represent the first manifestation of tuberculosis. The possibility of tonsillar tuberculosis should be considered when unexplained enlarged tonsils are observed in patients with pulmonary tuberculosis.

#### **PS-231-269 Intestinal tuberculosis with abdominal complications: radiologic and pathologic features**

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**Background:** The aim of this study was to investigate radiological and pathologic features of intestinal tuberculosis with abdominal complications.

**Methods:** 50 patients with 30 surgically complications (15 intestinal obstruction, 10 perforation, 3 fistulae, and 2 intestinal bleeds) were analysed. We have utilized abdominal ultrasonography, radiological examinations, barium studies, and computed tomography.

**Results:** Intestinal obstruction was the most important single feature (in 80% of cases). The primary cause of obstruction was bowel adhesion. In ten patients with intestinal perforation, both obstruction and ulcerations were the most important features in eight, and multiple ulcerations in two patients. In three patients with fistulae, the common features were focal or multiple strictures, and fibrotic bowel wall. In 45.45% of cases the abdominal complications occurred during anti-tuberculosis therapy.

**Conclusion:** The understanding of the radiologic and pathologic features of intestinal tuberculosis with complications helps in making an appropriate clinical decision for the treatment strategy. CT has an inherent limitation for demonstrating the mucosal abnormalities such as ulceration. Close observation is necessary, especially in those patients who are acutely ill during anti-tuberculosis treatment.

#### **PS-346-371 Success of DOTS implementation in Bosnia and Herzegovina between 1996 and 2003**

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**Introduction:** During the Bosnia defensive war (1994), the DOTS strategy was introduced and National TB Programme (NTP) started in Bosnia-Herzegovina (BH) is currently being considered as a country implementing the DOTS strategy now in 100% of the total population.

**Aim:** To show that implementation of DOTS strategy and the NTP have reduced TB incidence in post war period in BH.

**Methods and Results:** The DOTS strategy and the NTP were ascertained using the treatment efficacy indicator: cure rate, completed treatment rate, treatment failure rate, death rate, treatment interruption rate, rate of transfer out. In the time between 1996 and 2003, the cure rate for initial phase of treatment ranged from 95.4% to 97.8% for rate from 93.3% to 96.5%.

**Conclusion:** The NTP and DOTS strategy rate of all TB cases, notification and decreased the incidence rate of all TB cases.

#### **PS-387-411 Evaluation des connaissances et attitudes des médecins du CHU de Cocody en matière de tuberculose**

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Il s'agit d'une étude prospective qui avait pour but de guider le comité national de lutte contre la tuberculose dans les actions d'information et de sensibilisation à mener auprès des médecins. Pour cela nous avons évalué les connaissances et attitudes en matière de tuberculose des médecins de CHU de Cocody. Au total, 170 médecins ont participé à l'enquête. Les résultats sont les suivants : Les médecins ont des connaissances adéquates sur la prise en charge des malades tuberculeux ; cependant des lacunes existent. Au plan clinique, la toux est considérée comme étant un signe d'imprégnation par 73,53% des enquêtés. Au plan paraclinique, Le diagnostic de certitude de la tuberculose pulmonaire repose sur la radiographie pulmonaire selon 36,48% des médecins. Le prix de l'examen des crachats est inconnu par 87,65% des médecins. Au plan thérapeutique, environ 32% des médecins ne connaissent pas les molécules du PNLTCI. Les médecins, soient 67,05% ne connaissent pas les antituberculeux responsables de l'ictère. Les conseils à donner au tuberculeux sont inconnus par 81,18% des médecins prenant en charge des tuberculeux. La périodicité à laquelle il faut faire le contrôle bactéri-

ologique des crachats est ignoré par 89,41% des médecins. Devant une tuberculose, 82,36% des médecins font des transferts dont 59% à cause du risque de contamination. Plus de 90% des médecins souhaiteraient avoir une formation sur la tuberculose.

#### PS-385-412 Caractéristiques de 332 cas de tuberculose pulmonaire à microscopie négative

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**Introduction :** Les difficultés diagnostiques et de monitoring liées à la tuberculose à microscopie négative [TPM (-)] sont nombreuses. Sous l'infection par le VIH, la TPM (-) réalise une situation préoccupante.

**Objectifs :** Nous avons voulu déterminer la prévalence et les caractéristiques de cette entité au niveau du Service de Pneumologie de Cocody et au niveau du Centre Anti-tuberculeux (CAT) d'Adjamé, deux centres de référence du programme national antituberculeux.

**Méthode :** Il s'agissait d'une étude rétrospective qui a permis de colliger 332 cas de TMP (-) au niveau de ces deux centres.

**Résultats :** Nous avons enregistré une prévalence de 12,65% pour le PPH de Cocody et 11,52% pour le CAT. Les sujets de 20 à 40 ans constituaient 71,1% de l'effectif. La co-infection TPM (-) – VIH a été estimée à 62,10%. Les signes fonctionnels étaient la toux chronique (83,1%), la douleur thoracique (79,8%), les expectorations (68,4%) et la dyspnée (17,2%). Les signes généraux étaient dominés par l'amaigrissement (73,8%). Le syndrome de condensation pulmonaire a été mis en évidence chez 5,1% des patients. A la radiographie pulmonaire, il s'agissait d'images alvéolo-interstitielles dans 80,4% des cas. Le régime de 6 mois (isoniazide, rifampicine, pyrazinamide) a été administré chez 99% des malades. Il a été enregistré 48,2% d'évolution favorable, 1,2% de décès, 26,5% de perdus de vue et 17,2% des patients transférés.

**Conclusion :** L'absence de diagnostic de certitude de la tuberculose est sans doute à l'origine de diagnostic par excès de cas de tuberculose avec pour corollaire un faible taux succès thérapeutique.

#### PS-367-446 Factors affecting conversion period of sputum examination in pulmonary tuberculosis cases

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In our study we included 72 patients who were hospitalized in our clinic in 2003. All of them were male. Their mean age was  $37.28 \pm 14.04$  (18.77). They were all smear positive pulmonary tuberculosis cases.

All of the patients received standard antituberculosis therapy. Initially we investigated the conversion period of smear and the factors affecting it. The demographic features of the patients and the conversion period of smear are shown in Table 1. The mean smear conversion period was  $25.60 \pm 15.08$  days. Use of alcohol and smoking, concomitant diseases, age and presence of disease with cavities were not found effective over the period of smear conversion ( $P > 0.05$ ). Having no previous treatment and having minimal infiltration on CXR reduced the period of smear conversion. This finding was statistically significant ( $P < 0.05$ ).

Demographic features of patients and smear conversion period

	Demographic features		Smear conversion period	
Cases	New	53	$22.94 \pm 13.93$	$P < 0.05^*$
	Old	19	$33.00 \pm 16.08$	
Smoking	Use	61	$26.28 \pm 15.76$	$P > 0.05$
	Not	11	$21.82 \pm 10.35$	
Alcohol	Use	9	$33.44 \pm 15.84$	$P > 0.05$
	Not	62	$24.39 \pm 14.87$	
Concomitant diseases	Present	11	$30.36 \pm 22.21$	$P > 0.05$
	Absent	61	$24.74 \pm 12.49$	
Age	Young	43	$23.95 \pm 12.25$	$P > 0.05$
	Old	29	$28.03 \pm 18.48$	
CXR	Minimal	15	$17.33 \pm 9.96$	$P < 0.05^*$
	Extensive	57	$27.77 \pm 15.51$	

\* Significant.

#### PS-423-461 Development of a research center for tuberculosis clinical trials through the conduct of a Phase II study of moxifloxacin in the initial phase of tuberculosis treatment

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The capacity to conduct randomized clinical trials (RCTs), especially in countries where tuberculosis (TB) remains epidemic, needs to be enhanced. Russia, having trained personnel and large numbers of TB patients, is uniquely suited for such trials. A Biotechnology Engagement Program project has been developed by scientists from RIPP, SRCAM, and CDC. The goal of the project is to develop the capacity to conduct RCTs of new drugs and regimens for TB treatment in Russia. The specific aims of the project are to: 1) build the laboratory, clinical, and information technology infrastructure required for RCTs at RIPP; 2) enhance laboratory capacity at SRCAM for mycobacteriology in support of RCTs; 3) provide data management,



statistical, and laboratory training for the conduct of RCTs; 4) design and conduct a RCT of a TB treatment regimen that includes moxifloxacin in the initial two-month phase of TB treatment; and 5) provide data for registration of a new drug susceptibility test kit developed at SRCAM. A moxifloxacin-containing regimen was chosen because of recent studies in a murine model of TB that suggest that the drug has potent sterilizing activity and may permit significant shortening of treatment for both active TB and LTBI.

#### PS-621-699 Effect of serum cholesterol and albumin levels on radiologic and bacteriologic features of tuberculosis patients

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**Objectives:** To evaluate effect of serum cholesterol (C), albumin (A) levels on radiological and bacteriological features of pulmonary tuberculosis (TB).

**Methods:** Records of 221 TB cases hospitalised between January 2003 and January 2004 were reviewed. They were divided according to the radiological extent of the disease (minimal, moderate, advanced) and pathological lesions (cavitary, parenchymal, pleural effusion). Serum cholesterol and albumin levels and sputum smear positivity were compared accordingly.

**Results:** There were no statistical difference in mean C and A levels between the groups ( $P > 0.05$ ). There were a high statistical relationship between smear positivity and pathological lesions ( $P < 0.01$ ). Smear positivity was higher in cavitary lesions than parenchymal lesions (88.8%, 68.0% respectively). Eventhough C levels were not statistically different according to the extent of disease in cavitary lesions ( $P > 0.05$ ), in cases with parenchymal lesions C levels were statistically higher in minimal group ( $P < 0.05$ ). A levels of radiologically advanced cases were statistically lower than minimal and moderate groups in both cavitary and parenchymal lesions ( $P < 0.05$ ). In cases with cavitary lesions C level of smear (–) cases were statistically lower than (+) ones. By contrast, in cases with parenchymal lesions smear (–) cases, C levels were statistically higher than (+) cases ( $P < 0.05$ ). There was no statistical difference between A levels and smear positivity.

**Conclusion:** Serum cholesterol and albumin levels are related with the radiological and bacteriological status of pulmonary tuberculosis.

#### PS-751-825 Haemetogenous dissemination of *Mycobacterium tuberculosis* in patients with tuberculous lymphadenitis

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**Aim:** Tuberculous lymphadenitis affects mainly cervical lymph-nodes. The port of entry and the mode of dissemination of the organism are not well understood. Bacteremia due to *M. tuberculosis* was reported in immuno-compromised as well as in immuno-competent patients with pulmonary disease. Our aim is to determine whether *M. tuberculosis* spreads through the blood to different lymph node groups in patients with tuberculous lymphadenitis.

**Methods:** Blood samples from 39 patients with FNA cytodignosis of tuberculous lymphadenitis were tested for mycobacterial DNA by PCR using an oligonucleotide primer that amplifies a 123 pb sequence conserved in all Mycobacteria species. Blood samples from 9 and 4 cases with reactive and malignant lymphadenitis, respectively, served as negative controls. The presence of mycobacterial DNA was correlated to the number of lymph nodes involved and the cytomorphological pattern of tuberculous lymphadenitis. Clinical examination, chest X-ray and HIV ELIA-serology were performed as routine clinic producers for all patients.

**Result:** None of the patients were positive for HIV or had clinical radiological evidence of pulmonary tuberculosis. Mycobacterial DNA was detected in the blood samples of 30/39 (77%) patients with tuberculous lymphadenitis, but in none of the cases with reactive or malignant lymphadenopathy. The presence of mycobacterial DNA correlated strongly to multiple lymph node involvement and to granulomatous-necrotizing and necrotizing cytomorphological patterns.

**Conclusion:** The blood stream is the most probable route by which mycobacteria dissemination from one group to another in patients with tuberculous lymph nodes.

**PS-763-837 Transfrontier' demonstration of bioequivalence in a Pakistani product (Rifa 4+) containing rifampicin, isoniazid, pyrazinamide and ethambutol in combination**

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**Introduction:** The importance establishing the in vivo bioavailability of rifampicin-containing products is recognized internationally, most especially when they are formulated in combination with other drugs. However infrastructural and financial constraints often limit such testing. A capacity building project is described, in which costs were reduced whilst maintaining confidence in the quality of the data.

**Aims:** To conduct bioequivalence testing of a 4-drug FDC, Rifa 4+ (Schazoo Laboratories (Pvt), Ltd, Lahore), in a collaborative project between Pakistani and South African institutions.

**Methods:** Internationally accepted methods of bioequivalence testing were used to establish the in vivo quality of Rifa 4+; the clinical aspects of the study were performed in Lahore and the plasma samples were stored and transported in dry ice to Cape Town where the drug concentrations were determined by validated HPLC and LC-MS methods an accredited laboratory recognized for this purpose.

**Results:** The study was successfully conducted and Rifa 4+ was bioequivalent for all 4 drugs.

**Conclusions:** The product was tested amongst healthy volunteers from a local population, costs were limited, and the capacity of a site in Lahore, Pakistan, was developed to conduct bioequivalence testing according to international standards of GCP.

**PS-862-935 *Mycobacterium W* as an adjuvant to chemotherapy in management of pulmonary tuberculosis**

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**Objectives:** A placebo controlled randomized single blind study was carried out to evaluate the role of *Mycobacterium W*. (MW) as an adjuvant to DOTS therapy in management of pulmonary tuberculosis (100 category I, 100 category II).

**Methods:** MW or saline as an adjuvant was given 0.1 ml intradermally on 0, 15, 30, 60 days and every 2nd month till the end of therapy. The patients were evaluated at 0, 15, 30, 60, 120 days and at the end.

**Results:** Sputum conversion was 97% at 15 & 30 days and 100% at 2 months in MW group compared

42%, 75% & 90% in control in category I. In category II it was 41%, 60%, 62%, 71% and 75% at ½, one, two, four and eight months in MW group compared 17%, 29%, 39%, 48% & 50% in control group respectively.

**Conclusion:** Addition of MW propped sputum conversion at least by 45 days. It was associated with improved weight gain, clinical improvement and radiological resolution. The cure rate improved by 25% in category II patients.

**PS-195-238 Impact of immobilization stress on experimental TB development in vivo**

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Stress is one of the provocative moments in TB development. But mechanism of its impact remains unknown in some aspects. Target of this study was to investigate the influence of different stages of the stressogenic response on the development and course of the tuberculosis infection in vivo. Experience was carried out on 72 guinea pigs. To obtain the immobilization stress animals were placed into cages like pencil cases for 3 days (alert stage), for 5 days (adaptation stage) and for 12 days (stage depletion). In each stage there were infected by 9 guinea pigs with 0.1 mg of the culture H37RV. In a month after beginning of the experience survival animals were slaughtered and index of lung injury was evaluated. It was proved that inoculation to animals of *M. tuberculosis* led to the dissimilar development of TB inflammation. The most expressed development of TB inflammation in lungs was marked among animals infected in the alert stage and depletion stage, that is  $2.44 \pm 0.53$  and  $2.78 \pm 0.63$  accordingly, and minimal one in the adaptation stage  $2.33 \pm 0.50$ . Thus, stressogenic changes of the organism resistance greatly impact on TB inflammation development. Infection with TB in the stages of alert and depletion differs by its prognostic unfavorability.

**PS-485-527 Minimum sample size and sampling time requirements for assessment of rifampicin bioequivalence from fixed-dose combination formulations**

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WHO and IUATLD have recommended use of Fixed-dose Combination (FDC) formulations with proven rifampicin bioavailability and have developed a simplified protocol to evaluate the same. In order to harmonize the requirements for bioequivalence of rifampicin, studies were conducted that fulfill the criteria of WHO

and Indian regulatory protocols. Retrospective pharmacokinetic evaluation of earlier conducted studies were done and power of the test and bioequivalence limits were calculated using 8–22 volunteers and sampling points of 8–24 h. In this paper pharmacokinetic and statistical evaluation from three representative studies showing low (15%), moderate (18%) and high variability (23%) in rifampicin absorption is given with the objective to determine minimum requirements for rifampicin bioequivalence based on variability in absorption. It was found that irrespective of variability in absorption, sampling schedule up to 8 h was sufficient to compare the absorption process of rifampicin. Whereas for sample size requirements, there was no influence of reduced sample size on bioequivalence estimates of rifampicin from the trials that showed low or moderate variability with power of the test above 90%. However, in study showing higher variation, sample size of 14–16 subjects was found to be optimum. Thus, there exists a possibility of reducing the sample size requirement for determination of rifampicin bioequivalence from FDCs compared to standard separate formulations using WHO protocol.

**PS-586-657 The novel nucleoside antibiotic caprazamycin B and its derivatives aiming a new anti-TB drug. [Part 1] In vitro antimycobacterial activity of caprazamycin B**

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**Introduction:** A series of novel nucleoside antibiotics caprazamycins (CPZs) have been discovered from the culture broth of *Streptomyces* sp. MK730-62F2. CPZs are considered to be inhibitors of phospho-N-acetylmuramyl-pentapeptide translocase (MraY) in the biosynthesis of the bacterial cell wall.

**Objectives:** Development of a new anti-TB drug having a novel chemical structure with a new mode of action and a selective narrow-range antimicrobial spectrum against mycobacteria.

**Methods:** By using agar dilution method, in vitro activity of the major compound CPZ-B was evaluated against *M. tuberculosis* isolates, various nontuberculous mycobacteria and enteric anaerobes.

**Results:** MIC90s of the CPZ-B were as follows: drug-susceptible *M. tuberculosis* ( $n = 21$ ) 12.5; MDR *M. tuberculosis* ( $n = 12$ ) 12.5; *M. avium* (serovar-4 and serovar-8;  $n = 33$ ) 25.0; *M. intracellulare* (serovar-16;  $n = 17$ ) 25.0; *M. kansasii* ( $n = 20$ ) 3.13; *M. fortuitum* ( $n = 10$ ) 25.0; *M. abscessus* ( $n = 10$ ) >100 µg/ml, respectively. CPZ-B exhibited equivalent MIC90 value (25.0 µg/ml) to that of clarithromycin against

*M. avium* and *M. intracellulare*. CPZ-B demonstrated milder action than rifampicin and clarithromycin against 22 species of predominant anaerobes of the enteric normal flora in humans.

**Conclusions:** 1) CPZ-B did not show any cross-resistance with the current anti-TB drugs. 2) CPZ-B proved to be effective against both drug-susceptible and MDR *M. tuberculosis* isolates.

**PS-591-661 The novel nucleoside antibiotic caprazamycin B and its derivatives aiming a new anti-TB drug. [Part 2] In vivo antimycobacterial activity of caprazamycin B**

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**Introduction:** We tried different routes of administration of caprazamycin B (CPZ-B) in mice and it was found that the intratracheal route of injection give good absorption and the most long-lasting retention time in lung tissue.

**Objective:** Evaluation of the therapeutic efficacy and cytotoxicity of CPZ-B in murine TB model.

**Methods:** Numbers of cfu and histopathological features in organs were investigated after a short-course treatment with CPZ-B against the murine TB model, infected intratracheally with 106 cfu/mouse of *M. tuberculosis* H37Rv.

**Results:** Twelve-day intranasal administration of CPZ-B with dose sizes of 0.5, 1.5 and 5.0 mg/kg/day in a volume of 25 µl/mouse/day starting from the 7th day post infection, gave an excellent therapeutic efficacy in lung and spleen, dose-dependently. In the treated mice, any significant cytotoxicity was not observed in the tissue sections histopathologically; in lung, spleen, liver and cervical lymph nodes. In uninfected mice, CPZ-B did not demonstrate any significant toxicity in tests with a single (>200 mg/kg, intravenous) and repeated (100 mg/kg/14days) doses, as well as in genotoxicity and cytotoxicity tests (5000 µg/ml).

**Conclusion:** A short-course intranasal CPZ-B treatment with small dose sizes gave an excellent therapeutic efficacy in lung of mice, dose-dependently.

**PS-594-668 The novel nucleoside antibiotic caprazamycin B and its derivatization aiming a new anti-TB drug. [Part 3] Synthesis of caprazene derivatives and their anti-*Mycobacterium tuberculosis* activity**

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**Introduction:** Treatment of the whole mixture of caprazamycins (CPZs) in an acidic solution gave a core structure caprazene (CPZEN) in a high yield.

**Objective:** To study structure-activity relationships of CPZEN derivatives against mycobacteria.

**Methods:** MICs for the 122 CPZEN derivatives against *M. tuberculosis* ( $n = 21$ ), *Staphylococcus aureus* 209P, *M. avium* and *M. intracellulare* ( $n = 25$ ) were determined by using agar dilution method.

**Results:** CPZEN showed no anti-*M. tuberculosis* activity, but out of 122 its derivatives, four of them exhibited more selective anti-*M. tuberculosis* activity than that of caprazamycin B (CPZ-B). For example, MIC<sub>90s</sub> (range) for CPZEN-3, CPZEN-10, CPZEN-45, CPZEN and caprazamycin B (CPZ-B) against 21 clinical isolates of *M. tuberculosis* were 6.25 (1.56–12.5), 3.13 (0.78–3.13), 6.25 (0.78–12.5), >100 (100–>100) and 12.5 µg/ml (3.13–12.5 µg/ml), respectively. On the other hand, MICs for CPZEN-3, CPZEN-10, CPZEN-45, CPZEN and CPZ-B against *S. aureus* 209P were >100, 6.25, 12.5, >100 and 0.78 µg/ml, respectively. Moreover, out of 122 CPZEN derivatives, three of them showed more potential anti-*M. avium* and *M. intracellulare* activity than those of CPZ-B. CPZEN-45 demonstrated better therapeutic efficacy in lung than that of CPZ-B against the pulmonary TB model induced in mice.

**Conclusions:** Some CPZEN derivatives were promising compounds as anti-mycobacterial drugs.

**PS-594-671 The novel nucleoside antibiotic caprazamycin B and its derivatization aiming a new anti-TB drug. [Part 4] Synthesis of caprazol derivatives and their anti-*Mycobacterium tuberculosis* activity**

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**Introduction:** Treatment of the whole mixture of caprazamycins (CPZs) in a basic solution gave a core structure caprazene (CPZOL) in a high yield.

**Objective:** To study structure-activity relationships of CPZOL derivatives against mycobacteria.

**Methods:** Screening of MICs for 22 CPZOL derivatives against *M. tuberculosis* ( $n = 21$ ) and *Staphylococcus aureus* 209P by using agar dilution method.

**Results:** CPZOL showed no anti-*M. tuberculosis* activity, but out of 22 its derivatives, some of them exhibited anti-*M. tuberculosis* activity as strong as that of caprazamycin B (CPZ-B). For example, MIC<sub>90s</sub> (range) for CPZOL-7, CPZOL-19, CPZOL and CPZ-B against 21 clinical isolates of *M. tuberculosis* were 3.13 (0.78–3.13), 25 (6.25–50), 100 (50–100) and 3.13 µg/ml (0.78–3.13 µg/ml), respectively. On the other hand, MICs for CPZOL-7, CPZOL-19, CPZOL and CPZ-B against *Staphylococcus aureus* 209P were 0.78, 12.5, >100 and 0.78 µg/ml, respectively.

**Conclusion:** CPZOL, a core structure of CPZs, proved to be a good precursor of anti-TB antibiotics.

**PS-912-987 Tuberculosis detection in the South Region of Kazakhstan**

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South Region of Kazakhstan is one of those with dense population (2094.6 million as of 01.01.03). Epidemiological TB situation remains complicated as all over the country. However, it should be noted the positive trends in TB profile since DOTS implementation, i.e. in 2002 TB incidence increased: in 2001 it was 113.3 per 100 000, in 2002 123.3; in 2003 firstly the decrease of this index was registered to be 117.3. TB mortality index decreased: in 2001 to 15.2 per 100 000, in 2002 to 14.5, in 2003 to 13.5. TB detection is realized by 2 methods: 1) sputum smear bacterioscopy: i.e. in 2003 there were examined 7124 persons, while *M. tuberculosis* was isolated among 56 (0.7%), in the anti-TB service these figures constituted accordingly 9523 and 1783 (18.7%). Thus, effectiveness of TB detection is higher than that in PHC network. In 2003 frequency of drug resistance constituted 54.1%, while one of MDR-TB 24.4%. 2) Through roentgenofluorographic method there were detected 1007 patients with suspicion to TB, i.e. 1.7 per 1000 of examined persons. Among newly detected in 2003 (2466) 2340 (94.9%) were with pulmonary TB, with extrapulmonary TB in 126 (5.1%). Bacteria excretion was present in 100 detected patients with destruction. Percentage of the destructive TB forms among new cases was 49.8. Thus, these facts prove rather tense epidemiological situation on TB.

### PS-830-900 Additional yield of positivity in two sputum samples for follow up examination in the Revised National TB Control Programme (RNTCP) India

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**Introduction:** Two sputum specimens (early morning & spot) are collected for follow up to ensure that positive results are not missed (RNTCP guideline-India). This study was conducted in Anantapur district, India to determine the usefulness of this system.

**Objective:** To determine magnitude of additional yield of sputum positivity by sputum microscopy of second sample of follow-up sputum examination in RNTCP.

**Methodology:** Follow-up sputum microscopy was done at the end of Intensive Phase, at end of prolongation of Intensive Phase, end of second month of Continuation Phase and at the end of Continuation Phase. All these results were considered for this study for new sputum positive Pulmonary TB patients registered during the year 2002.

**Results:** There were 5086 follow up sputum examinations were done for new pulmonary sputum positives registered during the year 2002. Among these 416 (8.9%) was positive in first (early morning) sample. Only 6.1% was positive in second (spot) sample. None of the sputum negatives in first sample revealed positivity in the second sample.

**Conclusion:** Examination of second (spot) sample of sputum for follow up does not yield additional positive results and hence is not useful.

## DRUG RESISTANCE/MDR-TB MANAGEMENT-1

### PS-115-154 The character of drug resistance in Armenia

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**Introduction:** Drug resistance and particularly MDR is an increasing problem worldwide.

**Objective:** This study is aimed to reveal the character of drug resistance in new patients and previously treated patients.

**Method:** Clinical and microbiological findings from 71 patients with various types of drug resistance.

**Results:** Among new cases (70% of all patients) prevailed patients aged from 15 to 24 (52%). Streptomycin

resistance was 62%, MDR was detected in 8% of the cases and resistance to all drugs (HRSE) in 8% of the cases. Infiltrative form was the most common type of TB (72%) among new cases. In retreated patients (30% of all cases) prevailed patients aged from 44 to 54 (49%). Streptomycin resistance was 18%. MDR was detected in 35% of the cases and resistance to all drugs in 39% of the cases. Retreated patients clinically characterized by the prevalence of fibro-cavernous tuberculosis (88%). In both new and retreated patients, males prevailed.

**Conclusion:** Based on this study high prevalence of primary MDR is probably due to free and uncontrollable marketing of anti-TB drugs in pharmacy network and use of rifampicin for nonspecific diseases.

### PS-244-274 Drug monitoring and multiple drug resistance

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**Introduction:** Isoniazid (INH) and rifampicin (RIF) were re-evaluated for the treatment of multidrug-resistant (MDR) cases from the viewpoint of drug monitoring.

**Objectives:** To evaluate the possibility of INH/RIF use to some of the MDR cases.

**Methods:** The drug monitoring system has been established using high-performance liquid chromatography. The plasma specimens were collected from the tuberculosis patients at particular time intervals. The minimum inhibitory concentrations (MICs) of INH and RIF against the MDR *M. tuberculosis* were measured. The pharmacokinetic factors and MICs were evaluated for the possibility of administration of INH and RIF to MDR cases.

**Results:** Preliminary, 10 patients and 6 strains of *M. tuberculosis* were examined. The average C<sub>max</sub> of INH and RIF were  $1.30 \pm 0.49$  and  $4.68 \pm 0.7$  µg/ml, respectively. The MICs of INH ranged from 2.0 to 32.0 µg/ml and that of RIF were over 32.0 µg/ml.

**Conclusion:** It seemed to be difficult to utilise INH and RIF to MDR cases, evaluating preliminary cases. However, the pharmacokinetic factors implied that especially the cases with INH 0.2 µg/ml resistant and 1.0 µg/ml susceptible could be treated with the intermittent administration of 15 mg/kg of INH.

### PS-307-337 Results of treatment by second-line anti-TB drugs of patients with drug-resistant tuberculosis

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We analyzed results of standard treatment by anti-TB drugs of the second-line in 101 patients with drug-resistant tuberculosis hospitalized at the AntiTB clinic Aktau city. Among all cases in sputum tuberculosis have been found out by microscopy and culture methods. In the structure of clinical forms there were: infiltrative pulmonary TB in 80 (79.2%) cases, fibrocavernous pulmonary TB in 21 (20.8%). In 19 (18.8%) cases there were marked the following complications: in 10 cases lung bleeding and hemoptysis, in 9 cases cardio-respiratory insufficiency. The intolerance to anti-TB drugs and drugs cancellation was marked at 5 (4.9%) patients. From all surveyed persons drug resistance was determined at all patients: to HRSE in 95 cases, HRS in 4 cases, HRE in 2 cases. All patients were treated by standard regimens of chemotherapy DOTS+. After intensive phase for 3–4 months of treatment positive sputum conversion was marked at 80 (79.2%) patients. Full standard course of treatment sputum ended conversion was marked in 99 (98.0%) patients. Thus, it should be noted, that treatment of patients by anti-TB drugs of the second-line in the regional anti-TB clinics is effective and economically reasonable.

### PS-320-352 Clinical outcomes of MDR-TB patients with diabetes mellitus in Lima, Peru: a retrospective record review

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Tuberculosis (TB) and diabetes mellitus (DM) are often comorbid conditions. Numerous studies report an increased prevalence of TB among diabetics and patients with DM and TB have unique clinical issues that need to be addressed when managing both diseases. Little has been reported about patients with MDR-TB and DM. A retrospective record review was done to determine clinical outcomes of MDR-TB therapy among 32 patients with DM receiving individualized therapy as part of a larger cohort of patients in Lima, Peru. Mean age of these patients was 54.0 years and 59.4% were male. Patients were in treatment for a mean of 16.1 months. Patients were resistant to a mean of 5.2 drugs. Baseline chest radiographs were available for 29 of the 32 patients. A majority (75.9%) of patients showed bilateral disease; 10.7% developed renal failure. Clinical outcomes demonstrated the following: 15.5% cured; 43.8% in

treatment and culture negative; 18.8% died; 18.8% in treatment and culture positive; 3.1% abandoned. This study suggests poorer clinical outcomes in patients with DM and MDR-TB and factors responsible for these poor outcomes will be explored.

### PS-325-355 Treatment of multidrug-resistant pulmonary tuberculosis with interferon-gamma subcutaneous injection

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**Introduction:** The main potential use of interferon- $\gamma$  for patients with MDR-TB is its role in activation of macrophages to function as effective phagocytic cells. Interferon- $\gamma$  stimulates reactive nitrogen species production, probably via nitric oxide synthase pathways, and evidence shows that these pathways are critical to killing and growth inhibition of mycobacteria by macrophages.

**Objectives:** We designed a protocol to investigate the effects of interferon- $\gamma$  in the treatment of chronic, advanced MDR-TB cases who had failed in conversion with long period of chemotherapy.

**Methods:** Eight chronic MDR-TB patients were enrolled to this study. All patients were scheduled to receive recombinant human IFN- $\gamma$  (LG PhD, Seoul, Korea) in a subcutaneous dose of 2 000 000 IU three times weekly for 24 weeks—a total 72 doses for each patient.

**Results:** Adverse effects were consisted of muscle aches ( $n = 5$ ), fever ( $n = 5$ ), headache ( $n = 6$ ), nausea ( $n = 2$ ), and vomiting ( $n = 1$ ). Sputum cultures remained positive for all patients throughout the study period. CT scans done at entry were compared with scans done after completion of treatment. There was no scan interpreted by the radiologist as improved. On the contrary patient 2 showed aggravation including cavity formation and surrounding infiltrative lesion.

**Conclusion:** We have now presented preliminary evidence of no improvement with long-term use of IFN- $\gamma$  in a group of patients with chronic MDR-TB patients.

### PS-362-388 Identifying a subset of MDR-TB patients with bilateral pulmonary disease suitable for adjunctive thoracic surgery

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**Objectives:** To identify characteristics associated with favorable treatment response among patients with bilateral pulmonary lesions that underwent adjunctive surgery during DOTS-Plus.

**Methods:** Retrospective case-control study among bilateral DOTS-Plus surgery patients in Lima, Perú.

**Results:** All patients with bilateral pulmonary lesions on plain radiograph and/or computerized tomography who underwent adjunctive DOTS-Plus surgery were included in the analysis. Variables were assessed for association with favorable treatment response (defined as sustained culture-negative status after surgery and survival at the time of analysis). Variables included clinical parameters (e.g., comorbidities, nutritional status, degree of drug resistance), radiographic findings (e.g., degree of lung field involvement, cavitary disease), and pre-operative analyses (e.g., pulmonary function tests). Univariate and multivariable analyses were performed and are reported here.

**Conclusion:** In Lima, Perú, identification of a subset of individuals with bilateral pulmonary involvement who benefit from surgery is crucial to improve outcomes in DOTS-Plus programs with resource limitations.

#### PS-393-417 Problématique de la prise en charge des rechutes et des échecs de tuberculose à Abidjan

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**Introduction :** La résistance aux antituberculeux devient un phénomène préoccupant. Les résultats de la prise en charge des tuberculeux en situation de rechute ou d'échec (après le protocole standard rifampicine, isoniazide, pyrazinamide), sont peu encourageants.

**Objectifs :** Nous avons voulu évaluer la validité du protocole appliqué à ces types de patients en déterminant les proportions de bacilles résistants dans les prélèvements de crachats de ces malades.

**Méthode :** Cette étude était un audit de 43 dossiers médicaux de patients tuberculeux dont 24 cas de rechute et 19 cas d'échec aux antituberculeux.

**Résultats :** L'âge moyen des patients était de 32 ans et 67,27% des patients venaient des quartiers les plus populeux d'Abidjan. Sur 43 patients, 14 avaient une sérologie VIH positive. Les isolats de *M. tuberculosis* étaient tous sensibles à la ciprofloxacine. Les niveaux de résistance variaient de 20,93 à 90,70% pour l'isoniazide, la rifampicine, la streptomycine et l'éthambutol. La multirésistance était estimée à 83,72%. Les proportions de *M. tuberculosis* résistant variaient de 16,66% à 95,83%. Les profils de la résistance en cas d'échec et de rechute de tuberculose étaient superposables. Les résultats de notre étude mettent en cause le protocole de traitement (rifampicine, isoniazide, pyrazinamide, éthambutol, streptomycine) des échecs et des rechutes de tuberculose.

**Conclusion :** Les rechutes et les échecs de tuberculose semblent être associés à une multirésistance en Côte d'Ivoire. La ciprofloxacine devrait être une molécule de renforcement de ce protocole en vigueur.

#### PS-446-486 Side effects in the treatment of multidrug-resistant tuberculosis in a DOTS+ Program in Tomsk Oblast, Russia

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**Objectives:** To determine number of side effects, and their effect on treatment results.

**Methods:** We observed 143 patients who started treatment more than 2 years ago and already completed treatment. Kanamycin/capreomycin, ofloxacin, cycloserine, PAS, ethionamide, pyrazinamide, and ethambutol were used. Mean number of drugs per patient—5.3. The duration of the intensive phase—11.3 months, the total duration of treatment—19.2 months. All patients underwent a complex clinical, laboratory, and instrumental examination; consultations with specialists if needed.

**Results:** Side effects were observed in 86% of patients. 39.8% were treated only symptomatically, for 40.7% of patients, 1 to 2 TB drugs were suspended, for 19.5% drugs were temporarily suspended. 76% of all side effects were initially observed within first 6 months. Treatment outcomes for the entire group: cured—82.5%, default—5.6%, died—4.9%, treatment failure—7%. A  $\chi^2$  t-test performed (0.16). There is no significant difference between the group with drug suspension and without ( $P = 0.7$ ).

**Conclusions:** MDR TB treatment is accompanied by a significant quantity of side effects. The optimal approach of detecting and treating side effects enables to keep the majority of TB drugs in the regimens and provides a high level of treatment effectiveness.

#### PS-450-487 Ambulatory treatment of MDR-TB patients in the DOTS-Plus program in Day Care Hospital (DCH) of Tomsk Oblast TB Dispensary, Tomsk, Russia

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**Introduction:** 177 DOTS-Plus patients treated in DCH since 01/2001. Some started treatment at hospital, including after surgery. Mean duration of treatment is 18–24 months. Median number of bed days—276 (180–425).

**Objectives:** To show that ambulatory treatment of DOTS-Plus patients is possible.

**Methods:** 177 DOTS-Plus patients who were on treatment in DCH since 01/2001 were reviewed. 92 completed treatment, 13 defaulted, 72 still on treatment. Main reason of default was chronic alcoholism. Treatment provided under DOT from 9am to 6pm, BID/TID 6 days a week according to drug tolerance and schedule convenient both to patient and TB doctor. Hot meals provided TID, so as monthly food baskets, hygiene sets and transport passes. Medical personnel include psychiatrist and psychologist. Frequencies of side effects were compared in patients started treatment in TB hospital (19) and DCH only (15) during 6 months.  $\chi^2$  test performed with  $df = 1$ .

**Results and Conclusion:** There is no significant difference between side effect frequencies in in-patient vs. out-patient treatment of patients in DOTS-Plus ( $P 0.960$ ). DOTS+ treatment is possible in ambulatory conditions with adjusted schedule, DOT, incentives and enablers and psychological care. This increases adherence, compliance and effectiveness of treatment (culture conversion over 80%).

#### **PS-470-511 Use of a potential of the Tomsk Oblast prison system in MDR-TB treatment in Siberian Federal Region (SFR)**

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Backgrounds for TB development in prison: physical and emotional stress, concentration of marginalized population (primary TB patients: new convicts—77.4%, old offenders—22.6%, unemployed—43%), prison conditions do not always provide adequate TB treatment. In Russian prison (new TB cases 2001–2003: average drug resistance—41.2%, MDR-TB—16.4%, re-treatment: drug resistance—70.9%, MDR-TB—48.9%). Among active TB patients in Russian prison, 45% are in prisons of the Siberian Federal Region (SFR): primary drug resistance—55.5% (MDR—12%), acquired drug resistance—60% (MDR—34%). Seven regions have bacteriological laboratories (an interregional lab—in Tomsk). A unified system of TB services is organized in Tomsk Oblast, adequate treatment facility established in correctional colony 1. Training of TB doctors is provided at the Prison Department of Advanced Training and in the PIH training center. DOTS-Plus effectiveness—87.2%. TB mortality in 1996—6.7%, 2003—0.2%. In order to improve adherence to MDR-TB treatment, 'peer education' program is used. Perspectives of optimal use of forces and capacity available in Tomsk prison within SFR: Creation of an MDR-TB treatment center in Tomsk prison allows to provide medical care to 20–30 patients from neighboring regions each quarter. Training of medical workers and volunteers among inmates.

#### **PS-470-512 Organizational aspects in the treatment of multiple drug resistant tuberculosis in the Tomsk Oblast prison system**

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**Objective:** To develop a system of organizational activities, without which MDR-TB is difficult to treat within the prison system.

**Methods:** The intermediate results of the MDR-TB Treatment Program in the Tomsk Oblast Prison System, started in 2000, were analyzed. The main principles of drug resistant TB treatment have been well known, but the effectiveness depended on some conditions, which required management decision. They included: qualitative laboratory monitoring, good tolerance of second-line TB drugs, capacity for surgery in case of ineffective chemotherapy.

**Results:** Experience of MDR-TB treatment in the Tomsk Oblast Prison System allowed us to identify a system of organizational activities, which can be divided in the following categories:

- Presence of specialized in-patient facility;
- Bacteriological, biochemical and clinical laboratories;
- Trained medical staff
- Capacity for specialized medical care
- Availability of second-line drugs for complete treatment
- Surgery capacity
- Improvement of nutrition for TB patients treated on the DOTS-Plus program

#### **PS-477-514 Aspects of MDR-TB treatment in the Tomsk Oblast Prison Hospital, Russia**

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129 MDR-TB patients started treatment over 12 months ago. Average characteristics: age—32.6 years, time of disease—5.3 years, number of previous treatment—3.2. Bilateral TB—55.8%. 80.6% of patients were smear/culture positive at treatment start. Other patients were positive 2–7 months before treatment start and they had severe clinical and radiographic signs of active TB. Drug resistance: HR—100%, S—97.5%, E—87.5%, Eth—45%, Z—38.8%, K—30.6%, Cap—8.8%, OfI—2.5%. Drugs received by patients: K—52.7%, Cap—47.3%, OfI—100%, Cyc—99.2%, PAS—86.8%, Z—79.8%, Eth—76.7%, E—29.5%. Average resistance to drugs—4.8, number of drugs—5.2. Outcome: 63 (48.8%)—cured, 2 (1.5%)—failure, 2 (1.5%)—default, 3 (2.3%)—died, 32 (24.8%) on treatment, 27 (20.9%)—transferred out to civilian sector.



**Average data:** intensive phase—9 months, in 63 patients treatment was 20 months. Of 104 patients, who were positive at treatment start, 101 (97.4%) had sputum converted.

**Culture conversion by months:** 1—41.8%, 2—79.9%, 3—87.3%, 4—90.9%, 5—98.2%, 6—96.4%. Sputum conversion: in a month—52.9%, 2—64.7%, 3—79.4%, 6—100%. Three patients became positive after 6 months. Intermediate treatment effectiveness—90%. Clinical and radiographic data correlated with bacterioscopy changes. MDR-TB treatment proved high effectiveness.

**PS-480-520 On the role of laboratory services in the implementation of complex DOTS and DOTS-Plus programs for TB detection and treatment**

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A model of the laboratory services in the implementation of DOTS and DOTS-Plus programs to detect and treat TB patients has been introduced in Tomsk Oblast. The DOTS strategy has been used since 1995, and DOTS-Plus since 2000, both in civilian and prison sectors. Organizational, methodological and management activity to create bacteriological stations, leading reference laboratory to perform sputum microscopy in Tomsk, active use of these methods in all clinical and diagnostic laboratories of general medical services allowed to improve the quality of detecting active TB patients, as well as provide close organizational and methodological cooperation between medical diagnostic settings of general medical services and TB services. Concordance of DST results performed in Tomsk and Boston provided reliable results to first and second-line TB drugs among the majority of the DOTS-Plus patients.

**PS-480-522 On a positive impact of the DOTS and DOTS-Plus programs on TB epidemiological situation in Tomsk Oblast, Russia**

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Since 1995 an implementation of the DOTS strategy, adjusted to the local conditions of the Siberian Fed-

eral Region (SFR), and since 2000 of the DOTS-Plus program both in civilian and prison sectors allowed to speak on stabilization of TB epidemiological situation in Tomsk Oblast. TB incidence per 100 000 population in 2003 (105.5) is lower than in SFR (126.2), and TB mortality is significantly lower (17.8) compared not only to SFR rate (33.8), but to Russia as well (21.8). In 2003 among new TB patients, 88.0% had culture conversion (60.6%—SFR, 73.4%—Russia), 77.2% had cavity closure (49.5%—SFR, 62.6%—Russia). Between 12 September 2000 to 12 April 2004, 507 MDR-TB patients were enrolled in the DOTS-Plus program, of them 275 patients have already completed therapy. The number of MDR-TB patients both among new cases and TB reservoir decreased in 2003 compared to previous years.

**PS-481-519 Primary multidrug-resistant tuberculosis (MDR-TB) in medical doctors: morbidity and implications**

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**Objective:** The impact of the absence of infection control measures and the morbidity of MDR-TB in four immunocompetent doctors.

**Methods:** At a TB specialist hospital in a province in South Africa, the hospital files all(103) health care workers between 1999 and 2004 were reviewed.

**Results:** Thirteen had culture confirmed MDR-TB of which four were medical doctors with no previous history of tuberculosis. They were immunocompetent, had no known contact with TB outside their work environment, were under 30 years old and worked in anaesthesiology and out-patients departments. All facilities were poorly ventilated, had overcrowded waiting areas and no specific infection control measures in place. The average time to diagnosis of MDR-TB was three months. Two doctors had lobectomies, one developed TB meningitis and a hemiparesis, and all experienced significant side effects from the drugs.

**Conclusions:** This is the first report of primary MDR-TB amongst immunocompetent health care workers. The TB epidemic has been attributed to HIV infection and the impact of HIV negative individuals with TB has been largely ignored. In developing countries inadequate infection control measures, insufficient human resources such as doctors and nurses, and poor monitoring systems place a strain on a overburdened health system.

### PS-482-518 Genotypic and phenotypic drug susceptibility testing in serial isolates of *Mycobacterium tuberculosis*

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To analyze drug resistance development eighty serial *M. tuberculosis* isolates were collected from 17 patients (2–8 isolates/patient) on anti-TB treatment at Guliripchi Hospital of Sukhumi, Abkhazia (September 2000–December 2003). The time spans between the first and the last isolate of a patient ranged from 5 to 31 months. Drug susceptibility testing was performed for first-line and second-line drugs and confirmed by real time PCR and sequencing. Overall, 100% and 85% of the patients harbored isoniazid- and streptomycin-resistant strains at the beginning of the study; drug resistance was found to develop over time against rifampicin (5 patients), ethambutol (2 patients), ofloxacin (3 out of 8 treated patients), capreomycin (2 patients out of 7 treated patients), and kanamycin (1 patient). All resistances developed concerned drugs included in the treatment regimen. The longitudinal data collected describe drug resistance in *M. tuberculosis* in a homogeneous population of patients as the Guliripchi Hospital collects all cases in Abkhazia. These preliminary data confirm that despite appropriate therapy drug resistance develops in most cases recorded as treatment failure.

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### PS-497-543 La tuberculose multirésistante : difficultés de prise en charge. Etude sur 14 ans

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La tuberculose multirésistante (TMR), définie par la résistance à au moins l'isoniazide et la rifampicine, pose un sérieux problème de santé publique. Afin d'évaluer son ampleur et les difficultés de sa prise en charge, nous avons étudié sur 14 ans, de 1989 à 2003, 1011 cas de tuberculose pulmonaire. La TMR a été retrouvée chez 37 patients : 3,66%, avec 3 à 4 nouveaux cas par année, et une baisse depuis l'instauration du DOTS en 1993. Le régime adopté est de 18 mois minimum avec INH, pyrazinamide, éthambutol, fluoroquinolone, associés aux cyclines : 27 cas,

l'éthionamide : 8 cas et la cyclosérine : 2 cas. Il est fonction de la disponibilité des antituberculeux secondaires et des effets indésirables. Les hospitalisations sont répétées pour réajustements thérapeutiques ou en raison de nombreuses complications. Le retard du diagnostic de TMR, de la prise en charge et la mauvaise observance constituent des éléments de mauvais pronostic. La TMR est un défi pour les programmes de lutte antituberculeuse qui impose de renforcer la surveillance des malades. Le DOTS constitue un espoir pour voir diminuer la multirésistance.

## TUBERCULOSIS AND HIV

### PS-470-508 TB in HIV persons in the Tomsk Oblast prison

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**Objective:** To study diagnostic and clinical characteristics of tuberculosis in HIV patients, and their social status.

**Materials and methods:** Medical and social data of TB inmates with HIV (1998–2003) were analyzed. Cumulative number of HIV patients—337, of them 97 patients detected in prison. As of 04/01/2004, 129 HIV patients are in prison; 31 HIV+TB patients (5 cases developed TB in prison). TB in persons with pre-clinical HIV-infection was not significantly different from TB patients. Isolation of HIV patients from the major part of inmates contains the increase of TB incidence. Majority of TB-HIV patients are intravenous drug users from marginalized population. This cohort contracted HIV-infection prior to TB. In order to detect TB in HIV patients, clinical, radiographic, bacterioscopy methods were used. Skin test was not used. With the progress of HIV-infection and decrease of T-lymphocytes, TB process became atypical: with minor limited TB, severe intoxication, tachycardia, respiratory insufficiency and mouth mycosis were observed.

#### Results:

- In persons with pre-clinical HIV, TB could be atypical;
- Clinical and morphologic TB manifestations at late stages of HIV-infection become atypical;
- Increase of HIV patients in prisons if they are not isolated from other inmates may lead to HIV+TB epidemic.

**PS-501-546 A review of drug interactions between the non nucleoside reverse transcriptase inhibitors (NNRTI's) and rifampicin in HIV-infected patients with TB**

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This review of the literature provides an evidence-based description of the potential, clinically relevant drug interactions between Rifampicin and the NNRTI's, Efavirenz, Nevirapine and Delavirdine and is meant to afford recommendations to the health care provider regarding treatment choices and appropriate dosing of the chosen NNRTI and Rifampicin in patients co-infected with HIV and TB. Data regarding appropriate treatment choices in the setting of TB therapy and HAART is limited. Current recommendations suggest that the dose of Efavirenz be increased to 800 mg daily when used in combinations with rifampicin, Nevirapine dose remains unaltered although the AUC is decreased by 37–58%, however this combination may only be used if no other options exist and clinical and virologic monitoring is possible. Delavirdine and rifampicin should not be used together as the Delavirdine AUC is decreased by 95%. In this setting a case could be made for applying therapeutic drug monitoring to antiretroviral therapy to optimize efficacy and reduce toxicity.

**PS-505-593 Clinical and radiological profile of tuberculosis in HIV seropositive patients and effect of ATT in these patients in VIMS Bellary a tertiary level teaching hospital**

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**Background:** India accounts for 25% of TB cases with HIV coinfection world. The state of Karnataka where this study was done ranks second highest in TB patients with HIV in India.

**Objectives:** 1) To study prevalence, clinical and radiological profile of TB in HIV seropositive patients. 2) To study effect of anti-tuberculosis treatment (ATT) in these patients.

**Methods:** 76 patients (68 male and 8 female) with HIV infection were screened for TB. Inclusion criteria was all HIV patients with TB and exclusion criteria children less than 12 years. HIV was diagnosed with 2 tests (rapidELISA) detecting different antigens, CD4 counts were taken. Diagnosis of TB was based on clinical, bacteriological evaluation including sputum smear for acid fast bacilli and chest skiagram. ATT was given to patients as per RNTCP guidelines.

**Results:** 50 (66%) patients had pulmonary TB, 26 (34%) extra-pulmonary TB indicating disseminated

nature of disease in HIV seropositive patients. Sputum staining was positive only in 27 (36%) patients. 43% of patients had typical manifestations and 57% had atypical eg. diffuse bilateral reticulo-nodular infiltrates, pleural effusion and mediastinal adenopathy. Mean CD4 counts were significantly lower ( $P < 0.01$ , unpaired  $t$  test) in HIV seropositive patients with TB than without. CD4 counts were higher ( $P < 0.01$ ) in patients with upper zone lesion when compared to patients with atypical radiological manifestations. Mean CD4 count at beginning of therapy was 192 cells /mm<sup>3</sup>. Initially there was improvement in CD4 but significant decline was ther at the end of treatment.

**Conclusions:** Rates of sputum positivity are lower and atypical radiological manifestations much higher. Patients with HIV related TB, particularly those with no cavity formation and advanced stage of disease are more likely to be sputum positive than those with typical cavitary post primary disease. There is initial improvement with ATT but without concomitant anti-retroviral therapy condition deteriorates.

**PS-518-594 Apport du score de Keith Edwards dans la co-infection tuberculose-IVH**

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**Objectifs :** Evaluer le score de Keith-Edwards (SKE) obtenu dans le diagnostic des enfants tuberculeux co-infectés par le VIH.

**Méthodes :** L'analyse porte sur le SKE obtenu chez 261 enfants soignés pour tuberculose entre janvier 2002 et décembre 2003 à l'Hôpital Pédiatrique de Kalembelembe de Kinshasa.

**Résultats :** Sur 261 enfants, 132 avaient un score très élevé : 13 à 20 et 129 un score allant de 7 à 12. Parmi les 132 avec un score très élevé 101 étaient positifs pour le VIH (77%), 23 étaient négatifs pour le VIH (17%) mais certains présentaient une malnutrition et 8 dont le statut VIH n'était pas connu.

**Conclusion :** Le SKE, lorsqu'il est très élevé, pourrait être un important indicateur de présomption de la co-infection TB-VIH. Toutes fois, il faudra aussi noter qu'il pourrait également être très élevé chez les enfants malnourris non infectés par le VIH.

### PS-703-778 Tendances évolutives de la prévalence du VIH chez les tuberculeux traités dans les Centres antituberculeux de Côte d'Ivoire de 1994 à 2002

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**Objectif :** Décrire les tendances évolutives de l'infection à VIH chez les tuberculeux traités dans les centres antituberculeux (CAT) de Côte d'Ivoire.

**Méthodes :** Dans les 2 Centres antituberculeux d'Abidjan et dans les 6 Centres antituberculeux de l'intérieur du pays tous les nouveaux patients diagnostiqués tuberculeux ont bénéficié d'un conseil et d'une proposition volontaire du dépistage VIH. Tous les sérums ont été acheminés au laboratoire du Projet RETRO-CI pour le test VIH selon un algorithme standard: Elisa mixte pour le diagnostic et Elisa monospécifique pour le sérotypage. Les patients ont reçu le résultat de leur sérologie un mois plus tard et ont bénéficié d'un conseil post test.

**Résultats :** Le nombre de cas de tuberculose notifiés a varié de 12 000 en 1994 à 17 204 patients toutes formes confondues. Pour les nouveaux cas à bacilloscopie positive, elle a varié de 7 500 à 10 400. Au cours de l'année 2002 les 2 CAT d'Abidjan ont mis en traitement 44% des patients tuberculeux. La prévalence de l'infection à VIH est restée stable avec 45% chez les patients tuberculeux à Abidjan et 40% pour les tuberculeux de l'intérieur du pays durant la période de 1994 à 2002. La prévalence au VIH1 est restée prédominante, respectivement 40% pour Abidjan et 30% pour l'intérieur du pays. Le taux de consentement au dépistage VIH est élevé à Abidjan comme à l'intérieur du pays durant toute la période (90% pour à Abidjan et 80% pour l'intérieur du pays).

**Conclusion :** L'incidence de la tuberculose en Côte d'Ivoire ne cesse de croître. La prévalence de l'infection à VIH est élevée mais reste stable avec une prédominance de l'infection à VIH1. Les Centres antituberculeux subissent une affluence des patients doublement infectés par la tuberculose et le VIH. Il est nécessaire de renforcer le cadre de collaboration pour une politique de prise en charge plus efficace des patients tuberculeux VIH-positifs.

### PS-731-807 Multidrug resistance associates with molecular types among *Mycobacterium tuberculosis* isolates from HIV/AIDS patients in Latvia

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**Introduction:** The first HIV positive patient was registered in Latvia in 1987. Since then the number of HIV/AIDS patients exceeded 1000 and among them about 100 with dual TB-HIV infection (2003 data).

**Objectives:** To analyse genetic polymorphism and drug resistance profiles of *Mycobacterium tuberculosis* associated with HIV/AIDS in Latvia.

**Methods:** *M. tuberculosis* was successfully isolated in 70% cases of clinically confirmed dual TB-HIV infected patients. Drug resistance was determined by absolute concentration and BACTEC cultivation methods. Molecular typing of 20 isolates was performed by analysis of PvuII restriction patterns and spoligotyping.

**Results:** Number of dual TB-HIV infected patients increased in Latvia during 1998–2003 from 1 till 40 new cases respectively. Primary multidrug resistant TB forms increased from 10% in 1999 till 34% in 2003 in this TB-HIV group (in the non-HIV group—9.3%). Molecular typing of TB-HIV patient mycobacteria isolates showed quite different restriction and spoligo patterns—Beijing (30%), LAM, X1, Haarlem, ST254 spoligofamilies (the latter were drug susceptible). Of 7 multidrug isolates 4 belonged to the Beijing family. 40% mycobacteria isolates were clustered and the rate of clustering is 0.25, however direct epidemiological links between patients were not found.

**Conclusion:** Among dual TB-HIV infected patients there does not prevalent specific molecular types of *M. tuberculosis*, however rate of clustering indicates on possible recent transmission. The high amount of Beijing genotype among multidrug isolates indicates on specific properties of this genofamily. Serious monitoring of TB-HIV patients and introduction of individual DOTS-plus program allowed increase in the cure rate.

### PS-738-813 Programme of TB care for HIV-patients in the Russian Federation

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**Introduction:** TB notification rate increasing during last ten years in Russia was stabilized at the level of 83.6/100 000 in 2003. However HIV infection can become an obstacle for the further improvement in TB epidemiological situation in Russia. In 2003, 212 813

individuals were registered as HIV positive in Russia, 97% out of them were in early stages of HIV infection. **Goal:** Development the programme of TB care among HIV patients.

**Methods:** Retrospective and prospective analysis of epidemiological data, clinical and morphological specifics of HIV-related TB in Russia in 1997–2002.

**Results:** 7678 TB-HIV patients were registered in Russia in 2002. Majority of them (81%) were in early stages of HIV infection, and 42% were registered as TB patients prior to HIV detection. High rate of TB in early stages of HIV infection is resulting from the fact that HIV infected individuals belong also to risk groups for TB. Out of all HIV infected, 89% were IVUDU, 37.2% of the patients entered the penitentiary system, 16.5% homeless and 68.3% unemployed.

**Conclusion:** The analysis of this patient cohort helped to develop the programme of TB-HIV care, which is based on WHO recommendations, taking into account specifics of TB in the HIV infected.

#### PS-834-905 Tuberculosis and AIDS

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**Introduction:** In 2003, the association of tuberculosis (TB)/AIDS remains a problem in Portugal, especially in Lisbon (22.3%), Porto (17.2%) and Setúbal (15.4%).

**Objectives:** To evaluate the TB/AIDS problem in our CDC.

**Methods:** Review of all TB/AIDS cases in our CDC during 1994/1995 and 2001/2002 and comparison of the data.

**Results:** In 94/95, TB/AIDS represented 11.5% of TB cases while in 2001/2002 it represented 15.2%, with an increasing incidence in black race (29.3% to 63%), mostly from Cabo Verde (41.2%). 55.2% in 94/95 were drug abusers against 33.3% in 2001/2002. Pulmonary tuberculosis (PT) predominated in both periods, and disseminated tuberculosis was the second most frequent (19% and 20.4%). Three of the pulmonary cases were multidrug resistant (MDR). AIDS diagnosis was simultaneous with tuberculosis one in 44.8% and 27.8% of the cases, and it was done afterwards in 6.9% and 14.8% of the cases, respectively. The HRZE scheme predominated (74.1% and 90.7%), and treatment was completed, respectively, in 51.7% and 75.9% of the patients, including the MDR ones.

**Conclusions:** 1) TB/AIDS is an increasing problem in our CDC. 2) Marked increase in the black race. 3) Less drug abusers with TB/AIDS. 4) Marked increase of DST in PT cases. 5) HIV was unknown in a significant number of cases. 6) Treatment was successfully completed in an acceptable number of cases in 2001/2002.

#### PS-887-962 HIV seroprevalence among tuberculosis patients in Nkembo Hospital-Libreville

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**Introduction :** Le Gabon compte actuellement près de 30.000 cas cumulés d'infection par le VIH. La prévalence est estimée à 7.7% à Libreville, la capitale. Environ 2627 cas de tuberculose toutes formes confondues ont été notifiés à l'OMS en 2001, dont 43% de nouveaux cas à microscopie positive. La co-infection VIH-Tuberculose aggrave le pronostic global de nos patients. Le but de notre étude est de déterminer la séroprévalence du VIH au sein de nos patients tuberculeux.

**Matériel et méthode :** Il s'agit d'une étude transversale réalisée du 25 juin au 31 août 2001. Les patients sont tous des nouveaux tuberculeux ou des cas de rechute. Les types de tuberculose n'ont pas été différenciés. Le diagnostic de la TB était clinique, radiologique et bacilloscopique (selon la méthode de Ziehl Neelsen). Un consentement oral a été demandé pour la réalisation de la sérologie VIH. Deux tests ont été appliqués : un test rapide, suivi en cas de positivité, par un Elisa.

**Résultats :** 358 patients ont été examinés, dont 141 femmes et 217 hommes. Le sex ratio était de 1.53 et l'âge moyen de 32 ans. La proportion de nouveaux patients était de 61%. 97% des patients avaient une tuberculose pulmonaire, 58% une bacilloscopie positive et 26% une sérologie VIH positive. Par rapport à ce statut sérologique, il n'a pas été noté des différences statistique significative pour le sexe, le type de maladie ou de malade et les résultats de la bacilloscopie. Nous n'avons pas retrouvé de profil de patient à risque d'infection par le VIH.

**Conclusion :** On constate une augmentation de la prévalence du VIH au sein des tuberculeux. Cependant, nos résultats sont identiques aux données ivoiriennes camerounaises et sénégalaises.

#### PS-199-242 Collaboration between the national tuberculosis programme and a non governmental organisation in TB/HIV care at district level: experience from Tanzania

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**Objective:** To determine the feasibility of establishing collaboration between the tuberculosis programme and an NGO in TB-HIV care at district level in Tanzania.

**Methods:** Quantitative and qualitative study designs involving TB as well as HIV suspects and patients together with health workers, conducted between December, 2001 and September, 2002.

**Results:** A total of 72 patients and 28 key informants were involved. The collaboration was in the following areas; voluntary counselling and testing for HIV, diagnosis and treatment of TB, referral and follow up of patients and suspects, home based care, psychological support and training. Both the tuberculosis programme and the NGO benefited from the collaboration. TB case detection among PLWA increased more than three folds and TB treatment was integrated in home based care. The main barriers identified in this study were; poor communication, poor referral system and lack of knowledge and skills among health staff.

**Conclusion:** The study has shown that it is possible for a tuberculosis programme and a non governmental organisation to collaborate in TB-HIV care. The study has also identified potential areas of collaboration and barriers that need to be overcome in order to provide such comprehensive services at a district level.

#### **PS-693-768 Coinfection reduction strategies for TB-HIV/AIDS in the Dominican Republic**

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**Introduction:** TB incidence in Dominican Republic is about 85/100 000 population cases and 1% of the sexually active population live with HIV, in some population groups it is 5%. Health establishments that apply DOTS have incorporated TB prevention, diagnose and treatment activities in patients HIV/AIDS.

**Objectives:** To evaluate results in coinfection TB-HIV/AIDS.

**Methods:** DOTS was expanded in 2002 and NPT of Dominican Republic began Isoniacid administration like quimioprofilaxis for TB prevention in patients HIV/AIDS and treatment antiTB supervised and gratuitous in cases TB-HIV/AIDS. These results have been obtained by the NTP information system.

**Results:** HIV/AIDS patients who received Isoniacid for TB prevention increased of 55 (2002) to 700 (2003). In cases TB-HIV/AIDS treated with 2RHZE/4RH3 scheme 34% (2002) and 55% (June 2003) cured and deceased percentage diminished from 35% (2002) to 26% (June 2003). 200 HIV/AIDS patient advisors at 20 provinces in Dominican Republic have been qualify in TB advisory.

**Conclusion:** Joint action between NTP and HIV/AIDS Programs are required to diminish coinfection TB-HIV/AIDS

#### **PS-748-822 TB/HIV co-infection, Mariupol city, Donetsk oblast, Ukraine**

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**Introduction:** High TB and HIV prevalence rate is registered more frequently in Donetsk oblast and TB-HIV co-infection cases are more common in recent years.

**Objective:** The purpose of this analysis is to study the HIV-related TB epidemic situation and to define most affected population group.

**Methods:** In the Mariupol TB dispensary was analyzed HIV/TB co-infection data, based on out-patient cards and case reports.

**Results:** There were 239 TB-HIV cases registered in 1999–2003. Out of which 28.5% were employed people, 5%—disabled, 66.5%—unemployed. 82.4% of the TB/HIV cases detected at the dispensary were new. 89 out of 239 were officially registered drug users. During that period of time 29 patients changed their places of residence. There were 82 death outcomes, 19 of which were caused by HIV/AIDS, 38—by TB, 25—by other causes. In 2003 in Mariupol were registered 128 TB-HIV cases. Out of 128 cases by gender: 64.8%—males, 35.2%—females; by age: younger than 19—0.8%, 20–29—25.8%, 30–39—43.7%, 40–49—28.9%, 50 and older—0.8%; by smear: 42.2%—PTB SS+, 53.9%—PTB SS–, 3.9%—EPTB. Treatment success made 57.8%.

**Conclusions:** Thus, working age people (98.4%) make most vulnerable group, with 66.5% unemployment rate. In order to raise treatment efficiency it is necessary to combine anti-TB and ARV therapy.

#### **PS-778-852 Role of HIV/AIDS service in HIV/TB co-infection control in Donetsk oblast, Ukraine**

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**Introduction:** High TB and HIV prevalence rate is registered in Donetsk oblast (380,0 and 271,48 per 100 000 population correspondingly), and HIV detection rate among TB patients came to 6% in 2003.

**Objective:** Definition of effective diagnostic and prophylaxis methods for HIV/TB infection; determination of the role of HIV/AIDS service in control of epidemic HIV/TB co-infection.

**Methods:** Processing of epidemic monitoring data.

**Results:** 1283 cases of HIV/TB co-infection were registered for 1996–2003 years (which amounts 10% of total amount HIV-infected people). 556 persons among

all patients with HIV/TB co-infection were diagnosed with AIDS (50% of all patients suffering from AIDS). 460 patients with HIV/TB died for the observation period (60% of them from AIDS, 26.7%—from TB). Special system of clinical-diagnostic and epidemiological monitoring of HIV/TB were elaborated, analytical computer program of registration of all HIV/TB patients was created. The algorithm of interaction between TB facilities and HIV/AIDS services in Donetsk oblast was developed.

**Conclusions:** HIV/TB monitoring allows to analyze deeply diagnostic and epidemiological markers and to correct joint efforts on prevention and treatment of patients with HIV/TB co-infection according to the results of this monitoring.

### PS-831-902 ProTEST expansion in Zambia

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**Introduction:** The ProTEST (Promoting HIV TESTING) initiative has been widely adopted as a means of enhancing collaboration between TB and HIV activities.

**Objective:** To provide an effective and rapid way of scaling up ProTEST in Zambia.

**Method:** A ProTEST training curriculum, a ProTEST Manual and tools for monitoring and evaluation have been developed for use by districts.

**Results:** The ProTEST pilot sites started in 1999 in three high-density urban settings. These three sites have been successfully handed over from Zambart Project (a research organization) to Lusaka District Health Management Board. Using GFATM and WHO resources, Central Board of Health has started to expand ProTEST country wide. Key health personnel from six additional districts have been trained after which they are expected to train other staff in their respective districts. Implementation is on going. The lessons learnt from this initial roll out phase, especially those of the challenges of collaboration between government and other organizations, will be presented.

**Conclusion:** ProTEST has been implemented differently in different countries. Lessons can be learnt from implementing the program in a decentralized health care system like that in Zambia. However, the challenges of integrating this programme into the existing health care structures still remain.

### PS-674-747 Using a Laboratory Performance Improvement Programme to enhance quality of services for TB and HIV/AIDS in Uganda and the Philippines

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**Introduction:** Efforts to improve laboratory performance frequently focus on training in laboratory techniques and providing equipment and consumables. Leadership and management strengthening has not been sufficient to create an institutional environment to leverage these investments and maintain technical quality.

**Objectives:** To devise and pilot a programme to improve laboratory performance through strengthening the management systems and developing managers to lead.

**Methods:** Tools for strengthening leadership and management have been adapted to match the specific management components and challenges faced by laboratory networks in low-income countries with high prevalence of TB and TB-HIV and are being piloted and evaluated in Uganda and the Philippines.

**Results:** Preliminary results of a structured participatory self-assessment process to identify gaps in the laboratory management systems, and highlights of resulting management improvement plans will be presented. The framework for the Leadership Development Programme to address priority challenges affecting the efficiency and quality of services will also be presented.

**Conclusion:** Improving leadership and management capacity of laboratory networks is essential for sustaining the quality and efficiency of services.

### PS-729-805 Causes of pneumonia, needing hospitalization, in HIV infected persons in Cambodia

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**Rationale:** The knowledge of pneumonia causes in HIV infected patients living in developing countries with limited access to ARV is the major goal of the ANRS 1260 study conducted in Africa (Dakar, Bangui) and Asia (Ho Chi Minh City, Phnom Penh). The results of Phnom Penh site are reported.

**Methods:** From September 2002 to November 2003, all patients hospitalized in Sihanouk Hospital with pneumonia (clinical and radiological criteria) and (+) HIV serology got investigations, including sputum examination, blood culture, fiberoptic bronchoscopy

and BAL. Final diagnosis resulted from microbiological documentation:

- Definite diagnosis in case of pathogen identification (direct examination and culture) in bronchial aspiration ( $\geq 10^5$  CFU/ml) and/or BAL ( $\geq 10^3$  CFU/ml) products.
- Probable diagnosis in case of pathogen identification in sputum only (culture not done for FAB; positive culture with  $\geq 10^7$  CFU/ml for bacteria).

**Results:** 297 patients were included; 23 were secondarily excluded.

- AFB were positive by direct examination of sputum in 77 patients
- One or more pathogens were identified as cause in 156 other patients: *Pneumocystis carinii* ( $n = 80$ ), *M. tuberculosis* ( $n = 36$ ), Pyogenic bacteria ( $n = 56$ ), fungus ( $n = 15$ ), *Strongyloides stercoralis* ( $n = 14$ ), atypical mycobacteria ( $n = 18$ ).

**Conclusions:** Main causes of pneumonia in HIV infected Cambodian persons are tuberculosis, pneumocystosis and bacterial pneumonia. Mycosis, atypical mycobacteriosis, strongyloidosis, may in some cases be responsible.

#### PS-730-806 Epidemiology of bacterial pneumonia, needing hospitalization, in HIV-infected persons in Cambodia

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**Rationale:** European, American and African studies have shown that HIV-infected persons were at risk for *Streptococcus pneumoniae* (SP) or *Haemophilus influenzae* (HI) pneumonia, at a T CD4 level  $>100/\text{mm}^3$ , and for *Pseudomonas aeruginosa* (PA) or other Gram-negative bacilli (GN B) pneumonia, at a T CD4 level  $<100/\text{mm}^3$ . The goal of this study is to appreciate the relevance of these data in Cambodia.

**Methods:** In the ANRS 1260 study, 197 HIV-infected persons, hospitalized in Sihanouk Hospital for pneumonia, with AFB negative in sputum, have been investigated according an algorithm including fiberoptic bronchoscopy (FO).

**Results:** In 197 patients, 184 FO have been performed. Pyogenic bacteria (PB) pneumonia was diagnosed in 56 patients: Definite diagnosis in 44 patients with positive culture of bronchial secretion ( $\geq 10^5$  CFU/ml) or BAL ( $\geq 10^3$  CFU/ml) products: probable diagnosis in 12 patients with positive culture of sputum ( $\geq 10^7$  CFU/ml). PB found were PA ( $n = 21$ ), GN B ( $n = 14$ ), *Staphylococcus aureus* ( $n = 13$ ), SP ( $n = 5$ ), HI ( $n = 3$ ). PB was alone at cause ( $n = 19$ ) or associated with another PB ( $n = 8$ ) and/or *Pneumocystis carinii*, *Cryptococcus neoformans* or *M. tuberculosis* ( $n = 22$ ),

and/or atypical mycobacteria or *Strongyloides stercoralis* ( $n = 10$ ).

**Conclusion:** In Cambodia, PB and more particularly GN B are frequently at cause in HIV-infected patients hospitalized for pneumonia. Multivariant analysis are currently performed to identify risk factors (CD4 level, previous antibiotics . . .) predictive of GN B pneumonia.

#### TUBERCULOSIS IN HIGH-BURDEN COUNTRIES-1

##### PS-169-205 United National Register for patients with tuberculosis in the TB monitoring system in the Republic of Kazakhstan (RK)

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Our country believes to the Central Asia Republics with unfavorable TB profile. Implementation of DOTS strategy by WHO protocols adapted to the possibilities of RK has been regulated by President and Government of RK since 1998. In addition to TB monitoring system existing in the RK, a personified electronic United National Register for TB patients was created. At present the Register is constituted from 300 000 records including not only TB patients, but persons from risk groups, persons earlier suffered from TB, those in contact with TB patients, children and adolescents with conversion and hyperergic tuberculin response. Computer technology of notification and monitoring of TB patients will give the opportunity to centralize the control of TB patients and the epidemiological surveillance of TB infection through studying MDR-TB prevalence, expenditures for anti-TB drug purchasing and to evaluate the treatment effectiveness and anti-TB policies, in order to adopt the measures to stabilize and improve the epidemiological profile of TB in RK.

##### PS-209-248 Are females more at risk to develop extra-pulmonary tuberculosis? Results from Damien Foundation projects in Bangladesh

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**Methods:** Analysis of the patients' data files 1997-99 from the Damien Foundation projects in Bangladesh. TB diagnosis is based on direct sputum examination for AFB. Diagnosis of non-positive TB cases is based on X-ray or other tests.



**Results:** TB cases registered were 7802 in 1997, 10 098 in 1998 and 10 736 in 1999 respectively. F/M ratio was 0.36 for smear positive TB, 0.37 for smear negative pulmonary TB, but 1.07 for extra-pulmonary cases. The most common sites of extra-pulmonary TB are lymph nodes, pleura, bones and gastrointestinal tract. The gender distribution for each site shows that females are more prone to gland TB (F/M ratio: 2.08) and males for pleural TB (F/M ratio: 0.26).

**Discussion:** As more males than females are diagnosed with TB in Bangladesh, the observation that females are more often diagnosed with extra-pulmonary TB than males cannot be explained by a better accessibility to health services for males. The difference observed reflects thus likely the reality.

**Conclusion:** While in Bangladesh pulmonary TB is much more common in males, EPTB, particularly gland TB, affects more females.

#### PS-249-277 Drug resistance of *Mycobacterium tuberculosis* in rural and urban areas in Bangladesh

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**Objective:** Determine the drug resistance patterns of *Mycobacterium tuberculosis*.

**Methods:** A community-based TB surveillance system has been set up in 106 000 population in rural Bangladesh at Matlab. Trained field workers interviewed all persons  $\geq 15$  years to detect suspected cases of tuberculosis (cough  $> 21$  days) and sputum samples were examined for acid-fast bacilli. A systematic sampling technique was used to obtain samples from patients attending a reference tuberculosis laboratory in urban Dhaka. Smear positive TB cases diagnosed between June 2001 and June 2003 from both settings were cultured and drug susceptibility tests were performed using standard techniques.

**Results:** Of 657 isolates, resistance to one or more drugs was observed in 48.4%. Resistance to streptomycin, isoniazid, ethambutol and rifampicin was observed in 45.2%, 14.2%, 7.9% and 6.4% respectively. Multidrug resistance (MDR) was observed in 5.5%. It was significantly higher among persons who received tuberculosis treatment of one month or more (15.4% vs. 3.0%, adjusted OR: 6.12, 95%CI 3.03–12.34).

**Conclusions:** The magnitude of anti-tuberculosis drug resistance in Bangladesh is high. Further evaluation is needed to explain the high proportion of streptomycin resistant *M. tuberculosis*. Appropriate measures to control and prevent drug resistant tuberculosis in Bangladesh to reduce mortality and transmission are warranted.

#### PS-255-282 High rates of recurrent TB and mortality following DOTS treatment in a setting of high drug resistance in Central Asia

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**Introduction:** DOTS tuberculosis programmes have been demonstrated to be effective in several resource-poor settings. However, little data are available from settings with existing high levels of drug resistance.

**Methods:** A survey in Karakalpakstan, Uzbekistan showed levels of multidrug-resistant TB (MDR-TB) of 13% amongst new cases and 40% amongst previously treated cases. The 213 patients included in this survey were followed through DOTS treatment, for a mean of 23 months post-diagnosis.

**Results:** Treatment success rates were 73% for new patients and 44% for re-treated cases, ranging from 82% (new fully-susceptible cases) to 24% (re-treated MDR-TB cases). Of the 84 patients with sputum-smear confirmed cure, 11 (13%) were re-diagnosed with smear positive TB (average 10 months after cure); and a further 15 (18%) with smear negative TB (total TB recurrence rate 31%). Mortality rates at the time of follow-up were 11% for fully susceptible cases, 13% for those with one-drug resistance, 16% for those with resistance to more than 1 drug (excluding MDR-TB) and 55% for MDR-TB.

**Conclusion:** High TB recurrence and mortality suggest that in such settings, standardised short-course chemotherapy may need to be revised.

#### PS-294-329 Spatial distribution of tuberculosis cases in Ribeirão Preto city during 1998 to 2002

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Map usage and concerns about geographic distribution related to diseases are not a recent issue. A classical example of these is the John Snow survey—maps were used to locate cholera cases and related them with water supplies. This work begins from an assumption that the spatial distribution of tuberculosis is not uniform. The aim of this survey was to establish the spatial distribution of disease in Ribeirão Preto city from 1998 to 2002 by looking for a dependency of its occurrence and space. Secondary data from Municipal Health Department were used to elaborate this study. Spatial statistic analysis was performed utilizing Spring software. The spatial analyses during the years demonstrate that each year has its own tuberculosis spa-

tial distribution in Ribeirão Preto, which reveals homogeneous areas for disease risk. Many cases were concentrated in the northeast region in the city, which consists of areas of medium and low income. The results contribute to show the TB spatial distribution in RP-SP, and also reinforce the space category as a methodological alternative to manage, monitor and evaluate health actions by directing interventions to reduced inequality.

#### PS-300-334 Genotypic and phenotypic heterogeneity in single *M. tuberculosis* isolates from pulmonary tuberculosis patients

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**Introduction:** The existence of heterogeneous populations in *M. tuberculosis* isolates and mixed infections are now generally accepted although systematic studies on their relative importance are rare.

**Objective:** To estimate the frequency of heterogeneous *M. tuberculosis* populations and detectable mixed infections in PTB patients from a high incidence setting.

**Methods:** One pre-treatment sputum sample from consecutive newly diagnosed smear positive PTB patients from three hospitals in the Greater Mymensingh District in Bangladesh was included. After culture and identification, *M. tuberculosis* isolates were subjected to drug susceptibility testing, and plated on Dubos agar to obtain isolated colonies (clones). Ten clones were re-cultivated and screened for genotypic heterogeneity using spoligotyping. Clones with divergent spoligotypes were further typed by IS6110-RFLP and MIRU-VNTRs, and Minimum Inhibitory Concentrations (MIC) were performed on each clone.

**Results:** Samples from 87 (90%) of 97 isolates available for analysis showed identical genotypes. Minor variations in genotypes were observed in eight and major variations in two patients.

**Conclusion:** These results showed infection with bacterial sub-populations in 8.2% patients and estimated the frequency of detectable mixed *M. tuberculosis* infections in the study population to be 2.1%. Heterogeneous MIC populations were observed among some isolates.

#### PS-313-343 Population based method for active TB and HIV case finding in difficult to reach, high-risk individuals

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**Objective:** Develop a method for identifying areas of high HIV/TB transmission to find difficult to reach individuals with increased likelihood of co-infection.

**Method:** The Priorities for Local AIDS Control Efforts (PLACE) method was implemented in Kinshasa, Republic Democratic de Congo, and in Cape Town, South Africa to identify high HIV incidence areas (PLACE venues). TB symptoms and presence of active TB were documented.

**Results:** 3482 persons were interviewed. Chronic cough was present in 15% of 621 men and 12% of 356 women socializing at 221 Cape Town venues; in 15% of 948 men and 11% of 245 women socializing at 63 Kinshasa venues; in 11.5% of 69 male and 8% of 234 female clients at 7 Kinshasa STI centers; and in 2.4% of 1035 pregnant women. 15 (9%) of 163 Kinshasa participants reporting chronic cough had active TB confirmed by smear microscopy ( $n = 14$ , 67% HIV-infected) or culture ( $n = 1$ ).

**Conclusion:** The study demonstrated a high prevalence of TB suspects at PLACE venues and identified network venues at high risk of HIV/TB transmission. The method can be cost-effective for intensified case detection of HIV and TB in vulnerable hard to reach populations.

#### PS-323-354 Prevalence of pulmonary tuberculosis in a Pakistani prison

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**Objective:** To determine the extent of pulmonary tuberculosis among prisoners in Karachi central jail.

**Method:** From 7 to 14 February 2002, TB suspects were enrolled and their chest X-ray and sputum examination were done.

**Results:** Of 4870 prisoners, 79 (1.62%) were pulmonary TB suspects. All were male with mean age of 32. Sixteen suspects were already on anti-tuberculosis treatment (ATT), 11 gave history of ATT for incomplete duration. Twenty-two (28%) suspects were not expectorating while fifty-seven (72%) submitted the sputum for AFB (Acid Fast Bacilli). Out of which only one suspect was smear positive. Thirty-nine (49%) chest X-rays including those of 22 who were not expectorating were normal. Eight (10%) showed healed lesion. Thirty-two

(40.5%) were suggestive of active TB, so clinically and radiologically 32 prisoners were suffering from active pulmonary tuberculosis. The prevalence was determined by, number of persons with active TB in jail divided by the total number of persons booked into jail, which turned out to be 657 per 100 000.

**Conclusion:** Pulmonary TB is 3.75 times common than general population in Karachi central prison and concrete efforts are needed to eradicate tuberculosis from this segment of our population.

#### PS-369-392 Annual risk of tuberculosis infection in Tanzania, 1999–2003

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**Background:** In 3 survey rounds between 1984 and 1998, the annual risk of tuberculosis infection (ARTI) in Tanzania remained stable despite a two-fold increase in notification rates of smear-positive tuberculosis (60% HIV-attributable).

**Objective:** To estimate the current trend of the ARTI in mainland Tanzania.

**Methods:** Children aged 6–15 years attending randomly selected schools in 60 districts were skin tested using 2TU Rt23 in Tween-80. Methods were similar for all survey rounds.

**Results:** Data were available for 68 591 children from 12 of 20 regions. The ARTI was 0.70% (95% 0.62–0.78) among all children and 0.68% (95% CI 0.53–0.82) among 7441 children (11%) with no BCG scar. For the same regions the latter had been 1.14% in 1983–1987, 0.95% in 1988–1992 and 1.14% in 1993–1998. The average annual decline since the 3rd round was 8%. Complete survey results will be presented at the conference.

**Conclusion:** The decline in ARTI suggests that the increased HIV-related incidence has had limited impact on tuberculosis transmission and/or that a well-functioning DOTS programme is capable of controlling tuberculosis despite high a HIV-prevalence.

#### PS-366-395 Quality DOTS is working to reduce TB prevalence in the capital city of a high burden country, Cambodia

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**Objectives:** To evaluate TB situation in central Phnom Penh compared to the result of National Prevalence Survey.

**Methods:** TB Prevalence Survey was conducted in Nov 2003–Jan 2004 at 20 densely populated areas of Phnom Penh by cluster sampling method. Participants over 10 years of age were screened with health questionnaire and chest X-ray, and TB suspects identified were examined for smear and culture of their two consecutive sputa.

**Results:** Out of 5361 eligible subjects, 4912 (91.6%) were screened and 451 TB suspects were identified. Thirty bacteriologically positive cases including three smear positive cases were detected, besides four on treatment. Since expected numbers of patients from the results of the National Survey are 17 of smear positive and 55 of bacteriologically positive for this survey participants, the patients detected were much fewer than expected.

**Discussion/Conclusion:** It was implied that TB patients particularly with smear positive are less prevalent in central Phnom Penh where quality DOTS is readily available at least for smear positive TB through various sources. Easy access to DOTS might serve to reduce patients' delay than other areas of the country. Further analysis including impact of HIV is necessary to explain rather high prevalence of smear negative/culture positive.

#### PS-380-404 The risk of occurrence of tuberculosis in geographical areas with varying socio-economic levels in a medium-sized city in the Southeast of Brazil

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Tuberculosis (TB) is related to socio-economic development and its occurrence is generally associated with living conditions, highly populated areas, basic sanitary conditions and low-quality housing, hunger and poverty. The objective of this study was to verify the existence of a correlation between the incidence of the disease and socio-economic conditions in the municipality of São José do Rio Preto, Brazil in 2003. New cases of TB occurring in the urban area were geo-referenced on a vectorial map using the streets as axes and grouped according to 432 census sectors. The utilization of principal component analysis enabled the grouping of the sectors according to socio-economic levels, with calculation of the respective incidence coefficients for each of the sectors. This analysis that produced a factor that was considered very representative of the socio-economic levels of the sectors was used to divide the urban area in three groups with low, medium and high socio-economic levels. Calculation of the incidence coefficients identified that the

risk of falling ill due to TB is approximately 3 times higher in the worst areas (45 cases per 100 000 population) compared to areas with better socio-economic levels.

### PS-394-430 Tuberculose chronique : profil épidémiologique aux Cliniques Universitaires de Kinshasa (2000–2003)

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La tuberculose chronique, surtout multirésistante, est un indicateur de l'efficacité d'un programme national de lutte antituberculeuse. Nous présentons l'évolution, le type de patients et quelques données épidémiologiques à Kinshasa. Sur cette période : 281 patients sont enregistrés (142 hommes [H] et 139 femmes [F]) (tableaux 1 et 2).

Tableau 1

Année	Nombre	H	F
2000	50	23	27
2001	63	34	29
2002	65	33	32
2003	103	50	53

97% des sujets ont moins de 55 ans.

Tableau 2 Types de patients (/ année)

Année	Rechutes n (%)	Echecs n (%)	Reprises n (%)	Autres n (%)
2000	45 (90)	2 (4)		3 (1)
2001	45 (71,4)	12 (19)		3 (1,8)
2002	33 (50,7)	21 (32,31)		10 (15,4)
2003	54 (52,4)	35 (34)	2 (1,9)	12 (11)

**Conclusion :** La tuberculose chronique est en progression à Kinshasa. Pas de disparité de genre. La population active est la plus touchée (15 à 54 ans). Le principal facteur de risque est la tuberculose de rechute.

### PS-410-449 Tuberculosis-related hospitalizations in Brazil (1993–2003)

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This retrospective study aimed to analyze tuberculosis-related hospitalizations in Brazil between 1993 and 2003. Data were obtained from CD-ROM's about the Hospital Information System (HIS), by the Brazilian Ministry of Health/DATASUS. During this period, a decrease in the number of tuberculosis-related hospitalizations was observed in Brazil, with a significant decline in the Southeast. In 1993, this region was responsible for 77.1% of hospitalizations, but only half

(54.4%) of the total number of hospitalizations in 2003. In the North and Northeast, however, the number of hospitalizations increased for male cases. What age is concerned, the range from 0 to 9 years old stood out with a rising tendency, corresponding to 5.3% of the total number of hospitalizations. High hospitalization numbers attract attention due to the high resource volume spent on tuberculosis diagnosis in hospital, in view of the fact that, after the arrival of modern chemotherapy, emphasis has been given to clinical treatment, which presents lower costs and good results.

### PS-439-478 Beijing genotypes of *Mycobacterium tuberculosis* in three South American countries

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**Objective:** To describe occurrence of the Beijing family of *Mycobacterium tuberculosis* in groups of isolates from Argentina, Peru and Paraguay.

**Methods:** IS6110 restriction fragment length polymorphism (RFLP) profiles of a convenience sample of isolates obtained in Argentina (1992–2003,  $n = 1119$ ) were analyzed together with profiles of isolates recruited for drug-resistance surveys carried out in Peru (1999,  $n = 143$ ) and Paraguay (2002–2003,  $n = 106$ ). Profiles were then compared with those of a set of 19 Beijing prototype strains (Dice/UPGMA coefficients, 2% optimization, 2% tolerance, BioNumerics, Applied Maths, Belgium). Isolates showing at least 80% similarity with any of the prototype profiles were considered to belong to the Beijing genotype as described by Lillebaek et al. (Emerg Infect Dis 2003; 9: 1153).

**Results:** Beijing genotypes were identified in isolates of 22 (1.9%), 12 (8.4%), and 9 (8.5%) patients from Argentina, Peru and Paraguay, respectively. The frequency of Beijing RFLP profiles resulted significantly lower in the Argentina group than in the other two countries ( $P < 0.001$ ). Only 2 patients harboring Beijing strains were East Asian-born immigrants. The remaining patients in the study were native South Americans.

**Conclusion:** Beijing genotypes are present in South America and appear to be substantially more widespread in Peru and Paraguay than in Argentina.

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### PS-461-501 Assessment of epidemiological impact of DOTS programme in a district of south India

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**Introduction:** Monitoring trend of the disease over a period with a view to demonstrating the impact of the DOTS programme.

**Objectives:** To assess the epidemiological impact of DOTS by measuring the trend of tuberculosis disease over a period of time.

**Methods:** A random sample of population covered under DOTS programme in a rural area was selected for disease and tuberculin survey. All the eligible populations were covered for identification of chest symptomatics and chest X-ray abnormal for diagnosis of tuberculosis. All children were tuberculin tested and reaction read after 48–96 hours. It is proposed to conduct four surveys at intervals of 2.5 years to estimate the indices.

**Results:** First survey was completed and a population of 83 390 adults registered for screening tuberculosis. Coverage for different examinations was above 90%. A total of 44 176 children were registered for tuberculin testing and coverage was 92%. Of these, 22 310 children had no BCG scar. The prevalence of smear positive cases was estimated to be 323 per 100 000 adult population and ARTI of 1.6% among children.

**Conclusion:** The results of the first survey serve as baseline information and the outcome of the future surveys will provide information on epidemiological impact of DOTS programme.

### PS-462-504 Molecular epidemiological investigation of tuberculosis in Abkhazia, a high incidence region in the Caucasus

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In recent years increasing rates of tuberculosis (TB) and of resistant TB were reported from several parts of Eastern Europe. Among these is Abkhazia, a small country with 250 000 inhabitants, which was affected by impoverishment and the breakdown of economical, social and health care systems after the collapse of the Soviet system and the Georgian-Abkhazian war. In

this study, we aimed to gain the first data on the population structure and spread of *M. tuberculosis* strains in Abkhazia by means of molecular epidemiological methods. Between December 1st 2002 and November 30th 2003 143 *M. tuberculosis* strains obtained from 82 patients recruited at Gulripch Hospital of Shukumi in collaboration with Médecins Sans Frontières were investigated by IS6110 fingerprinting and spoligotyping. This sample included chronic patients as well as new cases. Thirty-seven patients (47%) were infected with a Beijing genotype strain. Based on identical fingerprint patterns of the bacterial isolates, 30 patients (38%) were grouped in 12 clusters comprising fully susceptible as well as MDR strains. These preliminary data confirm the importance of the Beijing genotype for TB in Abkhazia and forces the attention to early diagnosis, detection and interruption of transmission of MDR TB.

The LONG-DRUG study is supported by EC grant QLK-CT-2002-01612.

### PS-484-526 Risk factors associated with default among TB patients in Georgia, 2002

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**Setting:** In 2002, 5983 TB patients were registered in civil population of Georgia. The overall rate of defaulting from DOTS was calculated to be 18.3%.

**Aim:** The aim of the study was to identify associated factors for defaulting from DOTS.

**Method:** Case-control study was conducted. Cases were patients who default from treatment and controls were successfully treated patients.

**Results:** Of the 1094 patients who default from treatment, 70% did so by the end of intensive phase; the median duration from the onset of treatment to default was 86 days. The default rate ranged from 13% to 29% in the different regions. The mean age was 39, the ratio male/female was 2.7. Univariate analysis demonstrated that higher likelihood of default was significantly associated with patient age >35 years, previous history of anti-tuberculosis treatment, being male, unemployment, residence of rural area.

**Conclusion:** The finding of this analysis have prompted the importance of involvement of PHC services in TB control; better supervision, default tracing, motivation and health education should be used as an intervention to reduce default.

**PS-498-544 Follow-up of chronic tuberculosis patients in Ho Chi Minh City, Vietnam**

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**Background:** In Vietnam no second-line treatment is available. The impact of tuberculosis (TB) cases that fail on retreatment (chronic cases) on transmission of multidrug resistant (MDR) TB is unknown.

**Objective:** To assess survival, infectiousness and drug resistance among chronic TB patients.

**Methods:** 600 chronic cases accumulated during 1997–2000 were followed up 1–4 years after retreatment failure by interview and drug susceptibility testing (DST).

**Results:** 24-month survival was 59% ( $n = 428$ ). Sputum was obtained from 153/257 surviving patients (median follow-up 17 months). Of 129/153 (84%) positive cultures, 116 (90%) were MDR. Smear-positive MDR-TB was found in 105/153 (69%). Household TB cases were reported for 43/448 (10%) patients. Of 73 household cases (0.17/patient), at least 21 (0.06/patient) were likely to be secondary; 21/40 (52%) household cases failed or died during treatment.

**Conclusion:** A substantial proportion of chronic TB cases survive and remain infectious for several years; nearly all have MDR-TB. The high failure and death rates in household cases suggest that these MDR bacilli are transmitted and that untreated chronic cases contribute to the spread of MDR-TB.

**PS-502-552 Treatment outcomes by drug resistance and HIV status in Ho Chi Minh City, Vietnam**

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**Objectives:** To assess treatment outcomes by drug resistance, HIV status and treatment history among smear-positive (S+) TB patients in Vietnam.

**Methods:** A representative sample of S+ TB patients were offered HIV testing and submitted sputum for drug susceptibility testing (DST). Treatment outcomes were obtained from routine registers.

**Results:** 51/1834 patients (2.8%) tested HIV-positive. Treatment failure (TF) was 6% among new ( $n = 1433$ ) and 14% among previously treated patients ( $n = 401$ ) overall ( $P < 0.001$ ), and 42% and 33% respectively for MDR cases. Among new patients, the risk of TF was associated with monodrug resistance (adjusted

odds ratio 2.4), MDR (aOR 53) and polydrug resistance other than MDR (PDR, aOR 14), but not with HIV-status. Deaths occurred in 15 of 44 (34%) HIV-positive patients. Mortality was associated with HIV-infection (aOR 31), MDR (aOR 4.7) and PDR (aOR 2.2), but not with treatment history.

**Conclusions:** Treatment failure among smear-positive patients in Ho Chi Minh City is strongly associated with (multi)drug resistance, but not with HIV status. One third of HIV-infected TB patients die before or during treatment; mortality is also associated with resistance to two or more drugs.

**PS-535-595 Restriction fragment length polymorphism analysis of *Mycobacterium tuberculosis* isolates from the Philippines**

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**Objective:** To study the molecular epidemiology of *Mycobacterium tuberculosis* in the Philippines, a high burden country.

**Methods:** We studied the restriction fragment length polymorphism (RFLP) profiles of 331 *M. tuberculosis* strains from the 1997 National Prevalence Survey and from patients under treatment. The isolates comprised 172 pansusceptible, 119 multidrug resistant TB (MDR-TB), and 31 drug resistant TB (DRTB) other than MDR-TB.

**Results:** Except for six isolates, the strains had 7 or more copies of IS6110 fragments with a mode of 13. There were 296 distinct IS6110 patterns with an 89.4% rate of diversity. Sixty-four isolates belonged to 29 clusters with a clustering prevalence of 10.6%. An epidemiological link was confirmed in 11 clusters, it was probable in 2, possible in 4 clusters, with no known link in 8 clusters. Clustering was lower in MDR-TB and DR-TB compared to the pansusceptible strains.

**Conclusion:** The low per-cent clustering of the isolates studied suggest that majority of TB disease in the Philippines are due to reactivation. The low clustering of MDR-TB suggests that the emergence of MDR-TB resulted from inappropriate anti-TB treatment rather than an epidemic outbreak of recent infection.

**PS-513-561 Trend of deaths due to tuberculosis and factors associated with the prevalence of tuberculosis: from Indian experience**

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Despite of all the efforts from Indian government, the share of deaths due to tuberculosis is not declining much over the last three decades. The findings from Survey of Causes of Death Statistics is indicating that

in 1971 the share of deaths due to tuberculosis was 6.7% and even in the year of 1997 it was 6.2%. Comparing the findings from NFHS-I and NFHS-II, it is evident that the prevalence of tuberculosis is on rise in India. Apart, from trend analysis, attempts to study the association of behavioral and environmental factors with the prevalence of tuberculosis in Indian states from data of NFHS-II. The result of multivariate analysis has been indicating that each of the behavioral aspects like currently smoking, ever smoking and drinking alcohol are highly positively significantly associated with the prevalence of tuberculosis, whereas among the environmental factors, i.e., person living in pucca house and with electricity is significantly negatively associated with the prevalence of tuberculosis. The paper concludes that to reduce the prevalence of tuberculosis in Indian states change of behavioral aspects as well as improvement of socio-economic condition of people should be emphasized.

## EPIDEMIOLOGY OF TB: SPECIAL POPULATIONS AND INSTITUTIONS (MIGRANTS, HOSPITALS, PRISONS)–1

### PS-128-162 Tuberculosis in high risk groups and methods of improvement of TB control in Ukraine

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**Introduction:** The TB epidemic in Ukraine was registered from 1995 year and program of TB control was adopted in 2001.

**Objectives:** To appreciate the TB incidence in some risk groups (homeless, migrants, people that had returned from prisons and peoples from isolation with distributions) in Kiev for 2000–2002 years.

**Methods:** Observation of risk groups by fluorography.

**Results:** In Ukraine the TB incidence had increased on 25.7% from 60.1 in 2000 to 75.6 in 2002 per 100 000 population, the mortality had decreased on 9% from 22.3 to 20.4 per 100 000 ( $P < 0.001$ ). The TB incidence in social-unadapted peoples formed 2384–2798 per 100 000 for 2000–2002 years exceeding the TB incidence of all population in Ukraine at 44–37 times and at 68–79 times in Kiev. The high TB incidence was marked in the groups of returning from prisons (22 500–4201 per 100 000 respectively) and in group of peoples from isolation with distributions (1066–1322), in immigrants (3867–17 647) respectively.

**Conclusion:** was established the high TB incidence in risk groups, it is necessary to carry out the prophylactic fluorography observation of these groups before appearing of the clinic symptoms and to use new methods of bacteriological diagnostic, effective treatment of patients.

### PS-174-210 DOTS implementation in prisons in Bangladesh

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**Introduction:** Due to overcrowding, poor hygienic conditions and nutritional status of inmates, the TB problem is substantially higher in prisons than among the non-prison population.

**Objective:** Implement DOTS in prisons of Bangladesh, starting with two major prisons in Dhaka and Chittagong.

**Methods:** Implementation started at end of 2002. In Dhaka prison the microscopy services were established at the prison laboratory, in Chittagong suspect TB inmates were brought to the Chest Clinic for diagnosis. DOT is given by staff trained by the NTP.

**Results:** During 2003 103 new smear-positive case were diagnosed at the Dhaka prison and 115 at Chittagong prison. This corresponds with 930 and 1300 cases per 100 000 inmates; substantially higher than the 100 per 100 000 for non-prison adult males. In Dhaka prison the number of inmates is 4 times the capacity, in Chittagong even 8 times. Number of patients diagnosed during the first 6 months of 2004 will be presented and compared with those diagnosed during the first 6 months of 2003.

**Conclusions:** The TB prevalence at the prisons is very alarming. Overcrowding contributes to the high transmission of TB. Expansion of DOTS services to the other prisons is given highest priority. Plans will be presented.

### PS-177-213 TB resistance in Moldovan prison before and after DOTS implementation

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**Settings:** Drug shortage in 1996–2000 resulted in an eruption of high level of morbidity and TB resistance in Moldavian Prisons. In 2000 a DOTS strategy was implemented by Prison Medical Service supported by Caritas Luxembourg.

**Objective:** To evaluate the level of TB resistance in prisons in 2003, comparing with previously data (1996–2000).

**Design:** The method of absolute concentrations on L-J media was used for drug susceptibility-testing (DST). Were recorded DST results, previous treatment, age and sex.

**Results:** The combined TB drug resistance in Moldovan prison was increasing during 5 years (1996–2000) and was estimated to grow up to 72% any resistance and 49.6% MDR. For last two years, after DOTS implementation, the increase of TB resistance is not

marked. In 2003 any resistance of patients never treated was 47.4% and the level of MDR was 15.8%. **Conclusion:** The level of TB drug resistance in Moldovan prison remains high. However, after DOTS implementation has the tendencies to decrease.

#### PS-180-216 Drug resistance surveillance and monitoring of tuberculosis in the border districts, Thai-Myanmar Border

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**Introduction:** The survey was conducted between 2001 and 2002 to determine the burden of drug-resistant tuberculosis in the border area of Thai-Myanmar.

**Objective:** To identify the magnitude of prevalence of drug resistance in the border area and use as a performance indicator for the NTP and to assess whether recommendation is appropriate.

**Methods:** 133 cultured growing *M. tuberculosis* were performed drug susceptibility testing against dihydrostreptomycin, isoniazid, rifampicin and ethambutol. Resistance was defined as percentage of colonies that grew on critical concentrations of the substances being tested. **Result:** Data on a total of 133 bacteriological smear and culture confirmed tuberculosis cases were collected from 4 diagnostic hospitals. 83 (62.4%) had susceptible strains and 50 (37.6%) had resistance to any drugs. Resistance to one, two, three and four drugs were 22 (16.5%), 12 (9.0%), 5 (3.8%) and 1 (0.8%), respectively. Resistance to isoniazid alone was 9.0%, and any resistance was 22.6%. For rifampicin alone and any resistance were 0.8% and 5.3%, respectively. Multidrug resistance to isoniazid and rifampicin, with or without resistance to other drugs, was 7 (5.3%).

**Conclusion:** The results show that drug resistance has reached alarming levels among TB strains circulating on the Thai-Myanmar border and that it is a serious threat to TB control efforts. Sound strategies on TB control are urgently needed.

#### PS-181-227 Impact of immigration from countries with a high tuberculosis (TB) burden on incidence in Piedmont Region (Italy) in 2001

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**Introduction:** WHO estimated that TB incidence in Italy in 2001 was 8 cases/100 000 population. Few data are available to estimate the impact on TB incidence of immigration from developing to industrialised countries. These data are invaluable for targeting control interventions to appropriate socio-demographic at-risk groups.

**Design:** Linking four sources, we identified incident TB cases in Piedmont in 2001. Prevalent HIV-positive cases were identified from regional registry. Data on residents come from National Census performed during the same year.

**Results:** Piedmontese adult population was 3 706 059 (1 773 052 men; 3 611 754 from industrialized countries; 1 947 050 under 50). There were 640 incident TB cases (32 HIV-positive). A total of 168 immigrants had TB. The TB incidence was 17 cases/100 000 population (178 in immigrants and 13 in autochthonous residents; incidence rate ratio 13.6, 95% CI 11.4–16.2). The fraction of TB cases attributable to immigrant status was 24.3%.

**Conclusion:** Preliminary data indicate that annual TB incidence in Piedmont is higher than estimated for Italy and immigration impact on local TB incidence is highly significant. The findings are relevant in view of the current increasing trend of immigration to Italy from high-TB-burden countries.

#### PS-217-253 Is the current screening programme of new entrants to a Western European city effective?

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As the numbers of new entrants to Liverpool from countries of high Tuberculosis incidence has increased, the TB service has striven to maintain its screening programme to this group. Despite many initiatives to identify, find and screen new arrivals, only half of the 9000 entered on to a database completed TB screening. A 4 year retrospective review of TB cases who have been in the country for less than 5 years shows that the majority of cases presented at a later date to primary or secondary care facilities, and that 78% were not known to the TB Service (Tables 1 & 2).

Table 1 Results of TB screening for new entrants to Liverpool, 2000–2003

	2000	2001	2002	2003	Total
Number identified	3223	2113	2277	1293	8906
Number screened	1975	1024	1182	575	4756
Percentage screened	61%	48%	52%	44%	mean 51%
Partial screening	330	147	64	49	590
Screened previously	25	49	51	48	173
BCG	20	20	27	10	77
Preventive treatment	24	11	26	6	67
TB diagnosed as					
direct result	3	1	0	1	5
Low risk	260	244	33	43	580
Uncontactable	893	648	1012	309	2862
Refusals	8	1	8	5	22
Names removed/ outstanding	87	196	42	358	683



Table 2 TB in new entrants to Liverpool, 2000–2003

53/68 not on database when TB diagnosed
4 diagnosed before screening
2 unsuccessful screening attempts
4 previously screened and cleared
5 routine screens led to notification

**Conclusion:** Although TB screening has produced some positive results and possible prevention by BCG vaccination and preventive treatment, large numbers are not being screened.

### PS-242-273 The multidrug-resistant tuberculosis (MDR-TB) problem in Almaty city and Kazakhstan

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**Introduction:** In 1998, the Kazakh government approved the nationwide implementation of the DOTS strategy. First-line TB drugs became available without limitation in 1998. Consequently, TB mortality declined from 30.7 in 1999 to 22.4/100 000 in 2003. The TB case detection rate increased (141.0 to 161.0/100 000). Second-line drugs have been introduced into pilot areas since 1999.

**Objectives:** To describe MDR-TB dynamics in Almaty city from 1999–2003 and the need for TB control revisions and improved MDR-TB case management.

**Methods:** General country and Almaty city data obtained from Kazakh TB statistics supplemented by information from Almaty city and district TB registers.

**Results:** MDR-TB among new cases increased from 5.4% in 1999 to 12.7% in 2002 at the national level, and remains stable at 14% over the same period in Almaty city. MDR-TB cases comprise 76.2% of registered chronic patients in Almaty. The number of existing chronic cases reached 276 by the end of 2003. More than a half (56%) are not permanent residents of Almaty; 37% have an imprisonment history; 6% have used SLDs.

**Conclusion:** MDR-TB has reached alarming levels both in Almaty city and nationwide. Critical review of the National TB control program is needed and urgent measures needed.

### PS-348-372 Positive tuberculin skin test (TST) among undergraduate medical students (MS) in Rio de Janeiro State, Brazil

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**Introduction:** Tuberculosis is an occupational hazard. Increasing concern with the risk of *M. tuberculosis* infection among MS has emerged.

**Objectives:** To estimate the prevalence of positive TST and its associated factors among MS.

**Methods:** A cross-sectional study was conducted among MS in pre-clinical, early and late clinical years from five universities in counties with different TB incidences: Campos (35/100 000), Petrópolis (59/100 000) and Rio de Janeiro (114/100 000). Sociodemographic profile, BCG vaccination and exposure to tuberculosis were analyzed. TST (Mantoux technique) was performed by a standardized professional. The association of independent variables with a positive TST was tested using the odds ratio (OR) and prevalence during studies using  $\chi^2$  for trend.

**Results:** Among 1032 students aged 18–43, 71 (6.9%) had a positive TST. Prevalence was higher among males (8.8%  $\times$  5.1%, OR = 1.80, 95%CI 1.07–3.05) and students outside Campos (7.8%  $\times$  1.9%, OR = 4.36, 95%CI 1.30–17.57). An increasing prevalence was observed in pre-clinical, early and late clinical years (5.2%, 7%, 8.6% respectively) but this was not statistically significant ( $P = 0.09$ ). Exposure to TB patients, BCG vaccination, age and social class were not associated to TST results.

**Conclusion:** Strategies to deal with healthcare workers/students mainly in settings with high TB prevalence is necessary. The trend for an increased prevalence of a positive TST during medical studies suggests *M. tuberculosis* nosocomial transmission.

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**PS-422-460 Characteristics associated with large genotype TB clusters in NYC, 2001-2003**

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**Background:** TB cases in homeless persons increased from 49/1084 (5%) in 2002 to 86/1140 (8%) in 2003. Genotyping of TB isolates was used to assess TB transmission in this population.

**Methods:** TB isolates were genotyped using RFLP and spoligotype since 2001. Cases with identical genotype (clustered cases) were investigated to identify epidemiologic links. Patients in clusters >4 (large clusters) were compared to patients in clusters with <4 cases (small clusters).

**Results:** Of 2685 culture positive TB patients diagnosed from 1/1/01–12/31/03, genotypes were available for 2378 (89%) isolates; 830 (35%) patients were clustered. Of 2378, 214 were homeless; 151 (71%) had clustered isolates compared to 679 (31%) of non-homeless patients ( $P$ -value <0.001). Patients in large clusters were older (41.8 vs. 38.8yo) and more likely to be homeless, US-born, HIV infected, substance abusers and incarcerated compared to patients in small clusters. In multivariate analysis, being US-born and homeless were both associated with being in a large cluster. Among the 151 clustered homeless patients, 39 (26%) had epidemiologic links; 10 identified another person as a contact, and 29 were linked though common sites compared to 28/121 of non-homeless patients with epidemiologic links.

**Conclusion:** Despite declining TB cases in US-born, TB transmission continues among homeless. Epidemiologic links in homeless persons were more likely to be identified through investigations of common location rather than traditional contact elicitation.

**PS-429-468 Public-private mix in TB control: the Egyptian experience**

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Egypt launched its NTP in 1989. As a consequence the average success rate rose to more than 85%. However, case detection rate is currently around 60%, which is below the WHO target of 70%. From the beginning, the NTP recognised that the involvement of different providers of health care would be essential to the success of TB control in Egypt. Since then the NTP has established links with a variety of public and private providers of health care. There have been sev-

eral studies into the private sector. These suggest that although there is a huge potential to identify TB cases in the private sector, the best mode of collaboration is not clear. There is a study conducted in Sharkia governorate with a case detection level of 46.2% of the expected new pulmonary smear positives to compare the effect of 3 days training vs. half day orientation on the NTP guidelines in improving the notification by the private medical practitioners. The preliminary results of this study is promising and reflected as an increase in case detection

**PS-442-483 Latent tuberculosis infection: risks to health care students at a hospital in Lima, Peru**

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**Introduction:** A prospective study from 2002 to 2003 measuring prevalence, boosting, and conversion of tuberculin skin tests (TSTs) among health care students (HCS) and non-healthcare students (NHCS) in Lima, Peru.

**Objective:** To demonstrate the increased risk of acquiring latent tuberculosis (TB) infection in the hospital relative to the community.

**Methods:** All participants had initial two step TSTs over 1–2 weeks. If both were <10 mm they received a 3rd an average of 6 months later. A 10 mm TST was defined positive, a 10 mm increase at 2nd TST defined boosting, a 10 mm increase at 3rd TST defined conversion.

**Results:** Among the HCS prevalence of initial positive TST was 20.9% (117/559), conversion rate was 1.1% (1/93), and booster rate was 4.9% (9/184). Among NHCS prevalence of initial positive TST was 12.2% (47/385), conversion rate was 0% (0/127), and booster rate was 1.1% (2/187).

**Conclusion:** HCS are at greater risk than NHCS for having positive TSTs, boosting and conversion. We conclude that the hospital poses a greater risk than the community regarding transmission of TB, and greater attention to hospital infection control measures is warranted to try to reduce this risk.

**PS-479-521 Preliminary results of an evaluation of a tuberculosis undertaking program for control of TB in migrants to Australia**

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**Introduction:** Migrants to Australia who have evidence of past tuberculosis are required to sign a tuberculosis health undertaking (TBU) and be subject to follow-up for two years.

**Objective:** To evaluate the TBU program.

**Methods:** A database of all TBU migrants registered at one chest clinic between 1984 and 1994 was linked to the statewide TB notification database for the period 1984 to 2003.

**Results:** Among 3288 migrants, 41 TB cases were identified over an average 13.5 years follow-up (92/100 000 person-years), including 9 pulmonary smear-positive cases (20/100 000 person-years). 48.8% of cases were notified more than three years after arrival. Age over 50 years at arrival was a risk factor for TB ( $P = 0.03$ ), while Mantoux reaction, BCG status, gender, and country of origin were not significant. Only 16 (52%) of 31 cases were notified by TBU surveillance. The remainder presented symptomatically. On average, 155 TBU migrants underwent surveillance to identify one case.

**Conclusion:** The incidence of TB in this cohort is much higher than in the general Australian population but similar to the incidence in migrants from high prevalence countries. These preliminary results support the need for a more comprehensive evaluation of the effectiveness of the TBU program.

**PS-563-630 Screening programmes for tuberculosis in new entrants across Europe**

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Screening foreign born groups with high rates of tuberculosis may help to ensure that they can benefit from early treatment and minimise onward transmission. In January 2003, we surveyed new entrant screening programmes in Europe. Of the 26 countries from whom a response was received, 13 (50%) carry out no specific tuberculosis screening. Of 13 countries with programmes, none conduct pre-entry screening, three conduct screening at ports of entry, and nine

screen in other centres. All thirteen screen principally refugees and asylum seekers, in eight this is required by law. Switzerland, Malta, Belgium, the Netherlands, Norway and the United Kingdom also carry out screening on other groups of entrants including foreign workers and students. All programmes use chest X-rays as a screening tool, but no two countries take the same specific clinical approach. Few data are available to determine effectiveness of programmes.

**PS-565-632 Systematic critical review of existing literature on new entrant screening for tuberculosis**

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Our aim was to describe different models of screening and summarise their outcomes. Medline and Embase databases were searched from 1966 and 1980 respectively until February 2003. Of the 33 studies included in the review, 22 provided information on uptake of screening, which varied from 15% to 98%. In seventeen studies, screening was carried out within the first year after entry. The number of active cases identified varied from 0 to 4538 per 100 000 screened. In the majority of the larger studies the rate was between 150 and 850 per 100 000. All of the studies involved screening individuals from countries where the rate of disease was over 40 per 100 000. Seven studies conducted screening for active disease more than one year after entry. The rate of active disease detected in these studies ranged from 60 to 4022 per 100 000; the majority of studies provided a rate less than 650 per 100 000. Four studies provided data on the number of people with infection identified on screening within one year of entry. Between 38% and 55% had positive tuberculin tests.

**PS-463-502 Reactivation and new infection of *Mycobacterium tuberculosis* contribute to disease among immigrants**

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**Introduction:** The use of restriction fragment length polymorphism (RFLP) is of great value for studying the

epidemiology of tuberculosis. Traditional contact tracing may underestimate the number of clustered cases found by use of RFLP. It is however, uncommon that the use of RFLP reveals concurrent reactivation among patients with close social contacts with each other.

**Objective:** The current study was performed to aid the deciphering of a suspected outbreak of tuberculosis among African immigrants, living in Norway.

**Methods:** A total of 15 immigrants who had social contacts with each other developed tuberculosis during February–September 2003. Thirteen of these belonged to the same religious congregation. It was reasonable to believe that an outbreak was ongoing in this congregation.

**Results:** One patient was culture negative. By use of RFLP analyses we could demonstrate that 9 patients were infected with the same strain of *Mycobacterium tuberculosis* and 5 patients were infected with different strains, each with unique RFLP.

**Conclusion:** The outbreak was related to members of one family and transmission had taken place in their home. The other patients in the same community had concurrently developed reactive tuberculosis. This report illustrates how traditional contact tracing can obtain valuable supplementary information from molecular methods.

#### PS-939-1014 Tuberculosis in the Central Prison of Douala, Cameroon

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**Setting:** A large urban prison in Douala, economic capital of Cameroon.

**Objective:** To determine the prevalence of pulmonary tuberculosis (PTB) and of factors associated with PTB among a population of about 2850 prisoners and their 168 guardians.

**Methods:** A cross-sectional survey during a 3-month period (Oct 2003–Jan 2004). All prisoners and guardians were screened with a pre-tested questionnaire about personal characteristics, antecedents of TB treatment, and signs of actual TB disease. All individuals with cough of more than 2 weeks duration underwent sputum smear examination. The sputum of all TB patients was collected for culture and anti-biogram. Voluntary HIV testing with pre- and post-counselling was offered to all prisoners. Data were analysed using EPI-Info.

**Results:** Of a total of 2830 prisoners, 2475 (87.5%) and 98 (59.8%) out of 164 guardians were screened with the following results: Of the prisoners, 85 (3.4%) were identified with smear positive PTB and

40 (1.6%) with smear negative PTB (total PTB prevalence: 5%). HIV seroprevalence among PTB patients was 21.7%. None of the guardians was diagnosed with PTB nor accepted voluntary HIV testing. In all prisoners, symptoms of PTB developed after having entered in prison. Risk markers associated with PTB included body mass index <20 kg/m<sup>2</sup>, prolonged prison stay, and HIV co-infection.

**Conclusions:** The prevalence of PTB among prison inmates was much higher than in the general population. Only a comprehensive strategy for TB control, including active screening and case-finding and measures for preventing HIV-transmission, can cope with the TB burden in the prison system.

## TUBERCULOSIS AND POVERTY

#### PS-287-321 An anthropological exploration of endemic tuberculosis in a remote Aboriginal community in Northern Australia

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In the Northern Territory (NT) Aboriginal people are at risk of contracting tuberculosis (TB), where rates are six times higher than among non-Aboriginals. In 2000 of the 38 notified cases, 14 (37%) were associated with one Aboriginal community. Despite effective treatment of TB patients over the past decade, compliance with latent TB infection (LTBI) has been low. In 2003/04 a qualitative study was conducted in order to assess the level of awareness and understanding of TB and latent TB infection (LTBI) in this community, and the factors which mitigate against early presentation with TB, and acceptance and/or compliance with treatment for latent TB infection. The researchers found there to be a low level of knowledge of TB, and even lower of LTBI. While the seriously ill will usually seek treatment at the local health clinic, there is some reluctance to present early due to communication difficulties with non-Aboriginal staff. Men expect their bodies to heal by itself, and many feel uncomfortable dealing with its non-Aboriginal staff. There is insufficient funding for outreach by Aboriginal people speaking local languages to inform those most at risk of TB, a measure community leaders consider necessary, nor for the treatment of those with LTBI.

### PS-312-342 Knowledge and attitudes towards tuberculosis among patients of a high burden country

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**Objective:** To assess the knowledge and attitude of TB patients towards their disease, and recommend strategies for improvement in a high burden country.

**Methods:** Descriptive cross-sectional study was conducted in an out-patient setting of two tertiary care hospitals in Karachi, Pakistan.

**Results:** Of the 150 patients interviewed, 22% were illiterate. Nearly 15% did not know that TB is contagious and 52% were unaware that TB can affect organs of the body other than lungs. Almost 56% believed that TB can be caused by stress or emotional trauma and 40% wished to hide the diagnosis from other people. About 17% thought that TB treatment can be stopped once symptoms have improved. Almost 70% thought that TB is a preventable disease and 45% believed that there is a vaccine that can prevent TB. Nearly half of the patients considered TB to be a social stigma in the society. About 38% believed that there were less chances of getting married with TB and 21% thought that TB could result in infertility. Media emerged as the main source of information for these patients.

**Conclusions:** Extensive health education and community involvement is needed to create awareness and remove myths about TB.

### PS-349-374 Socioeconomic profile of patients with tuberculosis (TB) in a poor county of Rio de Janeiro (RJ) periphery, Brazil

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**Introduction:** Tuberculosis is reported to be a disease of the poor. Almost 95% of all TB cases occur in the poorest countries.

**Objectives:** To assess the socioeconomic profile of TB patients in a public primary care unit which notifies 85% of all TB cases in Duque de Caxias (incidence rate 156/100 000).

**Methods:** A questionnaire-based study comparing the socioeconomic class of TB with non-TB patients was conducted. DHS and Brazil (IBOPE) criteria were used for socioeconomic classification. In Brazil, all TB patients are treated in public units, since drugs are supplied upon notification.

**Results:** The survey included 529 patients (243 with TB). Compared to the 1996 DHS Brazilian survey, the

three lowest quintiles of both groups are wealthier. Regarding IBOPE criterium, 61% belonged to the two poorest classes in both groups, in contrast with 34% in the metropolitan RJ general population. There was no difference in socioeconomic class between groups by both criteria.

**Discussion:** These results suggest that public facility customers are underprivileged and that TB patients are poor, although not poorer than non-TB patients. DHS results may reflect changes in Brazilian socioeconomic status since 1996 or exclusion of very poor patients, who might not even reach public units.

Sponsored by: World Bank, Reaching the Poor Program.

### PS-359-381 Implementing a package of interventions to reduce the negative effects of stigma of tuberculosis in five municipios of Nicaragua

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Nicaragua has a well organised tuberculosis control program and is making good progress towards the WHO targets for case finding and holding. However, problems persist for person affected by tuberculosis. Stigma of TB, though under-recognised is one the reasons. We explored social stigma in five remote municipios of Nicaragua and selected in each of them one or more of five type of interventions:

- TB clubs to strengthen coping skills of people affected by TB
- Home visit to discuss the psychosocial problems of the people affected by TB with its direct social surroundings
- Revision of patient pathway to decrease stigmatizing features and bring care as close as possible to the community
- Involvement of the family in the care to people affected by TB from the starting of the treatment
- Case discussion of people affected by TB with care providers not directly involved in TB program to sensitise them about the difficulties encountered by TB patients.

This set of intervention is evaluated by a combined quasi-experimental study with qualitative evaluation of the process. A scale to measure changes in stigma and self-esteem has been designed for that.

This project is supported by the Damian Foundation.

### PS-375-403 Tuberculosis and society: a case study of major determinants of disease and planning for effective strategies in India

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Tuberculosis is a chronic illness that eventually leads to death. There are nearly eight million new cases of TB

per year and this is set to rise to 12 million new cases per year by the year 2005: The purpose of the present study to identify the causal links between the occurrence of tuberculosis, society and poverty and also to identify the major determinants with the help of a multivariate statistical approach to study the major dimensions between disease, sociocultural, socioeconomic and sociodemographic variables with an emphasis on nutrition and poverty. The study was based on primary and secondary data. The study with the help of a questionnaire survey collected data for the selected variables on a stratified random sampling in order to identify the major dimensions with the help of a factor analysis. The study thus identified the major dimensions with reference to causal links between Tuberculosis, Society (socioeconomic variation in the society) and Poverty (particularly with reference to onset of undernutrition and malnutrition indicators) including a poor environmental setting of the lower socioeconomic status.

#### **PS-458-499 Tuberculosis control in rural areas**

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The control of Tuberculosis in rural areas, where clinic and other health services are distant or non-existent, is reliant on the DOTS worker's knowledge and ability to work with patients and on community support. The paper will show the development of both of these in identified rural areas of South Africa over a three year period. It will also show the impact of educational activities on the community knowledge of both TB and HIV/AIDS.

#### **PS-611-675 Civil society mobilization for tuberculosis control in Rio de Janeiro State (RJ), Brazil**

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**Introduction:** Aids control program in Brazil is a success mainly because of the social mobilization and NGOs organization and political power. The RJ Tuberculosis Control Program (TCP) decided to use the same strategy to achieve political commitment and DOTS expansion.

**Objectives:** Sensitize, mobilize and qualify, the Civil Society Organizations (SCO) to participate in TB control activities.

**Methods:** First step was to conduct an Assessment of CSOs (working with AIDS, health and human rights). Then, CSOs were called for a workshop to discuss the TB situation and operational program strategies.

**Results:** Foundation of RJ TB Forum with 35 OSC. The Forum is promoting actions close to its affiliates

and to the general population, informing and alerting for the problem. The Forum has as its primary task to be properly structured in order to influence public health policy decisions and to denounce all kind of human rights omission, transgression and violation suffered by people living with TB.

**Conclusions:** The civil society mobilization is important to occupy, in a responsible way, institutional spaces where the population has for right to be represented. This experience has also shown the importance to create alternative places where population could claim and have their rights warranty.

#### **PS-714-786 Millennium Development Goal 6: limit the spread of HIV/AIDS, syphilis and tuberculosis**

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Goal 6 strives to eliminate diseases which represent a serious threat to security of life. The Bulgarian adaptation of this goal to limiting the spread of HIV/AIDS, syphilis and tuberculosis is related to their social importance and to the alarming increase in the incidence rates of these diseases during the last few years. Their prevention has not only social but also financial implications, since their treatment requires more resources than their prevention. The aim is to reduce twofold tuberculosis cases and full coverage of the country with the DOTS strategy and increased proportion of healed cases. Until 1990, Bulgaria, like some other countries in the Balkans, registered a long-term decrease in tuberculosis. At that time, the average incidence was 25.1 per 100 000. In 1998, however, tuberculosis incidence grew to 50 per 100 000, while in 2002 it stood at 47.8 per 100 000. By comparison, TB incidence in the EU is about four times lower (11.5 per 100 000 in 2000). Multidrug-resistant tuberculosis (MDR-TB) is a serious problem for Bulgaria both from the epidemiological and the financial points of view. Its treatment is much more difficult and about 1000 times more expensive than treatment of other patients. Until 1999 the incidence of MDR-TB grew to 10.7% due to interrupted and incorrect treatment. In order to reverse the spread of tuberculosis, there must be significant improvements in early diagnosis and treatment of patients. Specific tasks for the improvement of the tuberculosis management in Bulgaria include: 1) Improvement of the quality of bacteriological laboratories; 2) Improvement of the flow of information from the periphery to the center; 3) Reduction of the proportion of relapses and interrupted treatment in order to reverse the prevalence of the disease; 4) Prevention of MDR-TB by means of providing the correct type of treatment for all patients and monitoring the progress of all patients up to the end of the treatment.

**PS-766-840 Role of a system of social-medical protection measures in a decrease in an epidemic wave of tuberculosis in Moscow in the twentieth century**

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Decrease in an epidemic wave of tuberculosis was marked in Moscow in the twentieth century, except for the periods of world wars, both on relative parameters of death rate, and by annual absolute quantities of death from this disease. Relative parameters had been reducing during all century, annual absolute quantities of death from tuberculosis had decreased since the second half of the century. The correlation analysis of parameters of death rate from tuberculosis and social-demographic and social-economic parameters was carried out during 1953–2000 when the specified system of measures was realized in the conceptual, structural and technical attitude and 1910–1953 when only separate elements of this system have been realized. Mathematical models are constructed which allow probabilistic forecasts of development of an epidemiological situation under various social conditions during the investigated periods of time in case a hypothetical realization of a system of medic-social protection measures take place or its absence. A ratio of a real and predicted hypothetical death rate from tuberculosis during these periods determines efficiency of social medical protection measures. It is shown, that realization of medic-social protection measures is one of the leading factors causing decrease epidemic wave of tuberculosis.

**PS-101-147 A peer promotion strategy of DOTS in redlight areas in Calcutta: an experiment with HIV positive people**

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This investigation summarizes the behavioural changes amongst HIV positive people in 15 red light areas in Calcutta City and lesson learned regarding community based DOTS strategy to control the commonest opportunistic infection, TB and discusses the use of peer network evaluation to understand the dynamics of peer promotion. To examine the interpersonal communication process of peer education about the DOTS strategy this study tested a new approach using multiple semistructured interviews and peer network analysis to collect data on sixty-nine peer educators and three hundred forty five of their contacts. One hundred per cent questionnaires that were given to sixty-nine peer educators to complete with their typical contacts from fifteen locations in the city were returned. There was a high level of information regarding the

most commonest infections and successful DOTS among HIV positive people. The peer contacts data presented here a step toward understanding the process of peer promotion. In conclusion it can assure (network questionnaire and semistructured interviews) the competency of peer promoters to disseminate the information in a positive way to ensure DOTS for commonest infection amongst HIV positive people.

**PS-692-767 Society mobilization to fight TB in the Dominican Republic**

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**Introduction:** NTP of Dominican Republic commemorated World TB Day (March 24th) mobilizing secondary level students of some Santo Domingo schools integrating them in fight against the TB with activities where participated civil society, industrialist, churches, national and foreign cooperation organizations, NOG's that work with HIV/AIDS.

**Objectives:** To incorporate several society sectors to integrate them in fight against the TB.

**Methods:** Were organized activities whose messages were 'Each breathing counts, stop TB now' and 'TB control is a commitment of everyone'. It was recognized health personnel for fighting against TB; accomplishment artistic activities like theater performance, singers, boards with civil society representatives, painting aid with subjects related with the TB control.

**Results:** World TB Day celebration they attended thousand people of different social sectors. It was recognized 6 provinces by their high performance fighting against TB in 2003, 42 people between doctors, nurses, bioanalists who work for TB control at intermediate and local level and 3 secondary level students by their paintings were awarded.

**Conclusion:** The social mobilization for fighting against the TB increases the population access to DOTS.

**PS-745-819 Obstacles à la mise en œuvre de la stratégie DOTS dans la ville de Ouagadougou**

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**Introduction :** Malgré la mise en œuvre de cette stratégie, de nombreux cas défailants ont été observés dans les Centre de diagnostic et traitement de la tuberculose au Burkina Faso.

**Objectif :** Identifier les obstacles à la mise en œuvre

de la DOTS, notamment de la prise supervisée dans le contexte d'un pays à ressources limitées.

**Méthodes :** Cette étude transversale a concerné tous les malades tuberculeux en première phase de traitement dans les cinq structures de diagnostic et de traitement de la ville de Ouagadougou pendant la période d'août à Septembre 2002.

**Résultats :** Pour 71% des répondants ( $n = 74$ ), le nombre élevé de comprimés par prise constituait une contrainte à l'observance du traitement. L'obligation de se déplacer quotidiennement a été citée par pour 55,4% des enquêtés. Une majorité d'enquêtés (51,4%) affirme dépenser environ 1 euro par jour pour se rendre au CDT. Le manque de ponctualité des agents de santé à leur poste a été observé par 56,7% des enquêtés.

**Conclusion :** Pour une meilleure observance du traitement, une décentralisation des lieux de prise du traitement anti-tuberculeux impliquant les formations sanitaires de premier niveau est impérative.

#### PS-829-901 Social aspects of health education in Kazakhstan TB control program

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**Introduction:** Lack of knowledge of patients has negative impact on their discipline, attitude to disease, and consequently, treatment effectiveness. The problem of improving methods to inform population with the view of increasing effectiveness of TB control activities remains urgent.

**Objectives:** The aim of the present investigation is to study problems of health education quality among different groups of population.

**Methods:** During this research it is expected to determine the level of awareness on TB problems among medical personnel, patients and their families through questioning and interview. To solve the specified tasks the qualitative methods of investigation were applied such as involving of population in estimation and solution of problems (IPESP) through focus group discussions and individual interviews.

**Results:** During the investigation all focus groups have shown low level of knowledge of all studied aspects. Medical specialists dedicate not enough time to explanatory work. The existing image of TB is—disease of poor people. So, the investigation has revealed serious deficiencies in health education and also that present methods of health education are of no informative value.

**Conclusion:** 1) It is necessary to continue conducting educational training on TB issues for different population groups. 2) Medical specialists should dedicate more time to explanatory work using methods that increase the informative value of health education. 3) It is important to change the image of TB as a disease in

the community and accentuate its infectious nature. 4) Further efforts to increase awareness among the population should be directed at the development of new approaches to health education.

#### PS-193-236 L'approche centrée sur le patient tuberculeux, une stratégie pour l'amélioration continue de la qualité des soins et de l'organisation des services de santé

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**Objectif :** Mettre en place un processus régional de recherche-action basé sur l'échange d'expériences et l'acquisition de compétences entre prestataires, pour améliorer les soins au patient tuberculeux.

**Méthode :** 52 personnes de 6 pays d'Afrique francophone (Bénin, Burkina, Sénégal, Niger, Mali, Côte d'Ivoire) participaient, avec dans chaque pays un responsable des Programmes Nationaux Tuberculose et un chercheur en santé publique. La pédagogie était participative, organisée en plusieurs phases :

- Séminaire d'échanges : formation méthodologique et définition d'une recherche-action
- Mise en place de recherche-action
- Séminaire de restitution : partage d'expériences et de connaissances

**Résultats :** Les équipes, composées d'acteurs de différents niveaux du système de santé, ont mis en place une approche 'bottom-up' et 'top-down'. Un réseau de travail et de recherche a été initié : les participants ont enrichi leurs connaissances d'expériences de contextes similaires. Les RA ont amélioré la qualité des soins aux patients tuberculeux : décentralisation du diagnostic, du traitement, organisation de visites à domicile, implication de la famille dans le suivi des patients.

**Conclusion :** Cette approche a permis de motiver les acteurs et d'améliorer la qualité des soins, mais un travail à plus long terme est nécessaire pour assurer la pérennisation des acquis.

Projet financé par la Direction Générale de la Coopération au Développement (DGCD) belge et mis en place par l'Université Libre de Bruxelles, en collaboration avec la Coopération Technique Belge.

#### PS-258-284 Interagency cooperation as a mechanism to strengthen National TB Program (First experience of cooperation between Project HOPE Turkmenistan and NRCS Turkmenistan in DOTS implementation)

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**Background:** To date Ministry of Health of Turkmenistan and 8 international organizations work on im-



proving TB program in Turkmenistan. Project HOPE provides TB drugs, laboratory and office equipment supply, educational, monitoring components and technical assistance. National Red Crescent Society (NRCS) of Turkmenistan implements food support program in the city of Ashgabat. To create basis of this program, NRCS in cooperation with Project HOPE conducted program assessment and developed the selection criteria for the patients including in the food support program. Taking into account the objectives of Food Support Program a need to train patronage nurses on DOTS appeared.

**Objective:** To improve patients' adherence to treatment, to improve NRCS patronage nurses competence on DOTS, to improve the population knowledge on TB.

**Methods:** Trainings for patronage nurses, food packs distribution among TB patients on continuation phase, IEC materials development.

**Results:** So far Project HOPE trained 9 nurses of NRCS of Turkmenistan. To improve knowledge of general population on TB Project HOPE in cooperation with Ministry of Health, NRCS and Zdrav Plus developed and produced posters and leaflets on TB for distribution among general population and in out-patients clinics.

**Conclusions:** Collaboration between National TB program and International Organizations in DOTS implementing will raise the effectiveness of TB program in the aspects of: patients' treatment adherence, patronage nurses competence and population awareness on TB.

#### **PS-351-376 Appealing incentives for healthcare providers dealing with tuberculosis in a poor county in the periphery of Rio de Janeiro, Brazil**

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**Introduction:** Duque de Caxias (DC) has one of the highest TB incidence of the country (156/100 000 population). In 2001, DC Tuberculosis Control Program (TCP) has reported a treatment default rate of 20%. Insufficient medical knowledge, skills and attitudes have been associated to poor tuberculosis treatment outcomes. Patients in DC have reported that important incentives for treatment compliance include better health care.

**Objectives:** To access appealing incentives for healthcare providers dealing with tuberculosis in DC.

**Methods:** An anonymous questionnaire-based survey on appealing incentives was applied among all

healthcare providers of the TCP unit, which accounts for most case notifications (1020/1200).

**Results:** Out of the 13 healthcare providers, 11 answered the questionnaire (one on medical leave, another refused to answer). Ten were female, median age was 42 (32–64) years. There were three nurse assistants, two nurses, one social worker and five physicians. Incentives considered important/fundamental included laboratory test access, infrastructure/computers, access to hospital beds when necessary, opportunity for qualification and better salaries. DOTS, meal tickets, multidisciplinary teams, number of scheduled patients and incentive for each cured case were considered desirable.

**Conclusion:** Main incentives for healthcare providers dealing with tuberculosis concern better facilities and valorization of professionals. Surprisingly, DOTS is not a priority.

Sponsored by WORLD BANK, Reaching the Poor Program.

#### **PS-637-708 World COPD (Chronic Obstructive Pulmonary Disease) Day in Sombor Municipality (SM), Serbia**

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**Introduction:** In November 2002 and 2003 the GOLD (Global Initiative for Chronic Obstructive Lung Disease) coordinated World COPD Day worldwide.

**Aim:** To present the tools implemented and the results achieved in marking the World COPD Day in SM.

**Methods:** An article in the 'Somborske novine' weekly entitled 'Breath for Life' was published; information on COPD was broadcast on the local TV and radio station and a sound recording (a COPD patient coughing) was released; a presentation was hosted by the local internet provider (IP); the short COPD questionnaire was put up in all primary healthcare facilities; students of the secondary school for nurses applied the questionnaire on the general population; the poster 'Is it COPD?' was hung up in the town; a seminar for nurses was organized; a GOLD-created document for the general practitioners was distributed.

**Results:** The 'Somborske novine' issue was sold in more than 6000 copies, the local TV/radio attracted several thousand viewers/listeners, the local IP had hundreds of visitors/day, the number of patients in primary healthcare was >1000/day, the number of nurses attending the seminar was >200.

**Conclusion:** In both years at least 15 000 inhabitants of SM were made aware of the dangers of smoking and COPD. The local IP was successfully used for the first time to promote a health-educational programme.

### PS-649-718 Creating a social program: formation of an integrated DOTS-Plus team

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**Objectives:** To describe the process of social development through formation of a DOTS-Plus team.

**Methods:** Qualitative study using participant observation, focus groups, and key informant interviews.

**Results:** In Lima, Perú, community-based DOTS-Plus efforts have served as process of social program development. Community health workers, patients, and health professionals have all developed discrete, inter-dependent roles in the health care team. Informal and formal training allows each participant to develop the skills to work autonomously within his/her defined roles, adapt to the cultural and changing needs of the patient and community, and still work as members of a multidisciplinary team. Nurses have, in large part, overseen the development and supervision of this team. Benefits to the patient and community include social reintegration of tuberculosis patients, formation of a cadre of highly-trained community-health workers, tangible successes resulting in improved morale and cohesion within the community, and public-private collaborations that can adapt to other health problems.

**Conclusion:** The eight-year process of creating a flexible, multidisciplinary DOTS-Plus team in Lima, Perú, has led to enormous personal development among team participants and has far-reaching potential as a means of community mobilization.

### PS-690-762 Communication regarding the prevention of tuberculosis: a partnership among the community, patients and health workers at Oswaldo Cruz Foundation

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**Introduction:** This investigation is an unfolding of the project about tuberculosis chemoprophylaxis (TC) at ECCRI.

**Objectives:** Contribute for the knowledge of communication demands about tuberculosis prevention and to propose communication participative work strategies.

**Methods:** We interviewed 135 people, between 18 and 73 years, 2003. Health workers ( $n = 22$ ), TB patients (20) and co-infected by TB-HIV (23) originated from two assistance units inside Oswaldo Cruz Foun-

dation and the general public (70), configuring a heterogeneous sample.

**Results:** Seventy-six (56.3%) declared having at least high school level and 83 (61.5%) were women. The answers of the 135 people's interviews were categorized. Relating to the matter about TB's Etiology: 40 (29.6%) of the participants 'qualified the disease' (severe pulmonary disease, chronic, bad, boring, serious problem), 27 (20.0%) of the interviewed informed that it was a transmissible disease (contagious, pulmonary infection).

**Conclusion:** Although presenting a good education level, a great part of the sample, included health workers, presents doubts about the prevention and the means of transmission of TB, existing little information and myths related to the theme, in the analysis phase. The personal experiences' reports were extremely important for the success of this research and it will contribute to the elaboration of informative materials.

### PS-486-530 Mechanistic explanation to the catalysis of reaction between rifampicin and isoniazid by pyrazinamide and ethambutol

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Rifampicin (R) and isoniazid (H) interact with each other under stomach acid conditions and formulation environment to form isonicotinyl hydrazone (HYD), which is a matter of concern as it leads to decrease in effective concentration of R. It was indicated during a previous study that the reaction is catalyzed by ethambutol (E), and to a lower extent by pyrazinamide (Z). While E is known to influence by attracting moisture due to its hygroscopicity and by lowering of pH, it was felt that an additional mechanism also played part, as both R and H decreased to an extent of 80% in formulations without (RHZ) and with E (RHZE), when exposed unpacked to 40°C/75% RH for three months. To understand the mechanism, R and H were stirred together with ethanolamines, pyridine, pyrazine, piperidine, pyrrolidine and di-isopropyl ethylamine in aqueous media. Ethanolamines and di-isopropyl ethylamine catalyzed the reaction, yielding up to 80% HYD. Other bases showed less interaction. The extent of catalysis was dependent upon proton abstraction property of the base. It means E, and to a lesser extent Z, catalyze interaction between R and H through abstraction of proton during the reaction process. The mechanistic pathway will be discussed.

**PS-687-759 Smoking: preventable risk factor?**

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**Introduction:** Smoking is one of the major single preventable risk factor of chronic mass non-infectious diseases. In our Society smoking is a socially excepted way of behaviour: 40.4% adult population, 23.3% high school students and 49% students, 55% of medical staff are smokers. A constant increase of the tobacco-smoking epidemic imposes an urgent need for adequate tobacco control programmes.

**Objectives:** Define and analyse the activities on tobacco control and reduction of smoking prevalence in our country.

**Methods and Results:** The Indoors Smoking Prohibition Act and The Act Against Smoking Adversing were passed in our country as early as in 1995 and 1991, but obviously, the instruments for their implementation haven't been effective. Since 1998 our country has been taking part in the international anti-smoking campaign 'Quit and Win'. In 2002 the Ministry of Health of the Republic of Serbia initiated another anti-smoking campaign 'Extinguish' the cigarette—Prolong your life', marking it as a priority for all medical institutions, high and university medical profile schools. It was also aimed at formulating the National Anti-Smoking Plan in accordance with the European Strategy of Control and Reduction of Smoking.

**Conclusion:** The two on-going anti-smoking campaigns in our country have diverse goals but common long term effects, encouraging permanent activities on smoking control in our country.

**PS-838-913 La prévention contre le VIH**

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**Introduction :** La pandémie du VIH/SIDA est la guerre non déclarée la plus mortelle au monde, dont l'Afrique est la première victime. Aussi bouleversant que soient ces décès, l'impact du VIH/SIDA ne s'arrête pas là. Un effet moins bien connu mais désastreux du SIDA est le nombre très élevé d'enfants qu'il a rendu orphelin. Ainsi, l'ONG Les Bâtisseurs s'occupe de la prise en charge des enfants orphelins infectés et affectés victime du VIH/SIDA. Nous sommes convaincues que, partant de notre expérience, les enfant orphelins victime du VIH/SIDA sont sans doute vulnérables du fait des conséquences qui entoure cette pandémie et de la société qu'ils vivent. Ainsi, conscient de l'impact positif de la communication dans la limitation de la contamination et du changement de comportement au sein de la population, l'ONG Les Bâtisseurs entreprend différentes activités afin de permettre l'accès à l'information à toutes les couches de la population tout en respectant le cadre communicationnel VIH/SIDA. En-

fin, plus 2854 personnes sont sensibilisées depuis le mois de janvier.

**PS-934-1009 Gender and tuberculosis infection in Kalingalinga community in 2003**

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**Background:** In Kalingalinga community despite tuberculosis (TB) diagnosis and treatment being free of charge in public clinics, hospitals and Community Based Tuberculosis Organisations (CBTOs), females seek medical help late compared to their male counterparts. This is a pilot retrospective study to determine the sex which was more infected and why females delay in seeking medical help in this low income setting.

**Method:** In February 2004 we carried out a survey to determine the sex which is prone to TB infection in Kalingalinga. We checked the tuberculosis records at ZATULET TB Centre. A structured questionnaire was used to record the total number of patients seen in 2003 according to sex, their ages and sputum smear results, the cure and treatment completion rates, defaulters and died according to sex. A question was administered to the staff to find out why a particular sex did seek medical help early compared to the other.

**Findings:** A total of 243 TB patients (113 males and 130 females) were registered in TB treatment register. Eighty seven (35.8%) males and eighty four (34.6%) females were sputum smear positive. Nineteen males and 17 females were declared cured while those completed treatment were 23 males and 25 females. Defaulters for males were 24 while females were 20. More men died (12) compared to 11 females. Fifty percent of the males were either working in factories or running average businesses while only 10% females were working or selling at the market. Eighty percent of the females were house wives.

**Interpretation:** Females delayed seeking medical help because of poverty, either busy with the children or nursing the sick. The males had more financial power and more prone to TB than females because of working in cement, quarries and other dust factories.

**DOTS: PUBLIC-PRIVATE MIX****PS-98-144 Does routine home visiting improve the return of latecoming patients?**

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**Objectives:** To compare return of late comers with and without home visiting and compare the treatment success rate in both groups.

**Design and methods:** This study is experimental, which randomizes patients into either home visiting or non-home visiting. Four hundred and eighty new smear positive cases who came late for collection of their drugs from the health centers over a period of 6 months were selected and randomized to either home visiting or non-home visiting.

**Findings:** Home visiting was highly effective in improving return of late coming patients (out of 240 patients, 231 return and 9 did not return). The success rate was 94.1% compared to 76.7% in the control group. Defaulter rate in the intervention group was 0.9% while in the control group it was 10%. Smear conversion at the end of the treatment was better in the intervention group (92.9%) compared with the control group (75%).

**Conclusion:** Home visiting by trained personnel would significantly improve patient compliance and the treatment success rate, smear conversion rate and reduce the defaulter rate.

#### **PS-171-207 Public Private Partnership in Bangladesh**

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**Introduction:** In big cities many patients attend the private sector.

**Objective:** Establish partnership between the NTP and private sector to increase TB case detection and improve patient management.

**Method:** 63 chest physicians and general practitioners participated in the Public Private Partnership Project in Dhaka. Orientation on NTP policies was given and NTP guidelines for private practitioners were discussed. The project was initiated in September 2003.

**Results:** 44 of the 63 PP's treated patients at their practice, 5 referred suspects to public services and 14 did not participate. Of 589 patients diagnosed during first 4 months, 164 (28%) were smear-positive, 354 (60%) smear-negative PTB and 71 (12%) extra-pulmonary. Only 20% of smear-positive patients had two smear examinations; 81% of smear-negative PTB cases had only one smear examination. 11% of all cases were treated with NTP drugs, free of charge; they attended weekly-fortnightly; DOT was given by a family member. The remaining patients were given prescriptions to purchase drugs. They reportedly did not want treatment under DOT, and were excluded from free treatment.

**Conclusions:** Involvement of private practitioners in DOTS in big cities is very important. However, diagnosis and treatment should be closely monitored and results discussed with the PP's for improvements.

#### **PS-191-234 An assessment for improving quality and expanding coverage, especially in urban areas**

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**Introduction:** NGO service Delivery Program (NSDP) is a USAID funded implementing agencies providing Essential services Package including the Tuberculosis services.

**General objectives:** To assess the level of quality and coverage of TB-DOTS program implementing by the NSDP partner NGOs mainly in the urban areas.

**Specific objectives:**

- Assess providers' knowledge of TB case management.
- Review the existing record keeping and reporting system
- Explore evidence of an operational integration and a referral system between NGO clinics and government health facilities, general practitioners and private clinics of the catchment area.

**Methods:** The assessment was conducted over a period of six weeks between October and November 2003 through observation, interviews and reviewing records, reports.

**Results:** All the NSDP clinics found integrations with chest disease clinics, other NGOs and some have integration with general practitioners to referral TB suspect, treatment, investigation & medicine supply. All categories staff of NSDP clinic found deficiency in knowledge on TB DOTS program. Recording and reporting of various report forms of NTP are found to be incomplete.

**Conclusion:** All categories staff of the clinics assessed was found deficient in their knowledge of TB DOTS program. Irregularities and incompetence were identified in the recording and reporting system.

#### **PS-225-259 The primary health care system as an essential component of the TB program in pilot sites of Turkmenistan**

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**Background:** The DOTS program is being implemented in Turkmenistan since 1999. At present the decentralized detection system and treatment of tuberculosis cases is functioning within the DOTS pilot sites.

**Objective:** Review the role of Primary Health Care (PHC) system in the TB control program of Turkmenistan.

**Methods:** Monitoring of the program performance according to WHO indicators.

**Results:** PHC is an important component of the National TB Program in Turkmenistan. The microscopy

sputum exam became an effective tool of tuberculosis case finding used by PHC (out-patient clinics). The number of TB cases detected by smear microscopy increased more than 3.5 times in the year 2003 in comparison with the year 2001 in PHC facilities. PHC system is actively involved in the process of TB treatment. There were 1860 tuberculosis patients who were treated in the out patient clinics in the continuation phase. The cure rate increased from 55.5% in the year 2000 up to 80.4% in the year 2002 since PHC has been actively involved in case finding and treatment of the tuberculosis patients.

**Conclusion:** PHC system involvement in the process of TB detection and treatment allows improvements in case finding and treatment outcome.

#### **PS-282-307 Assessment of TB-DOTS program implemented by NSDP urban NGO clinics**

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**Introduction:** Although the government of Bangladesh, in coordination with NGOs, implementing TB program, there is scope for more integration with the implementing partners in order to strengthen capacity and quality.

**General objectives:** Assess the capacity and quality of TB-DOTS program in urban NGO clinics.

**Specific objectives:**

- Assess capacity of case identification
- Assess quality of laboratory services
- Review existing recording and reporting system

**Methods:** An assessment of 15 NGO clinics was conducted over a 6-week period (October–November 2003) through observation, interviews and reviewing records/reports.

**Results:** Only two-third of staffs was trained to identify symptomatic cases. Laboratories for sputum examination were available in one-third of the clinics, which fulfilled 84% of the required criteria in physical facility, equipment, staining quality, waste disposal and recording.

**Conclusion:** Capacity building efforts need to be generated through intensive training of all staff categories for identification of symptomatic and sputum positive cases appropriately. Laboratory services & recording need improvement and better tracking.

#### **PS-459-500 Improvement in quality of tuberculosis care through public-private mix (PPM)**

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**Introduction:** Private Medical Practitioners' (PMPs) participation in RNTCP initiated by PCMC; increased

from 9 to 92 during 1999–2003, majority from alternate system of medicine. PMPs referred suspects for diagnosis & categorization to Public Health System (PHS) & provided DOTS at their clinics. PHS did monitoring & evaluation.

**Objective:** Evaluation of PPM initiative to understand quality of tuberculosis care and assess needs for improvement in the Programme. It also explored PMPs expectations from PHS.

**Methodology:** Structured questionnaire was administered to 72 PMPs whose involvement in RNTCP was for minimum one year.

**Results:** Nearly half PMPs credited training/material and feedback system as good. But cooperation from PHS was unanimously rated good or excellent. PMPs reported that training helped them improve their own TB care services including suspecting (97%), diagnosing and treating patients (87%) but over half of them stressed the need for retraining and continuation of additional services for other diseases also.

**Conclusion:** World wide, this is probably the only PPM that initiated PPM at very inception of local RNTCP without any external agency's support. This makes it more sustainable & replicable. Results indicate extremely important lessons from this PPM that PHS needs to be equipped enough to cater to referrals from PMPs for cases other than Tuberculosis. Rigorous monitoring and retraining were equally important issues identified.

#### **PS-702-777 Projet de mise en œuvre du traitement directement observé dans la commune d'Adjame Abidjan, Côte d'Ivoire**

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**Introduction :** La tuberculose est un problème des grandes villes. Abidjan (10 communes), capitale économique, a enregistré, en 2001, 8836 cas de tuberculose toutes formes confondues/17 110 pour tout le pays (52%). Les difficultés d'accès aux structures sanitaires sont des freins à l'application du traitement directement observé (TDO). L'Organisation Non Gouvernementale (ONG) Fraternité a suivi pour la phase pilote, 288 patients tuberculeux pulmonaires à microscopie positive (TPM+), dans la commune d'Adjame de la ville d'Abidjan pour la mise en œuvre du TDO.

**Objectifs :**

- Réaliser une cartographie des patients TPM+ de la commune d'Adjame
- Déterminer à la fin du 2ème mois la conversion bactériologique
- Evaluer les résultats du traitement

**Méthodologie :** Etude prospective chez 288 patients >15 ans nouveaux cas tuberculeux à microscopie positive (TPM+) habitants la commune d'ADJAME

dépistés du 1er Septembre 2001 au 31 Mars 2002 au CAT d'Adjamé et mis sous traitement antituberculeux (2 RHZE/4RH) chez lesquels une surveillance communautaire du traitement antituberculeux a été menée par les conseillers de l'ONG Fraternité pendant toute la durée du traitement.

**Résultats :** 288 patients nouveaux cas TPM+, age moyen = 27 ans, sexe ratio = 3/2, habitant la commune d'Adjamé dont la cartographie en 5 zones montre : zone1(39), zone2(91), zone3(10), zone4(67), zone5(81). Conversion bactériologique à 2 mois = 98% (6 patients positifs au 2ème mois).

**Résultats du traitement :** guéris = 230(80%), échec = 3(1%), transférés = 27(9%), perdus de vue = 22(8%), décédés = 6(2%).

**Conclusion :** La mise en œuvre du traitement directement observé des patients tuberculeux est réalisable dans la ville d'Abidjan avec une implication communautaire. Le taux de succès thérapeutique 80% (taux national 64%) et le taux des perdus de vue 8% (taux national 17%) se sont nettement améliorés. Recommandation pour une extension de cette stratégie dans les 10 communes d'Abidjan.

#### PS-718-792 Private public mix DOTS in peri-urban areas in Dhaka city: experience of BRAC

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**Introduction:** National Tuberculosis Program expanded DOTS services in all large cities in collaboration with the NGOs. Beside rural areas, BRAC gradually expanded DOTS services to 18 peri-urban centers in Dhaka city since October 2002 covering approximately 1.8 million population.

**Objectives:** Increase accessibility of DOTS services in urban population to reach the national case detection and cure rates of 70% and 85% respectively by 2005.

**Methods:** Trained female community health workers (CHWs) provide education on TB to community, identify and refer suspects for sputum examination and ensure DOT. In addition, Private practitioners, pharmacists, village doctors and community leaders refer TB suspects and provide DOT. Decentralized sputum collection centers are organized in different slums and work places.

**Results:** Till February 2004, a total of 570 TB patients were diagnosed. Of them, 332 were new sputum positive and 44 retreatment sputum positive cases. Sputum conversion rate of new sputum positive cases was 89%. A total of 271 DOT providers are currently treating patients. Of them, 177 are CHWs and 94 are private practitioners, pharmacists, village doctors and community leaders.

**Conclusions:** DOTS expansion through CHWs, private practitioner and pharmacists is found to be effective to increase access of DOTS services in urban areas.

#### PS-777-851 Laboratory quality control system improvement in a public-private partnership in Yogyakarta Province

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**Background:** The Hospital DOTS Linkage Project (HDL) is a partnership between The Indonesian Ministry of Health, The Indonesian Hospital Association, KNCV and Gorgas TB Initiative/UAB. Through public-private partnership, HDL promotes DOTS by creating networks for: patient referrals between government health centers and government/private/chest hospitals; quality assurance program for hospital laboratories linked to the NTP laboratory system.

**Objective:** To establish a unified laboratory network for quality assurance and control among all hospitals engaged in TB diagnosis.

**Methods:** Hospital staff were trained in DOTS policy and implementation. Education about quality control and laboratory networking was inserted; seminars/coordination meetings were held.

**Result:** Since 2001, 143 health center staff and staff from 18 hospital laboratories received training. Initially, resistance was significant to network development, in particular for hospitals and lung clinics to submit materials to a unified quality control system. To overcome this barrier, the Microbiology Department of Gadjah Mada University offered to coordinate the cross-check system without reducing the central role of the NTP reference laboratory. After two years, a unified QC system began to function effectively, including all 18 hospitals trained in DOTS.

**Conclusion:** Creating a quality control system in the public-private context is possible and depends on involving all stakeholders from the public, hospital and laboratory sectors.

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#### PS-868-940 Hospital DOTS and Linkage (HDL) project for the integration of hospitals in tuberculosis control in Yogyakarta, Indonesia

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**Aim:** Creating a sound model for public/private partnership that promotes expansion of DOTS into public and private hospitals.

**Introduction:** In 1999 hospitals detected approximately three times as many TB cases as health centres,

yet the hospital cases were not reported through the NTP, as hospitals were not implementing DOTS. That year the HDL project began expanding DOTS into these settings.

**Methods:** The initiative involves such activities as advocacy, training, network creation, and common information systems. This process is monitored and evaluated by a DOTS Committee that includes stakeholders from the public (NTP) and private sectors, including academia and professional organizations.

**Results:** 18 of the 33 hospitals are participating and implementing DOTS. There is a 257% increase in TB case notifications, as well as a 446% increase in sputum smear-positive notifications. Conversion rates increased from 77.2% in 2000 to 85.05% in 2003, and cure rate rose from 69% in 2000 to 73.16% in 2002. Additionally, the NTP/MoH has recommended using the HDL as the basis for expansion of DOTS in hospitals nationwide with HDL collaborators serving as DOTS advocates in other provinces.

**Conclusion:** The HDL has improved case detection and treatment outcomes in Yogyakarta and is setting a model for standardizing DOTS in the hospital sector.

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#### **PS-869-942 Establishing a hospital-health center referral network for TB patients in Yogyakarta Province, Indonesia: a model for private-public mix (PPM)**

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**Aim:** To create a private-public TB control by establishing a mutual referral link between government and private hospitals and government health centers for TB case management.

**Introduction:** The referral of hospital (public and private) TB cases to public health centers for treatment initiation or continuation poses a challenge as many cases are lost to follow-up and potentially default from treatment.

**Methods:** A protocol for referring cases from 18 private and public hospitals to public health centers, including an information system, was developed in 2002.

**Results:** 79, 160 and 131 of smear positive cases detected in hospitals were referred early (before initiating treatment) to a health centers in 2001, 2002 and 2003 respectively. Among the referrals in 2001, 65% were registered at the health center and 66% of these were cured. In 2002, 72% of cases referred were registered at the health center and 68% were cured. In 2003 the per cent of cases registered at the health center increased to 78%, treatment outcomes are pend-

ing. Efforts to track patients referred in 2001, 2002 and 2003 were carried out and 52%, 79% and 82% were found for those years, respectively.

**Conclusion:** Referring TB patients from hospitals to health centers warrants a strong and coordinated system.

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#### **PS-874-950 Utilization of a private for profit TB microscopy diagnostic center under Private Public Partnership**

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**Introduction:** Private Public Partnerships are needed to achieve TB millennium goal. Lalitpur PPP demonstrated the success story of partnership. Under that umbrella, the utilization of a private for profit TB microscopy diagnostic center was analyzed.

**Objectives:** Determine the utilization of a private for profit TB diagnostic center to NTP under the umbrella of PPP.

**Methods:** Four years data was analyzed. Sputum microscopy was free of charge by the private for profit DOTS center. NTP trained two local laboratory staff, supplied one binocular microscope and logistic materials. NTP monitored the microscopy service regularly. The utilization by TB symptomatic and follow up TB cases was analyzed focusing on use of TB microscopy service by gender.

**Results:** The microscopy center applied NTP policies and achieved high performance in quality control. 943 chest symptomatics (48% male, 53% female) used the free microscopy service. 538 TB cases utilized it for monitoring treatment (48% male, 51% female). TB cases in the DOTS center show ~2:1 M:F ratio. Females utilize services more than males. Responsible factors were analyzed.

**Conclusion:** Establishment of TB microscopy center in private for profit institutions enhances accessibility to females. Minor investments by the NTP can contribute to the priority of identifying more women.

#### **PS-922-997 Role and involvement of private practitioners in TB control in Onitsha and Abakaliki, Southeast Nigeria**

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**Objective:** To describe the role and the involvement of private practitioners (PPs) in Tuberculosis control in Onitsha and Abakaliki, Southeast Nigeria.

**Methods:** A descriptive study using quantitative and qualitative methods was conducted from May to June 2003. For the quantitative part a cross-sectional survey was done using a self-administered questionnaire. Data derived from the survey were complemented with information gathered from the qualitative part (semi-structured and in-depth interviews with private practitioners and key informants, observations and group interviews of TB patients).

**Results:** Most of the PPs were seeing TB suspects (83% in Abakaliki; 92% in Onitsha) in their private clinics. For those PPs who refer TB patients, majority claimed they refer patients to government/NTBLCP facilities. Further investigations showed that there is no formal referral system in place. All PPs in Abakaliki and 95% in Onitsha said they saw less than 5 new TB cases on an average in a month. There were 29 regimens in different combinations of HRZEST and Vit B of different durations given by 34 PPs of which only 18% was consistent with NTBLCP/WHO guidelines. Majority of PPs in both areas (63% in Onitsha; 50% in Abakaliki) did not keep TB registry and 86% in Onitsha and 75% in Abakaliki did not trace defaulters. All PPs in Abakaliki and 76% in Onitsha did not do contact tracing. About 70% (71% in Abakaliki and 72% in Onitsha) answered they were never contacted by NTBLCP to inform them on TB guidelines and about three quarter (76%) of PPs in Onitsha had never attended any continuing medical education (CME) on TB while 47% in Onitsha answered the same. Most of the PPs (88% in Abakaliki; 92% in Onitsha) had never been involved in NTBLCP programs but said they were willing to collaborate (82% in Abakaliki; 92% in Onitsha) in any way (58% Abakaliki; 59% in Onitsha) without preconditions (54% Onitsha; 50% Abakaliki). Majority of the PPs (95% in Onitsha; 88% in Abakaliki) would appreciate it if NTBLCP would provide them free TB drugs for their patients but they would charge some service fees in doing so (59% in Abakaliki; 58% Onitsha).

**Conclusions:** Majority of private practitioners in Onitsha and Abakaliki see TB suspects and eventually treat them although diagnostic and treatment regimens were variable and inconsistent with NTBLCP guidelines. The majority of these private practitioners had never been involved in any TB control program of the government but wished to collaborate in anyway but with expectation of incentives. New programs that offer ways to increase awareness of national guidelines for TB care and strategies to effectively involve private practitioners as needed.

## TOBACCO AND AIR POLLUTION-1

### PS-508-585 Respiratory allergy and asthma in the textile industry

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Respiratory allergy and asthma in the textile industry could be related to either textile or dye particles. The aims of the study were: 1) To evaluate the respiratory allergy prevalence in the textile finishing industry and 2) To identify the incriminated agents and 3) To propose prevention clues. It consisted of a transversal descriptive and extensive inquiry among 141 male workers exposed to chemicals used in textile processing, conducted by a physician using a questionnaire and spirometry in a first step. All, except non symptomatic subjects or heavy smokers, were explored for bronchial hyperreactivity (BHR) prick testing for current allergens and textiles and peakflow monitoring in the work place as well. Interview revealed 34.8% of subjects with one or more atopic features with 12.8% ocular allergy, 11.3% otorhinolaryngology symptoms, 11.3% asthma equivalent and 1.4% asthma. Among all symptomatic patients who were tested for BHR and prick testing, 15 (10.64%) were considered to be suffering from occupational allergy (asthma-rhinitis). Two particularly exposed work sites were identified: dye mixing and tissue coloring. Metabisulfites, azoic colorants and hyposulfites seem to be incriminated. Specific technical preventive measures are proposed.

### PS-798-871 Perception des risques environnementaux chez les consultants des Centres de Soins de Fès, Maroc

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**Introduction :** Depuis plusieurs années, la population des pays du Nord a pris conscience des risques environnementaux. La question de la perception de ces risques se pose maintenant dans les pays du Sud confrontés à des situations identiques.

**Objectif :** Evaluer la perception des risques environnementaux chez des consultants de Centres de Santé de la ville de Fès.

**Méthodes :** Nous avons réalisé une enquête par questionnaire chez 152 consultants soit 93% des personnes concernées.

**Résultats :** 63% étaient des femmes. 50% avaient un



niveau d'étude égal ou inférieur au niveau primaire. Les problèmes environnementaux les plus préoccupants cités étaient : la pollution de l'air (21.4%) et de l'eau (20%). Une proportion élevée de personnes (86%) estimaient que la pollution de l'air présentait des risques importants pour la santé. Les risques les plus connus étaient les maladies respiratoires (77%) et 39% des personnes se plaignaient de troubles liés à la pollution. La source de pollution de l'air la plus citée était les usines (63.8%). Les deux-tiers des sujets se considéraient très mal informés sur la qualité de l'air. Pour les répondants, le principal acteur de la lutte contre la pollution devrait être l'Etat (65%).

**Conclusion :** Ces résultats bien que préliminaires mettent en évidence un début de prise de conscience de la part de la population face aux problèmes liés à la pollution atmosphérique.

#### **PS-876-951 La pollution domestique en Afrique : un problème majeur de santé publique**

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**Contexte :** L'Afrique compte 14% de la population mondiale où la pauvreté constitue le frein majeur pour le développement. Le continent vit une situation paradoxale : malgré l'abondance des ressources énergétiques fossiles et d'énormes potentialités en matière d'énergies renouvelables, neuf personnes sur dix n'ont pas accès à l'électricité et trois quarts de l'énergie proviennent de combustibles solides tels que la bouse séchée, le bois, les déchets agricoles et le charbon utilisés pour la cuisson et le chauffage. Ces éléments constituent sans doute la plus grande source de pollution de l'air à l'intérieur des habitations.

**Objectifs :** Réaliser un état des lieux de la pollution domestique et évaluer son impact sanitaire.

**Méthodologie :** Analyse de la revue bibliographique sur la pollution domestique et l'impact sanitaire dans le continent Africain.

**Résultats :** Des taux d'exposition ont été retrouvés plusieurs fois supérieurs aux normes de l'OMS, ou aux normes fixées par certains pays. La pollution domestique est classée par l'OMS parmi les 10 principaux facteurs de risque et occupe le 4ème rang avec 3,6% de la charge de morbidité totale. Les travaux font apparaître une relation assez constante et étroite entre l'usage de combustibles solides dans les habitations et certaines maladies. Selon ces analyses, cet usage causerait environ 35,7% des infections des voies respiratoires inférieures, 22% des broncho-pneumopathies obstructives chroniques et 1,5% des cancers de la trachée, des bronches et des poumons. La pollution de l'air à l'intérieur des habitations pourrait être aussi associée à la tuberculose, à la cataracte et à l'asthme.

Pour la mortalité prématurée et la charge de morbidité dues à la pollution de l'air domestique, la Banque mondiale estime en moyenne annuellement pour la période 2001–2020, à 530 000 décès prématurés et à 18.1 millions d'années de vie corrigée de l'incapacité (AVCI) en Afrique Subsaharienne. La part des décès prématurés et de la charge de morbidité due à la pollution domestique par rapport à la pollution atmosphérique urbaine est respectivement de 90% et 94%. **Conclusion :** La pollution atmosphérique domestique constitue un risque majeur de santé publique en Afrique, et sa réduction doit être favorisée par un développement durable et une diminution des inégalités sociales.

#### **PS-877-953 Effets sanitaires de la pollution atmosphérique urbaine en Afrique du nord : cas de la ville d'Alger**

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**Contexte :** La pollution atmosphérique dans la zone d'Alger est principalement d'origine automobile et les différentes mesures effectuées ont montré des niveaux de pollution très élevés pour de nombreux polluants.

**Objectifs :** Mettre en place un système de recueil de données sur la pollution atmosphérique, Mettre en place un système de recueil de la morbidité respiratoire en consultation ambulatoire ; évaluer l'impact sanitaire de la pollution atmosphérique urbaine par les poussières (PM10) à Alger.

**Méthodologie :** c'est une étude descriptive permettant d'évaluer l'impact sanitaire de la pollution atmosphérique par les poussières en population générale. Un capteur de poussières (PM10) installé a permis un suivi permanent et continu des niveaux du polluant. Le recueil de la morbidité respiratoire en consultation ambulatoire a porté sur les motifs de consultations. Notre analyse pour apprécier l'effet attribuable à la pollution, s'est basée sur les résultats de l'étude de S.HAJAT menée à Londres en prenant comme référence la relation dose—réponse trouvée dans ce travail.

**Résultats :** Pour l'indicateur d'exposition, le niveau moyen journalier est 61 µg/m<sup>3</sup> [29–93] et la saison hivernale est caractérisée par un taux élevé (DS < 10-6). Les données de morbidité extra-hospitalière montrent que le nombre moyen quotidien de consultations pour affections respiratoires est de 25,29 [14,67–37,91]. Cette moyenne est élevée en période hivernale (DS, P < 10-6).

**Conclusion :** Cette démarche d'évaluation de l'impact sanitaire a permis de déterminer le nombre de consul-

tations attribuables à la pollution atmosphérique par les PM10. Elle devrait être étendue à de plus vastes territoires englobant d'autres villes et impliquant plusieurs structures sanitaires pour déterminer la fonction exposition—risque spécifique par la mise sur pied d'étude de type écologique temporelle.

### PS-194-237 Asthma mortality: comparative analysis in São Paulo, Brazil

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**Objective:** To quantify the mortality rate of asthma according to multiple causes methods of analysis and compare to underlying cause of death.

**Method:** Data were provided from all death certificates of persons aged between 5 and 34 years, emitted in the years 1993, 1994, 1995, in São Paulo county, mentioning the word asthma were considered as valid information (code 493/IDC-9). In this second study the same date was submitted to the method of multiple cause of death analysis.

**Results:** The diagnosis of asthma has risen from 1 to 1.165. The coefficient of mortality has increased around 5 times in the male population.

**Conclusion:** The analysis showed a greater impact of asthma on the male group. The age range of persons which suffered more by this disease did not change: from 20 to 34 years old. Despite the fact that asthma is more frequently present when the method of multi causality is used, the increase found in the number of asthma diagnosis points out that it can still be considered among Brazilians as less notified cause in the chain of events that can lead to death.

### PS-370-393 Prevalence of asthma and allergy in children in Sudan

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**Introduction:** Prevalence of asthma is increasing worldwide. It has been observed that the prevalence of asthma is increasing in Sudan.

**Objectives:** To describe the prevalence and severity of asthma, rhinitis and eczema in children 13–14 years old living in Khartoum, Sudan, and to find out predisposing factors of asthma as apart of ISAAC.

**Methods:** Prospectively 500-school child were counseled between Feb–Sep 2003 in Khartoum, Sudan. The studies included any child in age 13 or 14 in different 55 schools. The data was collected by questionnaire. It was entered, and analyzed by Epi info 6.

**Results:** 53.4% of the samples were males, 41.6% were females. Prevalence of asthma according to wheeze hearing was 17.0%, and Incidence of wheeze was 12.2% in the past 12 months. 15.4% of children had exercise induced wheeze, 23.0% had Night cough without chest infection while 20.0% had Sneezing without cold infection. Skin rash occurred in 11.6% during the past 6 months. But only 4% of all had eczema. 27.1 of children with positive wheeze had dogs in there houses, 56.5 had cats and 50.6% of them had smokers in their families.

**Conclusion:** Prevalence of asthma found to be 17.0%, wheeze was directly related to animals & passive smoking.

### PS-511-570 Assessing allergic sensitisation by questionnaire

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**Setting:** Characterisation of the asthma fenotype such as separating allergic and non-allergic asthma is important in population studies. In order to do so one normally needs to do allergy testing, which, compared to questionnaire studies, is resource demanding.

**Aim:** The aim of this study was to compare the validity of children and parent reported allergic symptoms against skin prick testing.

**Methods:** In the study 374 schoolchildren (13–14 years of age) answered the ISAAC questionnaire and underwent skin prick testing. In addition the parents were asked questions on observed allergic symptoms in their children. Allergic sensitisation was defined as a positive reaction to any allergen. Validity was assessed using Youden's index (sensitivity + specificity – 1).

**Results:** The validity compared to skin prick testing was higher for parents reported symptoms than for the ISAAC questions. The highest validity was obtained when combining three questions on parents observed allergic reactions to cat, dog and pollen: 59% (sensitivity 70%, specificity 89%). Of the ISAAC questions N1: 'Ever having had rhinitis without a cold' had the highest sensitivity (66%) but a low specificity (69%) while N3. 'Having rhinitis and conjunctivits in the last year' had the highest specificity (91%) but a low sensitivity (42%).

**Conclusion:** Our survey indicates that parents reported allergic symptoms should be used when assessing allergic sensitisation if allergy testing can not be performed.

**PS-816-888 Incidence et gravité de l'asthme chez l'adulte**

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**Introduction :** L'asthme reste un sérieux problème de santé publique qui préoccupe les professionnels de santé malgaches.

**Objectif :** Evaluer l'incidence et la gravité de l'asthme.

**Méthodologie :** Asthmatiques adultes hospitalisés en pneumologie. Etude rétrospective et prospective de mars 2003 à février 2004

**Résultats :** Sur 132 patients recrutés, 60% sont des femmes, et 31% âgés entre 20 et 30 ans, puis ce pourcentage décroît parallèlement à l'âge. 54% ont un niveau scolaire secondaire et 70% dans le secteur tertiaire. L'atopie est fréquente, 32% des cas, l'antécédent familial de maladie asthmatique 20% et le tabagisme 17%. L'asthme se déclenche pendant la saison des pluies et pendant l'exposition au froid. L'interrogatoire révèle que les allergènes domestiques ou environnementaux sont prédominants. Les stades II et III représentent 32% et 27%. A l'admission nous comptons 45% attaque d'asthme, 26% asthme aigu grave ; le DEP moyen est 180l/mn.

**Conclusion :** L'incidence de l'asthme est en augmentation. L'asthme survient surtout chez les femmes d'âge mûr. Le rôle du tabac et les allergènes sont bien marqués. Le stade IV est rare. Les asthmes persistants modéré et léger sont fréquents

**PS-299-333 Tobacco use among adolescents in Kerala, India**

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**Introduction:** Tobacco use is increasing among adolescents of Kerala, the most advanced Indian state vis-à-vis education and health.

**Objectives:** To determine prevalence and correlates of tobacco use in a sample of 13–17 year old male school students in Trivandrum, the state's capital.

**Methods:** Using two-stage cluster sampling technique, 45 classes were selected from 14 schools in Trivandrum. Information on tobacco use pattern and demographic variables was collected from 1323 boys (mean age 14.7), using a pre-tested, anonymous, self-administered questionnaire. Bivariate and multivariate analysis was done.

**Results:** Overall, 34.6% had tried some form of tobacco. Prevalence of current tobacco use was 11.3%, current smoking 8.1% and current chewing (pan, pan masala, gutka, khaini) 3.2%. Current tobacco use was significantly higher among 17 years and older boys

(OR 4.2, CI 1.9–9.2) compared to 13 years and below. Fathers' tobacco use (OR 2.1, CI 1.4–3.2), friends' tobacco use (OR 2.5, CI 1.3–4.8) and low academic performance (OR 3.0, CI 1.4–6.7) were associated with higher current prevalence. Three fourths of current users reported wanting to quit.

**Conclusion:** School based health education programs involving fathers and interventions offering peer education, counseling and tobacco cessation services are required.

**PS-377-402 The effect of stop smoking to FEV<sub>1</sub> and FEV<sub>1</sub>/FVC**

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**Setting:** This research is the continue of previous research which started 18 months ago and it's results are published after the first 6 months.

**Aim:** To study the amelioration in FEV<sub>1</sub> and FEV<sub>1</sub>/FVC in the ex smokers after 6, after 12 and after 18 months.

**Methods:** We had made a group of 43 patients who stopped smoking. All of them had COPD and they stopped smoking by doctor's advice. We followed our patients 18 months with the spirometry's control every 6 months (first 6 months we followed our patients every month). In our research we were including lung function tests, FEV<sub>1</sub> the first and FEV<sub>1</sub>/FVC after that (Tables 1 & 2).

Table 1 FEV<sub>1</sub>%

	I	VI	XII	XVIII
<40 years	79	94	96	96
40–65 years	69	79	84	86
>65 years	62	65	70	70

Table 2 FEV<sub>1</sub>/FVC%

	I	VI	XII	XVIII
<40 years	61	71	72	79
40–65 years	55	62	68	70
>65 years	49	50	55	59

**Results:** All the patients had amelioration of the lung function tests. The youngest patients (<40 years) had the biggest amelioration during the observation period (18 months). Their results are as they have never been smokers. The older patients (>65 years) had very little amelioration.

**Conclusion:** Stop smoking has big effect on the younger patients, but all the patients have effect in some slight degree.

**PS-618-685 Tuberculosis surveillance in Manitoba, Canada: past, present and future**

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**Introduction:** Since 1993, all *Mycobacterium tuberculosis* isolates recovered in the province of Manitoba have been genotyped by the standard IS6110-RFLP method for routine surveillance, prevention and control purposes.

**Objectives:** To determine the utility of the accumulated data to date, to identify gaps this data can fill, and to determine how this information can be exploited for the future.

**Results:** Our laboratory has genotyped 1290 isolates with the following results: i. a predominant strain has been identified and is the object of ongoing virulence studies, ii. the epidemiology of TB in Manitoba has been well described, with risk factors for transmission established, iii. more efficient typing methods have proven acceptable for future genotyping, and iv. a model to institute nationwide molecular typing has been proposed based on our database. Unfortunately, a gap still exists between molecular and conventional epidemiology; this database is relatively unknown to other health care workers involved in TB control and prevention, and there is no policy in development to forward the concept.

**Conclusion:** Introducing molecular epidemiology to a region is a recognized asset in TB control. These tools need to be advocated to inform and encourage collaboration with control and prevention departments. Policies need to be drafted to strengthen and encourage this link. A nationwide surveillance system should be developed and adopted.

**PS-454-492 Large single-strain tuberculosis outbreak among Pacific Islands population in Auckland, New Zealand**

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**Objectives:** To screen exposed contacts of an infectious tuberculosis disease (TBD) case, search for new cases, and to identify factors contributing to the scale of the outbreak.

**Introduction:** Auckland has large a Pacific Island population (150 000 in 2001) with TBD incidence (56.2/105 in 2003) exceeding non-Pacific incidence (15.3). Diagnosis of a Tuvaluan woman with smear-positive pulmonary TBD led to large contact investigation.

**Methods:** Contacts screened using Mantoux testing and chest X-rays, TBD cases diagnosed from specimen culture or from radiology and clinical examination, latent TB infection (LTBI) diagnosed if Mantoux >10mm and absence of TBD.

**Results:** Tuvalu-born index case provided childcare within community of interlinked extended-family households. Investigation identified 130 household contacts of index or secondary cases. Of these, 25% (32/130) had TBD and 53% (69/130) had LTBI. TBD rate 47% (24/51) among children aged <16yrs. Overcrowding in some affected households, with peak household TBD rate 60% (6/10). All culture-confirmed cases had matching RFLP patterns. All TBD cases HIV-seronegative.

**Conclusion:** This outbreak demonstrates high infectivity of smear-positive TBD, even in HIV-seronegative groups. Although index case overseas-born, living conditions in NZ led to wide local transmission. TB control strategies in New Zealand must address adverse socio-economic conditions that promote disease transmission.

**PS-926-1001 Is low body mass index (BMI) a risk factor for tuberculosis contacts?**

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**Objectives:** To evaluate if low body mass index (BMI) is one of the risk factor for tuberculosis contacts.

**Methods:** 152 household contacts of 67 tuberculosis patients, who had bacteriologically or histologically confirmed tuberculosis in our clinic between December 2003 and March 2004, were evaluated according to height, weight, BMI and presence of active tuberculosis disease. Pre symptomatic BMI of detected tuberculosis cases were evaluated among contacts.

**Results:** 17 (11.18%) of the 152 contacts whose mean age was  $35.46 \pm 14.93$  found active tuberculosis.

BMI	Active tuberculosis		Total n (%)
	Positive n (%)	Negative n (%)	
Below 20	7 (41.2)	23 (17)	30 (19.73)
Above 20	10 (58.8)	112 (83)	122 (80.16)
Total	17 (100)	135 (100)	152 (100)

In the contacts it was seen that in the individuals whose BMI were below 20, and the risk of developing tuberculosis was significantly high. OR 3.409 (1.75–9.88) (Fisher's Exact Test) ( $P = 0.018$ ). When we did logistic regression analysis OR was 1.84 (1.08–3.14) ( $P = 0.024$ ), it was significantly high.

**Conclusion:** BMI should be taken into consideration for contact tracing of tuberculosis.

## SUNDAY 31 OCTOBER 2004

### THEMATIC SLIDE PRESENTATIONS

#### PROGRESS IN TB CONTROL

##### TS-99-145 Tuberculosis KAP study among health care workers and tuberculous patients in Iraq

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**Aim:** This study aimed at evaluating the knowledge, attitudes, and practice of tuberculosis patients and health care workers (HCW) regarding tuberculosis.

**Methods:** A cross sectional study was carried out in a random sample of 250 primary health care centers (PHCC) whereby randomly selected 500 patients and 500 HCWs were interviewed using pre-tested structured questionnaires.

**Results:** The frequency of optimum knowledge of tuberculosis among patients was 64.4% while 54.8% reported negative attitudes and practice towards tuberculosis (high degree of stigma). Also the optimum knowledge of HCWs towards tuberculosis was excellent (95.5%). HCWs knowledge increases steadily with increased age, and duration of their job, with elapsing of 20 years and with optimum knowledge. Unfortunately, health care worker practice towards tuberculosis suspects was not satisfactory, only 38.2% responded correctly. The two most important source of patient information about tuberculosis were their physicians and television. Education, training and supervision of our NTP showed good impact on the knowledge of tuberculosis among both TB patients and HCWs.

**Conclusion:** Knowledge is not the only determinant of health seeking behavior and compliance to treatment but mainly the attitudes and practice towards the disease, and the high level of stigma proved to be the main barrier hindering proper and timely health seeking behavior. Poor adherence of the HCW to national tuberculosis control (NTP) guidelines regarding tuberculosis suspects highlighted a major cause of low case detection in this community. These results call for the need to organize an awareness programme to destigmatize the disease and for regular training of the HCW on the NTP guidelines.

##### TS-175-211 Gender differences in tuberculosis in Sudan: the role of gender in access to TB services as a function of TB treatment

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This study analysed data from tuberculosis management units (TBMU) in eight states of Sudan, to examine the socio-economic characteristics in suspects and patients of tuberculosis (TB) in relation to gender and to examine the role of gender in the adherence to treatment. Nearly 32 460 patients with respiratory symptoms presented themselves to the TB MUS in the selected states. Of the 32 460 patients, 10 494 were TB suspects; The female: male ratio among TB suspect was 0.7:1. Of those suspected to have TB; 1797 were TB patients; the female: male ratio among TB patients was 0.7:1. The prevalence of co-infection was 5% among females compared to 3.4% among males. Females had a longer patient delay in diagnosis (7 months VS 6 months,  $P = 0.016$ ), longer duration of symptoms and worse TB treatment outcome than males. Success rate among females was 74.9% compared with 80.7% among males (Odds ratio 1.4; 95%CI 1.12–1.76). Default rate was 21% among females compared to 13.9% among males (OR 1.65; 95%CI 1.29–2.11). In terms of accessibility females have slightly less accessibility to TB health services than males TB patients. But in term of adherence to anti-tuberculosis treatment, females have worse adherence than males. National TB programme needs more research to identify reasons for non-adherence among females.

##### TS-492-539 The cost and cost-effectiveness of tuberculosis control in the Russian Federation

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**Objective:** To generate economic and epidemiological analyses relevant to the development and evaluation of TB control in the Russian Federation.

**Methods:** The cost, effectiveness and cost-effectiveness of TB control was assessed in four regions (Orel, Ivanovo, Kemerovo, Samara). Data for 1999 were used because this was the most recent year for which treatment outcome data existed at the end of the study period (2000–2002).

**Results:** In-patient care accounted for 50–60% of total TB control costs, followed by fluorography (10–20%). The average cost per new bacteriologically positive patient treated was around US\$ 1000–1400 (health

system: US\$ 750–1100; patients: US\$ 200–300). The cure rate varied from 50% to 89%; death and failure rates were high. The cost per DALY averted was about US\$ 100 in all oblasts, but would be US\$ 500–800 if in-patient care costs were in line with the country's average income levels. Total TB control costs in Russia are approximately US\$ 250 million.

**Discussion:** TB control is a good health care investment in the Russian Federation. However, costs are high by international standards, reflecting extensive reliance on in-patient care and fluorography, while cure rates are poor. There is much scope for improving the efficiency with which resources are used.

#### **TS-696-771 'Think PHC, Do TB.' Integrated scale-up of tuberculosis control in Japan'**

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**Introduction:** Failure of tuberculosis control in developing countries is often blamed on ill-functioning health system. Therefore, scaling-up of tuberculosis control needs scaling-up of health system. In 1950s, Japan faced a challenge: poor economy, extraordinary tuberculosis burden, and incomplete health system.

**Objectives:** We analyzed tuberculosis control strategy along with scaling up health system.

**Methods:** Historical descriptive analysis. Concept of control knobs for health system performance was used.

**Results:** Japan put immense inputs, and developed tuberculosis control within the framework of health-system scale up, without establishing a vertical system. Interventions identified in control knobs of health system were applied to tuberculosis control. Some tuberculosis-specific interventions were added, which were adapted for other control activities subsequently.

**Conclusions:** Political will translated in financial support, and integrated scale up of control activities were keys for Japanese success. Sufficient human resources and significant economic growth made this possible. Japanese experience is not simply replicable in developing countries, but still remains meaningful in the era of the Global Fund and the 3 by 5 Initiative.

#### **TS-737-812 Results of DOTS demonstration projects implementation in Russia**

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**Introduction:** In Russia 26 territories implement the WHO strategy (DOTS). The newly signed MoH Prikaz on recording-reporting forms is an important step in TB control. According to the Prikaz in 2004 the new cohort analysis forms should be gradually introduced

in 37 regions in 2004 and they should have been used countrywide by January 2005. The proportion of smear sputum (SS)+ cases in DOTS areas was 33%, and in non-DOTS areas – 27%.

**Methods:** Collection and analysis of the quarterly reports from DOTS areas.

**Results:** In 2003, quarterly reports from 26 territories of the country were submitted. More than 20 000 new cases were registered, 33% of them were SS+. It slightly exceeded the Russian average rate of 27%. In some DOTS territories (Vladimir, Novgorod, Tomsk, Orel and Ivanovo Regions, Republic of Mari-El) the number of SS+ cases was 42–53%. Treatment results of SS+ patients (2002 cohort) were received from 24 territories. Treatment success was 67% (37–80%). Orel, Ivanovo, Vladimir and Tomsk Regions reached higher treatment success that can be explained by the complex approach to programme implementation, regular training, supervision, monitoring and effective case management and social support. The observed suboptimal treatment results call for further investigations and research.

#### **TS-741-816 Progress in TB control in India, 2003–2004**

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**Background:** With 1.8 million new cases annually, India has the highest TB burden in the world.

**Recent progress:** Coverage of the Revised National TB Control Programme (RNTCP) expanded from 530 million (January 2003) to 851 million (March 2004). In 2003, 906 472 cases were initiated on treatment, with 358 496 new smear positive cases registered – 69% case detection. Despite rapid expansion, treatment success was 87% (2002 cohort). September 2003 saw a Joint Government of India/WHO RNTCP Monitoring Mission, with 20 international and 20 national TB experts involved. In 2003, RNTCP engaged with new partners and initiated new projects. To date, >3000 private practitioners, >800 NGOs and 80 corporate sector units are involved and RNTCP has launched public-private mix projects in 14 large urban areas. A network of task forces facilitate medical colleges' involvement in RNTCP, with 131 colleges providing RNTCP services. A consensus statement on the 'Management of Paediatric TB under RNTCP' has been issued by RNTCP and the Indian Academy of Paediatricians. Collaborative activities between RNTCP and the HIV/AIDS programme, focused on 6 high HIV seroprevalent states, are on-going. Updated protocols have been developed for EQA and DRS, intensified IEC activities undertaken, including piloting of COMBI in 1 state, and a 3-year national ARTI survey completed (1.5% ARTI).

### TS-756-830 Institutional development, manpower and funding in the National TB control programme of China

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**Introduction:** In 2001, the State Council of China developed the 'National TB Control Programme (NTP)—2001–2010' for implementation in all provinces.

**Objectives:** Determine the status of TB control institution, manpower and funding in the NTP.

**Methods:** Three governmental ministries—health, finance, and planning—jointly conducted an evaluation of the NTP during the 4th quarter, 2003. A standard evaluation form was used to collect information on status of TB institution, manpower, and governmental funding. Evaluation teams visited all provinces to verify the data accuracy.

**Results:** In 2003, all 31 provinces and 336 prefectures/cities and 2628 of 2683 counties/districts had established TB control institutions/units. Average number TB control staffs at provincial, prefecture, and county level was 25, 18, and 7.5, respectively. However, many counties and prefectures had <5 staffs. Governmental funding for TB control per capita (excluding central funding, salaries and World Bank loan) increased from US\$ 0.011 in 2001 to \$ 0.015 in 2002 and \$ 0.017 in 2003.

**Conclusion:** A network of TB control institutions exists to implement DOTS and number of staff is adequate in most but not all areas in China. Governmental funding for TB has increased but, as of 2003, was still inadequate for DOTS implementation.

### TS-788-860 Evaluation of a new diagnosis system for *M. tuberculosis* infection

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To diagnose *M. tuberculosis* infection, tuberculin skin test (TST) has been used for a long time. However, since PPD used for TST contains numerous antigens which are homologous to those from BCG or non-tuberculous mycobacteria, TST shows positive reaction in those who are only infected with *M. tuberculosis* but vaccinated with BCG or infected with non-tuberculous mycobacteria. Therefore, it is extremely difficult to diagnose *M. tuberculosis* infection based on TST in countries where BCG vaccination is carried out such as Japan. In this context, we have evaluated the new diagnostic system (QuantiFERON-TB Second Generation:QFT-2G) for *M. tuberculosis* infection. Whole blood was stimulated with *M. tuberculosis* antigens, ESAT-6 and CFP-10, which are absent from all BCG strains, and IFN- $\gamma$  produced by T cells was mea-

sured. Sensitivity and specificity were analyzed based on the data obtained from healthy individuals who are mostly BCG vaccinated (220) and culture positive tuberculosis patients (118). The data were analyzed by the statistical methods including Receiver Operating Characteristic (ROC) analysis to establish the appropriate cut-off value. By these analyses, the sensitivity and specificity resulted in 89% and 98.2%, respectively, indicating that QFT-2G is useful to diagnose *M. tuberculosis* infection without influence of BCG vaccination.

## POSTER DISCUSSION SESSIONS

### EPIDEMIOLOGY OF TUBERCULOSIS AND TOBACCO

#### PC-161-195 Passive smoking (PS) and self-reported asthma (A) symptoms in schoolchildren

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**Introduction:** Numerous studies estimate an increased risk of developing A in childhood due to the effect of environmental tobacco smoke.

**Objective:** To evaluate the influence of PS on the prevalence of A symptoms in ISAAC (International Study of Asthma and Allergies in Childhood) Phase III, Sombor center, Serbia.

**Method:** ISAAC written (WQ) and video questionnaire for the 13–14 year old, applied on all the children attending 7th grade (group I,  $n = 1105$ ), and WQ for the 6–7 year old, filled in by the parents of all the children attending 1st grade of all the 20 elementary schools (group II,  $n = 1029$ ). ISAAC Phase III environmental questionnaire applied on both groups.

**Results:** Wheezing ever—18% (I), 20.5% (II); wheezing in the past 12 months—11% in both groups; asthma ever—5% in both groups; wheezing during exercise in the past 12 months—11% (I), 4% (II); cough at night in the past 12 months—15% (I), 12% (II). Mother smokes (MS) in 47% (I) and 42% (II), father smokes (FS) in 55% (I) and 57% (II) of the families. Older age group (I): no positive correlation between MS and A symptoms; FS/night cough OR = 1.28 (95%CI 0.92–1.79); 2 or > members of the household smokes/night cough OR = 1.39 (95%CI 0.88–2.20). Younger age group (II): MS/wheeze ever OR = 1.60 (95%CI 1.18–2.17); FS/current wheeze OR = 1.48 (95%CI 0.98–2.22);  $\geq 2$  members of the household smokes/wheeze ever OR = 1.40 (95%CI 0.93–2.11).

**Conclusion:** There is a positive correlation between PS and A symptoms (wheeze ever, current wheeze) in 6–7 year old schoolchildren.

**PC-170-206 Report of the first smoking cessation clinic, Tehran, Iran, 2004**

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**Introduction:** Tobacco use is the leading cause of preventable death worldwide. 5 million people die from tobacco each year, the half of these deaths usually occur in developing countries. If current trends continue, it is estimated that it will be responsible for 10 million deaths by the year 2020, the majority of which 7 million will occur in low-income countries.

**Material and method:** Smoking Cessation Clinic, as a research project, was established for the first time in Iran by NRITLD in 1998. The quitting educational courses consist of 7 sessions of 90 minutes run by General Practitioners. In implementation of smoking cessation programs, the following are being employed: Providing education on smoking hazards and quitting methods, behavioral therapies, group discussion, nicotine replacement therapy. Among the ex-smokers, some are randomly selected for confirmation of CO expiratory smokerlyzer Test.

**Result:** Of 1936 (1527 male, 409 female) smokers registered on 1st March 2004, 515 (401 male, 114 female) were not able to completed the educational courses for different reasons and of the remaining 1426 (1131 male, 295 female), 1268 (1019 male, 249 female) have quitted successfully (88%) and others smoked cigarette in lower rate. Among those, 23.4% had a relapse into smoking a month after abstinence and the percentages in the 3rd and 6th months were 40.7% and 47.2%, respectively. One year after quitting, the rate of relapse was 52.4%.

**PC-383-408 The impact of smoking on adherence to latent tuberculosis infection treatment**

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**Introduction:** We wanted to estimate factors associated with compliance to latent tuberculosis infection (LTBI) treatment among a smoking population of recent immigrants to Canada.

**Method:** Between 1998 and 2000, a convenient sample of patients undergoing treatment for LTBI completed a self-administered questionnaire on health beliefs and smoking status. Smokers and non-smokers were contrasted according to their socio-demographic profile, general health beliefs, perceptions on TB and compliance to LTBI treatment.

**Results:** 320 patients were recruited, and 302 (94%) completed the questionnaire, of which 265 were recent immigrants. Smoking prevalence was 21%. Factors associated with smoking status were male gender, lack of

regular exercise and of regular dental check-ups, and the belief of the low impact of smoking on general health outcomes including TB. Adequate compliance with LTBI treatment was found in 72% of patients. Women (OR 2.0; 95%CI 1.2–3.3) and non-smokers (OR 1.8; 95%CI 1.03–3.3) were associated with compliance to LTBI treatment. Only gender was found as an independent predictor after adjusting for smoking status (OR 1.9; 95%CI 1.06–3.3).

**Conclusion:** Knowledge of demographic characteristics and health beliefs among smokers will help in the development of preventive interventions among this population at high risk for TB disease.

**PC-404-440 Time to diagnosis and treatment of tuberculosis in northern Lima, Peru**

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**Background:** Multiple behavioral and health system factors lead to diagnostic delay resulting in increased morbidity and ongoing transmission as tuberculosis (TB) patients go undetected.

**Methods:** Cross sectional study was performed in northern Lima to quantify time to TB diagnosis and treatment and to identify factors associated with delay.

**Results:** 259 newly diagnosed adult TB patients were interviewed: 84.6% pulmonary, 15.4% extrapulmonary TB; 74% smear(+). The median time between first symptom and treatment initiation was 41 days, and 11 days between the first health encounter and treatment initiation. Delay was significantly associated with smear negative status. No association found with sex, age, ability to read or bacillary load. Patient chose mainly physicians (73%) and pharmacists (22%) as the point of first health encounter. Sputum was requested from 65% of patients seen by physicians on their first encounter; 87% of patients delivered all samples; 91% of the smear results were available within 4 days.

**Conclusion:** Delays are primarily related to health-seeking factors and secondarily to low suspicion of TB diagnosis among physicians and the low sensitivity of smear microscopy. Educational campaigns targeting patients and physicians, and programs promoting high quality smear microscopy are required to reduce time to diagnosis.

**PC-455-495 Smoking and tuberculosis: a systematic review and meta-analysis**

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**Introduction:** Numerous studies on the relationship between smoking and tuberculosis (TB) have been



conducted, however, no systematic review exists. By assimilating studies on the topic we aim to: 1) systematically assess the literature and 2) quantify the relationship between smoking and TB using meta-analytic methods.

**Methods:** Eight major databases (including PubMed and EMBASE) were searched yielding 1198 papers spanning the time period 1953 through 2004. Two independent reviewers screened studies based on inclusion/exclusion criteria. The reviewers evaluated the full text of 208 studies in several languages and included 54 studies, primarily case-control and cross-sectional, from which data were extracted.

**Results:** Study outcomes analyzed separately were tuberculosis infection (8), active disease (32), and death (6). For active TB disease random effects summary odds ratio (OR) was 2.04 (95%CI 1.65–2.53) comparing smokers to non-smokers. For infection, OR = 2.02 (95%CI 1.60–2.55) and death OR = 2.13 (95%CI 1.39–3.28). Other analyses include dose-response, publication bias, quality assessment, subgroup analyses, and meta-regression.

**Conclusion:** TB and smoking are massive public health problems, especially in resource-poor countries. This meta-analysis demonstrates that risks for TB infection, disease, and death are approximately two-fold higher for those who have ever smoked versus never smoked.

#### PC-476-516 Respiratory disease trends in South African platinum miners: an autopsy study

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**Introduction:** There is a paucity of data on the respiratory health of platinum miners. Around 95 000 miners are employed in this industry in South Africa. Post mortem examinations are performed on approximately 3000 deceased miners from all commodities annually, irrespective of cause of death. Around 10% of these are platinum miners.

**Objectives:** To review autopsy data on platinum miners with a view to describing disease prevalences, time trends and associated risk factors.

**Methods:** Pathology findings at autopsy were analysed in platinum miners, from 1975 to 2003.

**Results:** Although the prevalence of PTB has been increasing in the mining industry as a whole, platinum miners appear to be most affected, with an increase of 350% over the last five years (currently 345 per 1000). The prevalence of silicosis is relatively high (53 per 1000 compared to 252 in gold miners in 2002) but may be explained by previous, undisclosed employment in the gold mines.

**Conclusions:** This is the largest series of platinum miners for whom lung disease has been analysed. Al-

though there appears to be less occupational respiratory disease in these miners than in gold miners, the high rates of PTB are a concern.

#### PC-544-601 Improved efficacy of multidrug-resistant tuberculosis treatment in patients given individualized therapy under DOTS-Plus, Latvia, 2000–2001

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**Background:** To manage multidrug-resistant tuberculosis (MDR-TB), Latvia has provided second-line drugs under a DOTS-Plus treatment strategy since 1999. The purpose of this study was to evaluate the improvement of treatment efficacy from the 2000 to 2001 cohort.

**Methods:** We conducted a retrospective record review of all civilian patients who began individualized treatment for MDR-TB in Latvia between January 1, 2000, and December 31, 2001.

**Results:** The treatment cohorts included 204 persons in 2000 and 215 persons in 2001. The proportion of patients never before treated for TB (primary MDR-TB) increased from 27% to 42.3%. The proportion of persons with positive human immunodeficiency virus antibody increased from 0.5% (1/197) to 3.9% (8/205). The median number of drugs that isolates were resistant to at treatment onset did not change (5 drugs, range 2–10). Among adherent patients, treatment efficacy (cure and completion versus death and failure) increased in 2001, from 75.8% (135/178) to 82.7% (149/180), and the death rate fell from 7.9% (14/178) to 4.4% (8/180). Overall, the proportion of defaulters increased from 12.7% (26/204) in 2000 to 16.2% (35/215) in 2001.

**Conclusions:** Under DOTS-Plus program conditions in Latvia, treatment efficacy has improved over time. Addressing treatment default is necessary to improve overall program effectiveness.

#### PC-558-622 Geographic distribution of drug-resistant (pyrazinamide) *Mycobacterium tuberculosis* in Quebec, Canada

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**Introduction:** With the increasing use of techniques to differentiate strains of TB using DNA (Genetic) fingerprinting come new challenges in the spatial analysis in transmission dynamics. We report on the spatial statistical results of a case-control study.

**Methods:** 77 TB cases having a clonally related pyrazinamide (PZA) drug-resistant strain in Quebec, Canada

between 1990 and 2000 were compared to 254 randomly selected Canadian-born PZA-sensitive controls and both mapped using 6-digit postal codes. We applied various spatial statistics to determine whether the cases had a similar geographic distribution as controls and whether or not there was evidence of a geographic concentration of cases based on the genetic profile of isolates.

**Results:** The results revealed: 1) no significant differences in the nearest neighbor distances between cases and controls, 2) cases tended to be closer to other cases indicating the drug-resistant strains were slightly aggregated in one region, and 3) no spatial-temporal structure between genetic and spatial distances.

**Conclusion:** These findings further corroborate prior analysis where we concluded that a clonally related family of PZA-drug-resistant TB isolates in Quebec represents historic rather than recent transmission.

#### **PC-560-624 Characteristics of tuberculin skin test positive children in a school-based tuberculosis screening program from a low burden country**

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**Introduction:** We describe the characteristics of tuberculin skin test (TST) positive children who were initially screened while attending a school-based integration program for newly-immigrated children.

**Methods:** We conducted a retrospective review of both classroom intake sheets for pupils and TB registry charts from TB clinic follow-up visits from September 1998 to June 2003. A positive TST test was defined as an induration  $\geq 10$  mm.

**Results:** Of 2524 children screened, 542 (21%) had a positive TST test and were referred to the TB clinic at the Montreal Children's Hospital. Of those, 484 (89%) presented at the clinic, 377 (78%) started on free self-administered therapy and 234 (62%) completed therapy. Two subjects were found with active disease. Of the subjects attending the TB clinic, 53% were boys, mean age was 12.4 years old, and the majority (25%) were from East/Southeast Asia. We obtained a TST result on 308 family members of which 73% were TST positive. Two active TB cases were found. Of those started on therapy ( $n = 160$ ) only 39 (24.5%) complied adequately.

**Conclusion:** This high latent TB prevalence and screening effectiveness suggest that this program is feasible and should be extended to all school-based immigrant integration programs. Follow-up of family members should be improved.

#### **PC-632-704 Health effects of particulate matter on human health in residential indoor environment in Ile-Ife**

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**Introduction:** The health effect of indoor pollution has attracted international concern. Indoor spaces form a significant part of man's environment.

**Objectives:** This study investigated the prevalence of respiratory symptoms and lung function abnormalities among residents living in residential environment in Ile-Ife.

**Methods:** This study employed a cross-sectional analytic design involving three dimensional data collection: indoor Pm10 assessment, questionnaire and lung function tests. Samples were collected in three different locations based on the type of working fuel used.

**Results:** The Pm concentration in residences with LPG was  $80.8 \pm 9.52 \mu\text{g}/\text{m}^3$  while residences with kerosene and firewood had  $236.9 \pm 265.3$  and  $269.4 \pm 93.7$  respectively. Lung function parameters of subjects using wood were significantly lower than those using kerosene and LPG. Correlation analysis revealed a strong negative correlation between residential indoor Pm10 concentration and lung function ( $r = -0.95$  and  $-0.98$  for FEV<sub>1</sub> and FVC, respectively, and a strong positive correlation ( $r = 0.80$ ) between residential indoor Pm10 and prevalence of symptoms among subjects.

**Conclusion:** Our study has demonstrated that wood fire is a risk factor for chronic lung diseases in adults. There is need for further studies on this subject and regulatory measures.

#### **PC-717-791 National TB Survey 2002, Cambodia, prevalence of pulmonary TB: preliminary report**

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**Objective:** To determine a burden of TB, especially prevalence of pulmonary diseases.

**Methods:** 42 cluster villages, a population of around 31 000, were sampled with stratified population proportionate method. Those who had cough for 3 weeks or more and/or any abnormality in chest X-ray were examined for sputum smear and culture.

**Results:** Among 23 040 eligible people of age 10 or more, 22 144 (96.1%) participated. 81 smear positive and 190 smear negative/culture positive TB cases

were detected. Crude prevalence rates of smear positive TB were 365/100 000 in this age group and 270 for all population. Male, 542, showed higher prevalence than female, 216. Older age group showed higher prevalence. Cluster villages with better access to DOTS center in distance tended to have lower smear positive prevalence, 276, than those with poorer access, 444. However, prevalence rates of smear negative/culture positive TB did not differ depending on accessibility. Crude prevalence rate of bacteriological positive TB was 1223 in participants of age 10 or more.

**Conclusion:** The prevalence rate of smear positive, 270, was lower than the WHO estimate, 548. However, the smear negative/culture positive prevalence rate was 2.4 times as high as smear positive. Cambodia still has a very high TB burden.

## DRUG RESISTANCE/MDR-TB MANAGEMENT

### PC-184-229 Preventing drug-resistant tuberculosis with a fixed-dose combination of isoniazid and rifampin

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**Objective:** To determine how well a self-administered fixed-dose combination of isoniazid and rifampin (CombinedHR) prevents acquired drug resistance (ADR) to *Mycobacterium tuberculosis*.

**Design:** Self-administered CombinedHR was given to 75% of patients and DOT or separate drugs to 25%. Approximately 75% of patients completed the treatment. We determined 1) how many patients had two drug susceptible cultures three or more months apart as a measure of drug susceptible failure or relapse, 2) how many patients whose initial culture was drug susceptible had a subsequent drug-resistant culture as a measure of ADR, and 3) the drugs taken by patients who developed ADR.

**Results:** Among 5337 drug susceptible tuberculosis patients who were known or presumed to be HIV negative, 152 (2.84%) treatment failures or relapses occurred of which 25 (0.47%) developed ADR. Among approximately 4000 cases taking CombinedHR and primarily CombinedHR, drug resistance occurred in 8 cases (0.2%) and 12 cases (0.3%) when patients with indeterminate histories were added.

**Conclusions:** Treatment with self-administered CombinedHR results in minimal ADR in HIV seronegative tuberculosis cases despite modest rates of incomplete treatment. This important issue needs prospective investigations among HIV positive and HIV negative pa-

tients in settings where interrupted treatment occurs more frequently.

**Note:** Published in the IJTLD. Moulding T. S., Le H. Q., Rikleen D., Davidson P. Preventing drug resistant tuberculosis with a fixed dose combination of isoniazid and rifampin. Int J Tuberc Lung Dis 2004; 8: 743-748.

### PC-478-517 Characterisation of *Mycobacterium tuberculosis* populations during infection: a longitudinal study on drug resistance development

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**Aims:** The first aim of the LONG-DRUG consortium is the generation of a collection of longitudinally collected samples from patients with MDR-TB. Primary objectives are 1) the molecular characterisation of multiple drug resistance development in MTB populations over time, 2) the clarification of the epidemiological relationship of the strains and sub-clones identified in the study population, and 3) the elucidation if the generation of resistant sub-populations of MTB are of clinical relevance.

**Methods:** Comparative strain and sample characterisation is carried out by determination of MIC to first and second-line drugs, resistance genotype determination by real time PCR, RFLP-PCR and sequencing and epidemiological control IS-RFLP and spoligotyping. The relative quantity of selected clones in clinical samples and primary isolates will be analysed by quantitative real time PCR using molecular beacons. All data are collected on an interactive web database accessible to all participants of the project.

**Results:** Sampling over the last two years yielded over 450 strains, 80 serial isolates from a total of 17 patients and over 150 baseline samples. DST data have been obtained for all strains and molecular work and data analysis is ongoing.

### PC-524-578 Clinical manifestations of multidrug-resistant tuberculosis in Southern Taiwan

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The prevalence and mortality of tuberculosis has rapidly declined over the past 4 decades in Taiwan, but the incidence remains high in Southern Taiwan. The emergence of drug resistance, especially multidrug re-

sistance challenges both physicians and health authorities in attaining the mutual goal of eradicating tuberculosis from Taiwan. An understanding of the clinical characteristics of this group of patients is the first step towards this goal. A retrospective review of cases with culture-proven, multidrug-resistant tuberculosis (TB), presenting to the Kaohsiung Veterans General Hospital from 1991 to 1999 was done. A total of 50 cases was included by review of our microbiological records. There was 40 males (80%) and 10 females (20%), and the mean age was 62 years old (range 35–86 years old). Most patients presented with pulmonary TB, and only 4 cases had extrapulmonary TB. The majority of patients (19 patients, 38%) had a history of TB and had received antituberculosis treatment. History of poor compliance during therapy was elicited in 12 patients. However, multidrug resistance was suspected by the physician in only 8 patients initially. Initial acid-fast smears of sputum was positive in 20 patients (40%) and negative in 30 patients (60%). Thirty-one patients (62%) had 2-drug (HR) resistance, 13 (26%) had 3-drug resistance (HR plus Z or S), and 5 (10%) had 4-drug resistance (HRZS). Anti-tuberculosis treatment was given to 44 out of 50 patients: 3-drug regimen (HRE) in 14 and 4-drug regimen (HREZ) in 30 patients. Twenty out of 50 (40%) patients died, 16 (32%) was referred to the Chronic Disease Control Bureau for treatment with 2nd line drugs, 4 (8%) patients transferred to another hospital, and 10 (20%) was lost to follow up. Patient compliance remains critical in the success of antituberculosis therapy and in the prevention of emergence of drug resistance. Future efforts should be directed toward this if eradication of tuberculosis is ever to be accomplished.

### PC-639-713 Comparing retreatment strategies for Category I failures

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**Objective:** To evaluate outcomes of two retreatment strategies for patients failing Category I.

**Retrospective cohort:** Two strategies for failures of Category I were implemented in neighboring regions in Lima, Peru beginning in February 2001. Failures were patients with positive bacteriology at four months of Category I. Strategy A: Category I was discontinued at four months, culture and DST were ordered, and an empiric regimen was initiated. Regimens were adjusted according to DST results. Strategy B: Category I lasted six months; failures started a standardized treatment regimen (STR); patients on STR with positive bacteriology after 6 months received an individualized regimen when DST results became available.

**Results:** 200 patients were treated between February 2001 and April 2003; 133 (of 161 with DST) had confirmed MDR-TB. In preliminary analyses, 86% of Strategy A and 64% of Strategy B patients had good outcomes (OR 3.5;  $P < 0.001$ ). Good outcomes were associated with resistance to  $< 5$  drugs (OR 3.9;  $P = 0.02$ ), which was more common in Strategy A patients. Hierarchical modeling will estimate the confounding effects of other individual, center, and strategy characteristics.

**Conclusions:** Patients referred to appropriate therapy for MDR-TB promptly had less resistance and experienced better outcomes.

### PC-740-815 Relevance of the preliminary results of DOTS Plus project in Orel Region, Russia, for revision of MDR-TB management in the Russian Federation

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**Introduction:** Data on MDR-TB in Russia are not sufficient and the management of MDR-TB does not comply with international recommendations. In 2002 the prevalence of multidrug resistance in Orel Region among new TB patients was 2.6% and 49% among previously treated patients. The DOTS Plus Programme in Orel started in November 2002.

**Objectives:** To evaluate interim outcomes and adverse events of the MDR-TB treatment.

**Methods:** The DOTS Plus data collection forms were reviewed for culture positive patients enrolled from November 2002 to April 2004 and the results were tabulated.

**Results:** 120 MDR-TB patients were registered. Of 102 patients treated for more than 3 months, 67 (65.7%) had culture conversion, 8 (7.8%) defaulted, 2 (1.9%) transferred, 6 (5.9%) died. One patient (0.9%) stopped treatment due to adverse reactions, 8 (7.8%) required removal of the suspected drug(s), 57 (55.9%) of patients with adverse events continued treatment.

**Conclusion:** Currently, 65.7% of MDR-TB patients treated for more than 3 months achieved timely culture conversion. Adverse reactions are not a major obstacle for the management of MDR-TB. Preliminary results are valuable for countrywide introduction of MDR-TB management according to international recommendations.

### PC-772-846 Developing of pilot project on biosocial determinants of successful MDR-TB control in Kazakhstan

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**Introduction:** An international research project on biosocial determinants of MDR-TB development in Kazakhstan was launched in Kazakhstan in 2003 in Almaty, Kazakhstan with consultation assistance of HMS and financial support from UNDP/World Bank/WHO-TDR grant.

**Objectives:** To identify biosocial determinants of TB and MDR-TB development in urban and rural areas of Kazakhstan.

**Materials and methods:** Study is a multi-method, multi-disciplinary research program, involving sociologists, microbiologists, epidemiologists, and clinicians to understand the fundamental biosocial problem of MDR-TB and develop further recommendations for prevention and control. Study employs both qualitative and quantitative methods of data collection. Analysis specifically aims to triangulate sources of evidence. Government documents and newspaper archives on tuberculosis problem from 1998–2004 were reviewed.

**Results:** Qualitative interviews with government officials, NGOs' representatives, focus group discussions with health workers showed different levels of commitment to TB problem. Different stimulation criteria for both patients and health workers give high adherence to treatment. There is a decrease in treatment interruptions and defaults.

**Conclusion:** A global threat of TB and especially of MDR-TB is not only a medical issue, but also has bio-social and socioeconomic impact. Both the medical community and society should increase their commitment to the problem of TB and MDR-TB.

### PC-779-853 TB drug resistance indicators in Donetsk oblast, Ukraine

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**Introduction:** In 2002–2003 DOTS strategy had been implemented in Donetsk oblast of Ukraine. 2442 medical workers, including 254 lab technicians, were trained; 90 centers of smear microscopy were set up, 46 microscopic, 3 bacteriological and 1 third level laboratories were equipped.

**Objective:** To analyze the contribution of laboratory service in TB control in the region.

**Methods:** Analysis of annual reports 2002–2003.

**Results:** 79 924 sputum smear microscopies and 40 924 culture examinations were carried out, 4503 susceptibility tests were done. It was found out that 36% of new TB patients had primary resistance to TB drugs before treatment, 67% of them to H, R, E, S in different combinations, 33% to 2 and more TB drugs, including 10.9% to H and R. In 64% of new TB patients drug resistance was discovered during chemotherapy, including resistance to H and R (36.3%). Drug resistance in patients with chronic forms of TB was discovered in 96.7% cases (including MDR in 56.5%), in patients with relapses, in 75% (including MDR, 41.6%).

**Conclusions:** The problem with resistant TB forms in Donetsk oblast needs to be solved by DOTS+ implementation in the region.

### PC-871-948 Multidrug-resistant tuberculosis on a university campus in Cape Town, South Africa

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Between January 1998 and March 2001 eight students from one university in the Western Cape were diagnosed with MDR-TB. The aim of this study was to investigate, by restriction-fragment length polymorphism (RFLP), whether transmission of MDR-TB occurred within the university campus and to explore epidemiological links by conducting detailed sociological interviews. The ages of the students ranged from 22 to 29 years, 5 were male, and 5 tested negative for HIV. A set of twins (S1 and S2) had the same strain of TB as demonstrated by RFLP. An additional student (S3) also had this strain, but on interview no epidemiological link to the twins was identified. S3 had a close friend with MDR-TB (S4) on whom no RFLP data was available. There were three students (S5, S6, S7) in the Law Faculty (two were room mates) – RFLP was identical in two and unavailable in one. The last student (S8) had an isolated strain and no epidemiological links to any of the other students with MDR-TB were found. Although we could not prove that all eight students were part of the same transmission chain, it is extremely worrying that there were three 'mini' outbreaks, which are under further investigation.

### PC-875-952 Utilisation of national MDR-TB surveillance data to illuminate sources of MDR-TB

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**Introduction:** A 20.5% prevalence of MDR was found among re-treatment patients in the 2001–2002 Nationwide drug resistance survey in Nepal. A sub-analysis of 171 re-treatment cases was carried out to examine prevalent resistance patterns and the sectors from which they report.

**Objectives:** To determine the MDR-TB prevalent resistance in patients by previous treatment regimen, sector treated in, and self-reported treatment outcome.

**Methods:** Analysis in EPI INFO of 171 re-treatment patients using, previous treatment regimen, outcome, and sector of previous treatment.

**Results:** MDR prevalence was 71.4% in cases previously treated with a Cat 2 regimen, and 30% treated with a 'non-standard' regimen. Patients who had failed Cat1 or Cat2 were more likely to have MDR than patients cured (or relapsed) by either of these regimens (24% v 12% for Cat 1) (88% v 20% for CAT 2). MDR was more prevalent (30%) in patients who had been previously treated in the private sector than in any other sector. Contribution to re-treatment MDR-TB was 43% in those previously treated with CAT 2, 31% previously treated with CAT 1, and 26% from other regimens.

**Conclusion:** National MRD TB Surveys MDR-TB can yield information about sources of MDR-TB.

### PC-924-999 Surveillance de la résistance aux anti-tuberculeux à Madagascar

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Le Programme National Tuberculose (PNT) à Madagascar a adopté depuis 1991 le schéma thérapeutique court et la stratégie DOTS. L'évolution de la résistance primaire de *Mycobacterium tuberculosis*, indicateur de l'efficacité du PNT, aux quatre antibiotiques : streptomycine (S), isoniazide (H), rifampicine (R), éthambutol (E), est évaluée par des enquêtes quinquennales chez les nouveaux patients tuberculeux pulmonaires à microscopie positive (TPM+). La résistance secondaire est déterminée chez les cas récurrents. Au cours

de la première enquête, réalisée en 1994–1995 dans 4 grandes villes, le taux de multirésistance aux deux antibiotiques majeurs H et R (Multidrug Resistance ou MDR) était faible : 0,25% pour la MDR primaire et 5% pour la secondaire. Si aucune MDR primaire n'a été observée à Antananarivo, le taux de MDR secondaire y a été le plus élevé (22%). Pour des raisons logistiques, la seconde enquête (1999–2000) a été réalisée uniquement dans la capitale, Antananarivo. Au total, 909 patients TPM+ ont été recrutés de manière consécutive dans 9 centres de santé. Les antibiogrammes ont été réalisés selon la méthode des proportions sur milieu de Loewenstein-Jensen à l'Institut Pasteur de Madagascar, et le contrôle de qualité assuré par le Centre National de Référence des mycobactéries à l'Institut Pasteur de Paris. Les résultats ont pu être analysés pour 789 nouveaux TPM+ et 99 cas récurrents. Les taux de résistance globale primaire et secondaire étaient respectivement de 11,2% et 11,1%. La monorésistance primaire était de 10,6%, essentiellement attribuable à la streptomycine (8,5%). Les taux de MDR sont comparables à ceux observés en 1994–1995 : 0,1% pour la MDR primaire et 4% pour la MDR secondaire. A Antananarivo lors de la première étude, les taux de résistance globale primaire et secondaire étaient respectivement de 18,8% et 34,9%. MDR primaire nulle et MDR secondaire à 22%. Ces résultats indiquent que dix ans après la mise en place du nouveau PNT, peu de souches MDR circulent à Antananarivo, témoignant de l'efficacité du PNT.

### PC-253-281 Amplification of tuberculosis drug resistance in a DOTS programme in Central Asia

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**Introduction:** Multidrug-resistant tuberculosis (MDR-TB) threatens tuberculosis control in many countries, including the Aral Sea Area in Central Asia. Without routine drug susceptibility testing (DST), all patients are placed on standard short-course chemotherapy (SCC).

**Objective:** To assess the amplification of drug resistance during SCC.

**Methods:** Of 382 smear-positive patients tested for drug resistance and DNA-fingerprinted, a repeat sputum sample was obtained from 77 during treatment; 64 had identical strains to that at diagnosis.

**Results:** DST revealed that 19 of these 64 strains had acquired resistance (5% 19/382). Of 172 initially drug-susceptible strains, 3 developed resistance (1.7%). Of 72 patients with single drug resistance, 1 amplified resistance (1.4%). Contrastingly, of 65 patients with

resistance to more than 1 drug (excluding MDR-TB), 9 (14%) amplified resistance, all becoming MDR-TB strains. Of the 68 patients with MDR-TB, amplification occurred in 6 (9%).

**Conclusion:** Significant amplification of resistance occurred in patients presenting with strains resistant to more than one drug. Amplification of resistance predominantly occurred during the intensive phase when doses are carefully supervised. These findings have widespread implications for DOTS programmes operating without routine DST in settings of high drug resistance.

## TRAINING, HUMAN RESOURCES AND COMMUNITY PARTICIPATION

### PC-154-188 Examining the strengths, weaknesses, opportunities and threats within tuberculosis information, education, and communication (IEC) campaigns for prisoners in Honduras: refining campaign content and prioritizing targets for future intervention

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**Background:** Since 2001, the Gorgas Tuberculosis Initiative and the Honduran National Tuberculosis Program have collaborated to implement DOTS throughout Honduran prisons. One outcome has been the widespread creation of information, education, communication campaign (IEC) materials and activities by prison staff and prisoners.

**Objective:** Assess strengths, weaknesses, opportunities, and threats within prison IEC campaigns.

**Methods:** Convenience samples of prison staff and prisoners participated in either: one-on-one interviews; focus groups; or a survey using a validated questionnaire to examine knowledge, attitudes, beliefs, and practices towards tuberculosis. IEC campaign efforts were cataloged by prison.

**Results:** Campaign strengths include distributing information related to seeking care for persistent cough, diagnostic procedures, treatment availability and consequences of defaulting on treatment. Measures of audience knowledge and attitudes indicated understanding of increased susceptibility to TB and acceptance of DOTS. Identified weaknesses include the integration of new knowledge with old beliefs. (84% of survey respondents recognize medications cure TB, yet 32% reported herbal teas help cure TB.) Opportunities to refine campaign content include incorporating behavioral theory constructs into messages.

**Conclusions:** To maintain campaign momentum and

avoid audience desensitization to TB messages, programs must prioritize targets for future intervention and expand beyond the medical model of patient education.

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### PC-200-243 Total quality management training to improve the quality of tuberculosis control services in Malawi

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**Background:** The National Tuberculosis Programme (NTP) in Malawi conducted a Total Quality Management (TQM) Course in February 2003, as a step towards improving the Management skills for NTP and district hospital staff working with TB patients. The participants identified problems in TB Control activities and worked on them to improve quality.

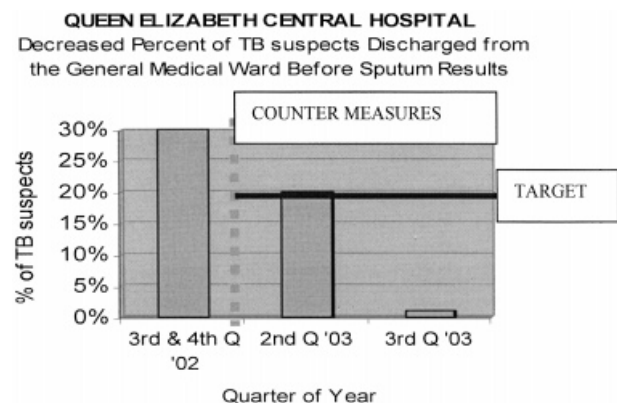
**Broad objective:** To equip tuberculosis control staff with valuable skills in quality improvement.

**Specific objectives:**

- Demonstrate a hands-on understanding of TQM.
- Apply the TQM concepts to TB control.

**Methods of work:** A one-week course was conducted. The teams carried out applied learning projects. Review of data collected between February and October 2003 and the implementation of countermeasures was done.

**Results:** An example of the project (Figure)



**Figure** The percentage of patients discharged before sputum results was reduced from 30% to 1% after implementing counter measures. The improvement target was 20%.

**Conclusion:** Training TB control staff in Total Quality Management skills and implementation of applied learning projects improves the quality of TB control activities. It is important for trained teams to put this as a routine in the day to day work for sustainability.

### PC-648-717 Integral role of community health workers in DOTS-Plus care

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**Objectives:** To describe the role of community health workers (CHW) in multidrug-resistant tuberculosis management, and highlight key aspects of CHW supervision and training.

**Methods:** Qualitative study using participant observation, focus groups, and key informant interviews.

**Results:** In addition to their primary responsibility of directly observed therapy, CHWs are responsible for surveillance and management of side effects, comorbidities, and TB-related complications, counseling and education to patients and families, active case finding in households and in the community, coordination of clinical and social services, and patient advocacy. Therefore, training must provide both specialized and broad-based knowledge and also foster initiative and adaptability in health care workers in order to respond to a wide range of medical and social problems in managing multidrug-resistant tuberculosis in a resource-poor setting. Close and systematic supervision by a supervisory team of nurses is essential to ensure excellent patient care.

**Conclusion:** CHWs play a multifaceted role in the management of MDR-TB patients. In order for CHWs to provide both clinical and psychosocial care of patients and communities, ongoing training and supervision is essential. Truly effective CHWs may adapt easily to managing a broad range of complicated health problems in resource-poor settings.

### PC-698-773 Extension de la prise en charge communautaire du traitement directement observé chez les nouveaux patients tuberculeux à microscopie positive (TPM+) de la commune d'Adjamé

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**Introduction :** Après le projet pilote de mise en œuvre du traitement directement observé chez 288 patients TPM+ dans la commune d'Adjamé avec des résultats de guérison de 80%, la prise en charge communautaire s'est étendue à tous les nouveaux cas dépistés en 2003.

**Objectifs :**

- Décrire la répartition géographique des patients dans la commune d'Adjamé
- Décrire la répartition géographique des patients dans les autres communes
- Comparer les résultats du traitement des patients

de la commune d'Adjamé à ceux non suivis des autres communes

**Méthodologie :** Etude prospective chez 645 nouveaux cas tuberculeux à microscopie positive (TPM+) dépistés dans la commune d'ADJAME du 02 Janvier 2003 au 31 Décembre 2003 par le CAT d'Adjamé et mis sous traitement antituberculeux (2 RHZE/4RH). Une prise en charge communautaire du traitement antituberculeux a été menée par les conseillers de l'ONG Fraternité pendant toute la durée du traitement.

**Résultats :** 645 patients nouveaux cas TPM+ dépistés dans la commune d'Adjamé, âge moyen = 32 ans, sexe ratio = 3/2, la répartition géographique en 5 zones montre : zone1 (129), zone2 (174), zone3 (65), zone4 (84), zone5 (193). Répartition des autres patients des autres communes dépistés au CAT d'Adjamé : Yopugon (736), Abobo (709), Attécoubé (381), Cocody (272), Plateau (27), Hors Abidjan (600). Résultats du traitement des patients de la commune d'Adjamé suivis : guéris = 548 (85% vs autres communes 56%), traitement complété = 6 (1% vs 12%), échec = 5 (1% vs 2%), transférés = 23 (3% vs 7%), perdus de vue = 11 (2% vs 15%), décédés = 52 (8% vs 7%)

**Conclusion :** L'extension de la prise en charge communautaire du traitement directement observé à tous les patients de la commune d'Adjamé donne un meilleur résultat par rapport aux autres communes. L'implémentation dans les autres communes serait souhaitable pour améliorer la prise en charge des patients tuberculeux à Abidjan.

### PC-710-784 Approches du diagnostic et du traitement de la tuberculose chez les internes des hôpitaux d'Abidjan, Côte d'Ivoire

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**Introduction :** Enquête menée auprès de 113 internes des hôpitaux d'Abidjan en vue de déterminer leur approche diagnostic dans le diagnostic de la tuberculose.

**Objectifs :** évaluer les approches du diagnostic et du traitement de la tuberculose chez les internes des hôpitaux d'Abidjan.

**Méthodes :** Il s'agit d'une enquête effectuée à l'aide d'un questionnaire anonyme auto-administré lors du choix des postes des internes des hôpitaux d'Abidjan qui s'est déroulé le 18 avril 2003.

**Résultats :** Parmi les 64,4% des internes (75/113) qui ont répondu au questionnaire, le diagnostic bactériologique de la tuberculose pulmonaire a été proposé comme examen de première intention par 92%. La combinaison de quatre médicaments antituberculeux a été préconisée pour la phase intensive du traitement des nouveaux cas par 52%. La combinaison la plus fréquemment choisie a été l'association Rifampicine-



Isoniazide-Pyrazinamide-Ethambutol (52%). Dans la majorité des cas (96%), la durée du traitement de première ligne a été estimée à 6 mois comme recommandé par le programme national de lutte contre la tuberculose. Pour les patients en situation d'échec, 62,7% ont jugé utile de référer les patients dans un service spécialisé. En présence d'une tuberculose chez la femme enceinte, 12% ont proposé que le traitement soit institué à la fin de la grossesse quand 38,7% ne se sont pas prononcés sur ce sujet. Quant à la stratégie DOTS préconisée par l'OMS pour lutter efficacement contre la tuberculose, 69,3% des internes ont déclaré n'en avoir jamais entendu parler.

**Conclusion :** Le diagnostic microscopique est l'examen pratiqué en première intention par les internes des hôpitaux d'Abidjan. Seul la moitié de ces médecins connaissent le schéma thérapeutique utilisé en Côte d'Ivoire pour le traitement de la tuberculose. La stratégie DOTS n'est pas connue par la majorité des internes. Il est nécessaire de renforcer les compétences et capacités des internes des hôpitaux par l'enseignement du programme.

#### **PC-720-794 Experience of cohort analyses trainings conducted in pilot DOTS program of Tajikistan**

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**Background:** Tajikistan's DOTS program has been implemented since July 2002. Training is an essential component of the program. Initial training in DOTS is followed by quarterly trainings in cohort analysis.

**Objective:** To examine the usefulness of cohort analysis training for acquisition of DOTS management knowledge and skills.

**Methods:** A quarterly training is held for TB Coordinators to analyze cohort data to determine management strategy of the DOTS program. During each seminar TB Coordinators from pilot polyclinics meet, exchange cohort data (Case finding, registration data, smear conversion, and treatment outcomes), and analyze the results of each others work.

**Results:** Over the period of five quarters, TB Coordinators went from never having analyzed TB the aforementioned data to taking an active role in analyzing cohort data and using this data in the management of the program (e.g., Analysis of quality of diagnostic sputum samples has led to additional training in sputum collection).

**Conclusion:** The training on the use of cohort analysis is an important component of the DOTS program. Cohort Analysis training promotes the development of analysis of program indicators and helps provide management skills for participants. Promoting these skills through cohort analysis training is necessary for the sustainability of the program.

#### **PC-769-843 Community based DOTS expansion in reaching global target of case detection and cure rates: Bangladesh experience**

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**Introduction:** National Tuberculosis Program expanded DOTS services in all 460 upazilas (sub-districts) in collaboration with the NGOs.

**Objectives:** BRAC, an NGO mobilized female community health workers (CHWs) to achieve the case detection rate of 70% and cure rate of 85% by 2005.

**Methods:** BRAC initiated a community based tuberculosis control program in Manikganj upazila, in 1984. This model was gradually extended to 283 upazilas out of 460 upazilas during last 10 years covering 78 million population. CHWs provide education to community, identify symptomatic persons, refereeing them for sputum examination and ensure DOTS. Decentralized sputum collection centers are organized in remote villages. Patients are requested to deposit Taka 200 (US\$ 3.5). After completion of the treatment, Taka 125 is given to CHW for her service and Taka 75 is returned to patient.

**Results:** Data of 60 upazilas where program started 5 years before was analyzed in 2004. Case detection rate reached to 66% in 2003 from 30% in 1999 and cure rate reached to 90% in 2002 from 87% in 1999.

**Conclusions:** Community based DOTS through CHWs was found to be one of the effective approaches in achieving the global targets of case detection and cure rates in Bangladesh.

#### **PC-775-849 Assessing the effectiveness of the Basic Food staples Basket (BFB) as an incentive to enhance patient adherence with treatment of active tuberculosis in El Salvador**

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**Introduction:** A number of studies have shown that incentives, primarily financial, provided to patients are effective in improving adherence to TB treatment (Volmink, 1997, Giuffrida, 1997).

**Objectives:** To evaluate the impact of the BFB on patient adherence to DOTS. To examine the programmatic benefits and limitations of the BFB from the perspective of public health workers. To evaluate the incentive value (positive, negative or neutral) of BFB on the follow-up care of patients with TB disease. To use the results of this evaluation to improve the El Salvador TB Program through modification of exist-

ing activities or through design and implementation of new interventions.

**Methods:** The review included case histories and records documenting patient receipt of the BFB.

**Results:** We surveyed 57 of the 71 eligible health care facilities, corresponding to 82% of all facilities in the 4 selected departments. Data were abstracted for 142 of 156 TB patients, or 92% of all eligible patients, in the 4 departments. 14 patients had their records in 12 very remote health care facilities which made data abstraction unfeasible. Of the 142 records from which data were abstracted, 21 patients were excluded due to missing outcome information, or were subsequently determined not to meet the inclusion criteria. Therefore 121 patients met the inclusion criteria as defined and were available for analysis. 61 patients were eligible; however only 27 (44%) actually received a basket. 94 (78%) of the evaluation patients did not receive baskets. Non-adherent patients received a median of 3 baskets and adherent patients received a median of 1 basket, but this difference was not statistically significant. The median age was 30–40 years and the majority were male.

**Conclusion:** Our evaluation of the basics Baskets program in El Salvador found that 20% of patients did not adhere to TB treatment as prescribed. This figure is similar to the 18% non-adherence rate found in Denver.

#### **PC-814-886 The education and training components of the United States-Mexico Binational TB Referral and Case Management Project**

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**Introduction:** The US-Mexico Binational TB Referral and Case Management Project seeks to ensure continuity of care and completion of TB treatment for patients who move between the United States and Mexico.

**Objectives:** Create education and training materials and courses for TB program administrators and health care workers (HCWs) on the project protocol and procedures. In addition, inform and educate TB patients about the project.

**Methods:** A multi-disciplinary team consisting of representatives from governmental and nongovernmental organizations in the US and Mexico created a bilingual protocol. Education and training materials were created and validated utilizing an expert panel with representatives from the US and Mexico.

**Results:** A bilingual protocol training manual was created for project administrators and HCWs. In addition, supplemental materials including protocol wall charts and information packets were created. HCWs in the US and Mexico were trained in several 2-day training courses. Patient education materials were also created.

**Conclusion:** In developing effective training materials and courses, it is essential to follow a systematic approach to use resources wisely, include the target audience in the development process, and enable collaboration and coordination. The use of multiple material formats and training methods were instrumental in reaching the target audiences.

#### **PC-841-914 Partnering to produce a low cost educational TB campaign in Lima, Perú**

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**Introduction:** Faced with limited resources, the PARTNERS TB Control Project partnered with the University of Lima to produce a mass media campaign to reduce stigma against TB patients.

**Methods:** University students from a communications class wrote scripts, produced, and validated TV and radio campaigns. The process was guided and monitored by PARTNERS personnel. An accompanying poster and pamphlet were created and printed. The Ministry of Health worked with TV and radio outlets to air the campaign at a substantial cost reduction.

**Results:** An effective partnership between the University of Lima and PARTNERS was established. The campaign was created with limited resources in only 7 weeks. The campaign was aired for 10 days on multiple channels. To augment the campaign, 10 200 posters and 120 000 pamphlets were distributed throughout Peru. Students gained valuable experience working with real clients.

**Conclusion:** Through partnering with a university, a successful model was developed to create a TB campaign at a fraction of the usual cost. University students can produce professional quality and innovative work. An effective partnership should: share resources; provide mutual benefits; include consistent coordination and communication. This partnership model may be used for other TB-related campaigns and in other health settings.

#### **DIAGNOSTIC METHODS AND DRUG SUSCEPTIBILITY**

##### **PC-230-265 Use of a PCR method for detecting *Mycobacterium bovis* in wildlife populations**

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An epidemiological survey in a French forest was performed in order to evaluate the existence of bovine tu-

berculosis (BTB) in wildlife population. Tissue samples from hunted-killed animals presenting or not macroscopic lesions were collected and processed for mycobacterial culture. *M. bovis* isolation was confirmed by culture and biochemical studies. We describe the development of a BTB-PCR method using the pathological samples of the above described survey in order to overcome classical bacteriology on terms of simplicity and specificity. Two mycobacterium adapted DNA extraction methods (kit+ sequence-capture) and two sets of primers based on IS6110 amplification for heminested PCR (already published+novel) were tested. All tissue samples from which *M. bovis* was isolated were also PCR-positive with either one or the two sets of primers. None of the culture-negative tissues were PCR-positive. Some non-specific reactions were observed with the already published primers on mycobacteria other than tuberculosis (MOTT) positive culture tissues. In our hands, sequence capture + hemi-nested PCR with new primers is the most sensitive and specific method. As we reach the sensitivity values of classical bacteriology, we propose this BTB-PCR as an interesting alternative method for this type of epidemiological studies.

**PC-360-387 Differentiation of the *Mycobacterium tuberculosis* complex from other mycobacteria by selective inhibition with p-nitrobenzoic acid (PNB) using the Bactec MGIT960 system**

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**Objective:** Selective inhibition of mycobacteria growth by inhibitory substances has been commonly used in the identification of species. Growth of the *M. tuberculosis* complex (MTB) is inhibited by p-nitro benzoic acid (PNB), whereas non-tuberculous mycobacteria (NTM) are resistant. The PNB test is known for a long time using solid egg-base media, which takes 3–4 weeks. The objective of the study was to develop a rapid PNB test using BACTEC MGIT 960 automated system.

**Design:** PNB differentiation tests were performed with well documented 86 *M. tuberculosis* strains and 24 NTM strains from Instituto Adolfo Lutz. PNB was added in the MGIT 960 medium. MTB strains were tested as a multi-center study with three different laboratories.

**Results:** The MTB strains were all PNB sensitive, confirming the original identification. For the 24 NTM strains all the PNB result were found resistant. Accuracy of the MGIT/PNB method to differentiate NTM strains from MTB was 100%.

**Conclusion:** The results showed that a simple, low

cost test, may be incorporated to a modern, safe and quick methodology, enabling exact accurate differentiation of MTB. After a presumptive identification by smear, this test may also be combined with MTB susceptibility testing protocol.

**PC-456-497 Efficacy of the string test with MODS in the diagnosis of pulmonary tuberculosis in HIV-infected adults with inadequate sputum production**

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**Introduction:** HIV-associated TB is associated with atypical symptomatology including unproductive cough. Sputum induction carries significant risks of nosocomial transmission. Retrieval of swallowed sputum using the string test may offer a safe, effective alternative diagnostic approach.

**Objectives:** To compare head-to-head the efficacy of the string test with sputum induction for the detection of pulmonary *M. tuberculosis* in HIV-infected adult TB suspects unable to provide an adequate sputum sample.

**Methods:** 160 consenting HIV+ TB suspects underwent the string test followed by sputum induction. All had previously submitted a smear-negative sputum sample deemed inadequate. All study samples (string test eluates and induce sputum) were cultured in Löwenstein-Jensen and MODS (microscopic observation drug susceptibility assay utilising Middlebrook 7H9 broth).

**Results:** 14 subjects had positive cultures for *M. tuberculosis*. In 8 subjects *M. tuberculosis* was cultured from the strings and sputum and in 6 subjects cultures were positive only for the string test ( $P = 0.03$ , McNemar's test). Two cases of MDR-TB were detected, one of which was only detected using the string test.

**Conclusions:** The string test is a safe and effective method for retrieval of useful clinical specimens for the diagnosis of pulmonary tuberculosis with sensitivity at least as good as sputum induction.

**PC-789-862 Investigation of *M. tuberculosis* infection among health care workers in Japan**

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Recently, a new in vitro diagnosis system for *M. tuberculosis* infection (QuantiFERON-TB 2nd Generation, QFT-2G) has been developed. Since ESAT-6 and CFP-10, which are absent from all BCG strains and most

of non-tuberculous mycobacterial species, are used to stimulate whole blood in QFT-2G, the results of QFT-2G are supposed to be unaffected by past BCG vaccination or infection with most of environmental mycobacteria. In the present study, we have analyzed *M. tuberculosis* infection among health care workers using QFT-2G in order to investigate the risk factors in the hospital where TB patients are hospitalized. A total of 332 workers including doctors, nurses, laboratory technicians were analyzed and the results were stratified by age, duration of employment, TB service and job categories. Using an appropriate cut-off value, 33 individuals were suspected to be infected with *M. tuberculosis* (QFT-2G positive rate: 9.9%). With the multiple logistic regression analysis for relevant factors, it has been revealed that the age and the duration of employment are independent risk factors for TB infection. The large size of erythema diameter (more than 80 mm) in tuberculin skin test (TST) strongly correlated with QFT-positivity. Thus, QFT-2G may be the useful tool to monitor *M. tuberculosis* infection among health care workers.

**PC-315-348 Rapid susceptibility testing for rifampicin resistance detection in *Mycobacterium tuberculosis***

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The rapid and accurate susceptibility testing of *Mycobacterium tuberculosis* is essential for effective patient treatment and to prevent transmission of the disease. 20 strains of *M. tuberculosis* was studied to compare different method for determine susceptibility to rifampicin. BACTEC (2 µg/mL), MGIT (1 µg/mL), Nitrate Reduction Assay (NRA) (40 µg/mL) and the colortimetric method MTT and Resazurin reduction assay (2-0.0625 µg/mL) were employed. The results were compared with the gold standard (Proportion Method) and InnoLipa test to detect mutations in the *rpoB* gene. By the BACTEC, MGIT and NRA were reported 10 strains as sensible and 10 resistant to RMP, and average of 10 days was necessary to obtain the results. The 10 resistant strains showed mutation in the *rpoB* gene. For the sensitive strains MIC value by the colorimetric assays were <0.0625 µg/mL, One of the 10 resistant strains showed 1 µg/mL MIC value, for the other 9 strains were >2 µg/mL. By the Proportion Method were confirmed these results. A complete correlation between all methods was observed. These results demonstrate the advantage of the new susceptibility testing because these reduce the time and are simple to perform.

**PC-395-419 Drug resistance of *Mycobacterium tuberculosis* in adult patients with miliary tuberculosis**

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**Background:** Miliary tuberculosis (TB) is a fatal form of TB. There is limited data on drug resistance pattern of *Mycobacterium tuberculosis* in adult patients with miliary TB.

**Objective:** To determine the drug susceptibility pattern of *M. tuberculosis* isolated from miliary TB patients at a tertiary care hospital in Pakistan.

**Material and methods:** All adult patients with miliary TB, admitted between 1994 and 2001, were identified using a computerized database. Culture positive isolates were evaluated for drug susceptibility using middle brook 7H10 agar according to NCCLS criteria.

**Results:** During the study period 110 patients were diagnosed with miliary TB. Of these 32 (30%) patients were culture positive (yielding 35 culture isolates). The sources of positive culture were sputum (37%), cerebrospinal fluid (18%), lymph nodes (12%), bone marrow (9%), bronchial wash (9%), urine (6%), lungs (6%) and liver (3%). Isoniazid resistance was found in 3 (9%) isolates. All the isolates were sensitive to rifampicin, ethambutol, pyrazinamide and streptomycin. There was no multidrug-resistant (MDR) TB isolate identified.

**Conclusion:** Despite the increasing prevalence of TB drug resistance in high burden countries, patients with miliary TB have infection with drug sensitive mycobacteria. First-line anti-TB drugs should be used as initial therapy in miliary TB patients.

**PC-667-740 Acquired resistance in *Mycobacterium tuberculosis* in previously treated patients in Peru: 2002–2003**

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**Introduction:** Resistance to multiple first-line antituberculous drugs is the most serious forms of mycobacterial resistance. It is essential to determine drug resistance in previously treated patients in order to design an adequate therapy regime.

**Objective:** To determine the frequency of *Mycobacterium tuberculosis* resistance to first line antituberculous drugs in previously treated patients.

**Methods:** 2059 strains from previously treated patients (relapses, withdrawals, and failures) from all over Peru were analyzed. Susceptibility testing was performed using the proportions method by Canetti, Grosset and Rist; and pyrazinamide susceptibility was determined using Wayne's method.

**Results:** Of 2059 strains assessed, 959 (46.6%) were failures; 927 (45%) were relapses; and 173 (8.4%)

were withdrawals. According to susceptibility testing, 647 (31.4%), 529 (25.7%), and 97 (4.7%) strains from the failures, relapses and withdrawal groups, respectively, were resistant to at least one antituberculous drug. 605 (29.4%), 479 (23.3%), and 82 (4%) strains were multidrug resistant, respectively.

**Conclusion:** The highest frequency of multidrug-resistant *M. tuberculosis* strains is found amongst therapy failures and relapses; consequently, the TB control program must pay special attention to these high-risk groups, in order to prevent multidrug-resistant *M. tuberculosis* dissemination in the community.

**PC-883-959 Clinical utility of a rapid, homemade microdilution colorimetric method for drug-susceptibility testing of *Mycobacterium tuberculosis***

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**Introduction:** New tools for rapid detection and drug susceptibility testing (DST) of *M. tuberculosis* (MTB) are needed in clinical laboratories to attempt an accurate treatment of cases due to resistant strains. In order to obtain a rapid and economical method to determine minimal inhibitory concentration (MIC) of antituberculosis drugs, a colorimetric microplate assay using 3-(4,4-Dimethylthiazolyl)-2,5-Diphenyl Tetrazolium Bromide (MTT) was designed (M-MTT).

**Objectives:** Evaluating a homemade, rapid colorimetric system for mycobacteria drug-susceptibility testing. Analyzing its performance and suitability for clinical laboratories.

**Methods:** The antituberculosis drugs were tested in the following concentrations (range in µg/ml): isoniazid 1.00–0.03; streptomycin: 8.00–0.25; rifampin 2.00–0.06, and ethambutol 32.00–1.00. DSTs were performed by the Löwenstein-Jensen proportion method (PM) used as the gold standard. The Bactec Mycobacteria Growth Indicator Tube 960 system (MGIT960, BD, Argentina). was also used and results from both methods were later compared. MICs and DST were performed on 323 clinical isolates.

**Results:** DSTs on MGIT960 and PM results were obtained in an average of 5 and 23 days respectively while MIC results by M-MTT were available in an average of 8 days. Sensitivity (S), specificity (ES) and area under the ROC curve (AUC) were used to estimate the general performance of the M-MTT. S and ES were >95% for all the tested drugs. The whole cost of 4 drugs MIC determinations for each isolate was almost US\$ 3.0.

**Conclusions:** Albeit MIGT 960 was the faster system it was also the most expensive. Therefore we concluded

that the M-MTT could be used as a simple, rapid and low cost technology for screening the susceptibility of strains to first-line antituberculosis drugs.

## POSTER DISPLAY SESSIONS

### BACTERIOLOGY AND IMMUNOLOGY

**PS-153-186 Trial of anti-TB activity of new chemical drugs for treatment of experimental multiresistant TB**

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High epidemiological danger for the society of the multi-resistant TB (MDR-TB) with its low treatment effectiveness leads to the need to intensify seeking the new drugs acting to the multi-resistant strains of *M. tuberculosis*. In the first phase we testify 22 drugs from 4 groups of the heterocyclic derivatives of acylformamid-oximes and  $\beta$ -oligopropionamides for anti-TB activity in vitro. Combination RK-44 from group 0-benzoyl- $\beta$ -morpholinopropionamidoximes from all of them had the highest anti-TB bactericidal activity being 10 times more higher than the rifampicin activity for the sensitive *M. tuberculosis* strains and 20 times more for multiresistant *M. tuberculosis* strains. Toxicity of this combination was tried in the white mouse experiences and RK-44 toxicity was 5 times lower when compared with rifampicin and 22 times lower while isoniazid. Experimental research in following phase was carried out to study the RK-44 medicinal effect on the guinea pigs infected with multi-resistant *M. tuberculosis*. Results reliably showed the higher activity of RK-44 in vitro and in vivo in TB treatment for experimental animals infected with MDR-TB strains if compared with basic drugs both rifampicin and isoniazid. It is of evidence of the promising effect of RK-44 as a new generation tuberculostatics having the high anti-TB activity both for sensitive and MDR strains of *M. tuberculosis*.

**PS-251-279 Frequency of isolation of nonsporulating anaerobic bacteria from the patients with drug-resistant tuberculosis complicated by empyema of pleura**

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One of the most widespread etiological factors of purulent-inflammatory processes promoting occurrence in various organs and tissues are nonsporulating anaero-

bic bacteria. Due to bacterial synergy pathogenicity of nonsporulating anaerobic bacteria can considerably amplify on background of tubercular infection and be the reason of the complicated current of tubercular process, lengthening terms and failures of treatment. Pathological material for study was a pleural liquid from 50 patients with drug-resistant tuberculosis complicated by empyema of pleura. Anaerobic bacterium have been found out in 20 (40%) of cultured specimens, in 4 (8%) cases—only monoculture anaerobic bacterium, and in 16 (32%) cases—associated anaerobic bacterium with aerobic microorganisms. The most frequently found representatives of bacterial population were Bacteroidaceae and Peptococcaeae. Among anaerobic strains, in 14 (28%) tests gram-negative bacillus were isolated (*Bacteroides fragilis* – 11, *Bacteroides serpens* – 3), and in 6 (12%) tests gram-positive anaerobic coccuses (*Peptococcus* – 5, *Peptostreptococcus* – 1) were isolated. Thus, results of bacteriological investigation of patients with tuberculosis complicated by purulent pathology have shown that in 40% of cases anaerobic microflora was isolated. Therefore along with identification of the agent of the primary disease it is necessary to give attention to the isolation and identification of nonspecific aerobic and anaerobic microflora at patients with tuberculosis.

**PS-338-364 Molecular characterization of *Mycobacterium avium* complex isolates from patients with respiratory symptoms in Guinea-Bissau**

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**Introduction:** Twenty-eight isolates of *Mycobacterium avium* complex (MAC) were cultured from sputum samples obtained from patients with suspected tuberculosis in Guinea-Bissau. These isolates were further characterized.

**Methods:** MAC probe positive isolates were characterized by hybridisation with probes (Accu-Probe) for *M. avium* and *M. intracellulare*, 16S rRNA sequencing and PCR detection of the DT1-DT6 sequences and the mig gene.

**Results:** One of the 28 isolates reacted with the *M. avium* probe and four with *M. intracellulare*. Six groups were identified by sequencing: 100% similarity was shown for two isolates with *M. avium* subspecies *silvaticum*, *paratuberculosis* and *avium*, for four isolates with MCR08, for five isolates with *M. intracellulare*, for seven isolates with IWGMT 90242 and subspecies HSC 1658, and for eight isolates with IWGMT 90238, 90237, 90247 and 90147. Two sequences were 97% related to IWGMT 90233. Two isolates expressed the DT1 sequence and three the DT6. The mig gene was detected in 18 isolates.

**Conclusion:** 16S rRNA sequencing showed the greatest power of discrimination. No absolute correlation was shown between the typing methods. The finding of the mig gene in 64% of the isolates was interesting since this gene has been associated with virulence of *M. avium*.

**PS-367-455 Evaluation of Gene Probe Amplified Mycobacterium Tuberculosis Direct Test (MTD) for direct detection of *Mycobacterium tuberculosis* in tuberculosis mediastinal lymphadenitis**

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**Aim:** Our aim was to investigate the diagnostic value of MTD in tuberculosis mediastinal lymphadenitis.

**Material and method:** In our study, we included 33 patients who were performed mediastinoscopy. 11 of them had tuberculosis, 22 of them had diseases except tuberculosis (9 sarcoidosis, 13 lung cancer). The yields of mediastinal lymphadenopathy obtained by mediastinoscopy were examined with Ziehl-Neelsen, Bactec radiometric broth, MTD, histopathological and their contribution to the diagnosis of *M. tuberculosis*, was investigated. We took the cut-off value for MTD as 30 000 RLU.

**Results:** The mean age of the patients (18 female, 15 male) were 45.27 + 17.75. The results are shown in the Table.

The results of diagnostic methods in cases

Method	TB cases	Control cases
Ziehl-Neelsen	0/11	0/22
Bactec	1/11	0/22
MTD	3/11	0/22
Histopathological	6/11	16/22

There was a significant difference statistically between the RLU values in tuberculosis and control cases (in TB cases 190 771.4 + 462 RLU, in control cases 3308.5 + 414 RLU,  $P < 0.05$ ). The accuracy of MTD was found as 75.7% in tuberculosis mediastinal lymphadenitis.

**Conclusion:** The MTD test is a diagnosis method that can be applied easily and rapidly (just in a day). The high cost is its disadvantage. It can be used as a complementary method for traditional microbiological analysis.

**PS-371-394 Drug resistance among recurrent tuberculosis cases in Kampala, Uganda**

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**Introduction:** Tuberculosis control is threatened by emergence of drug-resistant strains. Drug susceptibility testing and strain identification by use of RFLP can establish the true rate of acquired drug resistance and rate of reinfection.

**Objectives:** To determine the incidence of acquired drug resistance in recurrent tuberculosis cases. To estimate the rate of re-infection versus the rate of reactivation in tuberculosis recurrent cases using RFLP. To assess the predictors of re-infection versus reactivation in tuberculosis recurrent cases.

**Methods:** A retrospective study design of culture positive recurrent PTB cases.

**Results:** The frequency of drug resistance in recurrent tuberculosis cases was 6.9% for isoniazid, 8.6% for streptomycin, 10.7% for ethambutol, 6.9% for rifampicin and 4.4% for pyrazinamide. MDR-TB was observed in 3.2%. 20.6% developed any form of resistance. Participants who developed drug resistance were more likely to be HIV-uninfected (53.9% Vs 83.3%,  $P = 0.02$ ) and had a significantly higher mean hemoglobin (12.1 g/dL Vs 10.7 g/dL,  $P = 0.008$ ). Eight of 29 (27.6%) patients with RFLP results had evidence of exogenous re-infections.

**Conclusion:** The risk of reinfection is high and there is need to identify where transmission is occurring and build community interventions to curb transmission.

**PS-556-621 Drug-resistant tuberculosis**

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**Aim:** The aim of this study was to determine characteristics of drug-resistant tuberculosis.

**Material and method:** There are evaluated 172 patients with any drug resistance to INH, RFM, EMB, STM recovered during the years 1986–2002.

**Results:** The strains of *Mycobacterium tuberculosis* from 172 patients with any resistance, resulted 69 (40.1%) resistant to INH, 35 (20.3%) to RFM, 10 (5.8%) to EMB, 118 (68.6%) to STM; monoresistance to 131 (76.2%) patients, bi-resistance – 26 (15.1%), tri-resistance – 11 (6.4%), quadruplet – 4 (2.3%). MDR-TB were 28 (16.3%) patients. According to the gender were 128 (74.4%) males and 44 (25.6%) females; 81

(47.1%) from urban and 91 (52.9%) from rural zones; 27 (15.7%) patients to group age 15–24, 38 (22.1%) to 25–34, 31 (18%) to 35–44, 30 (17.4%) to 45–54, 31 (18%) to 55–64, and 15 (8.7%) over 64 years old. New cases were 121 (70.3%), relapse, 29 (16.9%), transferred, 5 (2.9%), treatment after default, 3 (1.7%), chronic, 14 (8.1%). Never treated were 69 (40.1%), previously treated, 68 (39.6%), and unknown, 35 (20.3%). Bad cooperation was to 51 (29.7%) patients, side effects of antituberculars to 16 (9.3%) with interruption to 14 (8.1%), with anamnestic familiar TB 44 (25.6%).

**Conclusions:** Drug resistant tuberculosis was more frequently to males with bad cooperation, often with familiar TB; higher to STM and INH. MDR-TB resulted 16.3% of patients with any resistance.

**PS-575-646 In vitro killing of *Mycobacterium ulcerans* by acidified nitrite**

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**Introduction:** *Mycobacterium ulcerans* disease (Buruli ulcer) is a serious ulcerative skin disease, which is a major health problem in many tropical countries, particularly in West Africa. It causes chronic, painless skin ulcers with undermined edges, usually on the limbs and predominantly in children. Treatment options for Buruli ulcer are surgery, antimycobacterials and topical preparations. However patients often present late with large ulcers, which require wide surgical excision, followed by skin grafting and the result is a long in-patient stay.

**Objectives:** The only topical treatment shown to increase the rate of healing in a double-blind controlled trial is acidified nitrite creams, which generate nitric oxide and other oxides of nitrogen (Phillips et al, submitted for publication).

**Methods:** *M. ulcerans* suspension was added to a fresh mixture of nitrite and citric acid. After 10 min and 20 min exposure the colony forming units were determined on Middlebrook 7H11 agar plates.

**Results:** Killing was rapid and viable counts were reduced more than 6 log<sub>10</sub> CFU to below detectable limits after only 10 min exposure to 40 mM acidified nitrite.

**Conclusion:** These results show that nitrogen oxides kill *M. ulcerans* even in 20 times lower concentrations to those, which were administered during a trial of topical treatment of human *M. ulcerans* disease.

### PS-228-261 Immune intervention and adaptive immune responses of V $\gamma$ 2V $\delta$ 2 T cells in active AIDS virus/mycobacterial coinfection

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V $\gamma$ 2V $\delta$ 2+ T cells play a role in anti-microbial responses. It is unknown whether adaptive V $\gamma$ 2V $\delta$ 2+ T-cell responses in active mycobacterial coinfection of HIV-infected humans can be generated during effective antiretroviral treatment. Here, SIVmac-infected macaques previously exposed to BCG were re-infected with BCG, treated with tenofovir or tenofovir + indinavir, and assessed for the development of V $\gamma$ 2V $\delta$ 2+ T-cell responses during active BCG coinfection. A restored capacity of V $\gamma$ 2V $\delta$ 2+ T cells to undergo major expansions and pulmonary migration in active BCG re-infection was detected after simultaneous BCG re-infection and tenofovir treatment of SIVmac-infected monkeys. Interestingly, a restored expansion of V $\gamma$ 2V $\delta$ 2+ T cells in SIVmac/BCG-coinfected monkeys was detectable even though antiretroviral treatment was initiated one month after BCG re-infection. Importantly, the restored expansion of V $\gamma$ 2V $\delta$ 2+ T cells coincided with increases in numbers of PPD-specific IFN $\gamma$ -producing CD4+ T cells and increases in the magnitude of their proliferative responses. In contrast, the control SIVmac-infected monkeys exhibited diminished responses of V $\gamma$ 2V $\delta$ 2+ T cells and mycobacterium-specific CD4+ T cells during active BCG coinfection. The results suggest that the development of adaptive immune responses of phosphoantigen-specific V $\gamma$ 2V $\delta$ 2+ T cells during active mycobacterium/AIDS virus co-infection requires control of viral infection and immune competence of peptide-specific CD4+ T cells.

### PS-317-349 Transforming Growth Factor- $\beta$ 1 (TGF- $\beta$ 1) pleural levels as a marker of pleural thickness in tuberculous pleural effusion

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**Objectives:** To evaluate the TGF- $\beta$ 1 pleural and serum levels from patients with tuberculous pleural effusion (TB) and determine if its levels were related with pleural thickness.

**Methodology:** Prospective clinical study of 55 patients with TB ( $n = 47$ ) or transudative effusion (control group;  $n = 8$ ). TGF- $\beta$ 1 pleural fluid and serum and were analyzed using the ELISA immunoassay. Thickness in TB group (PT) were evaluated by chest high-resolution computed tomography (HRCT) and divided

in three groups according to pleural thickness: A 0–2 mm, B >2 mm <9 mm and C >10 mm.

**Results:** TGF- $\beta$ 1 levels were significantly higher in TB than those in the transudative. In TB group, there were no significant difference between TGF- $\beta$ 1 and pleural fluid and serum levels and also no correlation between pleural fluid and serum. The median levels of TGF- $\beta$ 1 pleural fluid in the group C (12/47, 1025.8 pg/mL) were significant high than in Group A (17/47 657.0 pg/mL) and Group B (18/47 497.2 pg/mL),  $P < 0.05$ .

**Conclusion:** High levels of TGF- $\beta$ 1 in TB pleural fluid was correlated with pleural thickness and may be a useful marker predictor of development of pleural thickness.

### PS-396-421 Role of Th1 and Th2-derived cytokines on iron homeostasis in ACD (anaemia of chronic disease)

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Haematological alterations involved in the acute-phase response and chronic inflammation include leukocytosis, thrombocytosis, and decreased erythropoiesis, resulting in ACD. Interestingly, thus far, hardly any attention has been paid to the role of Th2 derived cytokines on iron homeostasis. We demonstrated to modulate iron metabolism by two different pathways: increasing ferritin translation via NO formation, and by an amplification of TfRmRNA expression. The objective of this study was to evaluate sTfR, sTfR/F, NO in healthy children, children with Th1 disorders, and with Th2 disorders there were symptoms of mild Fe deficit anemia (Hgb 10g/dl). sTfR value were determined using the Quantikine IVD Human immunoassay kit (R&D Systems), plasma NO concentration was measured by Cayman Chemical's photometric test.

**Results:** see Table.

	Ferritin	sTfR ( $\mu$ g/L)	sTfR/logF (nmol/L)	NO ( $\mu$ mol/L)
Healthy	27.4 $\pm$ 5.1	31.7 $\pm$ 5.8	24.97 $\pm$ 5.57	54.6 $\pm$ 13.75
Th1 disorders	80.7 $\pm$ 8.9	30.96 $\pm$ 4.1	16.3 $\pm$ 2.43	156.6 $\pm$ 59
Th2 disorders	64.4 $\pm$ 7.7	30.8 $\pm$ 4.9	17.18 $\pm$ 3.01	113.4 $\pm$ 42

**Conclusion:** Th-2 derived cytokines primarily enhance TfR-mediated iron uptake in activated macrophages, which is then stored in ferritin that this been effectively produced following stimulation with proinflammatory cytokines, which reveals a connection between iron metabolism and NO.



**PS-523-579 Serodiagnostic test (CapiliaR MAC) to detect anti-glycopeptidolipid-core IgA-Antibody in serum for diagnosis for pulmonary *Mycobacterium avium-intracellulare* complex (MAC) disease**

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We report the development of the serodiagnostic test using anti glycopeptidolipid (GPL) core IgA-antibody in patients with pulmonary MAC disease. GPL-core was separated as antigen from GPL which was purified from serovar 4 *M. avium* by column chromatography. This antigen was applied to an enzyme immunoassay suitable for the measurement of anti GPL core antibody in serum. This EIA meets all the requirements of routine clinical assay in term of sensitivity (detection limit: 1.0 U/ml), reproducibility (total CV: 5.2–11.3%), accuracy (recovery: 91.2–109%), simplicity and rapidity (<2.5 h). Clinical validation of the assay was confirmed by the measurement of anti GPL core antibody in the serum of normal subjects and immunocompetent patients with pulmonary MAC disease. The EIA tested in this study showed a high serodiagnostic discriminating power (76.3% sensitivity and 94.4% specificity).

**PS-553-610 Survival in whole blood culture: marker of virulence of IS6110 clustering strains of *Mycobacterium tuberculosis***

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**Objective:** To examine the ability of IS6110 clustering and non-clustering strains of *M. tuberculosis* to evade the killing mechanisms of the human host.

**Methodology:** Clinical isolates of 3 unique strains, and 2 endemic strains, the Beijing family and the KZN family, identified by IS6110 fingerprinting, were grown in a whole blood culture model (WBA) (Wallis et al, 2001) with minor modifications. The assay was performed in triplicate. Survival was measured by the number of days to positivity in a BACTEC 460.

**Results:** The differences in the survival values of each strain was computed by a spreadsheet for the WBA with the growth indices of the blood cultures. Significant differences in the survival rates were displayed by the different strains. Survival of the Beijing strain was significantly higher than that of all the other groups of strains. The survival rate of the KZN strain was lower than the Beijing strain but significantly higher than all others. With one exception, very little differences were observed among the 3 representative strains of each group tested.

**Conclusion:** This study has established that survival

rates in whole blood culture are useful as surrogate markers of virulence in clustering strains of *M. tuberculosis*.

**PS-273-299 Tuberculose étendue**

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Tuberculose : Probleme de santé publique mondial  
Dans le monde :

- 30% population infectée par BK
- 8 millions de Nx cas / année
- Pays en développement :
  - 95% des Nx cas & 98% de décès
  - 26% de décès évitables
- 75% d'infections et de décès (15–45 ans)
- Incidence :
  - 5–50 cas p. 100 000 hab/ an
  - 120–220 cas p. 100 000 hab/ an

En Algérie :

Maladie en régression

Incidence actuelle (M+) = 22–23 cas p. 100 000 hab/an  
Sétif :

- Incidence (M+) = 20,5–22,5 cas p. 100 000 hab/an
- Plusieurs formes de tuberculose :
  - Formes minimes
  - Formes étendues
    - \* Prognostic vital
    - \* Observées malgré tous les efforts de LAT

Etudier les caractéristiques

- Cliniques
- Radiologiques
- Evolutives

- Etude rétrospective
- 192 cas de formes étendues
- Hospitalisées au service de pneumo-phtisiologue
- Années : 2000–à2003

Recueil : fiche de dépouillement

Exclusions : Formes minimes  
Formes disséminées

Classification (Etendue III) :

Caractéristiques générales de la population d'étude :

Année : 2000 : 37 cas ; 2001 : 59 cas ; 2002: 53 cas ; 2003: 43 cas

- Sexe: Hommes : 126 cas ; Femmes : 66 cas ; Sex-ratio = 1,9
- Age-moyen: 43,4 ans

**PS-347-373 Lung cancer in patients 45 years of age or younger**

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**Aim:** The aim of this study was to determine if are differences between lung cancer patients 45 years of age or younger and elder one.

**Material and method:** There are evaluated two groups of lung cancer patients: A—21 cases 45 years of age or younger ( $38.6 \pm 6.6$ , range 21–45) and B—231 over this age ( $61.3 \pm 7.7$ , range 46–80). Respectively 15 (71.4%) males and 6 (28.6%), 212 (91.8%) males and 19 (8.2%) females. Were analyzed gender, profession, tobacco consumption, histologic type, symptoms and their duration before hospitalization, radiologic and bronchologic data, sedimentation rate, leucocytes, fibrinogen, stadium, treatment.

**Results:** Significant differences were found for tobacco habits, gender, anorexia, thoracic pain, fibrinogen and chemotherapy. Significant differences were not found for other variables analyzed.

**Conclusions:** Younger lung cancer patients are more likely to be non or less smokers, females, less frequently anorexia and thoracic pain, less fibrinogen level, receive more frequently chemotherapy compared with elder patients.

#### PS-444-484 Identification of in vivo expressed TB proteins in the body fluids of tuberculosis patients

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**Introduction:** *Mycobacterium tuberculosis* changes its protein expression profile depending upon environmental stimuli. Consequently, the most important biomarkers for disease progression are TB proteins expressed during active infection. To date, identification of these proteins has been confounded by the high concentrations of host proteins present in human body fluids.

**Objectives:** To use innovative sample preparative and proteomic techniques to identify in vivo expressed TB proteins in patients with active disease.

**Methods:** Advanced proteomic approaches were used to concentrate and identify TB proteins in the body fluids of TB patients.

**Results:** To date, 12 *Mycobacterium tuberculosis* proteins have been identified in the sputum and serum of TB patients. They fall into the general functional categories of DNA and protein synthesis (4), energy metabolism (2), mycobacterial cell wall synthesis (2), host survival (1) and hypothetical (3).

**Conclusion:** We have demonstrated that fractionation and enrichment strategies can be used to capture and concentrate low abundance TB proteins present in the body fluids of TB patients. This approach has broad applications for identifying biomarkers for pathogens that infect animal or human hosts.

#### PS-507-559 Yield of traditional methods for the diagnosis of pleural tuberculosis

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**Introduction:** Pleural tuberculosis (PTB) is one of the commonest forms of extra-pulmonary TB. Diagnosis is often a challenge because the traditional diagnostic methods lack sensitivity. From 1998 to 2003, during a study we developed on old and new diagnostic methods on PTB in Rio de Janeiro, Brazil, we verified the sensitivity of the traditional methods for the diagnosis of this disease.

**Methods:** From August 1998 to March 2003 all patients submitted to a thoracentesis because of a pleural effusion were analyzed. Acid fast staining (AFB) and culture (Löwenstein-Jensen medium) of pleural fluid and biopsies were carried out as well as histopathological examination of the pleural biopsy.

**Results:** From 137 patients, 95 (69%) were cases of TB and in 43 (45%) AFB, pleural fluid culture, pleural biopsy culture and histopathological examination were performed and sensitivities were 2%, 9%, 35% and 70%, respectively.

**Discussion:** PTB is a common extra-pulmonary form of TB, being responsible for up to 10% of all cases. Traditional methods for the diagnosis of PTB have low sensitivity, which was confirmed in our series.

**Conclusion:** As sensitivity of traditional methods is low, development of new diagnostic tests for the diagnosis of PTB is warranted.

**Methods:** From August 1998 to March 2003 all patients submitted to a thoracentesis because of a pleural effusion were analyzed. Acid fast staining (AFB) and culture (Löwenstein-Jensen medium) of pleural fluid and biopsies were carried out as well as histopathological examination of the pleural biopsy.

**Results:** From 137 patients, in 43 (31%) AFB, pleural fluid culture, pleural biopsy culture and histopathological examination were performed and sensitivities were 2%, 9%, 35% and 70%, respectively.

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**Conclusion:** As sensitivity of traditional methods is low, development of new diagnostic tests for the diagnosis of PTB is warranted.

### PS-536-599 BALF phospholipids in smokers and non-smokers with sarcoidosis and tuberculosis

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Altered composition of epithelial lining fluid may affect the outcome of the disease. The aim of the present study was to evaluate an influence of smoking on BALF phospholipid concentration in sarcoidosis and tuberculosis. BALF phospholipid composition was determined in 64 patients with sarcoidosis, 12 patients with tuberculosis and 10 healthy volunteers. The total lipid phosphorus (TLP) and level of phosphatidylcholines (PC) in BALF were found to correlate to each other and were decreased in sarcoidosis (1,6 fold) and tuberculosis (5,6 fold) as compared to controls ( $P < 0.02$ ). A mild not significant tendency to the reduction of BALF phospholipids in smokers was observed within controls, patients with sarcoidosis I and tuberculosis. Statistically significant decrease of TLP and PC was shown only in sarcoidosis II/III (TLP:  $20.7 \pm 3.5 \mu\text{mol/L}$  in smokers compared to  $31.9 \pm 2.6 \mu\text{mol/L}$  in non-smokers,  $P < 0.05$ ). Decrease of surfactant phospholipids in non-smoking patients seems to be due to alveolar and interstitial inflammation. Less BALF recovery ( $58.5 \pm 3.2\%$  versus  $67.5 \pm 2.1\%$ ,  $P < 0.05$ ), bronchial obstruction and starting fibrosis may contribute to more significant phospholipid reduction in smokers.

### PS-570-636 Malnutrition in multidrug-resistant tuberculosis patients in the Philippines

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**Objectives:** To describe baseline nutritional status of patients with MDR-TB in the Philippines and to determine its impact on sputum smear and culture conversions. **Methods:** Records of 168 MDR-TB patients at the Makati Medical Center DOTS-Plus Pilot Project in the Philippines were reviewed.

**Results:** The mean BMI was  $18.9 \pm 4$  with 53.8% patients malnourished ( $\text{BMI} < 18.5$ ); 36.5% had moderate-severe malnutrition ( $\text{BMI} < 17$ ). Thirteen (7.7%) patients had positive smears after 6 months of treatment, and 10 (5.9%) patients had a positive culture after 6 months of treatment. Malnutrition was significantly associated with a longer time to sputum smear conversion ( $P = 0.01$ ). Malnutrition was not associated with time to culture conversion ( $P = 0.18$ ).

**Conclusion:** Malnutrition is common in Filipino MDR-TB patients, and its in these patients far exceeds national prevalence rates of 13.2% for malnutrition and 4.4% moderate-severe malnutrition, in adult Filipinos.

There was a significant association between malnutrition and slower sputum AFB smear conversion; correlation with culture conversion was not demonstrated. Further studies are planned to better understand the relationship between nutritional status and treatment outcomes of MDR-TB.

### PS-614-682 Bioelectrical impedance analysis and anthropometric body composition among HIV and tuberculosis infected individuals in Uganda

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**Objective:** To determine the impact of HIV and tuberculosis (TB) on body composition in developing countries and the relationship between bioelectrical impedance analysis body composition measurements and anthropometry.

**Methods:** A cross-sectional descriptive study was used to examine 570 household individuals who were screened for tuberculosis and HIV at baseline from the Kawempe Community Healthy study.

**Results:** Body mass index (BMI) had consistent strong direct correlations with body fat while weight had a similar relationship with body cell mass (BCM). Hemoglobin and weight had direct correlations with fat-free mass and phase angle among the under 5 year olds. Among adults with HIV/TB co-infection, TB disease, and HIV seropositive, BMI was  $19.3 \pm 2.5$  ( $P = 0.001$ ),  $19.3 \pm 2.2$  ( $P = 0.0006$ ),  $23.4 \pm 5.0$  ( $P = 0.5$ ) respectively compared with healthy individuals  $22.5 \pm 4.5$ . BCM was  $14.3 \pm 3.1$  ( $P = 0.0048$ ),  $15.1 \pm 3.3$  ( $P = 0.05$ ),  $15.2 \pm 2.5$  ( $P = 0.4$ ) respectively compared with  $15.3 \pm 3.5$ . Similarly body fat,  $9.4 \pm 5.8$  ( $P < 0.001$ ),  $9.5 \pm 6.1$  ( $P < 0.001$ ),  $18.6 \pm 12.7$  ( $P = 0.4$ ) compared with  $16.5 \pm 9.9$ .

**Conclusions:** BMI is a direct measure of body fat while weight measures BCM. Individuals in this study experience semi-starvation and HIV infection does not appear to worsen the metabolic effects of tuberculosis. Bioelectrical impedance analysis is a useful tool to supplement the anthropometric nutritional evaluation.

### PS-867-941 Impact of the affluence of refugees from Angola on the management of tuberculosis at Kimpese in the DRC

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Most adults in Central Africa are latently infected with *Mycobacterium tuberculosis*. Tuberculosis is the first

cause of morbidity and mortality among adults in the DRC. An estimated 2% of the Congolese develop active TB during their adult lives, and probably all have been infected without any symptom. Tuberculosis has always been an important public health problem in the developing world and financial resources for implementing efficient tuberculosis control programs have generally been insufficient. The management of tuberculosis can be made more difficult by the presence of new parameters such as the migration of populations, especially refugees, due to the negative effect of a war. At Kimpese, there was a massive affluence of refugees from Angola from 1998 to 1999 due to the war in Angola. The population of Kimpese increased from 30 000 to 40 000; a quarter of the population are refugees from Angola. The present study reports the impact of the presence of refugees from Angola in the management of tuberculosis at Kimpese, a rural area in Central Africa, located 220 km south-west of Kinshasa in the DRC. The data present this impact regarding the number of cases, the supply of antituberculosis drugs, and the apparition of MDR-TB. According to the statistical data from the Leprosy and Tuberculosis Coordination Office for the eastern part of the province of Bas-Congo, the number of TB cases increased from 1597 cases in 1997 to 2219 cases in 1999. The percentage of refugees among TB patients ranges between 35% and 45%. During this period the National TB Program had a deficit in the supplies of antituberculosis drugs for one third of TB patients. During the period, 8 cases of MDR-TB are suspected clinically, 3/4 of them refugees from Angola. The massive affluence of refugees from Angola at Kimpese has dramatic consequence by increasing by 25% the cases of tuberculosis, by leading to a deficit in supplies of antituberculosis drugs and by the apparition of MDR-TB mostly among refugees from Angola.

#### PS-389-413 The 'Quebec' family of *Mycobacterium tuberculosis*: evidence against ongoing spread

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**Introduction:** We have recently characterized the genetic similarity between PZA-R isolates of *Mycobacterium tuberculosis* (TB) in the Quebec born. We now describe in more details the epidemiologic characteristics of this clone and further explore the evidence against an ongoing spread.

**Methods:** We selected isolates with the 'Quebec' mutation profile which share the 8 base pair deletion in the *pncA* gene and an amino acid substitution of Arg 140 - > Ser. We also identified 4 corresponding TB isolate without the specific PZA resistance profile as

controls. Molecular characterization was done with the IS6110 restriction fragment length polymorphism (RFLP) technique. Clustering was defined with identical RFLP matching or with a difference of one band for near-identical patterns. Baseline epidemiological information was obtained from surveillance data and participants were asked to recall their lifetime history to highlight potential circumstances of transmission.

**Results:** We defined 77 cases and 254 controls. They did not differ on demographic or clinical characteristics. No predictors of clustering could be found among interviewed (or not) cases or controls.

**Conclusion:** We identified a predominant and successful strain that has spread throughout Quebec for which transmission links could not in fact be documented for at least a generation.

#### PS-628-698 Development of a biosafety cabinet testing and certification program for TB laboratories in Peru

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The capability and capacity for maintaining acceptable operation of biosafety cabinets (BSC) are not available in many resource-constrained settings. As TB laboratories in developing countries begin to expand their testing, it is essential that they also develop a BSC certification program to ensure both the safety of the laboratory staff and the integrity of the testing. This requires strong administrative commitment, training of personnel, and funding for equipment and supplies for testing and maintenance of the cabinets. The National Institute of Health Perú, with Partners in Health, Socios En Salud, Vigía, the Massachusetts State Laboratory Institute, and the Eagleson Institute, developed a national BSC certification program for TB laboratories. This collaboration delivered a practical train-the-trainer program to qualify laboratorians and engineers as certifiers, and provided training for laboratory administrators. Comprehensive protocols are currently being implemented to assure a sustainable program. This project demonstrates the feasibility of developing a BSC certification program, while increasing the testing capacity in resource-limited settings, and can serve as a model in other developing countries.

## CLINICAL TUBERCULOSIS

### PS-107-151 The role of resistant *Mycobacterium tuberculosis* in relapses of tuberculosis

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**Introduction:** Relapses of tuberculosis occur even nowadays despite initial hospitalization and administration of full doses antitubercotics.

**Objectives:** To obtain the results, to analyse the histories from the patients with improved relapses of tuberculosis and find the possible causes of relapses of tuberculosis.

**Methods:** Analysis the important data in patients who suffered from relapses of tuberculosis.

**Results:** In previously period for 7 years, 149 patients were hospitalized due to respiratory and others symptoms and the relapses of tuberculosis were obtained in that time of hospitalizations. The number of male patients were higher than number of female patients and the more patients were in the fifth decade of life time. All patients suffered for respiratory symptoms and some of them were hospitalized due to haemoptysis (28–19.8%). The mean time of manifestation relapses of tuberculosis were 11.23 years. The resistance were obtained in 21–14.9% patients with the relapses of tuberculosis. Five—3.5% patients were with resistance to 4 drugs four—2.8% patients with resistance to three drugs, four patients were with resistance to two drugs and only two—1.4% patients with resistance to one drug. In these group with improved resistance to antitubercotics, accompanied diseases as COPD were obtained in 8–5.6% patients, diabetes mellitus in 5–3.5% patients and renal failure in 1–0.7% patient. The most frequent radiographic findings were bilaterally shadows with cavernas. Due to these findings, the therapies delivery were much longer in these group.

**Conclusion:** According to these results obtained from the previously time of 7 years, the manifestations of relapses of tuberculosis were found in 141 patients. One of the possible causes of relapses tuberculosis is the manifestations of resistances *M. tuberculosis*. Controlled therapy and hospitalization is very important in these cases.

### PS-141-176 Clinico-social aspects of pulmonary tuberculosis in women of reproductive age

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**Aim:** To study causes promoting the tuberculosis development in women at the age of 15–49.

**Results:** From 55 studied patients contact with tuberculous patients (mainly in families) was in 40%. Tuberculosis clinical structure was: infiltrative TB was found out in 40%, cavernous 36.3%, disseminated 9%, focal 3.6%, and the primary forms were diagnosed in the rest ones. Positive sputum smear was noticed in 74.5%, pulmonary tissue destruction in 80%. The duration of the disease before consulting the physician was from 3 to 6 months. In 27.3% tuberculosis was revealed in the patients of risk group diabetes mellitus, psychic diseases, ulcer. In 20% of cases tuberculosis was revealed during pregnancy and after delivery (in terms up to 6 months). 87% mentioned bad living and economic conditions and were unemployed.

**Conclusion:** The development of pulmonary tuberculosis in women of reproductive age is due to bad living conditions, lack of job, contact with tuberculous patients. The onset of the disease coincides with the period of hormonal change in female organism (pregnancy and delivery). Late reveal of tuberculosis in these patients demands medical service availability improvement and sputum study for *Mycobacterium tuberculosis*.

### PS-155-190 Treatment outcome among tuberculosis patients in Sarajevo

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**Objective:** To analyze the results of treatment of new and relapse tuberculosis (TB) cases in Sarajevo Canton. **Patients and methods:** Treatment cards of TB smear and culture positive patients in Sarajevo Canton in a 2-year period were analyzed. Data of Laboratory Registers of Referral Microbiological Laboratory were also notified.

**Results:** In 1998. and 1999. total number of 153 TB patients were reported as smear and culture positive with 81 men (52.9%) and 72 women (47.1%). 13.08% of all patients were considered relapse. Cure rate in 1998. was 85.1% and 91.8% in 1999. 3% patients completed treatment in 1998. and 1.2% in 1999. Death rate was 4.5% in 1998. and 3.5% in 1999.

**Conclusion:** Unsatisfactory outcome rate was 7.4% in 1998. and 3.5% in 1999. The situation was improved in 1999. as the result of better disease control.

### PS-165-199 The surgical treatment of TB spontaneous pneumothorax and pleural empyema

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The surgical treatment of TB spontaneous pneumothorax (SP) and pleural empyema (PE) was conducted on 220 patients (133—men, 87—women). 154 patients (69.1%) were aged 20 to 40 years. SP and PE devel-

oped at the fibro-cavernous lung tuberculosis in 108 patients (49.1%), at infiltrative—78 (35.5%), at focus tuberculosis—in 34 (15.4%). The duration of lung tuberculosis varied between 1 month and 10 years, SP—between 1 week and 2 years. 105 patients (47.7%) had sputum smear positive, 59 (27.7%)—in pleural liquid. Pre-surgical treatment was done during 3–5 months using anti-TB drugs (H,R,E,Z,S), including intra-venous and lymphotropic chemotherapy, and punctional sanation of the pleural cavity. Pleuropulmonectomy was done on 82 patients (37.3%), pleuroectomy and partial lung resection on 46 (20.9%), pleuroectomy and lung decortication on 92 (41.8%). 58 patients (26.4%) had post-surgical complications. Main complications included bronchial fistula and pleural empyema, relapses of TB-process and lung-cordial insufficiency. The majority of these complications were healed. Good results of the surgical treatment were in 198 patients (90.5%). Lethality occurred in 18 patients (8.2%).

**Conclusion:** Despite the clinical complexity of the disease and high operational risk the surgical treatment of the lung TB, complicated by SP and PE is the main and highly effective method of treatment.

#### **PS-198-241 Diabetes mellitus among firstly detected patients with pulmonary tuberculosis**

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Treatment of pulmonary TB with diabetes mellitus comorbidity is more difficult to be treated compared with their treatment apart. Records of TB disease of patients treated since 1999 till 2003 were analyzed. Out of 931 patients TB and diabetes mellitus comorbidity was registered in 44 (4.7%) cases. Men were 29 (65.9%) and women 15 (34.4%). 11 (25%) were from age group 40 to 49 years, 18 (40.9%) 50 to 59 years, 9 (20.5%) were older 60 years. Mainly infiltrative pulmonary TB (88.6%) was diagnosed. Diabetes mellitus type I was found out in 8 (18.2%), type II in 36 (81.8%). Diabetes mellitus of middle degree was marked in 35 (79.5%), with heavy course in 9 (20.5%). Complicated diabetes with retinopathy, encephalopathy, vascular disorder was observed in 25 (56.8%). Treatment tactics: 1. TB treatment under standard chemotherapy course during 2 months of intensive phase with parenteral streptomycin implementation, per rectum isoniazid and rifampicin or ethambutol, with following their taking per os during 4 months. 2. Diabetes treatment in intensive phase: insulin taking despite of type with following sugar decreasing drugs taking in continuation phase. As a result, sputum conversion was obtained in 39 (88.6%), cavity closing in 5 (11.3%) cases. Thus, patients with comorbidity of TB and diabetes should be treated in-patient to heal the destructive changes.

#### **PS-252-280 The research about the existence of risk factors in the new smear positive pulmonary tuberculosis patients**

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**Introduction:** The disease develops in the two years of the infection in 5–10% of the people who are infected with *Mycobacterium tuberculosis* and some risk factors are known to increase the possibility of the development of tuberculosis.

**Objectives:** We aimed to search the frequency of the those observable risk factors in our clinic.

**Design and subjects:** Risk factors were searched retrospectively in 114 new smear positive pulmonary tuberculosis patients who were hospitalised in 2003, in our clinic.

**Results:** All patients were male with mean age  $43.0 \pm 16.2$ . 91 (79.8%) of patients were heavy smokers, 35 (30.7%) were underweight, 25 (21.9%) had diabetes mellitus, 15 (13.2%) had chronic alcoholism, 6 (5.5%) patients were taking immunosuppressive treatment, 3 (2.6) had silicosis, 2 (1.8%) had chronic renal failure, 1 (0.9%) had leukemia, 1 (0.9) had lymphoma and 9 (7.9%) of them had close contact with people known to have active tuberculosis.

**Discussion:** In our studies we observed that the most frequent risk factor in the development of the tuberculosis disease is 'the heavy smoking'. As a result, the Smoking Cessation Programs should be inserted to the Tuberculosis Control Programs.

#### **PS-343-367 Lung tuberculosis in diabetes mellitus patients: some clinical aspects**

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The association diabetes mellitus and tuberculosis is unfavourable for both diseases and increases the tuberculosis morbidity. The aim of this retrospective study was to evaluate the impact of this metabolic disorder in tuberculosis. The study included 50 patients diagnosed with tuberculosis and diabetes mellitus, hospitalized in the Pneumology Clinic Cluj-Napoca between 2001–2002. We analyzed different parameters from the medical records. The results revealed the predominance of the diseases in males (64%). The most affected were people aged over 60 years (32%) and between 50–59 (28%). 70% cases were from urban environment. Other parameters analyzed were: occupation (58% retired, 18% workers), diabetes mellitus type (70% insulin independent, 30% insulin dependent), glycemia levels at admittance and hospital release (70% normal values under tuberculosis treatment), radiological pattern (38% fibrocaceous and cavitary pattern), bacteriological findings (54% BK positive, both mi-

croscopy and culture; 30% confirmed in culture), therapeutic scheme (76% standard scheme DOTS). We also studied the evolution of both diseases under specific treatments (14% gave up insulin therapy), the presence of other comorbidities, the diabetes complications (28%). Many important particularities of this association (tuberculosis and diabetes mellitus) are due to the camouflaged onset of tuberculosis in these patients, despite severe radiological patterns.

#### **PS-432-469 Pulmonary function in tuberculosis patients in a high-burden, poorly resourced setting: the Timika TB lung study**

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**Introduction:** There is a paucity of information from high burden, poorly resourced settings about pulmonary function in TB patients.

**Objectives:** To classify and quantify pulmonary function abnormalities in TB patients in Timika, Papua Province, Indonesia.

**Methods:** Ninety consecutive sputum smear positive pulmonary TB patients were enrolled and underwent spirometry. Treatment was according to the WHO DOTS strategy.

**Results:** TB patients had severe disease as measured by X-ray scores and sputum positivity. At enrolment, mean FEV<sub>1</sub> (1.88 versus 2.96 litres/min) and FVC (2.43 versus 3.60 litres) were significantly lower in TB patients compared to controls at baseline ( $P < 0.001$ ) after adjustment for sex, age, height and ethnicity. The FEV<sub>1</sub>/FVC was similar in patients and controls at enrolment and at two months.

**Conclusion:** There was biologically and statistically significant restrictive lung disease in TB patients at enrolment. Pulmonary function improves but doesn't return to normal after two months of anti-tuberculous chemotherapy despite improved chest X-ray appearance and sputum clearance. Further progression in the study will reveal whether the abnormalities result in significant pulmonary disability in the short term and if they are fully reversed by the end of TB treatment.

#### **PS-568-635 Chest radiograph findings in children with chronic symptoms in a region with a high prevalence of tuberculosis and HIV, Botswana**

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**Objectives:** To describe chest radiograph (CXR) findings of children with chronic symptoms admitted to two national referral hospitals in Botswana.

**Methods:** Children (<15 years) with chronic cough ( $\geq 2$  weeks), fever  $\geq 2$  weeks or failure to thrive  $\geq 3$  months were enrolled. PA and lateral CXRs and HIV testing were performed. CXRs were read in a blinded and standardized fashion.

**Results:** 197 children, median age 14 months, were enrolled of whom 90% had chronic cough; 136/177 (77%) were HIV-infected with a mean CD4% of 22%. The PA was technically acceptable in 124/156 (79%) and the lateral in 57/103 (55%) CXRs. Of the 124 children with PAs, TB was diagnosed radiologically in 10% and excluded in 66%. TB could not be diagnosed or excluded in 26% of HIV-infected children compared to 14% of HIV-uninfected children. Of all CXRs, patterns showing pneumonia/bronchopneumonia (52%), lymphoid interstitial pneumonitis (8%), and chronic lung disease (13%) were described; 15/16 with chronic lung disease patterns were HIV-infected.

**Conclusions:** Compared to HIV-uninfected children, more chronic patterns were observed and more difficulty was experienced in interpreting CXRs of HIV-infected children. The diagnosis of lung disease is complicated by sub-optimal CXRs at these hospitals, suggesting training and quality assurance needs for radiographers.

#### **PS-574-644 Clinical and radiographic aspects of spinal tuberculosis (TB)**

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**Objectives:** To describe the clinical and radiographic aspects of spinal TB in patients attending the Institute of Infectious and Tropical Diseases.

**Methods:** Chart review of spinal TB cases from 1999 to 2003.

**Results:** 25 cases of spinal TB were diagnosed over a total of 325 TB cases (8%). They were predominantly males (76%), foreign born (84%), median age of 35 y (range 23–84). Local pain was the initial symptom in

91% of patients; 28% had neurological deficit. CT and MRI were the imaging studies performed. Thoracic (40%) and lumbar vertebrae (36%) were more commonly involved. Paravertebral abscesses, disc involvement and vertebral deformity were detected in 80%, 76%, and 60% of patients at baseline, respectively. TB was confirmed in 23 patients, 68% had mycobacteria isolated by CT guided needle aspiration and 32% by histology finding of granuloma. The median length of anti-TB treatment was 12 months (range 7–19); 16% required surgical treatment.

**Comments:** Tuberculous spondylitis is a complex health issue, require costly, repeated, imaging studies and longer courses of anti-TB treatment. Medical therapy alone provided favorable outcomes in the majority of patients. CT and MRI represent sensitive tools to support clinicians in the management of spinal TB.

#### **PS-658-732 Side effects of TB drugs in the initial phase of TB treatment**

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**Background:** Standardized short course chemotherapy was implemented into TB treatment in Turkmenistan in 1999.

**Objective:** To study the incidence of side effects of TB drugs in 1077 patients treated using DOTS regimens.

**Methods:** Monitoring of the treatment outcomes according to WHO indicators.

**Results:** The treatment outcomes in 1077 TB patients were studied. Out of them 81 (7.5%) patients developed side effects (allergic reactions, toxicity and intolerance) in the initial phase of treatment. TB patients with concomitant pathology of gastro-intestinal system (in 60% cases) alcohol and drug addicts (18.3%) more often develop side effects. Treatment was recommenced in 66 patients (81.5%) after temporary abolition of the drugs and appropriate treatment carrying out.

**Conclusion:** Side effects of TB drugs complicate TB treatment and are often developed in TB patients with intercurrent diseases.

#### **PS-776-850 Experience of integration of TB service and primary health care within the framework of DOTS strategy implementation in Tajikistan**

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**Background:** Annually Tajikistan registers on average 2800 up to 3500 new TB cases and these numbers tend to increase. DOTS-strategy implementation began in July 2002 in two pilot areas: Dushanbe and Leninsky

rayon and covered 879 000 population (13% of Tajikistan's population).

**Method:** Abstract is based on data analysis from 1574 patient in DOTS pilots 2002–2003.

**Result:** The DOTS Program involves PHC workers in TB case finding and treatment observation. Family physicians have referred 69.7% of the TB suspects for sputum microscopy. As a result of integrated activities PHC and TB workers registered 449 new TB cases SS+, that is 40.4% of 1111 new cases. While working through PHC service facilities, smear conversion rates have steadily improved from 69.2% (3rd Qtr. 2002) to 90.2% (3th Qtr. 2003). During the same period treatment success improved from 74.4% to 86.6%. Smear conversion in areas without DOTS coverage was 20.6%/2001 and 27.4%/2002. While treatment success in the same regions was 56.2% and 55% respectively.

**Conclusion:** The integration of the PHC and the National TB program has contributed greatly to the DOTS pilots meeting the targets recommended by WHO for smear conversion and treatment outcomes.

#### **PS-802-875 Influence of co-morbidity in the interpretation of tuberculin skin reactivity in multi-ethnic adult patients with tuberculosis**

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**Background:** In the Malaysia setting of multi-ethnicity and high BCG coverage, interpretation of Tuberculin Skin Testing (TST) may be difficult.

**Objectives and methodology:** From 2001 to 2003, a retrospective study of all adult patients with documented TST results treated for tuberculosis (TB) in two government hospitals were conducted to determine the reliability of TST and factors affecting its interpretation.

**Results:** One hundred and three patients [mean age (SD): 43 (17); male: 67%] were eligible for data collection: 72% and 57% of patients had positive TST results based on cut-off points of 10mm and 15mm respectively. The only significant association with TST results was the severity of co-morbidity. A patient with co-morbidity score of 3 defined as those with any cancer, end-stage renal or liver disease, or HIV disease, are more likely to have a negative TST results [10mm cut-off points OR (95%CI) 6.6 (1.82 to 24.35),  $P = 0.003$ ; 15mm cut-off point: 4.8 (1.21 to 18.95),  $P = 0.012$ ].

**Conclusions:** Amidst all possible confounding factors like ethnicity and prior BCG vaccination, severity of co-morbidity remains strongly predictive of a negative TST. Caution should be exercised in interpreting TST in these patients.



### PS-853-926 Echographic diagnostics of exudative pleuritis of tuberculosis nature

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Ultra-sound investigation (USI) is not implemented as it could be for diagnostics of lung and pleura diseases because the air filling the lung tissue reflect the ultra-sound nearly completely while chest bones make difficult the approach to the chest organs. We analyzed pleural cavity USI results obtained through implementation of devices 'SHIMADZU-SDU-1200' and JUST VISION-200 (Japan). There were examined 98 patients with pulmonary TB. Right side location was in 49% left one in 32.6%, bilateral one in 12.2%. Encapsulated pleurisy at the right was revealed in 6.1%. There were clinical and X-ray allowed to determine that pleurisy was the complication of the infiltrative pulmonary TB in 2 cases, fibrocavernous TB in 19, TB of intrathoracic lymphatic nodes in 6 and in 3 cases. In 3% residual changes in term of the petrificates after pulmonary TB supported earlier were observed. Investigations allowed finding out the echodiagnostic signs of presence even of the minimal liquid quantity, and differentiating the free and encapsulated exudates as well. Thus, pleural cavity USI is high sensitive method to reveal even the small pleural liquid quantity. This method is the informative, non-invasive way and it could be used to determine the exact point for puncture, to control the liquid level and therapy carried out effectiveness.

### PS-854-927 Comorbidity of pulmonary TB and bone and joint TB

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TB situation in Kazakhstan deteriorated is characterized by increase of frequency of generalized TB forms development with complicated clinical course. Frequency of combined TB location forms, especially lung TB and osteo-articular TB constitutes 58.2% out of all patients treated in 2000–2003. Focal TB with infiltration and destruction was prevalent among lung changes. Bacilli excretion was revealed in 12 (11%). Disseminated TB diagnosed in 26.5 (9%) of patients. *M. tuberculosis* was isolated in 7 (19.4%). Infiltrative pulmonary TB was confirmed in 17 (22.7%). Other TB injuries forms occur not frequently. Thus, fibrocavernous TB was diagnosed in 3 (0.7%) of patients. Pleural injury was associated in 14 (3.2%). Generalized TB forms were notified among children, mostly spondylitis which was accompanied with intrathoracic lymphatic nodes TB in 36 (8.3%), with primary TB complex in 15 (3.5%) cases. Prevalent clinical manifestations in patients with combined TB forms were the expanded processes in the osteo-articular sys-

tems, complicated with abscesses, fistulae, neurological disturbances and skeleton deformation. Analysis of age groups showed that patients of younger and matured age (20–50 years) and children (1–7 years) are more vulnerable to the generalized TB process than persons of older age groups.

### PS-864-937 Candidiasis as the associated infection at TB

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**Target:** To investigate the frequency of candidiasis among patients with tuberculosis taken the anti-TB drugs of the first and second-line and determine the risk groups for candidiasis.

**Materials and methods:** There were examined 82 patients with TB. All were diagnosed by cultural method with mycoses isolation.

**Discussion:** Women were 20%, men 80%. Clinical TB forms were as followed: infiltrative pulmonary TB 46.2%, fibrocavernous pulmonary TB 50%, other forms 3.8%. Bacilli excretion was confirmed in 82.6%, destructive changes in 80.7%. *Candida albicans* from 600 to the entire growth were cultured from sputum of 82 patients examined for mycoses injuries presence. Risk factors leading to the *Candida* infection development. 1) Patients treated with anti-TB drugs of the first line: *Candida* injuries were revealed in 7%, among those treated with drugs of the second-line in 53.8%. 2) Patients with diabetes mellitus type II: *Candida* injuries were presented in 20%. 3) Immunodeficiency status in 40.0 of patients, 4. Double infection HIV/TB. Particularity of the candidiasis clinics among HIV-infected patients when high frequency of the mouth cavity and esophagus while injuries of the skin and nails are absent. 5) Comorbidities in term of diseases of liver, kidneys, gastrointestinal tract diseases in 40% and non-specific lung diseases in 25% of patients.

### PS-927-1002 Effectiveness and safety of FDCs vs. single drug formulations in the treatment of pulmonary tuberculosis, Pakistan study

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**Objectives:** To evaluate the clinical and therapeutic value of 4 drug FDCs verses single drug formulations and also to assess the pattern of age/sex distribution and socioeconomic involvement in the occurrence of tuberculosis.

**Method:** A total of 293 patients having sputum positive pulmonary tuberculosis were enrolled, out of which 187 were male and 106 were female. Patients

with renal, hepatic, diabetic, cardiac problem and pregnancy were excluded from study. Patients were randomly selected into three groups (A, B, C). Group A & B were given FDCs and group C was given single drug formulations (Table).

#### Results:

Group	Patients	Sputum conversion	Average days	Toxicity/side effects					
				None	N/V*	Itching	Jaundice	Others	Died
A	97	98.9%	37	83	12	1	0	1	0
B	97	93.8%	32	71	16	7	0	3	0
C	99	95.9%	40	70	22	3	2	0	1

N/V\*: Nausea/Vomiting.

**Conclusion:** Treatment regimens of group A, B, and C produced satisfactory clinical results. There was no significant difference in the efficacy among the three treatment regimens. However the side effects observed in all three groups strongly indicate that FDCs are safer for treating TB patients. Prevalence of tuberculosis in this part of the world is more in the age group of 15–24 years.

#### PS-409-448 Completion rates for treatment of latent tuberculosis infection in Florida among those born outside of the United States

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**Objective:** Very little information exists in the medical literature regarding the rate of completion for treatment of latent TB infection. The purpose of this study is to identify completion rates for latent TB infection treatment and compare rates for completion between the foreign-born and all other candidates for therapy of latent TB infection.

**Method:** Retrospective database review of data from 2001 in county TB registries of the seven largest counties in Florida.

**Results:** In 2001, the last year which completion rates are available, the seven largest counties in Florida evaluated 2916 individuals with latent TB infection. A total of 2407 started therapy and of these 1448 completed a course of treatment. The completion rate in the seven counties was 49.7% among eligible candidates. Among the foreign-born the completion rate among candidates was 62.8%. Significant variation between counties was noted. The most significant reason for terminating therapy was patient self-discontinuation of therapy.

**Conclusions:** Completion rates for treatment of latent TB infection remain unacceptably low, but appear better among foreign-born individuals. Further study investigating reasons for this and the need to improve completion rates needs to be further evaluated.

#### PS-689-761 Tuberculosis chemoprophylaxis in co-infected TB-HIV patients at Evandro Chagas Clinical Research Institute

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**Introduction:** The ECCRI has been developing the project 'Durability of the protective effect, tolerance and adherence to chemoprophylaxis (CP) concerning tuberculosis (TB)' since August/2002.

**Objectives:** Determine the TB/CP's abandonment; adverse events associated to the usage of isoniazid (INH) and TB occurrence.

**Methods:** Open prophylactic clinical trials of INH 300 mg/day during 6 months. Within 19 months, 42 co-infected TB/HIV were included in conformity to the eligibility criteria: Normal thorax X-ray, tuberculin skin test  $\geq 5$ mm, normal hepatic function evidence (NHFE).

**Results:** Mean age was 43 years (DP = 11.4), being 25 (59.5%) were males. We verified that 28 (66.7%) informed having income  $\geq 3$  minimum wages and 29 (69%) informed  $\leq 8$  years of education. Thirteen (31%) had minor side effects during the first 3 weeks, related to INH's usage. Thirty-eight (90.4%) are being observed, 2 (4.8%) were abandoned by lack of interest and 2 (4.8%) were suspended due to important alterations in the values of NHFE.

**Conclusion:** The adverse events were of low intensity, even when the majority of patients are in antiretroviral therapy. No cases of TB were detected until now. This cohort offers relevant information regarding the effectiveness and durability of INH's protective effect.

#### DRUG RESISTANCE/MDR-TB MANAGEMENT-2

##### PS-295-328 Isoniazid resistant tuberculosis in Denmark

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**Introduction:** Treatment of Isoniazid (H) resistant TB (not MDR-TB) in Denmark 1999–2002.

**Objective:** Examine treatment and prognosis of H resistant TB in Denmark and discuss this in the light of the evidence for safety of standard treatment of H resistant TB.

**Methods:** Information about patients with H resistant TB was from a central register. Patients' files were ob-

tained from the hospitals in charge and information on treatment modifications and result of treatment was extracted.

**Results:** 105 patients with H resistant TB were identified for 1999–2002. Information concerning treatment was available for 101. Continuation treatment was modified for 87 due to H resistance. Ten different treatments were used, all including at least one drug other than H additional to Rifampicin with a total treatment period of 6 months or more. All with modified treatment were cured. Only one relapse has occurred in 246 observation years.

**Discussion/conclusion:** Modified treatment of H resistant TB is safe. Further evidence concerning risk of failure and relapses with standard treatment in H resistant TB should be accumulated before it is considered a safe treatment.

#### **PS-516-569 Treatment failures in MDR-TB patients in Tomsk Oblast for 2001–2002**

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**Introduction:** 131 DOTS-Plus patients were observed during 01/2001–09/2002 with mean duration of treatment 18–24 months. 12 (9.2%) patients reported as failures.

**Objectives:** To show that treatment failures associate with late start of DOTS-Plus.

**Methods:** We studied clinical, radiographic, bacteriologic data, and adverse reactions to second-line drugs at the start of treatment and during therapy. Outcomes: 87 (66.4%) cured, 13 (9.9%) default, 1 (0.8%) transferred out, 6 (4.6%) died (of them 2 of TB), 12 (9.2%) treatment failures, 12 still on treatment. Among DOTS-Plus failures: disease history 2–5 years, with bilateral pulmonary TB, cavities and 2–4 courses of inadequate treatment before DOTS-Plus. 9 patients received second-line drugs during previous treatments (Of, Eth, K), 2 with unknown history of treatment. Their resistance pattern at the start of DOTS-Plus: 4 HRSEKZ; 4 HRSEZ, 4 HRSEK, 3 HRS, plus 1 had resistance to Of, 3 to Cap, 3 to Eth. DST were confirmed at MSLI, Boston, USA. All 12 remain positive on 12–24 months with amplified resistance pattern.

**Results:** All failures were reported as treatment ineffective.

**Conclusions:** Adequate therapy has to be started right after drug resistance reported according to DST results and those not used before.

#### **PS-537-598 Ambulatory treatment of MDR-TB patients with DOTS-Plus**

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**Introduction:** Observational study of 68 MDR-TB patients received ambulatory treatment from 09/2000–12/2002. Duration of DOTS-Plus is 18–24 months. In overall cohort of DOTS-Plus patients side effects to 2d-line drugs occur in 86% and require management and close monitoring by TB doctor. It's a concern that treatment of these patients is only possible in hospitals under doctors' direct supervision.

**Objectives:** To show that ambulatory treatment of rural DOTS-Plus patients is possible with DOT provided by trained medical personnel/volunteer.

**Methods:** Treatment outcomes of 68 rural DOTS-Plus patients treated in ambulatory sector from 09/2000–12/2002 were evaluated. All started treatment in hospital with mean duration of treatment 10 (7–14) months, doses taken TID. Intensive phase stopped after 3–4 consecutive negative cultures and smears. Doses changed to BID intake, patients referred to rural areas of residence. Treatment provided under DOT by trained rural medical personnel/volunteer who controlled and managed side effects under doctors' supervision. To prevent defaults all patients received various incentives/enablers (hot meals, food baskets and transport passes).

**Results:** 51.4% cured, 13.3% failures, 7.4% defaults, 1.5% transferred out, 26.4% still on treatment. Culture conversion was 69.7%.

**Conclusion:** Ambulatory treatment in DOTS-Plus program in rural areas is possible under DOT by trained medical personnel/volunteers.

#### **PS-609-674 Fluoroquinolones in treatment of multidrug-resistant tuberculosis (MDR-TB) in children: a multi-country analysis**

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**Objective:** Evaluate fluoroquinolone (FQ) use for MDR-TB in children.

**Methods:** Data from charts of children <15 years diagnosed 01/98–12/01 were reviewed. Cases were children with culture-confirmed MDR-TB or known contacts of MDR-TB cases with clinical evidence of TB.

**Results:** 185 cases were collected, median age 8 years; 17 were HIV+. Second-line drug treatment was begun in 126. Ninety children were treated with FQs includ-

ing 6/32 Latvian, 32/34 Peruvian, 5/56 Russian and 47/63 South African. There were no reports of arthritis/arthralgia. Toxicity was higher in FQ recipients (47% vs. 18%,  $P \leq 0.001$ ). FQ recipients were older (median age 11.0 vs. 4.0 years;  $P < 0.001$ ), and more often culture positive (91% vs. 30.6%,  $P < 0.001$ ). FQ users received a higher median number of drugs (6.0 vs. 4.0). Outcomes by FQ use or not were: cure/completed treatment (49% vs. 78%), death (7.8% vs. 6.3%), default (6.7% vs. 2.1%), failure (2.2% vs. 0%), and still on treatment (30% vs. 3.2%).

**Conclusion:** Children may benefit from using FQs to treat MDR-TB.

#### PS-634-700 Molecular characterization of *Mycobacterium tuberculosis* isoniazid resistant isolates from Brazil and Argentina

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**Background:** The *Mycobacterium tuberculosis* multidrug-resistant (MDR) strains is defined as resistant to at least isoniazid (INH) and rifampin (RMP). The multiresistant phenotype emerges with sequential acquisition of mutations in several loci of separate genes. The resistance for isoniazid these are known to be linked to: *katG*, *inhA*, *ahpC* and more recently *kasA* and *ndh* genes.

**Methods:** Eight-five isoniazid-resistant *M. tuberculosis* isolates from Brazilian states were characterized by automatic sequencing (31 from Rio Grande do Sul, 15 from São Paulo, 23 from Rio de Janeiro, 16 from Minas Gerais). Were analyzed the mutations in the *katG* and *ahpC* gene.

**Results:** In *katG* gene the codon most affected by point mutation was 315 with frequencies of 87.1% (RS), 60.9% (RJ), 60% (SP) and 78.6% (MG). The *ahpC* promoter region showed mutations in distinct positions in 12.9%, 21.7%, 6.7% and 25% in isolates from RS, RJ, SP and MG respectively. We observed association with mutation in *katG* and *ahpC* genes.

**Conclusions:** Current studies are being conducted to verify the characterization of the mutations involved in resistance in other regions of Brazil and Argentina.

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#### PS-650-719 Comprehensive management of diabetics with multidrug-resistant tuberculosis by the multidisciplinary DOTS-Plus team

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**Objectives:** To describe the impact of DOTS-Plus on diabetes control among diabetics with multidrug-resistant tuberculosis.

**Methods:** Retrospective case series of 12 patients enrolled to receive MDR-TB therapy in Lima Sur between 1 October 2000 and 1 October 2003

**Results:** Median age was 53 years old; 8 were female. The patients had received a median of 3 previous treatments, and demonstrated resistance to a median of 5 drugs. At baseline, 8 were insulin-dependent, and 9 had poorly-controlled diabetes. All but one patient culture-converted. At the time of analysis, four patients were cured, 2 died, and 6 were culture-negative in treatment. Intensive case management by the DOTS-Plus team resulted in improved diabetes control in almost all patients. Average glucose dropped from an initial 236 mg/dl to 167 mg/dl; although not routinely performed at baseline, average hemoglobin A1C during treatment was 8.5.

**Conclusion:** Intensive management of diabetes in this group of MDR-TB patients with poorly-controlled diabetes was an integral component of the DOTS-Plus approach. Multidisciplinary management of additional complex medical and social issues associated with chronic diseases is essential to successful MDR-TB treatment.

#### PS-677-750 MDR-TB surgical treatment, Lima, Peru

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**Setting:** In Peru the MDR-TB primary is 3% and acquired 12.3%, that have stayed from the year 1996. The mortality for MDR-TB is from 40% to 60% that is equal to not treated TB. Morbidity rates and incidence of TB positive smear are 155.6/100 000 and 88/100 000 respectively. The surgical treatment of the MDR-TB as adjuvant therapy is good alternative even in patients with bilateral TB lesions.

**Objectives:** To show the results of the surgery of lung resection as adjuvant therapy in patient with uni or bilateral MDR-TB lesions. To establish the surgical indications in the treatment of the MDR-TB in this group of patients and show the results of surgical treatment.

**Methods:** It was carried out a prospective and descriptive study in Lima, Peru (2000 to 2004) in patients with MDR-TB of high resistance degree with unilateral or bilateral resectable lung lesions.

**Results:** 106 patients MDR-TB with continuous or intermittent positive smear or culture, with continuous regimen DOTS-plus, 84.9% had resistance to 4 or more drugs. 60.38% was lobectomy, 24.53% pneumonectomies, 8.49% lobectomies with segmentectomies, 2.83% segmentectomies, 3.77% other procedures. Postoperative mortality 4.70% and morbidity 23.60%. High bacteriological conversion 73.33% unilateral and 67.39% bilateral TB lesions show efficacy of this treatment.

**Conclusions:** Adjuvant lung resection in MDR-TB is excellent treatment method due to high percentage of bacteriological conversion, with low postoperative morbidity and mortality, in patient with unilateral or bilateral advanced lesions. Cases with unilateral or bilateral cavitary lesions with intermittent or continuous positive smear or culture can be included in the surgical treatment, if VC > 50%, FEV<sub>1</sub> > 1000cc.

#### **PS-713-785 Drug resistance (DR) surveillance in a rural community recently covered by the DOTS programme**

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**Introduction:** DR monitoring is a useful tool to monitor effective functioning of tuberculosis control programmes.

**Objectives:** To determine the prevalence of DR among patients treated under the programme.

**Methods:** The study population was drawn from 500 000 individuals covered by DOTS programme in a rural area of Tamil Nadu, India. Patients registered under DOTS programme from 1999–2003 form the study population. Two sputum samples before treatment & whenever treatment failed or disease relapsed were examined by culture and sensitivity to all anti-tuberculous drugs.

**Results:** Of 1731 patients treated with category 1 & 3 85% and 57% of 429 category 2 patients were sensitive to all antituberculous drugs. INH resistance alone was 5% in category 1 and 3 and 18% in category 2. Pretreatment MDR-TB was 1.5% in category 1 and 3 and 12.1% in category 2. Of the 503 category 1 cured patients, followed up for 18 months, 12% relapsed, of whom 1% had emergence of MDR-TB.

**Conclusion:** MDR-TB rates in this rural community recently brought under DOTS programme are low. Effective implementation of DOTS will help to prevent the increases in MDR-TB rates.

#### **PS-715-787 Indication for surgery and postoperative results in patients with multidrug-resistant pulmonary tuberculosis**

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Between 2000 and 2003 a total of 11 patients underwent surgery for multidrug-resistant pulmonary tuberculosis (MDR-PTB). They were 4 female and 7 male with mean age of 32.2 years. Chest CT scan revealed localized unilateral cavitation in all patients. Pulmonary function tests and, in 6 cases, ventilation perfusion scans showed a predicted FEV<sub>1</sub>>0.8 in all of them. MDR-TB was verified by BACTEC TB 460, MGIT and Quantiferon test. Chemotherapy duration ranged from 1 to 4.5 years of categories II and IV according to WHO. The indications for surgery were chemotherapy failure in 10 (90.9%) of the patients and haemoptysis in 1 (9.1%) case. The operative methods included 8 (72.73%) lobectomies, 1 (9.1) lobectomy combined with resection of S6 and 2 (18.2%) pneumonectomies. No 30-day postoperative death was faced. Postoperative complications, as residual pleural cavity and prolonged air leakage, were found in 2 (18.2%) of the cases. The mean postoperative in-hospital stay was 13.2 days. The conventional anti-TB treatment varied from 8 to 18 months postoperatively. The postoperative results were excellent in 9 (81.8%) of the patients and very good in 2 (33.3%) of them. In conclusion, surgery for MDR-PTB as an adjunct to chemotherapy is followed by acceptable postoperative complications and good long-term results.

#### **PS-787-861 Outlook of the treatment with unazyn of drug-resistant tuberculosis forms and non-specific diseases of the breathing organs**

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**Introduction:** Secondary infection among patients with tuberculosis influences negatively on the specific process course.

**Objectives:** This study was to investigate the clinical course and cure of drug-resistant TB forms complicated with non-specific pathology of lower respiratory ways because of which additionally unazyn was administered.

**Methods:** Two groups of children and adolescents suffered from drug-resistant TB forms were included in this study. Patients with concomitant non-specific endobronchitis confirmed with bronchofibroscopy constituted the first group and patients without concomitant pathology the second one.

**Results:** Study carried out indicated that presence of the secondary infection complicated the TB process course inducing the fast infection spreading in the non-affected lung areas, led to the more expressed TB intoxication manifestations and persistent cough. *Streptococcus pneumoniae* (63.9%), *Staphylococcus aureus* (17.2%), *Haemoliticus influenzae* (9.4%), *Candida albicans* (38.4%) induced the concomitant pathology among patients more frequently. At this in 75.5% of cases microflora was resistant to all antibiotics with wide spectrum action really. Unazyn administration in dose of 1.5 g during 14 days before second-line anti-TB drugs implementation favored not only to cut short the non-specific process in the lower respiratory ways but lead to the faster positive changes in TB process. Among patients of 2nd group suffered also from drug-resistant TB positive dynamics was slower despite they did not have the concomitant pathology.

**Conclusion:** Data obtained give the reason to mind that including the unazyn into schemes of drug-resistant TB treatment not only promote the concomitant pathology fast cure but exercise the expressed favorable effect to TB course.

#### **PS-818-890 Using DOTS-Plus to improve DOTS and expand access to effective tuberculosis treatment in Tomsk Oblast, Russia**

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**Introduction:** DOTS-Plus programs are implemented in areas with existing DOTS programs.

**Objectives:** To describe how the implementation of a DOTS-Plus program was used to strengthen DOTS in Tomsk Oblast, Russia.

**Methods:** A three-year qualitative study using ethnographic methodology, including participant observation and key informant interviews.

**Results:** Despite the belief by some that the DOTS-Plus strategy draws resources away from the treatment of drug-susceptible TB, experience in Tomsk Oblast suggests that implementation of a DOTS-Plus pilot program in the civilian sector enhanced the pre-existing DOTS program and contributed to improving TB control in the region. This has been achieved through: 1) integrating management of TB in the civilian and penal sectors; 2) improving the capacity to provide daily DOT; 3) improving case detection through smear microscopy and contact tracing; 4) improving laboratory capacity; 5) training physicians, nurses, and health-workers in both rural and urban areas; 6) providing a choice of treatment sites for patients (e.g. ambulatory clinic, day hospital, home visits, etc.); 7) providing incentives and enablers to patients and health care work-

ers; and 8) enabling adequate program management and monitoring.

**Conclusions:** By implementing DOTS-Plus in Tomsk Oblast, the underlying DOTS infrastructure has been expanded and improved.

#### **PS-819-891 Treatment of alcoholic individuals with MDR-TB in Tomsk, Russia**

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**Introduction:** In Russia, a significant proportion of patients with MDR-TB also suffer from alcohol dependence.

**Objectives:** To describe the management of individuals with MDR-TB who suffer from alcohol dependence. We report on MDR-TB treatment outcome, medical and social characteristics, and management strategies of this subset of individuals treated in Tomsk, Russia.

**Methods:** Case-control study. Cases: patients diagnosed with alcohol dependency enrolled into MDR-TB treatment between Sept 9, 2000 and Sept 1, 2002. Controls: patients without reported alcohol dependency enrolled into MDR-TB treatment during the same period. Baseline clinical, radiographic, and bacteriologic characteristics, as well as treatment outcome and occurrence of adverse reactions, will be collected through retrospective chart review.

**Results:** Clinical and social characteristics and frequency of poor treatment outcome—treatment failure, default and death—will be compared between alcoholic and non-alcoholic cases and controls. Among alcoholic individuals, risk factors for poor treatment outcome will be identified using a univariate and multivariable analysis. Finally, we will describe our management approaches for clinical and social challenges related to this group.

**Conclusions:** Alcoholism is not a contra-indication to MDR-TB therapy. However, management of medical and social complications among alcoholic patients with MDR-TB can be challenging and require aggressive management strategies.

#### **PS-840-910 Frequency of adverse responses at anti-TB chemotherapy**

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Frequency of adverse responses at anti-TB drugs of the second line made by different pharmaceutical

companies for treatment of patients with MDR-TB was studied. Depending on chemotherapy regimens patients were divided in 3 groups. Gr I: 27 patients treated in the intensive phase (4 to 6 months) with capreomycin and cycloserin (Elly Lilli, USA), prothionamid (Sanavita, Germany), and sparfloracin (Ranbaxi, India). Gr II: 28 patients received zanocin (ofloxacin) (Ranbaxi, India) instead sparfloracin. Gr III: 31 patients treated with capreomycin, tibilin, ofloxacin, pyrazinamide (Adzhanta Pharma, India) and prothionamid (Lupin LTD, India). By clinical forms, age, presence of concurrent diseases and complications groups to were similar. In Grs I and II adverse reactions on anti-TB drugs were marked in 51.9% and 57.15%, and in Gr III in 74.2% ( $P < 0.05$ ). In Gr III complaints on prothionamid were in 48.45% ( $P < 0.01$ ) versus 14.8% and 25% in Gr I and II accordingly (nausea, vomiting, insomnia, pains in epigastrium). In Gr III prothionamid was canceled in 12.9%, in Gr II in 3.6%. Cycloserin was excluded in 11.1%, 7.1% and 12.9% accordingly (expressed changes in CNS: depression, fear, alert, psychosis). Articular syndrome and skin manifestations were the most frequent in Gr III (38.7%,  $P < 0.01$ ). In 16.1% (Gr III) ofloxacin was changed by levofloxacin (Hebst, Germany). Reliable difference on intolerance of capreomycin, cycloserin was not revealed.

#### PS-847-920 Bronchological methods in diagnostics of pulmonary MDR-TB

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We have analyzed 28 cases of pulmonary TB treated under DOTS category I and II with outcome 'cured'. But their control X-ray showed destruction and negative results of sputum smear and culture.

**Objectives:** Diagnostics of TB process activity and resistance to the main first line anti-TB drugs.

**Methods:** Bronchofibroscopy with BAL with sputum investigation 2 times for revealing *M. tuberculosis* was carried out to 28 patients. Additionally brush and transbronchial lung biopsy under and television control (BRTC) was implemented to 10 of them. At this *M. tuberculosis* in BAL was identified in 7 cases by smear microscopy and sputum sample collected after bronchofibroscopy in 7 cases also. In general out of 28 cases in 14 (50%) through the bacterioscopic method and in another 14 (50%) trough the cultural method implementing there were isolated *M. tuberculosis* resistant to anti-TB drugs of the first line. Pathomorphological investigation of the biopat in 10 cases allowed to confirm in 90% of cases the tuberculosis infiltrative ulceric endobronchitis at the positive results of BAL bacteriological investigation of BAL, BRTC made from injury foci preciously allows to determine the effectiveness of TB process. Results obtained lead to the adequate treatment of patients with MDR-TB.

#### PS-849-922 The clinical aspects of multidrug-resistant tuberculosis control in Kazakhstan

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Since 1999 in the pilot regions implementation of DOTS-Plus was started but sometimes because of absence of the comprehensive programme there are patients with super-resistant TB (SRT). It is necessary to treat the patients under medical worker observed control and limit the indications for administration of this therapy method for patients with bilateral expanded hyper-chronic processes because the prognostic in advance treatment failure leads to the SRT TB formation, that is a very dangerous threat for the community. In all cases treated under DOTS-Plus regimen stopping the intensive chemotherapy phase and transferring in the continuation phase should carry out only 2 times negative sputum culture results obtaining with one month interval. Minimal intensive phase duration should be 4 to 5 months. When sputum smear conversion becomes negative it is possible to continue the intensive phase out-patient taking into account the patient social status, control availability, presence of the available medical institution. Therefore personal responsibility of a physician from phthisiatric service and a medical worker of the Primary Health Care (PHC) are needed for daily anti-TB drugs taking under strict observation. Phthisiologists should organize the training in the PHC in the treatment monitoring methods, adverse responses control, health education on MDR-TB.

#### PS-851-924 Out-patient treatment of MDR-TB patients under DOTS-Plus regimen

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**Target:** To investigate the effectiveness of early transferring out-patient the patients with MDR-TB treated with anti-TB second-line drugs. We analyzed the results of treatment of 20 patients in age 20–57 years. Men were 12 (60%), women 8 (40%). Five of them were employed; three of them were working at anti-TB institutions. Remained patients were jobless or invalid (from TB). Forth patients suffered from alcoholism or drug abuse. All of them had BK+ in sputum. Standard DOTS-Plus regimen was administrated. Patients were hospitalized during 4 to 88 days. Average in-patient stage duration was 70.8 days. Main reason to not stay in-patient depended on desire of patients themselves. Six patients were discharged by reason of non-compliance to the hospital regimen. All the patients continued to be in the intensive phase of chemotherapy during 3–4 months in home conditions under medical

control. Bacteria excretion at 2 times microscopy every 3 months was not confirmed. All patients completed the treatment as 'cured'. Thus, implementing the treatment under DOTS-Plus regimen out-patient is indicated for patients with good living conditions, sufficient drugs tolerance and early sputum smear conversion. If one controls the second-line anti-TB drugs taking treatment is rather effective.

#### **PS-858-931 Treatment outcomes under DOTS-Plus regimen among patients with MDR-TB and diabetes mellitus comorbidity**

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Target of the study was to investigate the Diabetes Mellitus (DM) influence on the treatment effectiveness among patients with MDR-TB treated under DOTS-Plus regimen. We are surveyed 29 patients with MDR-TB with DM comorbidity in age of 20 to 64 years. 37.9% patients suffered from DM type I, 62.1% type II. In 51.7% cases diabetes course was of middle degree of heaviness, in 48.3% it was heavy. All the patients independently on disease type received the insulin therapy. Various toxic and allergic responses to drugs were observed in 55.2% cases. Out of them non-eliminable adverse reactions to cycloserin were observed in 24.1% of patients, absolute intolerance of anti-TB drugs of the second line was manifested in 2 cases. As a result of the treatment under DOTS-Plus sputum smear negativation after 3 first months of chemotherapy was obtained in (51.7%) only. In 20.7% cases negativation was not obtained. A total of 68.9% were cured, in 31% cases treatment failure was marked, 3 of them died from TB progressing. Thus MDR-TB treatment against background of DM is not sufficiently effective, because of bad drugs tolerance and torpid both diseases course.

### **TUBERCULOSIS AND LUNG DISEASE IN CHILDREN**

#### **PS-126-160 Characteristics of tuberculosis in children in Armenia**

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**Introduction:** TB morbidity and clinical structure was studied for the last ten years in 1270 children in Armenia.

**Methods:** Statistic data on TB and histories of diseases were studied and analyzed.

**Results:** Children's tuberculosis morbidity in 2002 was 8.0 on 105 of population. The ratio of children among new cases made 5.8%. The number of boys was twice more than that of girls. In 92% of cases the patients were vaccinated. 76.2% of new TB cases was pulmonary TB, including hilar adenopathy. Its distribution was following: hilar adenopathy 39.7%, primary complex 16%, infiltrative form 12.7%, disseminated 3.9%, focal 3.4%, cavernous 0.5%. In 15.7% of cases pulmonary TB was accompanied by destruction, and 10.2% of patients were sputum smear positive. Most often revealed forms of extrapulmonary TB were: pleuritis (6.7%), tuberculosis of bones and joints (4.2%), lymph nodes tuberculosis (3.2%), tuberculous meningitis (2.7%). All the patients were treated according to DOTS. The sputum becomes negative in 91% of cases. The treatment success was 91% after 2–3 months.

**Conclusion:** In Armenia epidemiological situation of children's tuberculosis is relatively favourable, and the treatment efficiency by DOTS is high enough.

#### **PS-166-202 Recurrent confirmed tuberculosis in HIV-infected children**

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**Objectives:** To determine the rate of recurrent TB in HIV-infected children and to identify possible causes.

**Methods:** HIV-infected children with  $\geq 2$  culture-confirmed TB episodes  $\geq 6$  months after completing treatment were identified. Clinical data and special investigations were collected per episode. Restriction-fragment length polymorphism (RFLP) analysis was done on available *Mycobacterium tuberculosis* isolates.

**Results:** Nine (10%) of 87 dually infected children had 19 confirmed episodes of TB. Median age: 29 and 54 months at first and second episodes, respectively. First episode treatment duration was 6 and 9 months in 6 and 3 children, respectively, with compliance problems in one each. Pulmonary TB was present in all episodes and extrapulmonary TB in ten, 4 of which in first episodes. Six had new TB source cases (second episode). Weight was  $< 3$ rd percentile in 6 and 5, and Mantoux skin test  $\geq 5$ mm in 6/8 and 3/6 in first and second episodes, respectively. Bronchiectasis was present in 5 in the second episode. Seven of 7 had drug-susceptible TB during the first episode. RFLP analysis was identical for both episodes in all 3 cases done.

**Conclusion:** TB recurrence is common in HIV-infected children. Both reactivation and reinfection occur.



**PS-269-292 Endobronchial tuberculosis and sepsis in children: case reports**

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Tuberculosis (TB), in some cases can be followed by sepsis, mostly by dissemination from unknown septic foci.

**Case 1:** Ten-year-old male, with positive contact with TB patient. Ten days before admission, with high temperature, anorexia, vomiting and cough.

**Status:** Afebrile, with pallor skin, dehydrated, with frequent cough. auscultation: Bronchial breathing on the right side.

**Investigations:** Mantoux test: 20 mm, sedimentation: 70/105, Perfusion scan: low perfusion in the right middle lobe. Haemoculture: *Staphylococcus* coagulase negative; Bronchoscopy: endobronchial TB on the right bronchus.

**Case 2:** Five year-old female, with positive intrafamilial contact with TB patient. Two weeks before admission, with high temperature and frequent cough. Status: febrile, with pallor skin, with frequent cough. On auscultation: pneumonic finding both sided, and mild broncho-obstruction. Investigations: Mantoux test: 12 mm, sedimentation: 138/146; X-ray of lungs: left-sided pneumonia with pleural drain and enlarged hilus; haemoculture: staphylococcus coagulase negative; ultrasonography of abdomen: hepatic enlarged, with supradiaphragmatic drain on the left. Bronchoscopy: endobronchial TB on the left bronchus.

**Treatment:** Both of the children were successfully treated with antibiotics, and modified antituberculosis therapy. Control investigations normalised after 9 months.

**Conclusion:** TB can be followed by other infections, which modifies the treatment and the prognosis, and requires more diagnostic procedures.

**PS-277-302 Improved confirmation of childhood tuberculosis using PCR: development of a diagnostic standard**

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**Rationale:** In spite of various attempts to improve and rationalise diagnostic approaches, the diagnosis of tuberculosis in children is mainly based on clinical signs and symptoms.

**Aim:** The objective of this study was to prospectively evaluate the use of IS6110 PCR in a high prevalence setting for confirming childhood tuberculosis.

**Methods:** This study was conducted in Yirga Alem, Ethiopia. A total of 503 clinical specimens (390 gastric aspirates, 113 sputum samples) from 268 children aged 0–14 years were processed for microscopy,

culture and PCR. Clinical parameters were assessed using standardized questionnaires.

**Results:** According to a modified WHO case definition, 142/268 children had suspected, probable or confirmed tuberculosis. We developed a diagnostic standard including PCR, microscopy, culture, and radiology that resulted in 13/39 (33%) additionally confirmed cases.

**Conclusion:** The inclusion of PCR clearly improved the confirmation of paediatric tuberculosis in a high prevalence setting confronted with additional problems such as malnutrition. The developed standard consists of predominantly objective parameters and may be used to evaluate (new) diagnostic methods.

**PS-296-330 HIV and multidrug-resistant tuberculous meningitis (MDR-TBM) co-infection in children: first case series**

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**Objective:** MDR-TBM in children has not been previously described. We describe the clinical presentation, diagnostic and management challenges and outcome of HIV and MDR-TBM in children.

**Methods:** Cultures of 6781 consecutive CSF samples collected showed that 362 yielded *Mycobacterium tuberculosis*. Forty-two were multidrug-resistant (MDR) of which five were children.

**Results:** All the children presented with vague signs and symptoms. The age ranged from 3 months to 11 years. Four children were HIV positive. The diagnosis of meningitis was confirmed on lumbar puncture. In 3 children, MDR-TB was diagnosed posthumously. Of the remaining 2 children, one is receiving appropriate TB and anti-retroviral therapy and has returned to school. The other child experienced several opportunistic infections and died despite appropriate TB therapy.

**Conclusions:** Every effort should be made to ensure directly observed therapy and completion of treatment. CSF studies should always include culture and susceptibility testing. There is an urgent need for diagnostic tests with improved sensitivity. Culture is too slow to aid in clinical decision. Diagnosis of TBM should be considered in all children with neurologic signs and symptoms. Mortality is associated with inappropriate treatment regimens, inadequate dosages, delays in diagnosis, delays in susceptibility testing.

### PS-345-369 Suprasternal cold abscess following successful treatment of pulmonary and mediastinal tuberculosis in a child

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**Case report:** A 10-year-old boy with pulmonary and mediastinal lymph node tuberculosis (TB) developed a suprasternal cold abscess six months into treatment, despite an improvement in his general wellbeing and inflammatory markers. After 6 months treatment, he developed a mass in the supra-sternal notch. He was otherwise well and ESR had decreased to 16 mm/hour. Radiologically, the right paratracheal lymphadenopathy was unchanged. Ultrasound of the neck showed a midline mass with an avascular necrotic centre. Computed tomography revealed a well-defined, thin-walled abscess extending inferiorly into the right paratracheal lymph node. Four months later, the suprasternal abscess burst spontaneously but the right paratracheal lymph node remained visible radiologically. Antituberculosis medicines were stopped after a total of 10 months.

**Discussion:** The phenomenon of lymph node enlargement, appearance of new lymph nodes and suppuration during or after therapy has been documented and it is thought to represent an immunological reaction rather than bacteriological relapse. Our approach now is if the patient is well and tests are negative, anti-tuberculosis therapy can be stopped. Surgery should be reserved for relief of obstruction. Glucocorticoids, under the cover of antituberculosis therapy, have been suggested when an enlarged mediastinal node causes either respiratory difficulty or collapse-consolidation.

### PS-456-498 La cuerda dulce: a tolerability and acceptability study of the use of the 'sweet string' test for the diagnosis of tuberculosis in children

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**Introduction:** Paediatric pulmonary TB diagnosis is hampered by non-specific symptomatology, paucibacillary disease and inadequate clinical samples. The string test shows promise for TB diagnosis in adults with inadequate sputum. If well-tolerated this simple tool might offer a breakthrough in paediatric TB diagnosis.

**Objective:** To determine the tolerability and acceptability of the string test to paediatric TB suspects, their parents and nursing staff.

**Methods:** 22 paediatric subjects aged 3–14 years (median 8) under investigation for TB were invited to undergo 2 string tests (four-hour downtime each). Validated subjective and objective pain and discomfort rating scales were used to assess the perception of the subject, parent and attending nurse.

**Results:** Patients as young as 4 years of age tolerated the procedure extremely well—84% willing to undergo a second procedure. Peak discomfort at the time of swallowing and of string retrieval was mild and brief as judged by visual analogue ratings and objective indicators. Good concordance of parent and child and objective and subjective ratings strengthened the validity of these findings.

**Conclusion:** The string test is well tolerated and achievable for most paediatric TB suspects as young as 4 years. A paediatric efficacy study is now needed.

### PS-589-658 New diagnostic methods for tuberculosis (TB) in children in Botswana

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**Objectives:** To evaluate TB diagnostic methods in children.

**Methods:** Hospitalized children <15 years with persistent cough, fever or failure to thrive were evaluated at 2 referral centers. Children ≤6 years had gastric aspirates; those >6 years expectorated sputum; stable children underwent sputum induction. Samples were evaluated by direct and concentrated smear, carboxy-propylbetaine (CB-18) and culture. Chest radiograph (CXR), tuberculin skin testing (TST), mycobacterial blood cultures, 4 serodiagnostic tests, and HIV testing were performed. The children were evaluated at 2 months. Clinical cases met ≥2 criteria: TST+, TB contact, response to TB therapy, or CXR suggesting TB.

**Results:** Among 195 children enrolled, the median age was 13 months, 53.3% were male, 139/187 were HIV+, 65 reported contact with a TB case; 12/191 were TST+. Children with ≥2 specimens included: 17 expectorated sputum, 157 gastric aspirates, 118 induced sputum; 191 had blood cultures. To date, 7 children have confirmed TB and 44 are clinical cases. Of the 7 confirmed cases, 2/2 were positive sputum, 5/5 gastric aspirates, 3/4 induced sputum, 3/6 blood cultures, and 3/7 CB-18 smears; 43 children died within 2 months.

**Conclusions:** Few children had bacteriologically confirmed TB. New methods did not increase case finding.

### PS-627-695 Score system in pulmonary tuberculosis among children and adolescents in Bahia, Brazil

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Since 2002 the Brazilian Ministry of Health has recommended a score system for tuberculosis diagnosis of children and adolescents. The aim of this study is to use this score system in patients with positive and negative bacteriology. An observational, transversal study was carried out. 164 patients with pulmonary tuberculosis, ages ranging between 1 and 15 years, were evaluated. Clinical, radiological, epidemiological and follow-up data were considered for diagnosis of tuberculosis. The mean age of the 164 patients was 6.62 years (SD  $\pm$  4.33). 65.2% of the sample reported a positive history of close contact. BCG vaccine coverage was 70.73% (116/164). 26.2% (43/164) of the patients had severe malnutrition. In this subgroup, 26/43 (60.47%) were  $\leq$ 5mm reactive to the tuberculin test. On the other hand, out of the 91 patients with tuberculin test  $\leq$  5 mm, 28.7% (26/91) had severe malnutrition. The use of the score showed the following distribution: a) very likely TB in 81.7% (134/164) of the patients; b) possible TB in 15.9% (26/164) and unlikely TB in 2.4% (4/164). Patients with probable TB and vaccinated more than 2 years ago had a 9-fold risk of having a tuberculin test above 10 mm than patients with possible or unlikely TB.

### PS-684-757 Compliance with unsupervised prophylaxis in children

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**Introduction:** The WHO and IUATLD advise 6 months unsupervised INH prophylaxis for all children less than 5 years of age, exposed to a sputum-positive household source case. With good compliance this regimen has proven efficacy, but little data exist on rates of treatment completion in high-burden settings. **Objectives:** To document treatment completion of unsupervised prophylaxis in children from a typical high-burden setting.

**Methods:** A retrospective file review of all children less than 5 years of age who were evaluated for tuberculosis after household exposure to a bacteriologically confirmed source case (January 1996–December 2003).

**Results:** The files of 386 children were reviewed (male 170, female 216). 336 were fully evaluated (Chest radiograph and Tuberculin skin test results recorded). Supervised therapy was indicated in 121 children of whom 101 (84%) completed the full duration. Unsu-

pervised prophylaxis was indicated in 169 of whom 73 (43%) completed the full duration. In 46 children no treatment plan was documented.

**Conclusion:** Compliance with unsupervised prophylaxis was poor. Supervised treatment greatly improved compliance. Due to poor compliance with unsupervised prophylaxis, alternative prophylaxis strategies may require evaluation in high-burden settings, especially in those children at high risk to develop tuberculosis following exposure.

### PS-725-799 Genotypic characterization of MDR *Mycobacterium tuberculosis* isolates from Cuba (1998–2003)

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**Background:** In recent years, multidrug-resistant (MDR) tuberculosis has been recognized as a potentially catastrophic challenge to global public health. In spite of MDR-tuberculosis is rare in Cuba, a few cases occurred in the last five years.

**Objective:** To characterize MDR *Mycobacterium tuberculosis* strains isolated in Cuba by genotypical methods.

**Methods:** IS6110 RFLP analysis and Spoligotyping were used to characterize 13 MDR *M. tuberculosis* strains isolated, from different cases, in Cuba between 1998 and 2003. The patterns were compared against a National Genotypic Database.

**Results:** Eleven out of 13 isolates were available for genotyping. RFLP and Spoligotyping analysis found only one cluster, formed by the same two strains in both cases, however no epidemiological connection between the patients could be done. The remained isolates showed unique RFLP and Spoligo patterns. The IS6110 DNA fingerprints from these MDR strains were not previously identified in the National RFLP Database. In contrast, the majority of Spoligo patterns were already listed in the Cuban Spoligotyping Database.

**Conclusion:** In spite of MDR-tuberculosis occurs infrequently in Cuba, the recent transmission is not still demonstrated. The creation of a Cuban MDR-tuberculosis Database will help to confirm the transmission of MDR-tuberculosis and to detect 'imported' cases in the future.

**PS-901-975 A case-control of TB risk factors in children under 5 years in Hanoi, Vietnam**

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**Background:** Every year, 30 000 children in Viet Nam suffer from tuberculosis (TB). Delayed detection and ineffective treatment result from poor TB diagnosis.

**Objective:** To assess risk factors for TB among children <5 years of age in Ha Noi (HN).

**Method:** A case-control study was conducted among ill children (<5 years) treated in the Infant Facility of the TB and Lung Disease hospital Jan 2001–Dec 2002, and among healthy children in different residential communities in HN. 156 controls per case were selected randomly in 35/135 communes/wards from infant vaccination lists.

**Results:** 78 cases and 166 healthy controls were enrolled. Among cases, 49% reported contact with a TB patient, of which 37% were smear-positive, 69% were pulmonary, and 73% were family members. Only 81% of the cases had a BCG scar. Contact with TB and missing BCG scar were significantly higher among cases than controls ( $P < 0.001$ ). Poor living conditions, malnutrition, and chronic disease were additional significant risk factors for TB (OR 4.8; 95%CI 1.7–13.2; 2.3; 95%CI 1.2–4.5; and 1.9; 95%CI 1.1–3.5 respectively).

**Conclusion:** Children in families with TB patients, especially if smear-positive, should be kept away from disease sources. Children living in poor conditions and who are malnourished are also at risk.

**PS-95-143 Comparison of clinical outcome with oral and inhaled bronchodilators in the management of wheezy children aged 1–59 months in the community: a randomized trial in Pakistan**

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**Background:** Wheeze is significant problem in children. There is gradual trend of switching over from oral to inhaled bronchodilator therapy. No randomized trials have been carried out in the community comparing the clinical outcome with two modes of therapy. If outcome with oral bronchodilators is same as with inhaled in young wheezers in developing countries, it will be easier to manage them.

**Methods:** In a randomized multicentre trial, wheezy children aged 1–59 months with fast breathing and/or lower chest indrawing received either oral or inhaled salbutamol at home after responding to up to three cycles of inhaled bronchodilators. They were re-assessed on days 3 and 5 for clinical outcome.

**Results:** From May 2001 to August 2002, 780 children

were enrolled. 390 were randomized to oral and inhaled salbutamol each. On day 5, 324 (83.1%) children in the oral and 328 (84.1%) in the inhaled group were completely well. There were no differences in the clinical outcome with both modes of therapy.

**Conclusions:** The clinical outcome of children aged 1–59 months with wheeze is similar when treated with oral or inhaled salbutamol. ARI control programmes in developing countries should continue using oral bronchodilators for the management of wheeze. It will save both time and money.

**PS-136-172 Etude communautaire d'intervention sur la prise en charge des maladies respiratoires : résultats d'une enquête préliminaire**

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Il s'agit d'une enquête préliminaire réalisé au niveau de 07 unités sanitaires de base d'une commune de l'agglomération d'Alger ; dont le but est d'analyser la réponse des services de santé à la demande de soins pour symptômes respiratoires. L'objectif de cette étude est d'adapter les guides techniques sur l'approche de la santé respiratoire (APSR) proposés par l'OMS pour améliorer la qualité et le coût des soins. Une enquête prospective a été réalisée du 1er au 31 Juin 2003 dans une commune urbaine d'Alger.

**Résultats de l'étude :** Sur 3830 consultants généraux tous âges confondus :

- L1078 ont consultés pour symptômes respiratoires soit 28%
- L908 soit 84% des cas ont présenté une IRA :
  - 74% sont des infections des voies aériennes supérieures
  - 10% sont des IRA basses dont 6% sont associées à une atteinte respiratoire haute.

Concernant les maladies respiratoires qui nécessitent des soins prolongés : 54 malades ont consulté dont 40 pour asthme (4%), 11 pour bronchite chronique (1%) et 3 pour suspicion de tuberculose pulmonaire (0,3%). L'analyse de la prescription médicamenteuse dans les infections respiratoires aiguës montre que 77% des consultants ont reçu une antibiothérapie.

**PS-314-344 Clinical characteristics and antibiotic prescribing in patients admitted with community acquired pneumonia: an experience from developing country**

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**Objective:** The aim of the study was to evaluate the epidemiology, etiology and outcome of Community

Acquired Pneumonia (CAP) at a tertiary care hospital in Karachi, Pakistan.

**Methods:** Observational case series on patients admitted with a diagnosis of CAP between January 2002 to August 2003. Clinical records were reviewed for demographic data, clinical features, investigations, treatment and outcome.

**Results:** A total of 329 patients (56.8% male) were admitted with CAP with mean age of 60 years. Two-third of patients had a co-morbid medical illness. Confusion was significantly common in the elderly population ( $P < 0.05$ ). A greater proportion of patients were admitted during the winter months. Organisms were isolated in 33.1% cases. *Streptococcus pneumonia* (8.2%) was the commonest pathogens followed by *Pseudomonas* (4%). Quinolones (47%) were most frequently prescribed followed by 3rd Generation Cephalosporin (41%). Mechanical ventilation was needed in 11%. Complications developed in 55 (15.7%) cases with a mortality rate 11%. Age  $\geq 65$  years, respiratory rate  $\geq 28/\text{min}$ , bilateral lung involvement, dyspnea, confusion and hypoxia at the time of presentation were significantly associated with mortality.

**Conclusions:** Risk factors associated with CAP mortality were similar to western studies. Concerns about penicillin resistant were reflected in frequent use of quinolones and cephalosporin.

#### PS-801-874 Addition of macrolide in treating adult hospitalised community-acquired pneumonia: a prospective study on clinical outcomes

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**Background:** Current clinical practice guidelines (CPGs), including those in South Asia, recommend the addition of a macrolide to a broad-spectrum antibiotic for the treatment of severe hospitalized community-acquired pneumonia (CAP).

**Objectives:** To assess the influence of macrolide addition on clinical outcomes of all hospitalized patients with CAP.

**Methodology:** Over a 16-month period between 2002 and 2004, 141 eligible patients were prospectively recruited from an urban-based teaching hospital in Malaysia.

**Results:** Of the 141 patients, 63 (44.7%) patients [age (SD) 56 (20.0) years; 50.8% male] received a macrolide-containing antibiotic regime while 78 (55.3%) [57 (20.2); 52.6%] were on a single broad-spectrum antibiotic. Thirty-nine (27.7%) and 102 (72.3%) patients had severe (SP) and 'non-severe' pneumonia (NSP) respectively. Irrespective of the pneumonia severity, there was no significant differences in mortality [NSP: 6.5%

vs. 5.4%,  $P = 0.804$ ; SP: 17.6% vs. 18.2%,  $P = 0.966$ ], need of ventilation [NSP: 8.7% vs. 3.6%,  $P = 0.274$ ; SP: 23.5% vs. 13.6%,  $P = 0.425$ ] and median length of hospital stay [NSP: 5.5 vs. 5 days,  $P = 0.954$ ; SP: 7 vs. 6,  $P = 0.401$ ] between the two treatment regime groups.

**Conclusions:** Macrolide addition did not convey any extra clinical benefits in hospitalized adult patients with CAP. Revision or refining of recommendations in current CPGs may be necessary.

#### PS-580-652 Indoor air quality and acute respiratory infections in developing countries with special reference to India: epidemiological perspectives and identification of major dimensions

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Nearly three-fifths of the total global exposure to particulate matter, one of the most ubiquitous air pollutants, occurs in the rural areas of developing countries. Worldwide, this translates into as many as three million deaths a year. In fact, nearly three-fifths of the total global exposure to particulate matter, one of the most ubiquitous air pollutants, occurs in the rural areas of developing countries. Worldwide, this translates into as many as three million deaths a year. The present study attempts to analyze the epidemiological perspectives of spatial distribution of acute respiratory diseases in relation to Indoor air quality and epidemiological perspectives related to age and sex wise variation in the distribution and also the risk factors associated with its occurrence and variation over space and in time. The study is based on both secondary and primary data collection (questionnaire survey particularly related socioeconomic, environmental and biomass consumption and exposure to various chemicals that affect severely the respiratory system). The study with the help of factor analysis identified the major dimensions and these dimensions emphasized the strategies essential to control and prevent the acute respiratory infection. Monitoring and estimating individual-level exposure to indoor PM10 from biomass combustion, longitudinal data on ARI, and demographic information have enabled us to quantify the exposure-response relationship for one of the most common diseases in developing nations.

## PRACTICAL APPROACH TO LUNG HEALTH (PAL) AND ASTHMA

### PS-373-397 Quality of life of patients with and without treatment with asthma preventive drugs

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Asthma is a chronic illness and a public health problem through the world. The aim of our study was to assess the effects of beclomethason-dipropionat (Beclorforte) treatment 2×500 mg daily, during 6 months, on asthma. We were analyzing the quality of life, frequency daytime symptoms, nighttime symptoms and exacerbations. Lung function measured by spirometry (FEV<sub>1</sub>, FVC and FEV<sub>1</sub>/FVC). We studied two groups of patients, with beclomethason-dipropionat preventive and without preventive. The groups were with 20 patients (Table).

	untreated	treated
Asthma manifestations vs. therapy	<i>n</i> = 20	<i>n</i> = 20
Patients experiencing		
daytime symptoms 3 time/weekly	11–55%	18–90%
nighttime symptoms 1 time/weekly	19–95%	
exacerbations within last month	13–65%	14–70%
	treated	untreated
Asthma symptoms control vs. therapy	<i>n</i> = 20	<i>n</i> = 20
wheezing	11–55%	19–95%
shortness of breath	10–50%	17–85%
cough	11–55%	18–90%

Quality of life of patients is better during the treatment with beclomethason-dipropionat. Asthma manifestations and asthma symptoms are significant smaller during the treatment with beclomethason-dipropionat.

### PS-400-426 Viral infection and role of oxidative stress in asthma exacerbation

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Viral infections of the respiratory tract are associated with oxidative stress which plays an important role in the injurious and inflammatory responses in airways diseases such as asthma and therefore are one of the most important triggers of asthma exacerbations. A large number of studies have demonstrated that increased oxidative burden occurs in airways diseases, shown by increased marks of oxidative stress in the airspaces and systemically in these patients. We ex-

amined NO plasma values (by Cayman Chemicals photometric test) and AOE activity of RBC (activity of SOD and GPx were determined by Randox commercial test, while the activity of catalase using Beutler's method) of 10 children with the symptoms of viral infection (RSV, CMV, EBV IgM+ using Elisa method) of the lung which brought about worsening of asthma and compared them with the group of children with asthma (*n* = 10) but without the symptoms of acute viral infection.

**Results:** Along with the symptoms of asthma as a persistent chronic inflammation of the airways, the children from the I group had in their anamnesis a IgG+ for more than two present viruses and/or IgG+ for more than two viruses in mothers. Analysis of anamnestic data, registred monocytosis and changes in the oxidative metabolism of peripheral blood phagocytes (elevated spontaneous activity was established, with insignificant difference in the values of the stimulated NBT test compared to the II group), suggested activation of oxidative stress with more frequent relapses and were using higher dosages of ICS. SOD and catalase activity significantly decreased according to values in II group. The concentration of NO showed significantly increased. The obtained results related to AOE activities indirectly indicate the higher production of ROS with disturbed immunological reactivity which contribute to asthma exacerbation.

### PS-428-467 The interrelationship of the inflammatory markers in blood of stable asthma patients before and after treatment with inhaled steroids and LRA

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**Background:** Airway and systemic inflammation has already been demonstrated in chronic airway inflammation, such asthma. This study was to characterize the relationship between inflammatory components in blood and antioxidative activity of RBC.

**Methods:** We studied blood from stable asthma patients (Mean FEV<sub>1</sub> 75.5% pred.) after 10 weeks treatment with IHC, 10 weeks treatment with LRA and 10 weeks without anti-inflammatory treatment (NoTr). Symptomatic treatment with short acting bronchodilators was allowed. We assessed IL-1, CRP, sNO levels and we compared them with markers of oxidative stress (SOD, GPx, Cat).

**Results:** Blood IL-1 correlated negatively with GPx (LRA: *P* = 0.006, *r* = −0.63; NoTr: *P* = 0.01, *r* = −0.6) and with Cat (IHC: *P* = 0.008, *r* = −0.65, LRA: *P* = 0.02, *r* = −0.62; NoTr: *P* = 0.05, *r* = −0.52). Cat correlated positively with GPx (IHC: *P* = 0.00006, *r* = 0.83; LRA: *P* = 0.02, *r* = 0.57; NoTr: *P* =

0.02,  $r = 0.59$ ). SOD, GPx correlated positively with FEV<sub>1</sub> (LRA:  $P = 0.002$ ,  $r = 0.7$ ; NoTr:  $P = 0.005$ ,  $r = 0.62$ ). Blood IL-1 correlated with NO (IHC:  $P = 0.002$ ,  $r = 0.67$ ; NoTr:  $P = 0.008$ ,  $r = 0.62$ ). There were positive correlations between IL-1, NO and NBT in exacerbation. Negative correlations ( $P < 0.05$ ) were recorded between the number of expressing sTfR and the concentration of IL-1 ( $r = -0.79$ ) in asthma exacerbation, as well as between GPx ( $r = -0.58$ ) and concentration of IL-1 during clinical improvement.

**Conclusions:** Inflammation promote oxidative stress of RBC. Our data suggest influence of IL-1 on expression of NO, IL-1 and NO on the expression of sTfR.

#### PS-508-568 L'asthme d'apparition tardive

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L'asthme débute dans plus de 85% débutent avant 40 ans, et dans seulement 3% après 60 ans. Ce travail étudie le profil clinique et évolutif de 14 patients avec asthme tardif tous de sexe masculin, âgés en moyenne de 65 ans, 13 étant tabagiques. La dyspnée sifflante constitue le mode de révélation le plus fréquent (10 cas), une toux sèche nocturne est notée chez 4 patients. La spirométrie a mis en évidence un trouble ventilatoire obstructif réversible. Un reflux gastro-oesophagien a été retrouvé dans 3 cas. Tous les patients ont été mis sous corticoïdes et  $\beta$ 2-mimétiques inhalés associés dans 12 cas à la Théophylline. Une corticothérapie orale au long cours a été nécessaire chez 2 patients. Tous les patients ont été hospitalisés en moyenne 3 fois pour crise d'asthme sévère. L'asthme tardif pose des problèmes de diagnostic différentiel avec les bronchopneumopathies chroniques obstructives nécessitant un test aux corticoïdes, de prise en charge thérapeutique du fait du terrain souvent taré et de pronostic lié à son caractère sévère persistant.

#### PS-815-887 Traitement de la rhinite allergique et prévention de l'asthme

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**Introduction :** La rhinite allergique est un facteur déclenchant la crise d'asthme. Cette comorbidité nous préoccupe.

**Méthodologie :** Malades avec rhinite allergique et asthme vus en pneumologie. Etude prospective pendant 15 mois pour déterminer l'exacerbation d'asthme.

**Résultats :** Nombre de malades recrutés : 120. homme 55% femme 45%, âge moyen 32 ans, niveau de vie bas,

antécédents familiaux allergiques fréquents. Les facteurs déclenchant les crises sont : poussières de maison 100%, variations météorologiques 25%. La rhinite apparaît avant la crise d'asthme. Nous avons noté 75% de rhinites simples, 60% d'asthme modéré à sévère. Le traitement des crises associe le dexaméthasone intranasal, salbutamol inhalé, dexaméthasone injectable, et du chlorphénamine 5 mg la nuit. Le traitement de fond dure 3 mois : chlorphénamine 5 mg et salbutamol inhalé à la demande. Aucun malade n'a présenté de crise d'asthme avec amélioration du DEP. Le coût du traitement est de 45.000 FMG (environ 4 Euros) par mois. **Conclusion :** Le traitement de la rhinite allergique, avec chlorphénamine 5 mg et salbutamol inhalé à la demande, réduit et ou empêche les crises d'asthme

#### PS-889-964 Prevalence of asthma symptoms, diagnosis and treatment among students of Obafemi Awolowo University, Ile-Ife, Nigeria

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**Introduction:** Asthma continues to be a cause of increasing morbidity and mortality among young adults in the developing world. The prevalence of asthma in this age group in Nigeria is not known.

**Objectives:** To determine the prevalence of asthma among undergraduates in Nigeria.

**Methods:** We studied asthma prevalence among the students using the Questionnaire developed by the IUATLD. 1000 questionnaires were distributed. 903 (90.3% response rate) were retrieved and analysed (469 males, 434 females). The items contained in the IUATLD questionnaire were taken as symptoms of asthma.

**Results:** The 12 month prevalence of wheeze, night waking with cough, chest tightness in the morning was 9% ( $n = 81$ ), 9.4% ( $n = 85$ ) and 8% ( $n = 72$ ), respectively. 14.1% ( $n = 127$ ) reported 3 or more symptoms or had been diagnosed with asthma by a physician previously. An additional 36 respondents (3.6%) reported 2 or less symptoms in the past 12 months. Thus a total of 18.1% (163/903) reported symptoms. Only 32.5% (53/163) of these symptomatic respondents had been previously diagnosed. 22.1% of these (36/163) were on occasional inhaler therapy.

**Conclusion:** These results indicate a relatively high prevalence of asthma among the students for which a great proportion had not been diagnosed and were not having proper treatment.

**PS-316-346 Lung function in patients with acute myocardial infarction**

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**Setting:** In patients with acute myocardial infarction (AMI), the presence of comorbidity, such as chronic obstructive pulmonary disease, may impede the clinical diagnoses of complicating heart failure.

**Aim:** To obtain, in an unselected group of patients with AMI, objective measurements of pulmonary and cardiac function and relation between these.

**Material:** 50 consecutive patients (mean age 69 years, 29 males) with enzyme verified AMI admitted to a district hospital. Forced expiratory volume at 1 sec. (FEV<sub>1</sub>), and forced vital capacity (FVC) were measured. Left ventricular ejection fraction (EF) was estimated by echocardiography. Examinations were carried out 3–7 days after the AMI.

**Results:** FEV<sub>1</sub> <70% of predicted values was found in 44%, FEV<sub>1</sub>/FVC <70% in 30% and EF <40% in 24%. Overall mean FEV<sub>1</sub> (95% confidence intervals) was 73% (67%–79%), FVC was 80% (74%–86%), FEV<sub>1</sub>/FVC was 0.72 (0.69–0.76), and EF was 45% (42%–58%). Lung function was correlated to smoking habits, but not to EF ( $P > 0.05$ ).

**Conclusion:** For unselected patients with AMI, significantly decreased lung function of obstructive type is almost twice as common as reduced EF. These findings may be important to clinical practice and choice of treatment modality.

**PS-419-458 C-reactive protein induces the expression of iNOS and interleukin-1 alpha**

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C-reactive protein (CRP) is the prototype acute phase protein. Previous studies have shown that CRP can induce production of pro-inflammatory cytokines (IL-1, IL-6, TNF- $\alpha$ ). The present study was undertaken to evaluate the relationship of CRP with IL-1 and oxidative metabolism of peripheral blood phagocytes (PBPh), and to assess the effect of CRP on IL-1, NO, and iNOS expression in alveolar epithelial cells. This study comprised 12 patients with interstitial lung disease (viral pneumonia, immune deregulations, and secondary IgA deficiency, ILD) and 6 healthy subjects. The concentrations in serum of CRP, IL-1, NO, iNOS were measured by ELISA. The spontaneous (SP-NBT) and PMA-phorbol-miristate acetate stimulated (ST-NBT) ability of the PBPh, a marker of PBPh activation, to reduce NBT (nitroblutethrasolium) into blue formozan particles, were measured. The concentra-

tion of CRP, IL-1 and NO were significantly increased in blood of ILD patients compared to controls. CRP was significantly associated with IL-1 and NO, iNOS and spont. NBT. CRP stimulation induced the expression of iNOS in a dose-dependent manner. These results suggest that CRP may increase the inflammatory response and the activation of the phagocytes in the peripheral blood by promoting the expression of IL-1 and iNOS from alveolar epithelial cells.

**PS-427-466 The proinflammatory cytokine is important in determining the severity of asthma enhancing the inflammatory process**

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**Setting:** Atopic and non-atopic asthma are characterized by chronic airway inflammation, but with different cythological and cythokinic profiles.

**Aim:** To evaluate the inflammatory markers from non-infectious exacerbation of AA and NAA.

**Methods:** We studied 8 subjects with moderate asthma (mean age 13.8y  $\pm$  09.9sd, basal FEV<sub>1</sub> = 57%pred.  $\pm$  16.8sd), and 11 NAA, mild-to-moderate asthmatics (mean age 09.3ys  $\pm$  05.9sd; FEV<sub>1</sub> 79%pred.  $\pm$  8.7sd). Spontaneous and stimulated was processed for cytological count and IL1 $\alpha$ , and TNF $\alpha$  measures (R & D systems);  $t$  test and  $P < 0.05$  accepted. No cause of exacerbation was assessed by the negative microbial cultures and direct identification of respiratory viruses.

**Results:** 1) both NAA and AA exacerbations proved characterized by elevated neutrophil and eosinophil counts, respectively, 2) a significative FEV<sub>1</sub>-neutrophil count correlation ( $r = -0.71$ ,  $P < 0.005$ ) was shown only in the case of NAA exacerbation; 3) NO did not discriminate any specific profile in AA and NAA exacerbation, even though IL-1 confirmed significantly higher in NAA. There is statistically significant difference between atopic and nonatopic asthmatics in SP-NBT and ST-NBT ( $P < 0.001$ ) suggesting different regulatory pattern for those two groups of patients (AA: SP-NBT 21.22  $\pm$  2.78, ST-NBT 72.65  $\pm$  14.43; NAA: SP-NBT 8.46  $\pm$  2.11; ST-NBT 28  $\pm$  3.14)

**PS-509-560 Effectiveness of integrated syndromic lung health-guidelines in patients with difficulty in breathing in rural Nepal**

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**Introduction:** Health effects of Practical Approach to Lung (PAL) Health guidelines were unknown in a real setting.



**Objective:** To compare health effects in patients with difficulty in breathing (DiB) visiting facilities with PAL-trained and non-PAL-trained health workers in a rural Nepal.

**Methods:** We grouped patients with DiB into two groups: with chronic cough (DWCC) and without chronic cough (DWOCC). We used 5 symptom-based questions from Juniper's Asthma Control Questionnaire (ACQ) to generate ACQ5 scores. Patients with DWCC ( $n = 296$ ) and DWOCC ( $n = 270$ ) were followed up after two months and two weeks respectively. *T*-tests and linear regression analysis were used to compare the health effects.

**Results:** Patients get better after visiting health facility. After correcting for age, the added health effect of visiting PAL facilities to patients with DWCC was reduction in ACQ5 score by 0.157 (95%CI -0.111–0.427) than visiting non-PAL facility, and by 0.359 (95%CI 0.135–0.584) in patients with DWOCC.

**Conclusion:** PAL guidelines were more effective than the usual practice guidelines in patients with DWOCC. Proper tools for measuring health effects of intervention using syndromic approach should be explored.

#### PS-510-584 Quality of life of patients with respiratory diseases included in PAL study in Nepal

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**Introduction:** Two health related quality of life instruments (WHOQOL and EuroQoL) were applied in Nepalese context for the patients with respiratory diseases included in Practical Approach to Lung Health (PAL) study.

**Objectives:** To find the quality of life in Nepalese patients with respiratory diseases and to compare WHOQoL and EuroQoL to find out their construct validity in Nepalese context.

**Methods:** 2243 adult patients (age  $\geq 15$  years) were interviewed in 42 primary health care facilities in Nepal.

**Results:** The mean WHOQoL and EuroQoL score were  $54.34 \pm 10.46$  and  $0.55 \pm 0.35$  respectively. Difficulty breathing patients had worse quality of life than cough or/and fever patients ( $P < 0.001$ ). Lower age group patients had better quality of life than higher age group ( $P < 0.001$ ). The EuroQoL score was substantially correlated with mean WHOQoL score ( $r = 0.493$ ) and physical dimension of WHOQoL ( $r = 0.536$ ; moderately correlated with psychological ( $r = 0.399$ ) and not significantly correlated with social (0.14) and environmental (0.283) dimension.

**Conclusion:** Quality of Life is related to disease severity. The correlation values gives their similar construct and its appropriateness in use in Nepalese context for the patients with respiratory diseases.

#### PS-500-564 Impact of training in Practical Approach to Lung-Health (PAL) guidelines on improving use of drugs

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**Introduction:** Widespread irrational prescribing problem resulting in inefficient use of resources. Among the various intervention options, training in clinical guidelines is one potential way to improve prescribing practices.

**Objectives:** To assess the effectiveness of training in improving adherence to Practical Approach to Lung-health (PAL) guidelines as well as adherence to other guidelines (Standard Treatment Schedule [STS] for health workers).

**Methods:** A stratified cluster randomized controlled trial conducted in primary health care outlets from a terai (flat land) district of Nepal. Randomized 21 and 19 health facilities in control and intervention group respectively from 76 health facilities. Health workers were trained in PAL guidelines adapted from World Health Organization (WHO).

**Results:** Significant increase in the percentage of correct prescriptions for lung disease which was 50% (95%CI 30.5–69.5) in intervention group compare to pre-intervention, where as in control group slightly increased but not significant and significant decrease in average drugs prescribed per encounter was 0.193 fewer drugs (95%CI -0.3835–0.0009) as compared to control group.

**Conclusion:** Training of primary health care workers in guidelines improves adherence to the guidelines focused on by the study but not to other guidelines.

#### PS-111-153 HIV and parasitic co-infections in pulmonary tuberculosis patients: a cross-sectional study in Mwanza, Tanzania

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**Background:** HIV and parasitic co-infections may affect the course of TB disease, but few data exist on disease burden among pulmonary TB (PTB) patients.

**Objective:** To determine the burden of HIV and parasitic co-infections in PTB patients.

**Methods:** Cross-sectional study was conducted from August 2001 to July 2002. Sputum samples were examined for mycobacteria by microscopy and culture. Stool and urine were examined for intestinal helminths and *Schistosoma* species. Blood was collected for determination of malaria and HIV.

**Results:** Of 655 PTB patients, 81.2% were PTB positive (PTB+) and 18.8% were PTB negative (PTB-). HIV, hookworm and *S. mansoni* infections were common (prevalence >10%); malaria, *A. lumbricoides*, *T. trichiura* and *S. stercoralis* were less common (prevalence <5%). PTB+ had lower HIV prevalence compared to PTB- patients (43.6 vs 62.6%,  $P < 0.0001$ ), but higher than controls (43.6% vs 10.7%). Higher HIV prevalence was associated with low intensity of mycobacteria.

**Conclusion:** PTB patients were burdened with infections that might impair cellular immune response and thus increase TB morbidity or complicate TB diagnosis and treatment. Hence, in high HIV and parasitic endemic areas PTB patients should be examined for these infections and be treated.

#### **PS-261-287 A case-control study of risk factors for tuberculosis (TB) relapse in 2 provinces: Thua Thien-Hue and Quang Tri, Vietnam, 2001**

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**Introduction:** In Viet Nam, the TB relapse rate is high, approximately 10%. In this setting, risk factors for relapse are poorly understood.

**Methods:** Collecting data from the first episode of all relapse TB patients with acid fast bacilli (AFB) positive smears registered in 2001 (cases), and previously cured new TB patients from 1999, who had not relapsed with TB in 2001 (controls). Two controls per case were randomly selected.

**Results:** Analysis based on 55 cases and 122 controls revealed that cases were significantly more likely to have had a detection delay (OR = 3.2; 95%CI 1.1–9.6). Those  $\geq 55$  years were significantly more likely to relapse than those <55 years (OR 2.4; 95%CI 1.1–5.6). Other variables significantly associated with relapse were treatment interruption in the intensive phase (OR 20.6; 95%CI 2.5–458.7), discontinuing treatment in the continuation phase (OR 2.6; 95%CI 1.1–6.0), and being an out-patient vs. in-patient in the intensive phase (OR 2.7; 95%CI 1.3–5.7). Finally, the cases were 2.2 times more likely to have had poor knowledge (95%CI 1.1–4.7).

**Conclusions:** The risk of relapse from TB increases with delayed detection, older age, and poor adherence during the primary TB episode, and poor knowledge.

#### **PS-354-377 Steroids and mineral density of bone tissue in sarcoidosis**

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**Objective:** To evaluate the influence of steroids on the mineral density of bone tissue (MDBT) in sarcoidosis.

**Methods:** We examined 65 sarcoidosis patients (median age 35 years) without any endocrinal diseases by the double X-ray absorptiometry method ('Dexa Scan DX-10').

**Results:** Nobody has been diagnosed osteoporosis, but osteopenia was revealed in 12% of patients. The value of MDBT was: in cavernous bones –  $352 \pm 29$ , in tubular –  $679 \pm 41$  mg/cm<sup>3</sup> ( $426 \pm 36$  and  $779 \pm 61$  mg/cm<sup>3</sup> in the control,  $P < 0.05$ ). There were no significant differences between the patients with various stages of sarcoidosis and sex. All patients were divided into 3 groups in accordance with the treatment regime: the group I received budesonide in the dose of 800mg/day, the group II was treated without steroids, the group III received prednisolone in the started dose 30mg/day. After 6 months the value of MDBT did not changed in booth of groups I and II and became lower in the group III ( $P < 0.05$ ).

**Conclusion:** Inhaled steroids in contradistinction to systemic steroids have no any influence on the mineral density of bone tissue in sarcoidosis.

#### **PS-356-378 Prognostic value of TNF- $\alpha$ level in pulmonary sarcoidosis**

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**Objective:** To estimate prognostic value of TNF- $\alpha$  level in sarcoidosis. We investigated 69 patients with newly diagnosed sarcoidosis (stage I - 38 patients, stage II - 31). All patients were monitored for 24 months.

**Methods:** TNF- $\alpha$  concentration in supernatants of cell culture were measured by ELISA.

**Results:** Spontaneous secretion level of TNF- $\alpha$  ( $7.2 \pm 1.1$  ng/ml/10<sup>6</sup> cells) of alveolar macrophages (AM) was increased as compared with control ( $P < 0.001$ ). TNF- $\alpha$  level was higher ( $P < 0.05$ ) in Löfgren's syndrome than in patients with less acute forms of disease. 28 patients remained stable, 25 improved, 3 show relapses and 13 deteriorated. Clinical-radiological improvement was typical for persons with high level of TNF- $\alpha$ . Relapses and deterioration of sarcoidosis were observed in patients with decreasing of secretory activity of AM.

**Conclusion:** High level of TNF- $\alpha$  (8–21 ng/ml/10<sup>6</sup> cells) may be used as favorable prognostic factor and reduction of cytokine-producing function of AM (TNF- $\alpha$  - 0.9–2.3 ng/ml/10<sup>6</sup> cells) can be estimated as unfavorable prognostic factor in sarcoidosis.

**PS-386-409 Aggregate nanoparticle formulations for TB treatment**

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Given the global epidemic of tuberculosis (TB) and emerging public health threat of MDR-TB, there is an unmet medical need requiring the development of new treatment approaches. To help fulfill this need, we have developed a new bioengineered drug form for TB treatment by forming TB drugs into porous nanoparticle-aggregate particles (PNAPs). PNAP systems, with aggregate size ranging from 1 micron geometric diameter to 100 microns, were formed by spray drying suspensions of drug-containing nanoparticles to yield drug formulations that 1) were highly dispersible, 2) allowed delivery of large masses of drug to mucosa, and 3) were easily disassembled upon delivery to body fluids to yield nanoparticles with their inherent attractive features for drug delivery (i.e., large surface area to achieve heightened solubility and targeting ability). Several TB drugs, such as rifampicin, PA824 and ESAT-6, were formed into PNAPs for delivery by inhalation or ingestion. This approach can be applied more broadly for other infectious diseases such as SARS and small pox.

**PS-391-414 Suivi et devenir des tuberculeux transférés à partir du Centre Anti-Tuberculeux (CAT) d'Adjamé, Côte d'Ivoire**

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**Introduction :** L'Afrique sub-saharienne demeure une zone dite à haute charge tuberculeuse en dépit de l'adoption et de l'application de la stratégie DOTS.

**Objectif :** Cette étude avait pour but d'évaluation de cette approche qui s'impose pour une amélioration continue.

**Méthode :** Nous avons alors réalisé une étude rétrospective descriptive portant l'audit des dossiers des tuberculeux diagnostiqués, mis sous traitement et transférés à partir du centre antituberculeux d'Adjamé durant l'année 1999. Nous avons retracé leur parcours.

**Résultats :** Il s'agissait de 376 tuberculeux transférés et 18,35% d'entre eux n'étaient arrivés à leur d'entre d'accueil. Concernant les 307 transférés enregistrés dans leur centre d'accueil, 80,78% avaient un âge compris entre 15 et 44 ans et le sex-ratio était évalué à 1,65%. La tuberculose pulmonaire à microscopie positive représentait 62,54% des cas. Nous avons noté 10,10% et 27,36% respectivement pour la tuberculose à microscopie négative et la tuberculose extrapulmonaire. La sérologie VIH était positive dans 48,15% des cas. L'irrégularité du traitement a été observée

dans 30% des cas. Au niveau du transfert, 80,78% des transferts étaient fait au cours de la 1ère phase du traitement et le temps mis pour accéder au centre d'accueil variait de 0 à 23 jours. De façon globale, on a noté 64,82% de guérison, 1,63% d'échecs thérapeutiques, 6,84% de ré-transférés, 17,92% de perdus de vue et 8,79 de décès. L'infection par le VIH n'avait pas d'influence sur le devenir des tuberculeux.

**Conclusion :** Le phénomène de perdus de vue représente un risque réel de tuberculose et un signe de l'échec de la prise en charge des tuberculeux.

**PS-435-472 Case-finding in tuberculosis patients: diagnostic and treatment delays and their determinants in Egypt**

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**Setting:** Study conducted in randomly selected Direct Observed treatment, Short-course (DOTS) centers nationwide.

**Objective:** To assess delay in diagnosis and treatment of new smear positive pulmonary tuberculosis patients in DOTS areas and their determinants.

**Design:** A nested-case control study has been conducted during one year period (2002–2003) whereby 800 new smear positive adult pulmonary tuberculosis patients were interviewed according to a pre-tested and structured questionnaire.

**Preliminary results:** The median diagnostic delay and total delay were 37 and 38 days, respectively, out of which the median patient delay, care, amounted to 10 days only. On the other hand, the median system delay, was 27 days. The private sector was the first choice to 64% of patients but the chest facilities were responsible for diagnosing 95% of patients. Determinants of different types of delay were also studied.

**Conclusion:** Delayed management of tuberculosis patients was mainly attributed to late diagnosis within the health care system. Increasing awareness among health care providers about the signs and symptoms of tuberculosis is therefore

**PS-493-537 Particularités de la tuberculose pulmonaire chez les tabagiques**

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Le tabagisme prédispose aux infections pulmonaires. L'objectif du travail est d'étudier l'effet du tabagisme sur la tuberculose pulmonaire (TB). L'étude est comparative cas-témoins de 90 patients TB divisés en 2 groupes : groupe I (G I), TB tabagiques (T = 45 cas) et

groupe II (G II), TB non tabagiques (NT = 45 cas). Les critères de comparaison sont cliniques (CL), bactériologiques (B), et radiologiques (RX), basés sur un score de gravité pré-établi. L'intoxication tabagique est de 19 PA. Il n'y a pas de différence CL ou B entre les deux groupes. Le score radiologique est plus élevé chez les T P < 0.001, K2 = 22,4. La guérison RX se fait avec 80% de séquelles dans le G I et 44,4% dans le G II. l'altération de la fonction oxydative du macrophage est au centre des mécanismes physiopathologiques, et dépend du gradient tabagique, avec extension des lésions, et retard de nettoyage. Le tabagisme augmente le risque d'infection tuberculeuse en altérant l'immunité locale et la clairance. Les programmes antitabac et antituberculeux sont complémentaires.

#### PS-678-751 Smoking cessation therapy in primary health care center 'Novi Sad'

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**Introduction:** Highly addictive nature of tobacco requires serious approaches for treatment of nicotine dependence.

**Objectives:** To present the main characteristics of patients who were treated by smoking cessation therapy (SCT) by MacFarland and Folkenberg (behavioural treatment in small groups) in the Department for Health Education in Primary Health Care Center 'Novi Sad'.

**Methods:** Evaluation of self administrated questionnaires of all 898 patients in the period of 1991–2003 at the beginning of 5 days treatment and 3 months follow-up evaluation of abstinence by telephone report and control meetings.

**Results:** The patients are being informed about start of a new SCT group through media, so they approach treatment on the voluntary basis. Almost the same number of both men and women were treated (48% M/52% W), mostly aged 40–49 years. Men were predominantly with high school degree and women with college degree. They smoked in most cases up to one pack a day. The most frequently length of smoking habit was between 10–19 years. The abstinence rate 3 months after treatment is about 60%.

**Conclusion:** This group behavioural SCM is attractive for all profiles of adult patients and it can be considered as an important method of clinical treatment of tobacco dependence.

#### PS-879-956 Feasibility of a standardised tobacco cessation intervention included in tuberculosis treatment

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A feasibility trial of smoking cessation intervention for tuberculosis treatment patients was undertaken in Sudan in 16 tuberculosis treatment centres. Eight other centres were chosen as controls. Feasibility measures to be examined included acceptability, effectiveness and tuberculosis treatment practices. Out of 875 new male tuberculosis patients, 381 (43.5%) were enrolled into the intervention component. Of those enrolled, 314 (82.4%) were cured or completed tuberculosis treatment and 44 (11.5%) defaulted, results that were similar to national results. Staff members involved became more positive about smoking intervention and a large percentage (65.5%) of tobacco users reported that they had stopped using tobacco by the end of the trial. This initial feasibility trial indicates the potential of tobacco cessation interventions for tuberculosis patients, being acceptable and effective and having no adverse effect on tuberculosis treatment practice.

#### PS-920-995 Activities of daily moxifloxacin alone and once weekly in combination with rifapentine against *M. tuberculosis* infection in mice

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The effectiveness of Moxifloxacin (M) against *M. tuberculosis* was assessed in vitro and in vivo. In vitro study showed that MIC<sub>50</sub> and MIC<sub>90</sub> against 18 strains of *M. tuberculosis* were 0.25 and 0.5 mg/ml, respectively. First experiment. M activity was evaluated in a preventive *M. tuberculosis*-infected mice model. The treatment began the day after infection and lasted for 28 days. M and Sparfloxacin (S) were given at 25, 50 and 100 mg/kg and Isoniazid (H) was given at 25 mg/kg 5 times per week as a positive control of activity. M 100 mg/kg was found to be more active than S 100 mg/kg and as effective as H. Second experiment. M 100 mg/kg was evaluated in combination with Rifapentine (P) and H in an established infection model in which mice were treated with 5 times a week RHZM then treated with once weekly PHM for 5.5 months. Mice are then left without treatment for 3 months to determine the relapse rate. Another group of mice is treated with the same regimen but M was replaced by streptomycin (SM). Another group was treated with the standard regimen of daily HRZ for 2 months followed by 2 months of HR. The results of this experiment have shown that the SM-containing regimen displayed a

relapse rate of 60% and the M-containing regimen displayed a relapse rate of 15% which was closer to that found in mice treated with the standard regimen of tuberculosis (7%).

**Conclusion:** M has a bactericidal and sterilizing activity against *M. tuberculosis*.

#### **PS-923-998 Tuberculosis management practices of private medical practitioners in an urban town in Nigeria**

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**Introduction:** This report describes the tuberculosis management practices of private medical practitioners in Enugu, Nigeria, which was previously undocumented.

**Methods:** Combination of TB case records review and a questionnaire study with cross sectional design undertaken in randomly selected private medical establishments.

**Results:** All 93 respondents were part or full time private for profit practitioners. Nearly all 92 see TB cases but only 54 (58.7%) treat TB cases. Main source of TB drugs for patients was the open market. Available NTP treatment centres are largely unknown. Major constraints encountered by practitioners were poor drug compliance (80.6%), poverty of patients (75.3%), and inadequate diagnostic services (54.8%). Of the 269 TB case records analyzed, 43.5% were seen within the first month of illness. Major diagnostic criterion is AFB positive smear plus a positive chest X-ray 149 (55.4%). Most cases 190 (70.6%) were referred out and only 79 were treated. Thirty-three (41.8%) cases received an approved regimen while the rest had 13 different drug combinations. Treatment monitoring parameters included AFB microscopy in 72 cases and chest X-ray in 60.

**Conclusion:** Private doctors are managing TB cases but at variance with national guidelines.

#### **PS-517-572 Risk factors for emergency room visits among asthmatic patients in a tertiary hospital, Rio de Janeiro, Brazil**

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**Introduction:** In Brazil, mortality attributable to asthma during hospitalization in publicly funded hospitals is approximately 0.3%. A more effective asthma care through all levels (out-patient assistance, access to free medication, emergency room visits and hospitalization) could change that figure.

**Objective:** To determine the risk factors associated with emergency room visits among asthmatic patients.

**Methods:** Cross-sectional study performed among out-patients at a tertiary hospital in Rio de Janeiro. From September 2003 to April 2004 a total of 68 patients were followed. Asthma diagnosis was performed according to international and national asthma consensus (IUATLD 1996, ATS 1997, Brazilian Consensus 2002). After approval from the ethic committee, all patients received free medication (inhaled steroids and/or beta2 agonists), answered a standardized questionnaire regarding socio-demographic features and had their ability to use inhaler verified (RN). Primary results: Asthma severity was represented as follows: 19.1% light; 35.3% moderate and 45.6% severe. Patients under inhaler misuse were four times more likely to look for emergency room assistance than those under correct use OR 4.21 (95%CI 1.05–17.42). Other factors were not associated with the outcome probably due to the small sample size.

**Conclusion:** A more effective training of this educationally and economically disabled population should be provided in this hospital pursuing an asthma program.

#### **PS-937-1012 Results of the international study of asthma and allergy in childhood (ISAAC), Phase III in Cameroon**

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**Introduction:** ISAAC was designed in response to the rapid increase of the prevalence of allergic diseases. The aim was to draw up a world map of prevalence of these diseases for the different countries. The prevalence data of these diseases are not known for Cameroon.

**Aim:** To assess the prevalence and severity of asthma, allergic rhino-conjunctivitis and atopic eczema in 13–14 year old school children in Bafoussam, West Province of Cameroon.

**Methods:** Using the written ISAAC phase III questionnaire, 2986 School children aged 13–14 years from randomly selected secondary schools in Bafoussam town were studied.

**Results:** The study revealed that in the past year 5.7% of the school children had wheezed while 0.54% had more than 12 attacks and 2.4% had experienced a speech limiting attack. A past medical history of asthma was observed in 51.96% of the children. Symptoms of allergic rhino conjunctivitis and atopic eczema were reported respectively by 11.8% and 11.3% of the children. The classic preponderance of asthma in boys was not confirmed in this study.

**Conclusion:** The prevalence of asthma, allergic rhino-conjunctivitis and atopic eczema in Bafoussam, Cameroon, appears to fall within the lower range of prevalence data recorded for these diseases in other centres.

**PS-940-1015 Occupational pulmonary hazards due to chronic exposure to benzene**

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**Objectives:** To find out the effect of chronic exposure to benzene on lung function (forced vital capacity, FVC, forced expiratory volume in the first second, FEV<sub>1</sub> and peak expiratory flow rate, PEFR).

**Design and setting:** A randomized cross-sectional study was performed in February 2004 in Khartoum city, Sudan. 123 subjects were included, 79 were workers at different petrol stations, 52 of them were exposed to benzene for more than 5 years and 27 were exposed for less than 5 years. The two groups were compared to 44 unexposed subjects (control). FVC, FEV<sub>1</sub> and PEFR were measured for both groups and the control. Reversibility tests using benzene were performed for some chronically benzene exposed subjects (38) and some unexposed subjects.

**Results:** Significant reductions in FVC and FEV<sub>1</sub> were shown as a result of chronic exposure to benzene ( $P > 0.01$ ). PEFR had shown statistically insignificant reduction ( $P = 0.239$ ). Reversibility tests using benzene produced significant reduction in PEFR and FEV<sub>1</sub> in benzene chronically exposed subjects ( $P > 0.01$ ) but not in benzene unexposed subjects.

**Conclusion:** Chronic exposure to benzene was shown to cause both obstructive and restrictive pulmonary problems and associated with pulmonary hypersensitivity to benzene rather than adaptation.

**TUBERCULOSIS IN HIGH-BURDEN COUNTRIES-2****PS-546-606 Descriptive TB epidemiology in the City of Harare**

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TB is a public health problem in the city of Harare with 9086 cases in year 2000 compared to 2000 in 1990. Over 70% of patients in Harare City are co-infected with HIV and TB. A desk study was done. Information on TB cases from 1975 to 2001 was obtained from Harare City Health Annual reports and TB electronic register kept with all TB patients in Harare City. The records were retrieved and analysed by use of graphs and percentages. Majority (90%) of the cases are between 20–54 years. Ratio of males to females is 2:1. High-density suburbs have most of the cases with Mbare suburb recording 800/ 100 000 cases in 2000, twice the average for Harare City. From 1993–1996 the peak age group with TB was 25–29 years and from

1997 to 2000 this had moved to 30–34 years. High-density suburbs remain the epicenter. Majority of the cases are between 20–54 years, the sexually active group and country workforce. This epidemic may be HIV and poverty driven. Resources must be put to prevention and care of HIV infected people as well as improving the standard of living.

**PS-554-615 Identification and drug resistance testing of *Mycobacterium tuberculosis* complex isolates from Chad: first results**

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**Introduction:** This is the first description of *Mycobacterium tuberculosis* complex (TBC) isolates from Chadian tuberculosis patients.

**Objectives:** To characterize TBC isolates from Chadian patients and to test isolates for drug resistance.

**Methods:** Thirty-five isolates from sputum or urine were confirmed by spoligotyping to belong to the TBC. Anti-tuberculosis drug resistance testing was done with the agar proportion method for INH (0.2 µg/ml), RMP (1.0 µg/ml), EMB (5.0 µg/ml) and SM (2.0 and 10 µg/ml). PZA was tested in liquid Bactec cultures.

**Results:** In total, 29 different spoligo-patterns were identified. One pattern was *M. africanum*, the others *M. tuberculosis*. Twenty-six different patterns belonged to one isolate. Two clusters of 4 and 2 isolates were comparable to the 'Cameroon family' characterized by the absence of inter-DR 23, 24, 25. Another cluster of 3 strains had the typical pattern of H37Rv. Twelve out of 34 strains (35.3%) were resistant to one drug and 3 strains (8.8%) were resistant to isoniazid and ethambutol. No strain was resistant either to streptomycin or to rifampicin.

**Conclusions:** The high proportion of drug-resistant strains underlines the necessity of a functional mycobacteria laboratory to make the Global Fund Programme a success in Chad.

**PS-571-639 Occurrence of adverse effects among patients treated for multidrug-resistant tuberculosis, Latvia, 2000**

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**Rationale:** To manage multidrug-resistant tuberculosis (MDR-TB), Latvia has provided second-line drugs under a DOTS-Plus treatment strategy since 1999.

We determined the frequency and association of adverse effects with individualized anti-MDR-TB therapy. **Methods:** We conducted a retrospective record review of all civilian patients beginning treatment for culture-confirmed pulmonary MDR-TB in Latvia between January 1 and December 31, 2000.

**Results:** Among 204 study patients, 55 (27%) had never been treated for TB before, 119 (58.3%) had been treated for TB with first-line drugs, and 30 (14.7%) had been treated with second-line drugs. Almost two-thirds (129, 63%) patients had an alteration (dose changed or drug changed) in their regimen due to side effects, and 2 patients discontinued anti-MDR-TB therapy. The most frequently reported side effects were nausea and vomiting (149, 73%), dizziness (73, 36%), abdominal discomfort/diarrhea (78, 38%), and hearing loss (58, 28%). More serious adverse effects such as psychiatric symptoms, convulsions, renal failure, and hypothyroidism all occurred in less than 8% of patients. The most commonly altered drugs were prothionamide (50 patients, 25%), paraminosalicylic acid (46 patients, 23%), kanamycin (40 patients, 20%), and thiacetazone (33 patients, 16%).

**Conclusions:** Treatment for MDR-TB with second-line drugs in Latvia requires continual monitoring, as two-thirds of patients required an alteration in their regimen due to adverse effects of second-line drugs.

#### **PS-576-650 Clinical outcomes of multidrug-resistant tuberculosis patients treated under the WHO DOTS-Plus strategy in Estonia, 2001–2002**

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**Background:** During the 1990s, Estonia experienced a dramatic increase in multidrug-resistant TB (MDR TB) cases. We assessed treatment outcomes for the first cohort of pulmonary MDR-TB patients treated in Estonia under the World Health Organization-recommended DOTS-Plus strategy.

**Methods:** We performed a record review of all patients who started MDR-TB treatment in Estonia between August 1, 2001–January 31, 2002.

**Results:** Of 87 patients registered, 43 (49.4%) were new patients without history of prior TB treatment, and 44 (50.6%) had previously been treated. The mean age was 43.6 (range 19 to 79), 69 (79.3%) were men, and 8 (9.2%) were prisoners. The patients' isolates were resistant to a median of 5 drugs (range 2 to 9) at treatment initiation. Five patients who died without MDR-TB treatment were excluded from the cohort. All patients were hospitalized to initiate therapy, with

82 initiating treatment with an individualized regimen. We excluded 7 who are still on treatment. Patients were treated for a median of 413 days (range 3 to 1270). Treatment outcomes included 39/75 (52%) as cure or treatment completion, 8/75 (10.7%) death, 14/75 (18.7%) default, and 9/75 (12%) failure.

**Conclusions:** Under national program conditions in Estonia, over half of patients with MDR-TB were cured despite high levels of drug resistance. Treatment default remains a significant issue in the DOTS-Plus program in Estonia.

#### **PS-578-648 Comparative differential analysis of risk factors between chronic cough and pulmonary tuberculosis in rural South Africa**

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The analysis takes place in the rural population of Agincourt, Limpopo Province, South Africa. A chronic cough survey was conducted in 1999. The results show a prevalence of 1.57% (CI 95 [1.44%–1.69%]). A hospital survey was conducted in the meantime in the same area among pulmonary tuberculosis ( $n = 315$ ). The risks factors were analysed for both diseases in the whole population of 10 years old and above ( $n = 33015$ ). We retrieve from the control population the tuberculosis cases in treatment and the chronic coughers to avoid any bias of selection. Analysing the odds ratio of chronic cough and PTB, by multivariate logistic regression, we observe that having ever worked ( $P < 0.001$ ) and having ever been a miner ( $P < 0.001$ ) are specific risk factors of PTB, whereas the lack of education is specific to chronic cough ( $P < 0.001$ ). We observe no evidence of specific risk factors associated with age, sex, and the size of the household for the lung diseases studied. The findings indicate that the comparative differential analysis of risk factors has implications in terms of public health of respiratory diseases. The analysis put in evidence the specific risk factors of morbidity of PTB by comparison with the general morbidity of lung diseases.

#### **PS-593-664 Modelling the diagnosis of tuberculosis to predict the impact of new technologies**

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Inadequate diagnostic tools and weak health systems contribute to poor TB case detection in many high burden countries, both in terms of the number of cases reported and the speed with which they are detected. New diagnostic technologies are being developed

which might improve both the speed and level of detection. A mathematical model has been developed to describe the diagnostic process and predict the impact of new tests across different geographic settings. The model encompasses TB biology, steps of the diagnostic process and the organization and utilization of health care services. Innovatively, the model separates pulmonary disease into 4 stages, each linked to the performance of multiple diagnostic tests. Clinical symptoms and health seeking behavior are also functionally related to these stages. HIV, extra-pulmonary TB and their association with pulmonary TB are included. Individual behavior and the properties of the health system can be flexibly defined according to country specific data. The latter is derived from field studies in Peru, Zambia, India and Thailand. The impact of 4 new diagnostics within the context of these health systems, using active and passive TB case finding strategies, is explored.

#### PS-600-669 Tuberculose à Abidjan

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**Introduction :** 50% des cas de tuberculose en Côte d'Ivoire sont dépistés et traités dans les 2 centres anti-tuberculeux d'Abidjan, Capitale économique avec environ 3.118 777 d'habitants avec une densité de 1475 habitants/km<sup>2</sup>.

**Objectif :** Apprécier l'importance de la tuberculose à Abidjan.

**Méthode :** Etude rétrospective portant sur les cas de tuberculose diagnostiqués et traités à Abidjan du 1<sup>er</sup> janvier au 31 décembre 2000.

**Résultats :** 6316 dossiers ont été analysés avec 60,7% de sexe masculin et 39,3% de sexe féminin, 63,4% de nationaux et 31,1% de non nationaux, 79,5% des malades ont entre 15 ans et 44 ans. La prévalence de la tuberculose à Abidjan est de 202,5 cas pour 100 000 habitants. Dans certaines communes elle varie de 148 à 306,3 cas pour 100 000 habitants. L'incidence annuelle est de 117,2 cas pour 100 000 Habitants. La densité moyenne des formes bacillifères est de 8 malades/km, mais varie selon les communes de 7 cas à 47 cas par km<sup>2</sup>. L'incidence annuelle des formes bacillifères est de 177,5 cas pour 100 000. Le rendement du dépistage est de 54,7%. Selon les communes, il varie de 26% à 87%.

**Conclusion :** La tuberculose à Abidjan demeure encore malgré la décentralisation un gros problème de santé publique.

#### PS-602-676 Descriptive analysis of tuberculosis in a demographic surveillance area (DSS) at Manhica District (Mozambique). Improvement of TB indicators and establishment of a TB research platform

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**Introduction:** Mozambique is a high tuberculosis burden country with serious challenges in TB control as 47% HIV prevalence among TB cases, 77% treatment success (2001) and 45% case detection rate (2002). The Manhica Health Research Centre, located in Southern Mozambique District, is based on its Demographic Surveillance System linked to clinical assistance and also research. The Centre started TB project on 2002.

**Objective:** To obtain tuberculosis descriptive analysis at Manhica District and to establish a TB research platform.

**Methods:** The project includes TB data collection (clinical, epidemiological and microbiological), supervision and technical support of TB activities at Manhica District.

**Results:** It has been created a clinical and laboratory TB research group following GCP and GLP standards. This team performed TB training of District health staff that facilitates extending TB treatment at peripheral Health Posts of Manhica District. These activities have derived on improving TB indicators as 65% increasing on newly TB cases (2001 incidence: 211/100 000pop versus 2003 incidence: 348/100 000pop), cure rate has grown from 56% (2001) up to 66% (2002), non-compliance rate has decreased to less than 8% however lethality rate has maintained on 22%, probably due to HIV co infection (50% HIV positive among TB patients). It has also set up a mycobacterial laboratory with culture and susceptibility tests facilities that have been able to process about 3000 samples/year for bacilloscopy and culture.

**Conclusion:** It has been created a TB research platform in Mozambique that allowed to improve TB indicators and to create facilities for future intervention studies (clinical trials).

#### PS-615-686 Tuberculosis mortality in Ile-Ife: a five year review

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**Introduction:** Death from tuberculosis (TB) is the longest indicator of TB epidemics in industrialised countries. In developing countries, morbidity and mortality is rising despite advances in TB management. There is scarcity of data on mortality due to TB in this environment, hence this study.



**Objective:** This study aims at investigating various factors associated with death among TB patients in OAUTHC, Ile-Ife.

**Methods:** We review all cases of deaths due to TB during the period under review. Data are presented using descriptive statistics.

**Results:** A total of 268 cases of TB were admitted. There were 49 deaths attributed to TB, this gives a mortality rate of 18.3%. The highest mortality was observed among patient with a M:F ratio 1:3:1. About 70% of the patients died within week of admission. Pulmonary TB was responsible for 69% of death followed by TB meningitis 14%, retroviral illness 24%, anaemia 60%. Delayed presentation, and diagnosis were identified as factors commonly associated with death.

**Conclusion:** This study corroborates with other studies in which delayed presentation and diagnosis were commonly associated with death. The extent to which TB continues to kill amongst other things depend on the extent to which modern intervention is available to the low income countries of the world.

#### **PS-647-716 Tuberculosis (TB) operational research: a need in low-medium income countries**

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**Introduction:** In Rio de Janeiro, Brazil, 86% of TB cases are pulmonary forms (PTB). In 1997, 57% of the laboratories reported performing <20 specimens per week. Therefore, TB diagnosis could be mostly based on chest X rays (CXR) which are supposed to be read by the attending physicians.

**Objective:** Pilot study to determine the prevalence of TB diagnosis based on CXR only.

**Methods:** From October 2003 to April 2004 a convenience sample of 85 respiratory patients was followed in one publicly funded primary care clinic in Rio. Patient's socio-demographic and clinic characteristics were evaluated through a standardized questionnaire. TB diagnosis was performed according to available resources following international and national TB guidelines (IUATLD, ATS, Brazilian Ministry of Health 2002). CXR abnormalities were classified using a categorization scheme developed for Immigration Canada (from normal to more extensive lesions: 1–5).

**Primary results:** Up to now, 39 PTB cases were identified: 32 (82.1%) patients presented more extensive lesions (CXR), among those 17 (53.1%) were sputum (–) or did not present sputum (NS). Seven patients (17.9%) were classified as less extensive lesions on CXR, 4 (57%) patients were sputum (–) or NS.

**Conclusion:** Training and radiology supervising in

good diagnosis practices will strengthen TB control. Operational research on CXR TB diagnosis will be proposed.

#### **PS-655-729 Drug resistance survey in the Russian Federation: challenges and future plans**

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The most urgent problem for Russia nowadays is the prevalence of drug-resistant strains of *M. tuberculosis*, including those with multidrug resistance (MDR). In some territories of the Russian Federation quite effectively performing projects are being implemented in collaboration with the international partners. The projects stipulate the external quality assurance (EQA) of DST performed in the international and federal reference laboratories. The implementation of these programs allowed determining the main tendencies of drug resistance prevalence. In particular, it was demonstrated that between 2001 and 2003 the level of primary MDR changed: in Orel region from 6.6% to 3%; in Ivanovo region from 6.1% to 1.5% and in Vladimir region from 2% to 4.4%. While the level of acquired MDR in 2002 in Orel, Ivanovo and Tomsk was registered between 42.4%–43.6%. According to the official statistics, the prevalence of primary MDR in the federal districts of RF in 2001 was: Southern 4.6%, Urals 5.9%, Siberian 6.7%, Central 7.4%, Far-East 7.6%, North-West 8.3%, Privolzhski 10.3%, the average rate of primary MDR in RF was 8.9%. While the primary MDR in RF in 2001 without active EQA programs was registered as the following: in Vladimir region 2%, and in Krasnoyarski krai 50.5%. Under these circumstances, the support of EQA programs for DST performed in the framework of collaborative international projects involving MH RF, MJ RF, leading federal research institutes, local TB facilities, WHO and international partners is especially important. The implementation of the long-term large-scale project on the study of a true level of *M. tuberculosis* drug-resistant strains prevalence has been initiated on the basis of randomized representative studies, which cover no less than 10% of the population of Russia.

#### **PS-656-730 Drug resistance survey in the Russian Federation during realization of TB monitoring program**

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The main goals of establishing the Russian Federal reference laboratories (RL) are: implementation of *M.*

*tuberculosis* drug resistance levels monitoring, prevention of spreading the strains with drug resistance as well as developing the service of bacteriology tests external quality assurance and integration into the net of international RL. In order to evaluate the readiness of laboratories to perform the reference functions, the quality and quantity evaluation criteria were developed for the bacteriology laboratories (BL). The criteria are transformed into questionnaires adapted for the computer processing. The first questionnaire, which includes 100 basic and over 160 specific questions, is the one on macro rates of main parts of BL activities. The preliminary analysis demonstrated the different stages of readiness among the district RL and the necessity of their gradual inclusion into the full extend external quality assurance program. In this respect, starting 2004 the long-term large-scale project on the study of a true level of *M. tuberculosis* drug-resistant strains prevalence has been implementing in the RF on the basis of randomized representative studies. The project provides for 6 cycles of studies performed in 2 phases with the coverage of no less than 10% of the population in Russia in each cycle, including the studies in the penitentiary facilities. The external quality assurance consists of testing the regional laboratories by means of a coded set of *M. tuberculosis* cultures and also randomized re-analysis of clinical *M. tuberculosis* cultures in the federal and international RL. As the result of the project implementation, the mechanism of the external quality assurance programs implementation under the condition of interaction of subordinated laboratories will be developed.

**PS-694-769 Cohort evaluation for new pulmonary tuberculosis positive bacilloscopía. Dominican Republic 2000–June 2003**

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**Introduction:** One of the goals for DOTS is to cure 85% of diagnosed new cases. 45.7% of the new cases positive pulmonary tuberculosis with positive bacilloscopía was cured in the 2000 and DOTS was expanded in 2002.

**Objectives:** To evaluate cohort of new cases pulmonary tuberculosis positive bacilloscopy since 2000 until June 2003.

**Methods:** The information in cohort of new cases pulmonary tuberculosis bacilloscopias positive was reviewed since 2000 to June 2003, treated with treatment scheme 2RHZE/4RH<sub>3</sub> and it was analyzed the exit condition.

**Results:** The cured percentage increased from 45.7% in 2000 to 67.6% June 2003 due diminution in finished cases from 29.9% to 11% in same period. Abandon-

ment percentage diminished from 14.9% to 12% in the same studied period.

**Conclusion:** The DOTS expansion has contributed to increase percentage of new cases pulmonary tuberculosis positive bacilloscopía cured. Abandonment treatment and finished cases percentage has diminished.

**PS-716-788 Estimation of new smear positive TB incidence and case detection rates in Cambodia**

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**Introduction:** According to the result of National TB Survey, 2002, the prevalence rate of smear positive TB, 270, was only a half of WHO estimate, 548.

**Objectives:** To have best estimate of the incidence and case detection rates of new smear positive TB for 2002.

**Methods:** In addition to the results of National TB Survey both on disease prevalence and patients' behaviors, results of a delay study, National HIV sero-prevalence survey among TB patients, a follow up study of HIV/AIDS patients in Phnom Penh, and National TB Drug Resistance Survey as well as National HIV/AIDS sentinel surveillance, and revised data of routine surveillance by quality assurance activities were utilized to make assumptions on disease durations and patients' proportions for three by two categories of TB patients under NTP, DOTS, under private, Non-DOTS, and undetected with and without HIV to calculate the incidence.

**Results:** Point estimate of new smear positive incidence rate was 202/100 000. 15% among them were attributed to HIV/AIDS. Estimated DOTS case detection rate was 52% and another 10% were treated by private sector.

**Conclusion:** Although the prevalence rate became around 50% of previous estimates, the incidence rate still remains at a very high level even excluding impact of TB/HIV.

**PS-758-832 The tuberculosis situation remains worrying in the countries of the Former Soviet Union**

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**Background:** The overall situation of tuberculosis (TB), in the 15 countries of the Former Soviet Union (FSU) has worsened since the early 1990s, due to broad societal changes.

**Methods:** Descriptive analysis of data from national TB case reporting, drug resistance surveillance, treatment outcome monitoring and AIDS case reporting, available at European level.

**Results:** TB notification rates increased by 82% between 1995 and 2002, reaching 104/100 000 in 2002 (300 725 cases). Highest rates were in the age group 25–44 years (137/100 000). Among the 917 AIDS cases reported in 2001, 70% of those with information on initial AIDS indicative disease had TB. Representative drug resistance data were available only from the Baltic States. The range of prevalence of initial multi-drug resistance in 2002 was 9–17% among new cases ( $n = 2259$ ), stable since 1999, and 43–51% among retreated cases ( $n = 866$ ). In 2001, in 8 countries providing complete treatment outcome data for sputum smear positive cases ( $n = 9766$ ), success ratios were low among new cases (64–77%; median 69%) and retreated cases (15–70%; median 43%).

**Conclusion:** Increasing notification rates, high drug resistance, poor treatment outcomes and emerging TB morbidity among AIDS cases indicate that the tuberculosis situation remains worrying. Large scale tailored interventions and strengthened surveillance are urgently needed.

#### **PS-780-854 TB and gender: SAARC regional perspective**

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**Introduction:** Reported data reveals low case detection rate as well less number of female TB patients.

**Objective:** To assess the gender differences among TB suspects and registered patients in NTPs of SAARC countries.

**Methods:** Sex disaggregated data were collected under the categories of TB case detection, TB suspects under going sputum microscopy, sputum positivity and treatment outcomes of registered TB patients during the last 2 quarters of 2001 (1 July–31 December 2001). Five TB diagnostic and treatment centres from each of seven member countries were randomly selected. The data were collected locally under the supervision of local TB programme managers according to the guidelines prepared by the STC. Analysis was done in STC using MS excel and Epi-Info software.

**Results:** Over all female/male ratio of less than one was observed in case of TB suspects undergoing sputum examination, sputum positivity and in total (all types) TB case detection. Higher treatment success rate and lower default rate were observed among female patients.

**Conclusion:** The existing gender inequalities in SAARC region may reflect gender differences in TB epidemiology.

#### **PS-783-857 Success of DOTS in SAARC Region**

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**Introduction:** Since 1993 Directly Observed Treatment Short-course (DOTS) strategy are being implemented globally to tackle tuberculosis (TB). By 1996 all SAARC Countries have started DOTS implementation. SAARC TB Centre is preparing SAARC regional report annually.

**Objective:** To provide progress of TB control in the SAARC region.

**Methods:** Analysis of data from Member Countries.

**Results:** Incidence rate (per/100 000) of estimated TB cases in SAARC region has decreased from 181 in 2001 to 174 in 2002 while it has increased globally from 138 in 2001 to 141 in 2002. In the year 2001 SAARC region was bearing 29% of the global new TB cases. In the year 2002 this proportion has come down to 27.4%. Case detection rate (Global/37%; SAARC/ 44%) and treatment success rate (global 82%; SAARC 85%) of this region are also in a better position.

**Conclusion:** TB control in the SAARC region is showing a positive progress. For this success to continue SAARC region must overcome the present challenges like sustainability of quality in diagnosis and treatment, expansion of DOTS to hard to reach areas, focusing cross boarder issue and migration, tackling of TB/HIV co-infection and MDR-TB.

#### **PS-809-881 TB & health education**

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**Objective:** Study of health education of TB patients, correlated to socio-economic conditions.

**Methods:** 200 TB patients answered a 30 items questionnaire on: TB (transmission, implications, treatment, protection, ways of information and socio-economic status. Patients were aged between 18–77. 87.5% workers and 12.5% retired, had low monthly incomes, with periods of unemployment, or performing illegal work. A third of them had precarious hygienic conditions of life. Although all of them had lyceum as minimum study, the test showed differences in basic knowledge for TB according to age, gender, social/ educational status. Women, younger and educated people were more informed than the others. Patients prefer to speak about their disease with the specialist doctor, instead of GP. As sources of information, they preferred any kind of leaflets, magazines and TV news. People under 50, having a medium level of understanding prefer to obtain information from the web.

**Conclusions:** There is a strong connection between

TB epidemiology and socio-economic factors. People have a lower level of health education than expected. Prevention and treatment of TB means more specific health education.

#### **PS-823-895 Meta-analysis of tuberculin skin test reaction in a school community**

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**Objective:** Study the risk of TB children infection, in a school collectivity.

**Material & Method:** 1200 students (594 boys and 606 girls, between 6 and 14 years old), in contact with a smear positive patient, school worker, were tested with 2UT of PPD. The test was considered positive ab 10 mm induration, Palmer I and II, at 6–7 years old pupils and >14 mm/any Palmer, at 7–14 years old pupils.

**Results:** 247 (20.5%) pupils presented hyperergia. 12 cases received chemotherapy in the past. All the other 235 (18%), proposed for chemotherapy, attended chest X-ray examination. 3 cases were hospitalized; only 1 was confirmed with primary TB and treated 6 months HRZ. The 2 others received HZ chemotherapy/6 months.

**Conclusions:** Hiperergic Mantoux reaction can be regarded as indicator of high risk infection: 18% of the students patient were infected, percentage accepted only in conditions of a high TB morbidity. Chemotherapy to prevent the risk of progression to clinical manifested disease or development of complications from primary TB is necessary.

#### **PS-837-908 Effects of low level conflict on National Tuberculosis Programme (NTP) as shown by routinely collected indicators**

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**Introduction:** The Nepal NTP has been implementing DOTS since 1996. At around the same time a low level conflict started mainly in districts in the Mid and Far West Region. The conflict has occasionally involved restriction of movement of people and goods. To what extent has this conflict affected the Tuberculosis Programme.

**Objectives:** To compare trends (1997 to 2003) in smear positive TB case finding and levels of cure rates between 16 conflict affected districts and the rest of the country.

**Methods:** Case finding and cure rates are routinely collected by the NTP at district level. The 16 districts were choosen on basis of being in Phase 3 of the UN Security staging in May 2003. Comparisons in case

finding were made between 1997 and 2003 for each district and cumulative totals.

**Results:** 2.9 million people in conflict affected areas experienced an increase of 65% (708 to 1107 new S+ve cases per year) between 1997–03, a faster increase than the rest of the country 24.37%. Both case-finding (69% vs. 72%) and cure rates (81% v 85%) are slightly lower than in the rest of the country.

**Conclusion:** The conflict has not significantly affected the outcome indicators of the Tuberculosis Programme so far.

#### **PS-935-1010 Impact of late/no sputum collection on apparent smear conversion rates, South Africa**

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**Introduction:** Smear conversion rates (SCR) provide a useful tool for evaluating program performance and are a marker for shifting from intensive to continuation phase of TB treatment. Anecdotal reports suggest that some specimens are collected a few days late, excluding them from analysis.

**Objectives:** To understand the relative impact of non-collection and late collection of sputum with regard to apparent SCR and to inform decision-making for program improvement.

**Methods:** Data from 9 sub-districts in 3 provinces were exported from the SA Electronic TB Register. SCR data for Quarter 2/2003 were evaluated using Epi-Info and Excel.

**Results:** Of 1446 records reviewed, 1021 (70.6%) converted. 184 (12.7%) had 'No result' recorded. Of these, 135 (73.4%) did not have any specimen collected; 45 (24.5%) had specimens that were collected late (after 100 days). 4 (2.2%) were missing for other reasons. Assuming a similar distribution of results as among those with recorded specimens, an increase in SCR to 80.9% would have been possible if sputa had been collected in a timely manner.

**Conclusion:** Observance of NTCP guidelines concerning follow-up sputum collection is essential to meet national targets. Late/non-collection of sputum has resource and program management implications vis-à-vis changing phases of the regimen. Follow-up evaluations need to investigate causes for non-adherence to program guidelines.

## PATIENT TREATMENT ADHERENCE/ MANAGEMENT-1

### PS-127-161 Effect of ayurvedic immunomodulator on sputum conversion under RNTCP regimen: a case control study

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**Introduction:** In RNTCP(DOTS) TB Drugs are given intermittently and sputum is examined periodically to assess responded treatment. Sputum conversion is found not satisfactory in highly positive (3+) cases. So an adjunct drug to enhance sputum conversion and infectivity is relevant in DOTS treatment.

**Objectives:** To study the effect of ayurvedic immunomodulator supplementation on sputum conversion in patients with sputum positive pulmonary tuberculosis on anti TB drugs under RNTCP.

**Methodology:** 21 cases of sputum positive pulmonary tuberculosis registered for RNTCP treatment in Alappuzha TU were selected randomly to be included in the study. They were given one tablet of ayurvedic immunomodulator twice daily during the entire intensive phase of the treatment. Sputum examination, weight and ESR were recorded at the start and end of intensive phase. 21 identical cases were taken as control.

**Findings:** Of the 21 cases, 19 cases are converted to negative by end of second month. 2 cases remained positive (9.5%). Of this one was Category II and both results were scanty on follow up. The average weight gain was 2.5 kg and the average reduction in ESR was 30 mm/hour. In control group, of 21 cases, 15 were converted to negative and 6 remained positive. The average weight gain was 1.5 kg and reduction in ESR as 20 mm/hour. There was one death in control group.

**Conclusion:** Ayurvedic immunomodulators seen to have a beneficial effect on sputum conversion of pulmonary TB cases getting anti TB treatment.

### PS-207-247 The level of care, response time and outcomes of TB cases in a Western European City, 1998–2003

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This retrospective study, using information currently recorded by the TB Unit in Liverpool, seeks to discover whether we have met the 85% cure target, how quickly the Unit has responded to being advised of a case or suspected case and what involvement the TB Service has invested in Patient care. 218 confirmed cases of whom 12 were found on post-mortem examination

were included. 66 had smear positive disease. 89% of cases or suspected cases who were later confirmed as cases, were seen within a week. 86% of patients were cured or completed treatment. Cases were scored according to factors which may influence their level of drug concordance (e.g., Substance abuse, language difficulties etc.). These were then measured against the levels of medical and specialist nurse input which were scored nil to intense (0–4). The study shows that in 98% of cases, factors affecting possible non-concordance with treatment has been identified and a higher level of care given.

**Conclusion:** The unit is achieving good cure and level of care rates by using selective levels of care and DOT according to need.

### PS-215-252 The increasing workload of the tuberculosis service in a Western European City

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Until 1995 the work of the TB Nurses was mainly concerned with support to TB patients and their families, contact tracing and clinics. In the subsequent 8 years Liverpool has experienced a rise in new entrants that has had a significant effect on the workload of the unit, both in routine tuberculosis screening and in the management and support of cases and suspected cases of TB. The figures also reflect the disproportionate burden of tuberculosis on the ethnic minority of Liverpool, given the ethnic population of 8.2% (Table).

Effect of immigration on workload of the TB service in Liverpool 1995–2003

	1995	1996	1997	1998	1999	2000	2001	2002	2003
New entrants identified	118	145	149	293	1179	3223	2113	2278	1294
New entrants screened	97	71	91	167	691	1975	1024	790	539
% TB cases in new entrants (in UK >2 years)	8	2	5	11	3	17	25	27	43
% TB cases in new entrants (in UK 2–5 years)	2	2	5	9	3	17	8	11	20
% cases in foreign-born (in UK longer than 5 years)	12	18	23	20	14	23	4	22	4
% Total cases non UK-born	20	22	33	40	20	57	37	60	67
% of those on preventive treatment who are new entrants	N.D.	N.D.	N.D.	N.D.	5	48	72	89	88

N.D. = No data.

### PS-219-254 The first report of DOTS supervised by a pharmacist and Japan's first experience with intermittent chemotherapy

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**Objective:** To evaluate the efficacy of intermittent chemotherapy based on a DOTS system under the supervision of a pharmacist.

**Methods:** Patients eligible for the study were new cases of pulmonary tuberculosis who were admitted at Fukuji Hospital between June 1, 2001 and January 31, 2004 whose isolates were susceptible to both isoniazid and rifampin. The treatment regimen consisted of two months of daily isoniazid, rifampin, pyrazinamide, and ethambutol followed by twice weekly isoniazid and rifampin. The enrolled patients were given the opportunity to select a pharmacy most convenient to them and took the medications under the direct observation of a pharmacist.

**Results:** Of the 578 patients admitted during the study period, 305 met the study criteria. Ninety-three of the 305 patients gave informed consent. Of the 93 participants, 70 completed the regimen, 20 are still enrolled, 1 defaulted, and 2 were referred to another provider. With respect to the default rate, the three-year mean rate decreased from 5.5% during 1997–1999 to 2.4% during 2001–2003.

**Conclusion:** DOTS with intermittent chemotherapy at the pharmacy is effective and safe. The default rate was improved by DOTS. DOTS with intermittent chemotherapy at a pharmacy should be expanded in Japan.

### PS-284-315 Outcome of neurotuberculosis patients put on DOTS: a report of 32 cases from South India

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With the introduction of DOTS Neurologist all over India are reluctant to accept intermittent regimen for Neuro Tuberculosis. We are reporting outcome of 32 cases of Neuro Tuberculosis put on DOTS (intermittent therapy). Thirty-two patients diagnosed to have Neuro Tuberculosis and registered in the 4 TUs of Alappuzha district during the year 2002 were selected for the study. Five patients died with mortality rate of 15.6%, four were changed to NTP regimen because of drug toxicity. One patient defaulted. The rest of patients (22) completed treatment with cure rate of 69%. Out of them 15 were followed up at 6 to 12 months after completion of treatment. Except for hemiparesis in one and minor problems like headache in two all are doing well. In our study the cure rate of Neuro TB is much higher than that for meta analysis of daily regimen. The mortality rate is also lower (15.6% vs 27%)

compared to a similar study from South India. The default rate is only 3% which is also significantly low.

### PS-288-322 Assessment of treatment outcome and adherence to treatment of lymph node tuberculosis patients put on DOTS

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**Aim:** To assess adherence and treatment outcome to anti TB drug by patient with lymph node TB put on DOTS.

**Method:** All lymph node tuberculosis patients put on DOTS (intermittent therapy) in Alappuzha District from 1st Jan. 2002 to 31st Dec. 2002 were analysed retrospectively. Diagnostic algorithm as per RNTCP policy is strictly followed up. Data are collected from four tuberculosis register maintained in the district.

**Result:** Of the 125 cases registered 121 (96.8%) successfully completed the treatment. There was only 3 default (2.4%) and 1 death (0.8%). There were no serious side effect requiring change in regimen.

**Conclusion:** Intermittent 3 drugs (H,R,Z) regimen is highly effective regimen for lymph node tuberculosis when given as DOTS with high adherence.

### PS-355-379 Follow-up of tuberculosis patients defaulting treatment in a high incidence area

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**Objective:** To determine what proportion of tuberculosis patients defaulting from treatment dies or has TB 2–10 years after defaulting, and what were reasons for defaulting.

**Methods:** All new TB patients from a high TB incidence urban community in Cape Town, who interrupted treatment for more than 2 months during 1993–1998, were visited in September 2003. They were interviewed and asked for a sputum sample.

**Results:** 188 out of 1138 (17%) TB patients defaulted treatment at least once. 34 (19% of 188) of them were successfully treated during retreatment. The remaining 154 defaulters were visited. Of these, 35 (23%) could not be found. From the remaining 119, 22 (18%) had died. Of the 97 patients alive, 51 tried to give a sputum sample; 7 were dry and 4 (8%) were culture positive, of whom one also smear positive. 59% of those interviewed still had symptoms that could be related to TB. The main reasons for defaulting were the understanding that they had completed treatment, or did not have TB anymore.

**Conclusions:** Although the moving rate is high, the majority of defaulters can still be found. The high proportion of defaulters that dies or still has TB indicates the need for more intensive follow-up of defaulters.

**PS-372-396 The prevalence and evolution of leukopenia during first-line anti-tuberculosis medication**

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**Introduction:** Although the cure rate of current short-course anti-tuberculosis (TB) treatment based on isoniazid, rifampicin, pyrazinamide, and streptomycin/ethambutol is essentially 100%, these drugs can cause various adverse reactions include hematological abnormality.

**Objectives:** To elucidate the prevalence and evolution of leukopenia during the treatment with first-line anti-TB drugs.

**Methods:** We enrolled the 15 year- or older patients with TB took 1st line anti-TB medication between June 2000 and May 2001 in Seoul National University Hospital, Republic of Korea. We retrospectively reviewed medical records including serial leukocyte counts.

**Results:** Among 900 TB patients enrolled in this study, leukopenia less than 4000/ $\mu$ l developed in 185 (20.6%) patients. Out of 109 (100%) patients in whom first-line anti-TB medications were continued despite of leukopenia, leukopenia resolved spontaneously in 32 (29.4%) patients and were persistent in the other 77 (70.6%) patients. The lowest leukocyte counts in majority of patients with leukopenia (152 (82.2%) out of 185 patients) were higher than 3000/ $\mu$ l through the treatment period. In multivariate analysis, lower initial leukocyte counts ( $P < 0.001$ ) and female sex ( $P < 0.001$ ) were associated with the development of leukopenia.

**Conclusion:** Leukopenia developed during anti-TB treatment with 1st line drugs was common, but usually mild and benign.

**PS-453-490 An interagency TB control program in Tomsk Oblast**

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Since 1997 Tomsk has become a site for implementation of the WHO TB control protocols. Since 2001 an interagency program 'TB detection and treatment, including MDR-TB' has functioned in Tomsk Oblast. TB treatment is coordinated between civilian and prison sectors, and in-patient and ambulatory stages. Ambulatory treatment has been improved. The participants of

the interagency program also focus on the problem of TB detection. TB doctors prepared recommendations, which were published as a pocket manual 'Detection of tuberculosis of various locality' for medical workers of the general medical services. It reflects: clinical characteristics of TB symptoms; types of laboratory tests; TB detection among risk groups through radiography; methods of TB detection in children; extra-pulmonary TB diagnosis. The difficulties of TB control strategy are that the patient should make the first steps toward TB detection. The words 'save yourself and thousands will be saved around you' require further development of health education in community.

**PS-491-535 L'allergie médicamenteuse aux anti-tuberculeux**

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Les anti tuberculeux (ATB) peuvent être responsables de nombreux effets indésirables conduisant au changement du régime thérapeutique. Le but du travail est de préciser la fréquence de l'allergie (A) aux ATB, et proposer une attitude pratique devant ces manifestations. Sur 1011 malades hospitalisés pour tuberculose pulmonaire de 1990 à 2003, 16 cas d'A aux ATB sont notés : 1,58%, au pyrazinamide : 37,25%, à la rifampicine : 31,25%. L'atteinte cutanée est plus fréquente (81,25%), souvent bénigne avec urticaire ou érythème. Un cas de thrombopénie et un cas d'anémie hémolytique ont été notés. Le délai moyen d'apparition de ces manifestations est de 8 jours. La conduite était l'arrêt des ATB et leur réintroduction un par un pour éliminer le produit en cause. Le recours aux anti-H1 a été nécessaire dans 5 cas. Un malade a nécessité une hémodialyse. La durée du traitement ATB était en moyenne de 9,5 mois. L'évolution était toujours favorable. L'hypersensibilité peut constituer un effet indésirable incitant à l'arrêt de ATB avec difficultés thérapeutiques.

**PS-520-574 The efficiency of the control system of tuberculosis patients in cooperation with public health centers**

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**Objectives:** To evaluate the efficiency of the control system of tuberculosis patients in cooperation with public health centers, not using DOT.

**Subjects:** 193 tuberculosis patients with smear-positive were enrolled in this study from April 2002 to March 2003 in our hospital. These patients underwent WHO short-course chemotherapy including pyrazinamide.

58 patients, who were at risk of treatment interruption, were selected according to our institute criteria and were followed up by public health nurses after their discharge.

**Methods:** We evaluated the treatment outcome of tuberculosis patients in our hospital.

**Results:** Treatment outcomes were as follows: 155 (81%) were cured, 18 (9%) completed their treatment, 7 (4%) died and 12 (6%) were defaulted or transferred out. The level of treatment success was 90%, which was higher than that of the previous year (84%).

**Conclusion:** TB control based on the cooperation with public health centers was effective in our region. In each country, it is important to establish the appropriate system of tuberculosis control according to the circumstances of public health care.

#### PS-532-659 Evaluation of the effects of an incentive program on treatment adherence of TB patients in Ivanovo, Russia

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**Introduction:** In 1995, WHO and the Ivanovo TB control program started a DOTS demonstration project in Ivanovo. Results fell short of the WHO target of 85% successful treatment partially owing to the high default rate. To improve adherence, an incentive program was implemented beginning in July 2000.

**Objectives:** To evaluate the effects of an incentive program on treatment adherence among tuberculosis patients in Ivanovo, Russia.

**Methods:** Data were collected from medical records and treatment cards on all patients registered for TB treatment in year 2000 in Ivanovo Oblast.

**Results:** Comparing 6 months before and after implementation of the incentive program, the median number of missed doses per month decreased from 2.1 in 1959 patient-months to 0.9 in 2557 patients-months. Within 1 year missed doses increased again. Qualitative analysis showed patients and providers became accustomed to the incentive.

**Conclusion:** The incentive program appeared to improve adherence, but the improvement wasn't sustained without further intervention.

#### PS-630-696 Hospitalization for tuberculosis (TB) in New York City (NYC)

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**Introduction:** The majority of patients with TB in NYC are diagnosed as in-patients. Many could be diagnosed as out-patients.

**Objective:** To determine factors associated with initial TB hospitalization in NYC and the proportion of admissions that could have been avoided.

**Methods:** Patients with TB confirmed during April-June 2003 were reviewed. Data was collected through medical records review and patient interviews. Patients with a definite need for hospitalization were those meeting one or more of these criteria: clinically unstable on admission, receiving home/nursing care, homeless, nursing home resident, alcohol/drug user, or suspected of a severe form of TB.

**Results:** Of 316 confirmed TB patients, 71% were initially admitted. Hospitalized patients were more likely to be black-non-Hispanic, US-born, homeless, HIV-positive, alcohol/drug users, medically insured, have a positive AFB smear, culture or nucleic acid amplification test for *M. tuberculosis*, both pulmonary and extra-pulmonary disease, a cavitary chest X-ray, and to die during hospitalization. Our analysis showed that, based on the above definition of justified hospitalization, 49% of hospitalized TB patients had a documented need for hospitalization.

**Conclusion:** More than half of hospitalizations for TB could be avoided. Better guidelines for management of TB patients in the out-patient setting need to be developed.

#### PS-672-745 Gender disparity in TB treatment outcomes in Gugulethu, South Africa: implications for health systems

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**Introduction:** Reported incidence of Tuberculosis (TB) is consistently higher amongst adult men than women. Gender differences in health-seeking behavior, perceptions of stigma and access to care have been implicated. Within the health system, the potential of gendered institutional norms for creating disparate experiences for men and women has been posited.

**Objectives:** To assess gender-specific treatment outcome amongst a cohort of TB patients in a highly endemic area.

**Methods:** Patients initiating TB treatment at NY1 Clinic Gugulethu, Cape Town, South Africa between 1 April 2002 and 31 March 2003 were followed prospectively. Interviews were conducted at intake, 2 and 6 months.

**Results:** Amongst  $n = 822$  patients enrolled, the male:female ratio was 1.4:1. At six months  $n = 479$  were cured/completed (M:F1.1:1), with 63 still on treatment. Excluding those who died, were transferred out, discharged (not TB), refused or imprisoned, male patients were disproportionately lost to follow-up ( $n = 106$ , M:F3:1). Male defaulters interviewed indicated that their itinerant lifestyle and/or employment interfered with long-term treatment adherence.



**Conclusion:** Current case-finding and case-holding practices, including DOT, meet patient needs differentially. Given increasing HIV-related TB incidence, gender sensitive services must reach women and retain men proactively. Extended workplace services plus a system permitting multisite service utilization would further these aims.

**PS-681-754 Integrating evaluation into project implementation: the Binational Referral and Patient Management Pilot Project (BRPMP)**

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**Introduction:** The BRPMP was designed to improve patient tracking and TB therapy completion among patients traveling between Mexico and the US. Evaluation activities have been an integral component of the Project.

**Objectives:** To evaluate the feasibility, effectiveness, and cost of the BRPMP.

**Methods:** A two-phase evaluation was designed, the results of Phase I informing the design of Phase II. Data sources include monthly progress reports, site visits, BRPMP databases, focus groups, and interviews. Stakeholders buy-in and input has been continually sought.

**Results:** Phase I identified missing links in the referral chain between the two countries, confirmed patients' acceptance of the referral system, and highlighted the need for deported TB suspects to be included in the Project. Phase II, focusing on these issues, will be implemented by August 2004.

**Conclusion:** Ongoing evaluation helps pinpoint difficulties and challenges, improve operations, and document lessons learned to inform Project expansion and replication decisions.

**PS-682-755 DOTS expansion of TB detection in NTP Mexico**

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**Background:** Mexico records more than 16 000 new pulmonary TB cases and 2900 deaths per year. The National TB Program is a priority in the National Health Program 2001–2006, with the vision 'A México Free of Tuberculosis'. It consists of three substantive and six strategic components; the first of the substantive components: 'TIMELY PROTECTION', to guarantee the case finding between respiratory symptomatic patients.

**Method:** During 2001 to 2003, have been performed intensive activities of case finding with fine sieve in selected groups through epidemiological focusing door

to door, epidemiological enclosing, groups of people with HIV/AIDS, indigenous and prisoners.

**Results:** With successful actions of DOTS expansion including community leaders participation, volunteers and social organizations, has been performed 127 operations in population, identified 789 new cases between respiratory symptomatic, case finding door to door (3%); epidemiological enclosing (1.3%); HIV/AIDS (1%); indigenous (9%); prisoners (3–14%), 100% enter to DOTS. This study, and inclusion of new cases identified to the treatment have avoided 11 835 of infected persons and may be almost 592 new cases, and 12 MDR cases.

**Conclusion:** Although the active search is complex, the need to be prioritized in focus has been demonstrated, moreover to DOTS expansion, making the control simple to achieve with support of the society.

**PS-941-1016 Delay to treatment of pulmonary tuberculosis in Montreal**

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In the management of Pulmonary Tuberculosis, delay to time of treatment is clearly an important issue for individual and public health: the longer a patient remains in the community before diagnosis and treatment, the greater the morbidity and likelihood of a significant outbreak. The phenomenon of delay-to-treatment is well-recognized, but more thoroughly studied in the developing world than in developed countries, where comprehensive surveillance programs have tended to insure promptness of medical response. However, with the increasing of movement of populations across borders and concomitant breakdown in continuity of preventive health care, health conditions in the cities of the developed world have come to reflect in part the social and political conditions of countries from which they receive immigrants.

The present study will address the delay-to-treatment in Montreal, Quebec from 1997–2002. In Canada, Tuberculosis is a reportable illness, and information is maintained on all cases in a province-wide database (MADO—Maladies Infectieuses à Déclaration Obligatoire). We will examine the delay-to-treatment based on documented onset of symptoms, date of first medical encounter, date of diagnosis, and date of report to Santé-Publique, with calculation of intervals reflecting delay attributable to the patient, to the community physician or health care workers, and to the diagnostic and Public Health apparatus. Multivariate statistical analysis will be undertaken to establish correlation among important demographic variables (sex, country of origin, lack of linguistic competence in French or English, time of residence in Canada, level of education and socio-economic standing) and significant intervals in the initiation of treatment.

Preliminary results show, as expected, a large representation of recent immigrants to Canada from countries with endemic Tuberculosis. With the combination of statistical database studies and detailed chart review, supplemented by patient interviews where possible, we hope to show a measurable impact of patients' personal history and circumstances on the public health realities of the city.

## **POLICY AND PROGRAMME IMPLEMENTATION: TB CONTROL IN SPECIAL POPULATIONS AND INSTITUTIONS**

### **PS-124-158 Adherence to TB treatment in the nomadic population of West Pokot District, Kenya**

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**Setting:** The Manyatta at Sighor, West Pokot District and the Chest Clinic, Kapenguria district hospital.

**Objectives:** To determine the knowledge of TB patients on TB and treatment, to determine the proportion of patients who miss treatment for more than one month and to determine the proportion of patients whose drug intake is observed.

**Design:** Cross-sectional study conducted between October and December 2003 with use of questionnaire as exit interviews. Results were analyzed using SPSS.

**Results:** Interviews completed by 398 patients: males constituted 62%, only 17% thought TB is caused by Germ and 47.5% did not know how long they would be on treatment. Of the patients in the District Hospital 53% were not observed while on treatment. More than 62% of the patients had missed treatment in varying times due to several reasons including too many tablets (35.5%) and side effects (25.5%).

**Conclusion:** Adherence to treatment in the nomadic population was poor due to several reasons. A lot of patients had little knowledge on length of treatment and cause of TB.

### **PS-172-208 DOTS implementation at the garment industries in Bangladesh**

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**Introduction:** The garment industry is one of the major industries in Bangladesh, employing almost 2 million people of whom over 80% are females between the age of 18–45 years. Implementation of DOTS addresses one of the health needs of a large vulnerable group.

**Objective:** Include the garment industry in the DOTS program in order to improve health of its employees.

**Method:** In 2000 DOTS was implemented in Young-one company garment factory in Chittagong which employs over 24 000 employees. Staff were trained by the NTP which also provides drugs and laboratory supplies. The factories (para) medical staff identify TB suspects, carry out smear microscopy and deliver treatment under DOT. During 2004 the services were extended to the family members of the employees.

**Results:** During the first 2 years on average 126 smear-positive cases per 100 000 employees were diagnosed. This is over three times the case detection among females of the same age group in the general population.

**Conclusion:** The extent of the TB problem, as well as the large group of concerned employees has urged the garment industry to extend DOTS. During World TB Day 2004 DOTS services were initiated in the Dhaka Export Processing Zone, involving over 50 000 employees.

### **PS-260-286 Tuberculosis screening in a prison in Hong Kong**

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**Objective:** To investigate the possible role of chest X-ray screening in prison.

**Background:** There is no regular tuberculosis screening programme for long-stay prisoners in Hong Kong.

**Method:** In a maximum security prison, all prisoners without chest X-ray examination in last six months as at 31/10/2001 were screened.

**Results:** 814 male prisoners aged  $34.6 \pm 9.6$  (SD) years underwent CXR screening. Of 53 cases (6.51%) with radiographic abnormalities, 10 active tuberculosis cases (8 culture-negative, 2 culture-positive) were diagnosed, at an overall yield of 1.23% (95%CI 0.59–2.26%). There was no statistical difference in age, ethnicity, place of birth, and residency status between those with or without tuberculosis (all  $P > 0.05$ ). Incarceration  $\geq 2$  years, staying in current prison  $\geq 2$  years and no CXR within 2 years were associated with tuberculosis in univariate analysis (all  $P < 0.05$ ), but only the last remained an independent predictor (OR 16.8, 95%CI 2.1–132.9,  $P = 0.008$ ) in multiple logistic regression. Among that group, the yield was 3.1% (95%CI 1.42–5.89%). Among those screened, no further cases were detected in the subsequent 2 years.

**Conclusion:** Two-yearly X-ray screening may worth further evaluation in prison.

### PS-290-325 Prevalence of pulmonary tuberculosis and comparative evaluation of screening strategies in a Brazilian prison

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**Objectives:** To determine the prevalence of active pulmonary tuberculosis (TB) and to assess the performance of several screening strategies.

**Methods:** In a cross-sectional study, all inmates ( $n = 1171$ ) from a Rio State prison underwent chest radiographic screening; subjects with abnormal findings had sputum smear examination and culture of sputum. Taking this strategy as the reference, we assessed three targeted screening strategies to identify TB suspects: strategy 1: cough  $>3$  weeks; strategy 2: WHO score  $>5$ ; strategy 3: presence of at least one potentially TB-related symptom.

**Results:** The prevalence of TB was 4.5% overall (48/1059), and 3% among patients with no TB treatment history. If TB suspects identified by targeted screening had smear examination alone, 37 (86%) of the 43 cases would have been missed by strategy 1, 36/43 (83.7%) by strategy 2 and 34/43 (79.1%) by strategy 3. If TB suspects had smear examination and, for smear-negative subjects, chest radiography, respectively 28/43 (65.1%), 22/43 (51.1%) and 13/43 (30.2%) of cases would have been missed.

**Conclusion:** All three targeted screening strategies were unreliable. Given the importance of early TB diagnosis in such overcrowded and highly endemic settings, routine radiography-based screening may be warranted.

### PS-304-335 Partnership and policy developments in the treatment of TB in the homeless: the London TB Link Project

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**Introduction:** Approaches to TB must address the underlying social and economic problems that complicate treatment. For example, 36% of patients at the Middlesex hospital presented with at least one of six risk factors in 2002/3 known to affect treatment outcomes

including: HIV (14%); housing need (36%); alcohol/drug use (13%); mental health (6%); economic (48% receiving social security benefits/nil income).

**Objectives:** The LINK project aims to develop an effective model of care for homeless people with TB to secure better clinical and social outcomes. This is being achieved through the development of a network of local service providers and the role of a link worker to enable access to the network.

**Methods:** A process evaluation employing both qualitative and quantitative methods. We share our experiences of joint working with allied community services. The relation between TB control and developments in local policy making are discussed.

**Results:** A number of 'institutional' barriers to the treatment of TB are explored suggesting the limitations of link worker models in the absence of general policy initiatives.

**Conclusion:** The growing complexities of managing TB in marginalised urban communities embodies the need for effective joint working between the housing, health and voluntary sectors.

### PS-333-359 Proportion of different case finding methods in detection of tuberculosis cases in prisons of Georgia

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**Introduction:** ICRC has supported the Ministry of Justice to implement a 'Tuberculosis Control Project in Georgian Prisons' since 1998.

**Objectives:** To determine which method of screening was more effective in detection of Pulmonary Tuberculosis (PTB) in 2001–2003 years.

**Methods:** Combination of Passive (PS), Entry (ES) and Massive (screened of all imprisoned population) (MS) screenings were conducted for identification of suspect patients for PTB. Selection of suspect prisoners was based on clinical Questionnaire. Diagnosis was confirmed bacteriologically and sputum smear positive (ss+) cases received DOTS.

**Results:** Proportion of PTB suspects through MS was 24.3%; 38.2% and 55.7% in 2001–2003 years. Proportion of PTB suspects through ES and PS together were per year: 75.7%; 61.8% and 44.3%. In 2001–2002 MS in colonies was done once a year, in 2003 - every 6 month. ES was weekly and PS - daily activity.

**Conclusion:** ES and PS together were more cost-effective, identified more cases of PTB and provided higher detection rate of ss+ cases than MS when it was done once a year. Only more frequent (every 6 month) MS rounds showed higher detection rate, which still is not significantly different than ES and PS proportion together.

**PS-335-362 DOTS programme in prisons of Georgia in 2001–2003 years**

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**Introduction:** ICRC has supported the Ministry of Justice to implement a 'Tuberculosis Control Project in Georgian Prisons' since 1998.

**Objectives:** To monitor the trend of Pulmonary Tuberculosis (PTB) in prisons of Georgia in 2001–2003.

**Methods:** Combination of Passive (PS), Entry (ES) and Massive (screening of all imprisoned population) (MS) screenings were conducted for identification of suspect patients for PTB. Selection of suspect prisoners was based on clinical Questionnaire. Diagnosis was confirmed bacteriologically and sputum smear positive (ss+) cases received DOTS.

**Results:** In 2001 the number of suspect cases of PTB was 3106 inmates and ss+ patients were 410 (13.2% out of all suspects). In 2002 these data were respectively: 3271 suspects, and 324 ss+ patients (9.9%). In 2003: 1840 suspects and 193 ss+ patients (10.5%).

**Conclusion:** The trend is the reduction of the number of suspect prisoners and ss+ patients. In 2003, compared to 2001, suspect cases of PTB decreased by 40.7% and the number of smear positive patients decreased by 52.9%. The proportion of ss+ patients out of suspects also decreased from 13.2% in 2001 to 10.5% in 2003.

**PS-357-380 Tuberculosis outbreak in a psychiatric clinic in Rio de Janeiro, Brazil**

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**Background:** There is scarce data regarding tuberculosis (TB) in psychiatric settings. At a psychiatric clinic, 18 TB cases were reported in 2002.

**Objective:** To describe TB prevalence and rate of infection among patients and employees during an outbreak investigation between January 2003 and January 2004.

**Methods:** All in-patients ( $n = 374$ ) and employees ( $n = 200$ ) were submitted to a tuberculin skin test (TST), sputum smear, culture with susceptibility testing and chest X-ray.

**Results:** Of the 374 in-patients, 336 had TST done and 185 (55%) were positive ( $\geq 10$  mm). Among 127 initially negatives, 21 (16.5%) converted after 6 months. TB was diagnosed among 20 in-patients, which gives an incidence rate 31 times greater than the city inci-

dence rate in 2002 (113/100 000 population). Bacteriological confirmation was obtained in 11 (58%) of the 19 pulmonary cases. Among employees, 127 performed TST. In 46 (36%) the result was positive and 6 (16%) converted in 6 months. TB was not found among employees. Treatment for latent TB was started in 27 subjects.

**Conclusion:** TB incidence, TB infection and tuberculin conversion rates were very high, suggesting the high risk transmission environment and the need to increase infection-control practices in this setting.

**PS-447-485 Access to TB services in Nepal: a study in a conflict and in a non-conflict area**

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The study was to determine amongst TB patients, whether the existing burden of disease, physical availability, financial affordability, acceptability, geographical accessibility, and level of civil conflict affect the access to TB services in areas with conflict (CA) and without civil conflict (NCA). A questionnaire was administered to 180 randomly selected TB patients in each of the Districts of Lalitpur (NCA) and of Dang (CA). The data was analyzed using the chi-square test and logistic regression; with only  $P < 0.05$  being considered as statistically significant. By univariate analysis, only one variable was associated in both areas, i.e. dogmatic behavior of health workers. In the NCA all of the following were associated with access: knowledge of TB services, and of drugs; within walking distance; availability of separate examination rooms and of microscopy; satisfaction with services. In the CA the additional factors were: female staffs in health facilities; satisfaction with services; presence of closures and killings were associated with access. Logistic regression model shows that only knowledge about TB drugs, and dogmatic behaviors of health workers are statistically associated with access. Based upon the findings, plans were recommended for implementation by District Health Facilities.

**PS-475-513 Family DOTS in Middle Hill Districts of Western Nepal**

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**Introduction:** A study was conducted in April 2001 to respond to the difficulty of Tuberculosis (TB) patients affording time off work to come for Directly

Observed Treatment Short Course (DOTS) in the two hill districts of Nepal where a flexible DOTS strategy is adopted since 1999.

**Objectives:** To assess family based DOTS as an alternative to daily DOTS in hard to reach area and to interpret its relevance while implementing the flexible DOTS strategy.

**Methods:** The data were collected by reviewing 220 patients records who were registered for treatment between July 2000 and March 2001; interviewing 38 patients, health workers, family and community; and observing 11 DOTS centres.

**Results:** Although DOTS protocol is not being implemented thoroughly as per the guidelines, the outcome of family based DOTS were encouraging and nearly the equal numbers of TB patients from hard to reach area were appeared to seek their TB treatment through family based DOTS. The majority of patients (86%) preferred family based DOTS and results showed an 88% treatment success rate under the family based DOTS strategy.

**Conclusion:** Family DOTS is equally beneficial to the patients who are living in hard to reach area.

#### **PS-531-592 Evaluation of the district tb control programme by the Rapid Appraisal Method**

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**Aim:** To evaluate the performance of the district tuberculosis control programme at Kabokweni district in Mpumalanga province of South Africa.

**Objective:** To assess the performances of four major aspects and its components of TB control programme at the Primary Health Care services.

**Design:** This was a descriptive cross-sectional study, which includes a cohort analysis. The principle adopted was the Rapid Appraisal Method. Selected indicators were used to evaluate the programme components.

**Results:** District support was very poor. Only 37% of professional nurses had adequate knowledge to manage a tuberculosis suspect. Information in TB register was inadequate. Involvement of community health workers was poor. 245 patients were included in the cohort analysis. 96% were diagnosed by sputum microscopy. Only 50% of patients were under direct supervision. Cure rate was 41% and interruption rate was 31%.

**Conclusion:** Rapid appraisal method can yield reliable information of the performance of Tuberculosis control programmes. Even though the treatment outcome indicators were well below the national programme objectives overall assessment showed that DOTS is a very successful strategy for TB control.

#### **PS-550-609 Training and advocacy for improved tuberculosis control in prisons in Latin America and the Carribean**

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**Introduction:** An International Workshop on TB in Prisons brought together Ministry of Health and Ministry of Security officials from Latin America and the Carribean for training and advocacy.

**Objectives:** To familiarize ministry officials with TB control issues specific to prison settings; to promote collaboration between national TB programs and the prison sector.

**Methods:** A 3-day workshop took place in August 2003 in Honduras. Officials from 11 countries attended, as well as speakers from 4 countries and the International Red Cross. The lecture content was based on WHO prison guidelines and experiences in Brazil, Colombia, Mexico, Venezuela, and Honduras, where GTI is sponsoring a national project to implement DOTS within the prison system. Participants toured a local prison, developed action plans, and received written and electronic reference materials.

**Results:** Participants developed an 11-point document committing themselves to improving TB control within their prison systems. A follow-up conference is scheduled for August, 2004 in Lima, Peru, to measure progress.

**Conclusion:** This collaboration between a US university and PAHO was successful in raising awareness of the problem of TB in prisons from health and human rights perspectives, and providing participants with tools for implementing their own programs.

#### **PS-669-742 Tuberculosis hospitalization in a large urban center**

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**Introduction:** Tuberculosis is currently treated in out-patient services, and hospitalizations are left for more severe cases or for patients with social problems. In large urban centers the tuberculosis hospitalization seems to be higher than in others cities. From 2000 to 2002, respectively 1885, 2473 and 2493 patients were hospitalized in São Paulo city. The total number of tuberculosis cases were 6667, 6660 and 7331.

**Objectives:** To calculate indicators of morbidity and mortality for tuberculosis in-patients from 2000 to 2002.

**Methods:** Place: São Paulo city with 10 millions inhabitants. Data are from the São Paulo State information system for tuberculosis (EPI-TB). Indicators of morbidity and mortality were calculated for in-patients.

**Results and discussion:** The in-patient rate was 18.1, 23.5 and 23.5/100 000. The mortality rate was 5.5, 4.1 and 5.3/100 000. The fatality rate was 30.9, 17.5 and 22.6%. These indicators show us the dangerous situation of tuberculosis in the hospitals. Reasons to explain these indicators are probably delay in diagnosis and to start treatment.

**Conclusions:** It is therefore necessary to improve case-finding in hospitals, start early treatment and implement others infection control measures.

#### **PS-722-796 Expansion of DOTS in medical institutions: lessons learned in Bangladesh**

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**Introduction:** National Tuberculosis Program expanded DOTS services in 16 medical institutions in collaboration with the NGOs. In 2003, BRAC and Damien Foundation jointly established a DOTS center in Mymensingh Medical College hospital. Following this experience, BRAC expanded DOTS services to 13 medical college hospitals in 2004.

**Objectives:** Establish linkage between community based DOTS services and medical institutions to increase the case detection and cure rates to 70% and 85% respectively by 2005.

**Methods:** A DOTS corner is established in every medical college hospital and inaugurated on World TB Day 2004. All doctors were given orientation on DOTS strategy. Trained staff is posted to each hospital. Sputum examination of TB suspects is done at hospital laboratory. After examination, the diagnosed cases are referred to the respective upazila (sub-district) or district chest clinic in case of urban areas. Patient residing closely to the hospital is given DOT from hospital.

**Results:** During last 4 weeks, a total of 55 TB patients were diagnosed. Of them, 29 were new sputum positive, 3 retreatment sputum positive, 13 sputum negative and 10 extra-pulmonary cases.

**Conclusions:** DOTS expansion in medical institutes is found to be effective to involve medical practitioners in DOTS strategy in Bangladesh.

#### **PS-799-872 DOTS strategy in isolated communities**

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**Boquerón:** 92 000 km<sup>2</sup>.

**Population:** 40 452; 44% indigenous people, mainly agriculture

**Population affected by tuberculosis:** 99% indigenous.

**Introduction:** In 1995 for the first time the Ministry of Health contracted a physician for the Tuberculosis (TB) Programme Coordinator. A TB Team was organised and together with the local Government many vis-

its were made to control TB. In 1999 the incidence rate reached 653 (per 100 000 inhabitants), the national rate was 38.

**Objective:** To reduce TB and prevent multidrug resistance (MDR) applying the DOTS strategy.

**Methods:** Visits to the communities, more than 35 000 km per year to all communities, selection of the Local Health Workers (LHW) and training of the communities, the LHWs receive intensive training every semester for two days, there after regular visits in their work with ongoing training in: control of all coughing patients, collecting materials, fixing the slides to be sent to Laboratories, and applying DOTS strategies.

**Results:** In the year 2000 the National TB programme selected Boquerón to be one of the first geographical area in Paraguay to apply the DOTS strategy. The LHWs prepare the slides, they supervise together with the trained community members the patients. The incidence rate (IR) started to fall, so the success rate. In 1999: IR 653, success rate (SR): 89%; 2000: IR 315, SR 98%; 2001: IR 238, SR 95% (when Deutsches Aussaetzigen Hilfswerk, Wuerzburg [DAHAW] introduced their support to the TB/leprosy Programme in Boquerón). 2002: IR 124, SR 93%. The default rates were: 8%, 4%, 1% and 3% in these years. The DOTS strategy is very useful, the community participation is vital and very helpful.

#### **PS-800-873 Correlation of monitoring indicators with improving the results of the TB control program of the penitentiary system in the Republic of Kazakhstan**

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**Introduction:** The study examined the correlation between improvement in checklist monitoring indicators and results achieved in TB control in the penitentiary system.

**Objective:** To demonstrate that selected monitoring indicators measure quality of TB control activities as reflected by better program results.

**Methods:** Retrospective analysis of data from monitoring visits and WHO indicators on microscopy diagnostics, registration, statistics, drug supply, hospitalization, and patient outcomes.

**Results:** Monitoring data improvements correlated with improved quality of TB control activities and higher ratings on standard program indicators. Comparative data analysis showed monitoring indicators improved 30–50%, reaching the ideal level of 100% on a number of indicators. For example, the indicator 'Percentage of DOT observance' at the beginning of the program was 60%, and by the end of the program

reached 100%. That improvement, along with improvement measured by other indicators, correlated with smear sputum conversion among new smear-positive cases increasing from 79% to 88.8% for the same time period. This intermediate treatment outcome is a clear indicator of program performance.

**Conclusions:** Regular standardized monitoring with using established checklists based on the methodology of Quality Improvement in Health Care enables and encourages the analysis of data to identify problems the solutions to which result in higher overall program achievement.

**PS-821-893 Gradual integration is gradual sustainability: an evaluation of BNMT supported TB Control Programme in eight hill districts of eastern Nepal**

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**Introduction:** Observational studies conducted between 1998 and 2002 to evaluate the impact of integration of tuberculosis control programme of BNMT with the National Tuberculosis Control Programme (NTP) of His Majesty's Government of Nepal.

**Objectives:** To provide a critical review of impact of integration of NGO-supported TB control programme.

**Methods:** For integration evaluation purposes, both primary and secondary information have been collected using qualitative and quantitative techniques.

**Results:** In the second year after integration, the following result were seen:

- Case detection rates increased (varying from a low of 17% to a high of 61%).
- The quality control (QC) showed very high agreement rate. The sputum conversion rate increased to 83.2% from 81.6%.
- Treatment success rate in study-districts increased remarkably.

**Conclusion:** Although integration as a process has been established in the study-districts, it needs to be strengthened technically and managerially and that will take some more years.

**PS-824-896 Epidemiological and operational situation of tuberculosis (TB) in prisons of the Latin American Region, 2003**

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**Introduction:** Prisoners are a vulnerable population for TB because the high transmission of TB and lack of TB control programs in prisons. In Latin America,

there are scarce epidemiological and operational information about this issue.

**Objective:** To describe the epidemiological and operational situation of the tuberculosis in Latin American prisons.

**Methods:** Transversal study; a questionnaire was sent through the PAHO country offices to the NTP managers of 20 countries. The collection period finishes in June 2004.

**Preliminary results:** Four countries answered the questionnaire. The incidence rate is 956.3/100 000 pop; 96% of the cases are pulmonary and 66% BK (+). The age group most affected is 25–54 years; 92% are male patients. The HIV prevalence in TB patients is 8.5%. Of the BK (+) patients (2002) 49% cured, 69% succeed, and 17% defaulted. All countries perform contact follow up. One country screens the prisoners. Every country follow treatment guidelines; 20% don't apply DOTS.

**Conclusions:** TB rate is 10 times higher in prisoners than in general population. The TB/HIV rate is also higher. Cure is low and default high, which increase drug resistance. There is a need for advocacy and training for DOTS in Latin American prisons.

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**PS-860-933 Improving TB control program in prisons of Kazakhstan through application of a quality improvement approach**

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**Objectives:** To generate knowledge and experience on implementing methodologies in quality improvement and assurance; strengthen quality of TB control activities through improving job performance by use of quantitative indicators; create TB control model for quality improvement in prisons

**Methods:** Retrospective data analysis of pilot program effectiveness during base-line assessment and midterm review showed need to improve both managerial and individual medical worker's job performance. Therefore we have developed innovative curriculum 'Improving health care quality within the DOTS strategy' including a quality evaluation model of the TB control system, a problem solving methodology, and a quality assurance triangle. Curriculum is focused on process indicators of job performance coupled with analysis of TB case notification rate, conversion rate and treatment outcomes.

**Results:** Observance of smear sputum collection protocol increased from 60 to 100%; saliva in diagnostic material decreased from 9 to 4%; correct TB case classification increased from 50 to 100%; and observance DOT protocol increased from 60 to 100%

**Conclusions:** TB program effectiveness can be in-

creased through improving job performance as measured and encouraged by specific quality indicators. TB education for medical workers and health managers should include on quality improvement methodology and use of quality indicators.

#### **PS-861-934 Laboratory service development in penitentiary system of Karaganda oblast**

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**Objectives:** Establish effective laboratory service in penitentiary system of pilot site.

**Materials and methods:** Based on laboratory network evaluation a plan of interventions was developed including material resources, training of laboratory staff, establishing organization structure and quality control, and monitoring and supervisions of laboratory system activities. The information management system for clinical aspects of the program was then developed with the laboratory service.

**Results:** Bacteriological laboratory was equipped and standardization of procedures and reporting forms was instituted according to the requirements of National laboratory service of the country. Sputum smear preparation protocol by the Ziehl-Neelsen method is now applied in 100% of cases, and compared to 25% of cases in 2001. The system of horizontal control of laboratory examinations quality was established within penitentiary system with vertical quality control of laboratories by the civil sector. As a result, the percentage of confirmed consistency of laboratory results reached 90%. As a result, feedback with clinical service has been improved and the proportion of saliva in sputum samples collected has decreased 4% in 2003. Effectiveness of infectious TB patient identification has increased from 4.6% in 2001 to 10.8% in 2003.

**Conclusions:** To improve laboratory component effectiveness of TB control program in the penitentiary system it is necessary to assure adequate materials provision, regular specialists training and supervision focused on individual work performance, as well as through feedback from clinical services.

#### **PS-863-936 Effective implementation of TB control program in prisons of Kazakhstan via 'Monitoring-Training-Planning (MTP)' methodology**

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**Introduction:** MTP is a methodology to implement health programs—it helps people to get things done

in their facilities and learn useful techniques for meeting their goals and responsibilities.

**Objective:** to demonstrate a meaning of implication of 'MTP' methodology to improve effectiveness of TB control activities in prisons.

**Materials and methods:** based on data obtained by means of staff supervision and routine program monitoring reports from worksites a document was made where obtained data was analyzed and based on this information potential obstacle were defined, developed recommendations, determined a target group, and made changes in content and methodology of the following training. Results of data analysis were disseminated to appropriate audience to get feedback. After that 'MTP' session was conducted, where in Monitoring segment - presented results of correlation analysis of TB control program aspects. In Training segment—conducted revised training course and developing a deeper understanding of the problem and understanding alternative solutions. In Planning segment—participants prepare a calendar of activities to be carried out within the time-frame specified

**Results:** Effectiveness of case detection through microscopy increased to 10,8%; smear conversion rate increased among new TB cases to 88,7%; number of relapse SS+ case decreased; cure rate increased on 13% during the first year of the project; mortality rate decreased to 40%, incidence rate decreased to 27%

**Conclusion:** 'MTP' is effective tool to improve quality of TB control activities.

#### **PS-870-943 Treatment outcomes of tuberculosis patients under DOTS and Non-DOTS**

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**Aim:** 1) To compare outcomes of tuberculosis patients treated under DOTS and non-DOTS conditions in private and public hospitals; 2) To increase adoption of DOTS by hospital doctors.

**Introduction:** Resistance from some doctors to adopt DOTS may hinder efforts to establish a uniform TB control program, and may lead to MDR-TB. Anecdotal accounts point to the lack of knowledge and awareness of the benefits of DOTS among this group.

**Methods:** Review of medical records of TB patients and NTP registries in 7 hospitals is underway to determine case management, diagnosis, treatment prescribed, duration of treatment, follow-up, DOTS and outcome. Treatment compliance and outcomes will be compared and results will be shared with the targeted group.

**Results:** Results are pending.



**Conclusion:** In Yogyakarta, hospital doctors manage numerous TB patients. From an epidemiologic and individual standpoint, these need to implement.

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#### **PS-910-985 Post-release TB treatment among Russian prisoners**

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We investigated post-release follow-up rate to TB dispensaries for prisoners with active TB in St. Petersburg, Russia. We found that only 28% of 80 active TB patients released from prison in 2002 had a single post-release visit to the out-patient TB dispensaries. We also examined characteristics of and barriers to medication adherence for prisoners and former prisoners with active TB. Self-administered surveys were administered to 100 TB patients (60 prisoners and 40 released prisoners). Preliminary results show that 90% of prisoners expressed the desire to continue with their TB treatment once released, with 91.5% of the sample stating that completion of their TB treatment was 'very important.' Despite the optimistic outlook, few participants had plans for a job or money for food and clothing after release. Of the imprisoned sample, 41.5% stated that they had experienced a disruption in their TB treatment. The most common reasons were transfer among correctional faculties, lack of adequate supply of medication at the facility and a reluctance to take medication because patients did not 'feel sick.' Our next step is to design and pilot test an intervention that identifies soon-to-be released prisoners and offers them an array of incentives to attend a TB dispensary and to complete treatment.

## **MONDAY 1 NOVEMBER 2004**

### **THEMATIC SLIDE PRESENTATIONS**

#### **EDUCATION, ADVOCACY AND SOCIAL ISSUES**

##### **TS-276-338 A framework to understand the 'new' stigma of tuberculosis**

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This paper reviews the old and the new stigmas that surround tuberculosis. It develops a conceptual framework for understanding the consequences of the new stigma(s) associated with TB. We examine the history of TB stigma from the early 20th century public health campaigns to the emerging idea that TB now carries HIV stigma, with its associations with fear, discrimination, morality and risky or illegal behavior. The older stigma symbolized TB as a sign of extreme poverty and dirt, which led to the notion of TB as 'that sentinel disease of poverty and decline.' The newer stigma is the stigma of being an opportunistic infection to AIDS. Indeed, TB and HIV are so closely associated in many people's minds, that they are virtually regarded as the same thing. An implication of this new stigma is its potential impact on treatment seeking for TB, which could have direct negative consequences for the MDG of reducing the TB burden. The paper reviews the stigma literature, and develops a framework to summarize our understanding of stigma and TB today. This includes the impact of stigma on NTPs, as well as how communication strategies can potentially help reduce stigma. Finally, a series of suggested directions for research are provided in the context of TB advocacy.

##### **TS-368-450 Perception and practices among vulnerable populations toward tuberculosis (TB) and continuation phase treatment compliance in Romania**

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**Objective:** To identify perceptions and practices toward TB and continuation phase treatment compliance among vulnerable populations in Romania, which has the region's highest TB burden. Vulnerable populations include poor Romanians, poor Roma, TB patients in continuation phase and their families.

**Materials and methods:** Quantitative research consisting of 600 KABP surveys (approximately 150 each) with Roma, poor Romanians, discharged TB patients and family members during January 2004 in Ilfov county, Neamt county and Sector 5 of Bucharest city in Romania.

**Results:** Perceived causes of TB included a cold or flu, sharing space or objects with an infected person, and other interpersonal contact, including blood and at birth. TB patients also listed excess work and smoking heavily. Knowledge about TB was lowest among Roma and women and highest among TB patients. Cough and fatigue were the most common TB symptoms for which care was sought. Younger people were likely to avoid hospitalization; women were almost twice as likely as men to refuse it. Key reasons included loss of work and not understanding the necessity. Stigma was extremely important to each target group; fear of isolation and pity from friends and family were the most significant related perceptions.

**Conclusions:** A lack of understanding of the duration and necessity of continuation phase TB treatment leads to poor compliance. Social stigma from TB must be addressed in health education campaigns. For Roma, poor patient-provider relationships led to little knowledge and treatment seeking. Educational programs, promoting basic knowledge regarding TB and its treatment, and focusing on both vulnerable patients and health providers are required.

#### **TS-469-509 Monitoring and evaluation of sustained clinical performance and tuberculosis management in the South African mining industry**

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**Introduction:** A previous population-based study in South African miners, who have a high prevalence of HIV, showed that around 60% of pulmonary tuberculosis (PTB) detected at autopsy, was undiagnosed during life, despite the comprehensive health services that are available to the miners during employment.

**Objectives:** To reduce missed diagnosis of PTB by means of an intervention program.

**Methods:** A structured, one-page process based performance review flow chart was designed. This intervention was implemented and evaluated in several health care facilities and with a broad range of health care workers.

**Results:** The proportion of cases of PTB diagnosed at autopsy, that were missed during employment, decreased from 65% in 1999 to 54% in 2003. The platinum industry was targeted in particular, as it currently has the highest rates of PTB, and the greatest

decrease was found in these mines: from 65% to 47%. Although health workers were enthusiastic about the intervention program, participation was dependant on a number of identified factors. The greatest improvement took place where the intervention was supported by senior management.

**Conclusion:** This intervention program for improving clinical PTB practice was effective. This method could be utilized in a wide range of health care settings.

#### **TS-583-653 Health education needs regarding tuberculosis among prison staff members, Thailand: implications for prison nurses**

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**Setting:** Nonthaburi, Thailand.

**Objectives:** To assess knowledge and beliefs regarding tuberculosis (TB) among prison staff members.

**Method:** A cross-sectional survey was conducted in 199 prison staff members from 146 prisons. The staff members were asked to participate in the survey when they attended a health training program in July 2003. A self-administered questionnaire was used to assess TB knowledge and beliefs regarding TB susceptibility in prison environment, severity, and benefit-barriers of prison TB control.

**Results:** About 97% of the participants were male and 80% of those held bachelor degrees. The median age was 36 and the median duration of working as the staff was six years. There was variation in TB knowledge. About 94% correctly reported TB symptoms and transmission, however 83% did not agree that TB can be cured. Beliefs regarding TB were low. Correlation analysis indicated that prison staff members who had high level of TB knowledge significantly reported higher level of beliefs regarding TB ( $P < 0.05$ ).

**Conclusions:** The majority of the participants had several misconceptions regarding TB. The findings emphasize that prison nurses need to provide health education for the staff to enable him/her to perform particular roles necessary for TB control in prisons.

#### **TS-629-694 Effect of supportive-educative nursing intervention on self-care behavior among Thai prisoners diagnosed as having pulmonary tuberculosis**

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**Setting:** Two correctional institutions for male drug addicts in Bangkok and Pathumthani.

**Objective:** To compare self-care behaviors between experimental and comparison groups.

**Method:** This quasi-experimental study was pretest-posttest two-group design conducted from March–April 2002. The experimental group comprised 37 patients from the correctional institution in Pathum-thani and the comparison group included 38 patients from another institution in Bangkok. The experimental group attended four sessions for weeks one, two, three, and eight (90 minutes/10 participants/session). Each session included: 1) teaching self-care behavior, 2) discussion about self-care experiences among group members, and 3) use of health diary for self-care. The comparison group received regular health education. Self-care behavior was measured by a questionnaire with 33 items in 6 subscales (transmission, treatment, side-effect, medication adherence, physical exercise, and nutrition).

**Results:** Socio-medical characteristics of participants and self-care behavior before implementing the intervention in both groups were similar. However, after the intervention, self-care behavior in the experimental group (mean score = 109.83) was significantly higher than that of the comparison group (mean score = 82.94) ( $P < 0.05$ ).

**Conclusion:** This study demonstrated that the nursing intervention could enhance self-care behavior. This intervention may be an alternative approach to provide health education for this special population.

#### **TS-706-781 Microfinance results in high tuberculosis cure rates and poverty reduction in rural Cambodia**

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**Objective:** To improve compliance with tuberculosis (TB) medicines and to address poverty as an underlying cause of TB within a comprehensive TB treatment and education program in Cambodia.

**Methods:** A female-managed village bank microcredit scheme targeting patients with TB and their families was established.

**Results:** 8007 women (including 590 from TB-affected families) in 96 villages participated in this microcredit program linked to a non-governmental (NGO)-sponsored TB case management program and received a total of \$653 657 in loans from 1994–2001. Village bank funds provided for the training of 96 Village Health Agents responsible for TB patient identification and community education about TB. Loan repayment rates approached 100% amongst TB-affected bank participants. Compliance and cure rates among TB patients in bank participant families were >95%.

**Conclusion:** The microcredit scheme within a TB case-finding and treatment program enabled TB-affected individuals and others in their community to improve their financial situations while providing for the sustainable expansion of health promotion activities within the community. Activities undertaken by village-bank-sponsored Health Agents promoted links between the community and local health centers. Microcredit should be considered in other resource-poor areas.

#### **TS-882-958 Knowledge, perception and TB transmission restricted behaviors of pulmonary tuberculosis patients in Danang City, Vietnam, in 2003**

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A cross-sectional study of knowledge, perception and TB transmission restricted behaviors among 387 TB patients living in Danang city, Vietnam. Data were collected by using structured interview from February to March 2004. In Danang city, TB is still public health problem. This study was carried out to assess the levels of knowledge, perception and TB transmission restricted behaviors of TB patients and to determine the associations of patients characteristics, knowledge, and perception with TB transmission restricted behaviors among pulmonary TB patients in Danang city. The results of this study showed that majority (75.7%) of the respondents were male, 77.5% were between 15–54 years old, 70.0% were married, and 69.8% had secondary level of education or less. Out of 387 respondents, 79.3% of them had good knowledge, 55.8% had positive perception, and only 44.2% had good TB transmission restricted behaviors. This study found that education, knowledge, perception about TB were significantly associated with TB transmission restricted behaviors among TB patients ( $P < 0.05$ ). As a result, it is recommended that to improve TB transmission restricted behaviors among smear positive pulmonary TB patients; it is essential that all actions must be systematic carried out: policy, health education program to increase knowledge, perception and TB transmission restricted behaviors for TB patients to improve TB transmission behaviors. It is also necessary to strengthen TB knowledge of Health workers so that they can effectively provide TB information to the patients. Besides, health information dissemination regarding TB should be encouraged by using mass media such as radio, television and newspapers to help TB patients, their families, and community to correctly understand TB, develop the right perception about TB, and practice TB transmission restricted behaviors if having TB.

**TS-911-986 A shared responsibility for TB control: DOTS committees succeed in Nepal**

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**Introduction:** Tuberculosis is a major public health problem in Nepal. About 45% of the population is infected with TB. 5000–7000 people die from TB every year. DOTS introduced in 1996 covering 1.7% of the population. Gradually DOTS has been implementing with commitment from the head of state right up to patients at community level.

**Objectives:** To document how the NTP has implemented DOTS to community level using DOTS committees.

**Methods:** DOTS committee, using written protocols, were formed involving social workers, political leaders, health workers, journalists, teacher, students, private practitioners, TB patients, patient's family member, traditional healers, local organisations, local political and administration units, mothers group, female health volunteer, medical colleges, schools, industries, and so on at each DOTS treatment centre. In addition, DOTS orientation was carried out with each individual group to ensure participation in controlling TB.

**Results:** With around 2000 functional DOTS committees the NTP programme has increased case finding and treatment success rate from 30% to 71% and 40% to 90% respectively (1994–2003). DOTS has been expanded through out the country covering 94% of the population.

**Conclusion:** By using DOTS committees for participatory partnership with allies, the NTP has made the Tuberculosis Programme a success.

**TS-79-127 The concept of an Asthma Drug Facility**

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Asthma is a widespread disease that is affecting between 10 and 15% of the population. However, the majority of patients in developing countries have no access to the essential drugs such as bronchodilators and inhaled corticosteroids. This means that many patients receive inadequate treatment or no treatment at all. This is causing increased costs to the health care system due to unnecessary hospitalisations and visits to emergency departments. Good quality asthma drugs could be purchased through pooled procurement and delivered to interested countries at a cost of less than 30 US \$ for a yearly treatment. The precondition for establishing a virtual procurement agency would be the willingness of Ministries of Health, Central Pharmacies and interested NGOs to participate in pooled

procurement and guarantee the payment of at least 20 000 treatments per purchase. The Global Drug Facility (GDF) for tuberculosis has been evaluated to be an excellent mechanism to facilitate the availability of good quality drugs in low income countries, either through drug grants or through direct procurement mechanisms offered to interested countries. The GDF could be used as the starting point for purchasing essential asthma drugs that could be used in the Practical Approach for Lung Health (PAL), promoted by the World Health Organization. The availability of good quality asthma drugs in all countries would greatly reduce the burden of asthma and also the workload in asthma and emergency departments.

**POSTER DISCUSSION SESSIONS****EPIDEMIOLOGY OF TUBERCULOSIS****PC-262-288 Chronic worm infection affects the epidemiology of TB**

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Helminth infections induce Th2 type immunity whereas resistance against TB is mediated mainly by Th1 type responses. It is not known whether Th2 inducing worm infections could affect the epidemiology of TB. This study was aimed to evaluate the association between TB and helminthes in a third world country setting. All patients had clinical features consistent with TB supported by positive sputum smear microscopy and the controls were healthy household contacts of the patients. 230 smear positive TB patients and 510 controls were included in the study. 71% of the TB patients and 36.2% of the controls had infections with one or more intestinal helminthes. Moreover 46.9% of the TB patients and 11.8% of the controls had HIV infection. Double infection with both intestinal helminthes and HIV was found in 33% of the TB patients and 4.5% of the controls. Regression analysis showed strong association between helminthes and TB (OR 3.5, 95% CI 2.1–5.9,  $P < 0.001$ ), between TB and HIV infection (OR 7.4, 95% CI 3.9–14.3,  $P < 0.0001$ ). HIV and helminth double infected individuals were more likely to have TB compared to individuals with either infection alone (OR 10.4, 95% CI 6.2–18,  $P < 0.0001$ ). These data show a strong association between TB and worms.

### PC-311-339 Dépistage positif chez des contacts étroits : infection récente ou ancienne?

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**Introduction :** Le dépistage des contacts étroits des cas de tuberculose (TB) pulmonaire fait partie de tout programme de contrôle des pays de faible incidence.

**Objectifs :** Évaluer les résultats du dépistage des contacts étroits identifiés après déclaration des cas de TB pulmonaire au Québec en 1997–1998.

**Méthodes :** Recueil rétrospectif de certaines variables et du résultats des tests cutanés à la tuberculine (TCT) auprès des 18 Directions de Santé publique du Québec.

**Résultats :** 372 TB pulmonaire ont été déclarés. 1422 contacts étroits ont été identifiés. Parmi les 1046 contacts avec dépistage complet, 464 (44,4%) ont eu un 1er TCT  $\geq 5$ mm et 57 (5,4%) ont présenté un virage tuberculinique. L'âge du contact, la naissance hors Canada et, dans une moindre mesure, la présence de cavités chez le cas index étaient associés à un dépistage positif.

**Conclusion :** Sauf pour ceux avec un virage tuberculinique, un dépistage positif représente probablement pour plusieurs contacts étroits une infection tuberculeuse acquise avant l'exposition au cas.

### PC-365-391 Tuberculin skin test anergy in HIV-infected patients: limited gain of reducing cut-off values

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**Background:** Because of decreased sensitivity of the tuberculin skin test (TST), recommended cut-offs for detecting latent tuberculosis infection are lower in HIV-infected than in non-infected patients. This may be ineffective if loss of sensitivity is due to anergy in some patients.

**Objective:** To assess the effect of anergy on TST sensitivity in HIV-infection.

**Methods:** All patients with smear-positive tuberculosis in 6 hospitals in Tanzania were skin tested using 2TU Rt23 in Tween-80 and tested for HIV antibodies with two ELISAs.

**Results:** 451/991 patients tested HIV positive (46%). Anergy (TST reaction  $< 3$  mm) was observed in 111 (25%) HIV-positive and 18 (3%) HIV-negative pa-

tients ( $P < 0.001$ ). Mean  $\pm$  Sd TST reactions among non-anergic patients were  $15.9 \pm 5.0$  mm in HIV-positives and  $16.8 \pm 3.0$  mm in HIV-negatives ( $P = 0.048$ ). Among the HIV-positive patients, the sensitivity of the TST at 10 and 5 mm cut-off was 64% and 72%, respectively.

**Conclusion:** In HIV-infection, most loss in TST sensitivity is due to anergy. Reducing the cut-off from 10 to 5 mm in this population provides limited gain in sensitivity whereas it is likely to result in considerable loss in specificity.

### PC-417-457 Factors associated with abandonment of tuberculosis treatment in Nicaragua

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This is a study designed to identify risk factors for the abandonment of tuberculosis treatment. This is a case-control study, matched by age and municipality in Managua and Matagalpa, Nicaragua. Cases were tuberculosis patients who had discontinued treatment during 1998–2001. Controls were TB cases cured. 251 pairs were included in the analysis. Questionnaires were used for data collection. The variables were grouped, in accordance with a hierarchical model. The odds ratios were estimated with respective 95% confidence intervals, using conditional logistic regression. The following characteristics were important: being male (OR 2.51; IC 1.63–3.94); without fixed residence (OR 3.08; IC 1.57–6.49) or having moved residence recently (OR 4.22; IC 2.06–9.93); being a smoker (OR 4.83; IC 2.56–9.88); consumer of alcoholic beverages (OR 4.83; IC 2.56–9.88) or illegal drugs (OR 5.25; IC 2.43–12.94); to have already received prior treatment (OR 2.14; IC 1.25–3.78), allocated a different treatment schedule (OR 1.77; IC 1.12–2.85); difficulty in accessing health services (OR 2.64; IC 1.39–5.29), and a negative perception of the healthcare received (OR 5.33; IC 1.52–28.56). Identification of these risk factors are important to prevent treatment abandonment.

### PC-441-479 Spatial distribution of tuberculosis mortality in Rio de Janeiro State, Brazil, during the last two decades

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**Introduction:** Brazil is one of the 22 countries with highest tuberculosis (TB) incidence in the world. In

the last few years, the risk of death by TB is greater in Rio de Janeiro than in the others states of Brazil with similar incidence rates.

**Objectives:** (1) analyze the spatial distribution of the mortality rates in the municipalities of Rio de Janeiro state in the last two decades, divided in four periods of five years from 1981 to 2000; (2) identify risk areas using spatial analyses techniques.

**Methods:** Exploratory data analyses were done with raw rates, Freeman-Tukey and empirical Bayes transformations. Spatial autocorrelation measures used were global Moran's I and Geary's C statistics. LISA maps and Moran scatterplot were drawn.

**Results:** The highest rates were observed for the metropolitan and northwest areas, while the lowest rates were found in the northeast of the state. Global Moran's I values were 0.505, 0.489, 0.588, 0.499 ( $P$ -value = 0.001) for the periods of 1981–85, 1986–90, 1991–95 and 1996–2000, respectively. LISA maps showed the evidence of the occurrence of high-risk zones in the metropolitan and northwest areas.

**Conclusions:** TB mortality was not spatially randomly distributed in Rio de Janeiro state in the study period.

#### PC-623-687 Global survey of tuberculosis laboratory services

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**Objective:** Quantify the availability and volume of tuberculosis laboratory testing in WHO Member States.

**Methods:** Questionnaires distributed to 207 countries. Questions included: total public and private facilities offering: smear microscopy, culture, and drug susceptibility testing (DST) and volume of these tests performed annually. For countries not submitting a questionnaire, the total tests performed was estimated using a regression equation.

**Results:** 109/207 (53%) countries responded. Over 65% provided national figures for the number of laboratory facilities and number of tests performed. Microscopy services range from 0.1/100 000 population (Sweden/Uruguay) to 8.3/100 000 (Russia). The average across the 22 HBCs is 1.6/100 000. The estimated global number of smears performed in the public sector is 44 375 000 (culture, DST figures pending). The ratio of smears performed per notified case is inversely proportional to TB incidence and ranged from 1:1 to 1084:1. The unweighted average for the 22 HBCs and globally is 26:1, 65.5:1, respectively.

**Conclusions:** Smear microscopy is the only widely available diagnostic service. The ratio of smears performed:cases detected varies markedly and is likely

influenced by TB incidence, health-seeking behaviour and availability of diagnostic centres.

#### PC-652-726 Diagnosis delays in contagious tuberculosis (I.R.Iran–2003)

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**Introduction:** Delay in diagnosis increases morbidity, mortality and transmission of tuberculosis (TB).

**Objective:** To determine the factors affecting the elements of diagnosis delay in TB.

**Methods:** A cross-sectional study based on a structured interview with 400 newly diagnosed sputum smear-positive TB patients aged over 15 years of Iran in a 3 months period in 2003.

**Results:** Median Total delay was 92 days. Medians of 'Patient' and 'Health care system (HCS)' delays were 20 and 46 days respectively, consequently they had a significant difference ( $P < 0.001$ ). In multivariate Linear Regression analysis, HCS delay (the longer delay) has shown significant increasing association with 'female sex, Iranian nationality, not requesting sputum smear for Acid Fast Bacilli 'AFB', not taking chest X-ray in the first visit, having at least a negative sputum smear for AFB, history of chronic respiratory disease'; and in absence of requesting sputum smear, 'attendance a private clinic as the first health facility'.

**Conclusion:** To reduce diagnosis delay, the interventions should be focused on HCS delay, especially (re)training of private physicians, especially about the importance of requesting sputum smear for AFB in TB diagnosis and thinking about TB in patients with history of chronic respiratory diseases.

#### PC-709-783 Tuberculosis control in remote regional Australia, 1998–2003

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Tuberculosis control in remote regions of developed countries remains a persisting problem. Over the past 5 years there have been 27 notifications of tuberculosis reported in the remote Kimberley Region of northern Western Australia, translating to an average notification rate of 14/100 000 per year. Seven of the notifications were from Indigenous Australians suggesting local transmission. Five were reported from an immigration detention centre where asylum seekers were detained until the Centre's closure in mid 2002 and where local acquisition is unlikely to have occurred. Of the remaining 22, all but one occurred in residents in the western part of the region. Al-

though the local populations are mobile across state lines, TB rates are higher in the Northern Territory of Australia (16 notifications/100 000 in 2003) which abuts the eastern part of the Kimberley. Annual notification numbers have remained stable at 2–6 cases/year, translating to notification rates of 6–17/100 000 per year. These findings have implications for case finding and identification within the Kimberley and indicate that local transmission continues to occur.

### PC-836-907 A survey on tuberculosis in prisons in Bangladesh

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**Introduction:** The magnitude of the TB problem in the prisons of Bangladesh is very little known. The living conditions of prisoners probably favour the spread of tuberculosis.

**Objective:** To assess the severity of the problem in prisons at the district level.

**Methods:** The survey was carried out in the prisons of Rajshahi, Naogaon and Nawabganj districts. Damien Foundation paramedical workers organized health education sessions for prisoners and invited suspects to produce three sputa. These were examined by direct microscopy for AFB. Quality control has shown the high reliability of the results.

**Results:** A total of 3477 prisoners were surveyed, among whom 319 were identified as suspects and 5 diagnosed as smear positive TB (150/100 000). In the 2 to 5 months following the survey, 8 additional suspects were referred, of whom two were smear positive.

**Discussion:** Although these data are not representative of the situation in all the prisons of the country, the prevalence figure presented here surprisingly does not seem higher than the estimated incidence of 105 smear-positive cases per 100 000 population for Bangladesh.

**Conclusion:** More extensive surveys of the TB situation in prisons should be carried out in Bangladesh.

## CLINICAL RESEARCH AND TREATMENT OF LUNG DISEASE

### PC-220-255 Dates of beginning of treatment of tuberculosis patients

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Dates of beginning of treatment of SS+ lung TB patients are one of the factors affecting TB spread and treatment outcome. According to WHO recommen-

dations SS+ lung TB patients should start treatment within the first 3 days from TB detection. We analyzed the dates of hospitalization of all 444 new SS+ lung TB patients from 8 pilot sites in 2003. In the 1st quarter of 2003 94 new SS+ patients were detected, while only 25 (26.5%) started treatment within 3 days from TB mycobacteria detection. The reason of untimely hospitalization is the lack of integration between laboratory service, PHC and TB facilities. Not always a patient was informed about the importance of urgent hospitalization. Having learned about the diagnosis some patients started self-treatment or at sorcerers. Project HOPE specialists developed series of activities and recommended them in pilot sites. During the monitoring visits Project HOPE controlled the accomplishment of the given recommendations. As a result, the number of the patients started treatment within the first 3 days after detection has increased up to 56.3% (97 out of 172 patients) in the 2nd quarter, 63.9% (76 out of 119 patients) in the 3rd quarter and 74.6% (44 out of 59 patients) in the 4th quarter. SS- lung TB patients can also be contagious during the late treatment. Therefore, control over timely hospitalization of all new TB patients is necessary.

### PC-327-370 Clinical guidelines to diagnose smear-negative pulmonary tuberculosis in a country with high-TB/low-HIV prevalence

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**Introduction:** Nearly half of all pulmonary tuberculosis patients have negative smears. In the absence of better diagnostic tests, clinicians in resource-poor health systems are expected to diagnose or exclude smear-negative tuberculosis using only their clinical judgement.

**Objectives:** To develop and evaluate guidelines to assist primary care physicians in diagnosing or excluding smear-negative tuberculosis in resource-poor health systems.

**Methods:** Clinical guidelines and an associated training package were developed based on current evidence and a consensus development process. These guidelines were evaluated for their efficacy in diagnosis and exclusion of smear negative tuberculosis against sputum culture as the 'gold-standard'.

**Results:** There was a significant improvement in the mean knowledge score subsequent to the training (47–66%  $P = 0.026$ ). The sensitivity and specificity of the guidelines in diagnosing smear-negative tuberculosis were 0.60 (95% CI 0.48–0.72) and 0.85 (95% CI 0.83–0.88) respectively. Amongst false negatives ( $n = 24$ ), six were attributable to non-compliance by clinicians to the diagnostic guidelines. The rest were mainly

due to exclusion subsequent to response to antibiotics. The sensitivity of the detection of various X-ray lesions (built as diagnostic criteria in the guidelines) ranged from 63 to 94%.

**Conclusions:** These guidelines (with local adaptation) can help primary care physicians working in resource-poor health systems in diagnosing or excluding smear-negative tuberculosis.

### **PC-179-215 The prevalence of TB-associated symptoms in children from a high-burden community**

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**Introduction:** A recent critical review of diagnostic approaches used in childhood TB emphasized the absence of standardized symptom definitions and poor validation.

**Objectives:** To describe the prevalence and duration of TB-associated symptoms in children without TB from a high-burden community, and to compare symptoms in children without TB to those in children with newly diagnosed TB.

**Methods:** A cross-sectional community survey on a 15% random sample of residential addresses, with completion of a standardized symptom based questionnaire and tuberculin skin test (TST) in all children <15 years of age. Symptoms evaluated were cough, chest pain, haemoptysis, anorexia, weight loss, fatigue, fever and night sweats during the preceding 3 months. **Results:** 1800 children were enumerated, 1415 (78.6%) completed both a questionnaire and TST. 451 (32%) were TST positive with a cumulative, age-linked increase. TB-associated symptoms were common (cough was reported in 68% of children). Symptom-duration showed a bimodal distribution. Both short duration (<1 week) and prolonged duration (>3 weeks) were common. Symptoms reported in 18 children with newly diagnosed TB did not differ significantly from those without TB.

**Conclusion:** The symptoms evaluated were too common to be of diagnostic value. It illustrates the need for improved symptom and outcome definitions in high burden settings.

### **PC-413-452 Diagnosis of pediatric tuberculosis in the HIV era**

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**Background:** Diagnosis of pediatric TB is based on clinical scoring systems developed before the HIV pandemic.

**Objectives:** Evaluate the performance of published TB scoring systems in HIV-infected and uninfected children.

**Methods:** Retrospective study in Kinshasa of 111 TB cases, 91 with known HIV status. Scores were calculated for 9 scales (Edwards, Fourie, WHO, Stegen, Nair, Seth, Brazilian MOH, Ghidey & Habte).

**Results:** Mean age at TB diagnosis was 3.7 for 49 HIV-uninfected and 2.4 years for 42 HIV-infected children ( $P = 0.04$ ). HIV-infected children were more likely to have TB exposure, a TB history, lymphadenopathy and malnutrition. Proportions presenting with cough, fatigue, dyspnoea, positive PPD, weight loss, fever, and nightsweats did not differ significantly. The locally adapted Edwards score was on average 11.6 in HIV-negative and 14.1 in HIV-positive children ( $P < 0.001$ ). While  $\geq 87\%$  of children were classified as requiring treatment by different scales, 76% met this criterion for all scales (71% HIV-uninfected, 80% HIV-infected cases).

**Discussion:** Clinical presentation of HIV-infected and uninfected children was similar. Disagreement in the decision to treat exists among the 9 published scoring systems. Improved methods for pediatric TB diagnosis are needed.

### **PC-627-692 A brief questionnaire for screening asthma among pediatric and adolescent patients in Rio de Janeiro, Brazil**

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**Setting:** Asthma is the most common chronic disease in childhood with recognition and detection still unsatisfactory. Questionnaires focusing on referred symptoms showed as a very promising and useful tool. This study aimed to determine the accuracy of a simplified questionnaire (SQ) as a diagnostic test for asthma in children and adolescent patients.

**Methods and results:** An observational, transversal study was carried out. A SQ was used for screening. Gold standard for asthma was a minimal increase of 12% in the first second of the forced expiratory volume after a bronchodilatation test. 211 patients with 5 to 15 years of age were evaluated. Prevalence of asthma was 22%. Family's annual income was less than US\$ 3600 in 67% ( $n = 141$ ). 60% ( $n = 127$ ) of support providers were illiterate or had less than four school years. Positive tests had at least one positive answer to the four SQ questions. Results showed: sensitivity = 82.98 (95% CI: 68.70–91.90), specificity = 53.66 (95% CI: 45.70–61.40), likelihood ratio = 1.79 (95% CI: 1.45–2.21), positive predictive value = 33.91 (95% CI: 25.50–43.40), negative predictive value = 91.67 (95% CI: 83.80–96.10) and accuracy = 60.19% (95% CI: 53.47–66.63).



**Conclusion:** SQ is a high sensitivity and negative predictive value tool of easy use and implantation, although unspecific.

**PC-631-697 Acute respiratory infection (ARI), wheezing and the Integrated Management of Childhood Illness (IMCI): are children over-treated with antibiotics and under-treated with bronchodilators?**

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**Methods:** Cross-sectional study. 217 children of two months to five years of age with ARI, wheezing and fast breathing (FB) were treated with aerolized  $\beta_2$  agonist ( $A\beta_2$ ). Chest radiographs (CXR), obtained in children with FB after this treatment, were evaluated for the diagnosis of pneumonia by pediatricians and by two radiologists after study. All children with pneumonia were treated with antibiotics.

**Results:** 27 subjects had FB after  $A\beta_2$ . 74.1% (20/27, radiologist diagnosis) or 29.6% (8/27, pediatrician diagnosis) had normal CXR. 24 children had no audible wheeze. 79.2% (18/24, radiologist diagnosis) or 33.3% (8/24, pediatrician diagnosis) of these children had normal CXR.

**Conclusion:** The rate of children with FB after the treatment and with normal CXR was high. As they should be classified as having pneumonia by the IMCI algorithm, antibiotics would be inappropriately prescribed. The rate of children with no audible wheeze was also high. It is essential to use the stethoscope to recognize these wheezing children. They should be classified as having pneumonia and would be inappropriately treated with antibiotics and without bronchodilator. Other studies are necessary to refine the IMCI algorithm.

**PC-506-565 Prevalence and risk factors for defaulting tuberculosis treatment among out-patients followed up at a tertiary hospital in Singapore**

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**Aims:** We sought to identify the prevalence and risk factors for defaulters from tuberculosis (TB) treatment among patients followed up at a tertiary care hospital in Singapore.

**Method:** Retrospective, case-controlled study of patients who had positive culture for *Mycobacterium tuberculosis* (MTC) between 1st July to 31st December 2003.

**Results:** Defaulters (16 out of 156 patients) were compared with 60 randomly selected controls. There

were no significant differences in sex, race, age, or comorbid conditions between compliant patients and defaulters. Comparing non-defaulters with defaulters, an initial follow-up appointment of longer than two weeks (25% vs 20.5%,  $P < 0.001$ ), increased incidence of treatment side-effects (9.1% vs 18.8%,  $P = 0.006$ ), impaired patient mobility (25% vs 4.5%,  $P = 0.03$ ), and starting TB treatment with four drugs rather than three (50% vs 20.5%,  $P = 0.005$ ) were factors strongly predictive of default. Most patients who defaulted did so within the first two months of treatment (68%). Directly observed therapy (DOTS) decreased the default rate (22.7% of non-defaulters vs. 12.5% defaulters were on DOTS,  $P = 0.011$ ).

**Conclusion:** Patients with risk factors for default should be identified early and put on DOTS.

**PC-721-795 The impact of food enablers and incentives on treatment outcomes in Tajikistan's DOTS Programme**

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**Background:** The enabler/incentive component (Food Support) in Tajikistan's DOTS program began in December of 2002. This program targets vulnerable patients. To date more than 800 patients have received food support. Treatment outcomes are available for 340 recipients of food support.

**Objective:** To determine the effect of a food support program on treatment outcomes (vulnerable vs. non-vulnerable patients) in the Tajikistan DOTS programme.

**Method:** Patient selection determined by vulnerability based on economic situation, land and animal ownership. Food support: Included Wheat flour, vegetable oil, peas, salt and sugar to cover basic daily needs. Distribution from central locations in three allotments at two month intervals covers patient and immediate family members.

**Results:** The treatment outcomes for those receiving enablers/incentives showed: higher cure rates (new S+ 86% cured vs. 60%), lower percentages of treatment failures (10.7% vs. 16%), lower percentages of 'died' patients (2% vs. 12%) and lower default rates (1% vs. 12%). The disparity in cure rates between new S- and extra-pulmonary patients was even greater; favoring those enrolled in the food support programme.

**Conclusion:** Food support made a major contribution to the program. Food Support and other enablers/incentives should be considered for all vulnerable patients enrolled in DOTS treatment in Tajikistan.

### PC-884-960 Risk factors for tuberculosis in renal failure, dialysis and transplant recipients in northern Alberta, and impact of INH prophylaxis in reducing risk

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High incidence of TB in renal failure (RF) (300–11 000/100 000) has led to recommendations that those at risk of TB infection receive treatment of latent TB infection (LTBI). We report a retrospective examination of the Northern Alberta program of LTBI in RF, risk factors for TB and impact of program. All patients of Northern Alberta, referred for dialysis and transplant suitability, were assessed for TB risk with TB skin test (TST), and if positive or historically infected, were referred for isoniazid (INH) prophylaxis. 1682 files were linked with the provincial TB Registry of 50 000 to identify 348 confirmed matches, and 29 confirmed cases of tuberculosis. The risk factors for development of tuberculosis analyzed were age, country of birth, ethnic origin, gender, tuberculin reactivity, underlying disease, INH prophylaxis, duration and tolerance. In a community with rates of tuberculosis ranging from 5–10/100 000 per year, the finding of 29 cases in over 1682, or 1724 over 11 years, gives an estimated mean 156.7/100 000 per year. Time of onset of 29 cases, with respect to RF, and LTBI will be reported. The cost of LTBI and cost saving based on estimated prevalence of infection and risk of disease will be analysed.

## TUBERCULOSIS AND SOCIETY/POVERTY

### PC-319-351 Appealing incentives for treatment compliance among tuberculosis patients in a poor county in the periphery of Rio de Janeiro state, Brazil

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**Introduction:** Duque de Caxias, a poor county in the periphery of Rio de Janeiro, has one of the highest tuberculosis incidence rate (156/100 000 inhabitants) in Brazil. Its reported treatment default rate was 20% in 2001. The aim of this study was to assess appealing incentives for treatment compliance among tuberculosis patients.

**Methods:** An anonymous questionnaire-based survey was carried in a primary care unit, which notifies 85% of all new TB cases in the county.

**Results:** A total of 243 questionnaires were answered. Mean age was 40.4 ± 15.1 years, 170 (69.9%) were male, 133 (54.7%) lived in couple. Incentives considered fundamental/important were: laboratory tests access (96.7%), more medical attention (93.4%), contact consultation (90.9%), scheduled appointments (89.3%), food supply (88.4%), transportation (84.6%), home drug delivery (80%), social worker support (79.5%), psychological support (76.2%), meal tickets (75.2%), home care visits (70.6%), Saturday appointments (50%), evening appointments (30.3%), permission to drink (5.4%) and smoke (5%) during treatment.

**Conclusions:** Main incentives for treatment adherence include better general assistance with a multidisciplinary approach. Most required incentives are already proposed in the State Control Program Guidelines and should be in practice. Professional commitment for changes is necessary as is financial support to warrant food and transportation supply.

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### PC-449-488 Health seeking behavior survey in the capital city with public and private sectors mixed in Cambodia

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**Objectives:** To examine health seeking behaviors (HSB) of TB suspected people in urban areas with public and private sectors mixed.

**Methods:** The CENAT/JICA TB Control Project conducted a HSB survey at 20 cluster sampled areas of Phnom Penh in Nov 2003–Jan 2004. All participants over 10 years of age were screened for TB through health questionnaire and chest X-ray. TB suspects identified were additionally interviewed about their HSB for the treatment.

**Results:** Through the survey, 4912 participants were screened and 451 (9.2%) were identified as TB suspects. Among them, 52 have had TB patients in their family members and 66 have been diagnosed as TB. As to the medical facilities of diagnosis, 47 (71%) out of 66 were at public hospitals including NGOs and 12 (18%) at private sectors. Although 244 suspects have sought the treatment before the survey to alleviate their respiratory symptoms, 170 (70%) of their first visits were pharmacies, 32 (13%) private clinics, and only 6 (2%) health centers.

**Conclusion:** In Phnom Penh with public and private sectors mixed, the involvement of private sectors, especially pharmacies, in National TB Control Program should be considered in order to shorten diagnostic delay.

**PC-466-505 Do vulnerable groups have equal access to TB diagnosis and treatment? Social assessment case study in poor rural China**

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**Background:** In the new TB control project jointly funded by the Chinese government, the World Bank and DFID, Social Assessment is regarded an effective way to identify barriers associated with low TB case detection and poor treatment completion.

**Objectives:** To identify barriers influencing TB diagnosis and treatment in rural China.

**Methods:** 120 TB patients and 300 suspected patients from three districts in Inner Mongolia were interviewed using structured questionnaires.

**Main findings:** The survey found that 73% suspected TB patients seeking care at village level did not obtain any specific diagnosis. Only 5% of them sought care at district TB dispensaries. 33.3% patients had a delay before seeking their first out-patient visit, 64.3% waited more than 2 weeks to obtain diagnosis after first out-patient visit. The cost of one out-patient visit in district hospital was 397 RMB, 73% of the total monthly household expenditure. On average, direct cost of TB health care including diagnosis and treatment was 1190 RMB, while the indirect cost including transportation and nutrition etc was higher at 1400 RMB.

**Conclusions:** Poor and vulnerable groups face delays in seeking diagnosis and treatment for TB. High costs (direct and indirect) are a key barrier to early access of care.

**PC-468-506 To assess how TB suspects are diagnosed and TB patients are treated under DOTS in China**

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**Objective:** To assess how TB suspects are diagnosed and treated under DOT in China

**Methods:** The China MoH National Household survey 2003 collected information on self-reported chronic cough, TB patients, diagnosis experiences and treatment seeking behaviour. Analysis of the differences between different social groups was conducted.

**Results:** Chronic cough rates in rural and urban areas were 1.6% (M:1.7% ; F:1.5%) and 1.8% (M:1.9%; F:1.8%) respectively. TB prevalence rate was 126 (M:155; F:95) per 100 000 and 85 (M:107; F:63) per 100 000 respectively. 63% of chronic cough patients sought care. There was no clear gender or rural/urban difference. Among those who sought care, only 15% of rural and 24% of urban patients were prescribed sputum smear tests for diagnosis. About 43%

of rural patients and 60% of urban patients were given X-ray examinations. 58% of rural patients and 74% of urban patients claimed they were treated under DOT, mostly supervised by family members (62% in rural areas and 82% in urban areas).

**Conclusions:** Over one third of TB suspects did not seek any professional care. Those seeking care were often not prescribed sputum smear tests. Majority of TB patients, particularly in urban areas, were supervised by family members.

**PC-474-510 Piloting pro-poor activities in poorest settings of urban Lilongwe, Malawi**

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**Objectives:** To equip community leaders with health promotion skills and storekeepers and volunteers with advisory skills to refer chronic cough cases and provide advice on appropriate home management of childhood fever in poorest urban communities of Lilongwe.

**Design:** Participatory approaches are used to empower community members to enhance their own health by developing participatory health promotion package and training of community leaders, volunteers, and storekeepers. The impact of the intervention on delay for chronic coughers and appropriate management of childhood fever will be assessed through household surveys, audits of chronic cough and TB registers to assess proportion of cases accessing health centres and qualitative assessment of storekeepers' practices.

**Progress/results:** Although the participatory approach is contributing to delay of implementation of activities, there is ownership of the process by both health workers and community members. The participatory health promotion-training package has been developed and pilot-tested. Collection of baseline data is almost through awaiting analysis.

**Conclusion:** Partnership with communities and private providers such as storekeepers can be one way of improving access to TB and Malaria services. It is feasible for disease programmes such as Malaria and Tuberculosis to harmonise resources at both community and district level to improve access to services.

**PC-564-631 Perceptions of pulmonary tuberculosis in a rural South-African society**

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A semi-qualitative study on perceptions of tuberculosis was conducted in 1999 among pulmonary tuber-

culosis patients ( $n = 315$ ) in Bushbuckridge hospitals, South Africa. The area is characterized by a high level of circular migration, a growing AIDS epidemic and a high incidence of tuberculosis (212 cases per 100 000 population). Among the patients interviewed, 39.5% responded they didn't know the origin of their disease. Among the others, 27.7% attributed TB to bewitchment, 25.1% to contact, 20.4% to work conditions, 14.7% to alcohol and tobacco, 7.3% to chronic cough, 3% to intercourse, and only 1% to poverty. According to demographic and epidemiologic factors (sex, age, education, and duration of cough), findings show that men were more likely to link their illness with work (sex ratio = 8.8), with alcohol and tobacco (sex ratio = 8.0), whereas women were more likely to perceive that their illness was due to contact with a tuberculosis person within the household (sex ratio = 0.6). Attributing the illness to flu and to bewitchment was associated with longer duration of cough (66.4 and 23.3 weeks). The results of this investigation indicate that much remain to be done to improve knowledge of disease causation in this population, an important element for disease prevention and appropriate care.

**PC-878-954 Where are the women in TB detection? Adding to the picture using other data sources**

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**Introduction:** In Nepal new TB cases are 2 times as likely to be diagnosed in men than in women. General assumptions are that access particularly to young women is part of the reason. Additional routine sources of data may help shed light on this issue.

**Objectives:** To see if other sources of data help explain gender differences.

**Methods:** Hospital TB and other respiratory in-patient data, census reported deaths data, and US and UK data were used to calculate age and sex ratios and compared with Nepal Tuberculosis Programme smear positive detection rates.

**Results:** Death data showed similar ratios to NTP data (M:F ratio: overall 2.08; 15–65 years 1.78; >65 years 3.3) vs. (M:F ratio: overall 2.01; 15–65 years 2.06; >65 years 3.23,) while hospital data shows lower ratio (15–70 years) 1.67 and female preponderance in in-patient admissions for other respiratory diseases (15–70 years: M:F = 0.79). International comparisons (UK/US) suggest a higher gap in women >55 years and young women aged 15–24 years.

**Conclusion:** Mortality, hospital and international comparative data show similar ratios to NTP data and this suggests that access to TB services for women may not be the main factor in explaining the Tuberculosis Gender Ratio in Nepal.

**MANAGEMENT INNOVATIONS TO IMPROVE THE QUALITY OF DOTS**

**PC-152-187 Quality assessment of tuberculosis care in the context of the DOTS strategy: implications for high-burden countries**

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**Background:** In theory, the DOTS strategy has five components, but modification in practice occurs when resources are limited. Identifying quality of the modified strategy is therefore important.

**Purpose:** To review evidence of the quality of care for TB patients in the context of DOTS and to propose indicators for high quality based on structure-process-outcome model.

**Method:** A literature search using the PUBMED database was conducted from January 1990 to March 2004. Studies were eligible for inclusion if conducted in one of 22 high-burden countries and had at least one component of DOTS.

**Findings:** Of the 24 eligible studies, 12 had five components of DOTS and 12 had at least directly observed treatment. Eight studies, which implemented five components incorporated with additional interventions, reported success rates for more than 85%. The use of cure rate may not be sufficient in identifying high quality programs. Indicators of structure, process, and outcome including patient satisfaction were proposed.

**Conclusion:** Quality of care for TB patients in high-burden countries varied across the studies. The more number of the components with additional interventions, the better successful outcomes were reported. Additional indicators for structure, process, and outcome are needed to guarantee that the care has quality.

**PC-173-209 Tuberculosis control in Dhaka, Bangladesh**

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**Introduction:** Presence of several providers' make TB control in big cities more complex than in rural areas, requiring multiple initiatives.

**Objectives:** Discuss initiatives undertaken in Dhaka city to implement and expand DOTS.

**Methods:** DOTS implementation and expansion in Dhaka through involvement of NGO general health services, PPM initiatives, DOTS at the workplace and in prison.

**Results:** During 2003 the number of TB microscopy centers increased from one to 41 and the number of DOT facilities from 1 to 74. During 2003 3784 new smear-positive patients were diagnosed, an increase of 21% compared with 2002. During 2002 94% of the patients were reported by 2 chest clinics, during 2003 59% were reported through the NGO network. Although case detection increased from 28% in 2002 to 34% in 2003, it is lower than the 38% country-wide. During 2002–2003, DOTS was expanded to prison and garment industries. Industry and PPM was initiated. Results will be presented.

**Conclusion:** TB control in big cities is complex. In addition to the public sector, public-public and public-private partnership should be established in order to increase DOTS coverage. A particular challenge is coordination of services delivered by the different providers and maintaining high quality diagnostic services.

#### PC-248-276 Use of budgeted workplans for DOTS implementation in China

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**Introduction:** Local TB staffs at local levels frequently lack the capacity to develop a good work plan for DOTS implementation and to monitor availability of funds to implement this plan.

**Objectives:** Develop budgeted workplans for all administrative levels responsible for DOTS implementation and use it to track completion of programme activities and availability of funding.

**Methods:** Quarterly workplans were developed for each administrative level in 3 provinces implementing a DOTS programme funded by CIDA/WHO. Each programme activities associated with DOTS had a detail budget requirement, the amount of funding, and funding sources. Implemented activities and available funding were reported against the workplan every quarter.

**Results:** The budgeted workplan and quarterly reports were used to monitor the programme. Percentage of planned activities completed (in parenthesis) include: training (114%), supervision (100%). Percentage of planned governmental funding for the project at each level (in parenthesis) include: provincial funds (105%), prefecture/city level (95%), and county/district level (100%). In one year, smear-positive case-notification increased from a baseline of 17 to 32 cases per 100 000.

**Conclusion:** A budgeted workplan is a simple tool to assist local programme staff to plan and implement programme activities and to monitor availability of funds.

#### PC-522-582 Directly observed therapy (DOT) in tuberculosis control: study of the time spent on journey and assistance during home visits in a health service of the city of Ribeirão Preto, São Paulo state, Brazil, 2004

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It is an exploratory study that intended to describe and analyze the time spent by the health team on assistance and journey during the home visits of the Directly Observed Therapy, in a Program of Tuberculosis Control (PCT) in the city of Ribeirão Preto (2004). The methodological references used were the same of the health system's evaluation: Structure - Process - Result. The variables were: Time the vehicle spends waiting for the procedures; Time spent on the journey; Time spent on the assistance inside the house; Total number of patients assisted by the DOT; Total number of home visits and Total number of hours spent on the assistance of each patient. The study verified that the average number of patients assisted by the DOT is around 15. The time the vehicle is available for the DOT is around 2 hours a day. The results showed that the way the health team organizes itself for the home visits, influences on the time available for the patient's assistance. It was concluded that the planning of the home visits, based on the location of the patients' residences, not only rationalizes, but also improves the time and the human and material resources of the services.

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#### PC-538-626 DOTS in Afghanistan—logistic aspects: a year later

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**Introduction:** Logistic difficulties to implement DOTS programs include lack of infrastructures, poor roads, weather conditions, territory, unskilled personnel and insecurity.

**Objectives:** To provide logistics know-how to the NTP.

**Intervention:** Central warehouse organization has been improved in order to ensure a safe environment for the workers and appropriate storage conditions for drugs and chemicals. Items are regularly country-wide distributed. Sub offices and NGOs receive items in accordance with the number of reported and forecasted patients. Stock control is improved by the sensitization of staff on the importance of a rational request based on calculated drug needs in order to

avoid drug expiration, shortage and stock ruptures. A MOU signed between WFP and WHO/NTP ensure food to the TB patients. Vehicles and motorcycles have been distributed to carry on monitoring and supervisory activities.

**Results:** At central level logistics activities have reached a good level and even at peripheral level the situation has improved. Staff have acquired skills through workshops and training on the job.

**Conclusions:** Much has been done during the last year, and strategic procedures have been decided on and undertaken. More has to be done in terms of capacity building, training of staff and providing a good quality of DOTS.

### PC-539-600 Development of an annual report card for country-level TB control in the WHO Regional Office for Europe through surveillance indicators

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**Introduction:** Annually, 52 countries provide WHO with TB notification data. TB control interventions and quality of reporting vary from country to country. We hypothesize that such factors correlate with the strength of TB control programs.

**Objectives:** We wish to measure the quality of TB control through data submitted. Such a tool may better guide WHO to assist countries.

**Methods:** We developed twenty indicators to evaluate the quality of country-level TB control via data submitted in 2003. Each indicator was graded numerically: 1-inadequate 3-somewhat adequate 5-adequate. Indicators were grouped into 4 categories: 1) DOTS elements 2) representativeness 3) program indicators 4) quality of reporting.

**Results:** See Table:

Mean grades with ranges

	West	Center	East	WHO Europe
DOTS elements*	25 (19–35)	31 (27–35)	29 (7–35)	27 (7–35)
Representativeness*	14 (3–15)	13 (3–15)	9 (3–15)	12 (3–15)
Program indicators*	19 (11–25)	16 (5–21)	16 (5–21)	16 (5–25)
Quality of reporting	19 (15–25)	18 (9–25)	18 (5–25)	18 (5–25)
Total*	77 (50–100)	77 (58–88)	66 (22–96)	74 (22–100)

\* P-value  $\leq$  0.05.

**Conclusions:** The mean grade was significantly lower in the East e.g., Newly Independent States. These preliminary findings correlate with higher notification rates in the East. WHO should increase support for countries with lower performance.

### PC-547-663 Implementation of a new strategy to improve compliance of tuberculosis treatment in Senegal

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**Objectives:** To develop and implement a new strategy to deliver tuberculosis treatment in order to improve patient's adherence to treatment.

**Methods:** On the basis of a study using an interdisciplinary approach (epidemiology and social sciences), innovative methods were developed. They are now being tested in 16 health centres in Senegal, using the cluster randomised controlled trial design.

**Results:** The proposed strategy is a package of several interventions aimed at improving patient adherence to treatment, including improvement of the relationship between health workers and patients, training of health workers, decentralisation of treatment, and close monitoring of DOT activities. At first, several training sessions were organized for districts staffs, health workers and community health workers, in order to explain these various components. In parallel, documents of new methods and communication supports were developed. Then, regular meetings were organized to maintain continuous training and exchange in order to maintain health workers' involvement in the implementation of the intervention.

**Conclusion:** Through a well-prepared implementation accompanied with on-going training, it is expected that the new strategy will have a positive effect on cure rates of TB patients in Senegal.

### PC-675-748 A novel approach for the assessment of management capacity to improve TB programme performance

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**Introduction:** The Philippines NTP has made important advances in expanding TB DOTS. Although treatment success rates are reported to exceed the global target of 85%, case detection rates remain low at 58%. There is also considerable variation in the quality of TB DOTS throughout the country. The USAID-funded LEAD Project is working with the Philippines NTP to improve the quality of services in selected Local Government Units (LGUs).

**Objectives:** To adapt and pilot an innovative approach to improve management skills, including problem solving capacity, of mid-level TB managers.

**Methods:** The MSH Management and Organisational Sustainability Tool (MOST) is a structured par-

ticipatory process which allows organizations to assess their own performance and develop a plan of action to improve their management practices under complex and changing conditions. The MOST instrument was adapted to address specific roles and responsibilities outlined in the NTP manual for the LGUs. Facilitators, including provincial and regional TB programme managers, were trained and conducted a 2-day MOST workshop. In addition to the participatory assessment of the TB systems and services, each LGU was responsible for preparing an action plan to address priority areas.

**Results:** Preliminary findings will be presented and discussed.

### **PC-753-827 Estimation of the financial requirement of the national TB control programme in China**

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**Background:** China has performed costing of its TB control programme as part of planning for various TB control projects.

**Objectives:** Develop a national method for estimating the financial requirement of the national TB control programme (NTP).

**Methods:** Experience from costing various TB control projects in China from 2000–03 was reviewed to develop a method for estimation. Using this methodology, all provinces collected data using a standard format and software. After provincial financial requirements were estimated, the central level aggregated provincial data to produce an estimation of the national financial requirement.

**Results:** The method for estimation had the following elements: 1) DOTS expansion by population and implementation units; 2) case-notification rate; 3) supervision, training and IEC activities; 4) equipment/vehicle requirement; 5) drugs; 6) case-finding and management fee. Using provincial data, the total requirement for the NTP was determined.

**Conclusion:** The costing methodology enabled the NTP to calculate its financial requirement.

### **PC-826-898 Ten years of DOTS regimens: success story in a developing country**

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The DOTS Programme in India was launched as Pilot Project in Chest Clinic Gulabi Bagh in North Delhi (India) covering one million population. The norms of one DOTS-Microscopy Centre per 100 000 population were established with one TBHV and Lab tech-

nician. The various parameters were collected from the period 1 January 1994 to 31 December 2003. The cure rate in Category I positive patients has been on an average of 87.8%. The annual cure rate ranges from 84.8% to 93.7%. The cure rate of Category II positive patients averages 75.7%. The failure rate of Category I patients averages 3.3% while the failure rate of Category II patients during the same period was 7.4%—these were potentially multidrug-resistant cases. During the period 1 January 1994–31 December 2003, 4018 patients were registered as Category I positive cases. Of these 3526 (87.8%) were cured/completed treatment. Of 2556 patients registered as Category II positive cases, 1935 (75.7%) were cured/completed treatment. Significant points to note: 1) Gradual acceptance of DOTS by patients; 2) Category-II positive patients started to fall significantly from 345 to 184 at present. Thus it can be concluded that DOTS can succeed.

## **POSTER DISPLAY SESSIONS**

### **TUBERCULOSIS DIAGNOSIS**

#### **PS-103-149 External quality assessment for AFB microscopy in Cebu Province, the Philippines**

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**Setting:** 64 microscopy centers in Cebu Province.

**Objective:** To assess applicability of blinded slide rechecking as EQA stated in APHL document for NTP in the Cebu Province as well as in the Philippines.

**Methods:** The sample slides selected by using Lot Quality Assurance System were reread blindly at the Provincial Quality Assurance Center. 80% sensitivity and zero acceptance error were employed as sampling condition. In addition quality of smear preparation of sample slides were assessed.

**Results:** 1) The number of sample slides were reduced from 6748 in the previous method to 3502 (almost half) in this method. As a result NTP coordinator and controllers were able to spend more time for monitoring including corrective action. 2) 37 major errors (1.1% of total slides) were found. These were closely related to the poor quality of smear preparation which requires retraining.

**Conclusion:** The new blinded slides rechecking is applicable as an effective EQA method of smear microscopy service of NTP in Cebu Province and is consid-

ered also applicable for the Philippines. The results ensure future improvement of quality of AFB microscopy service NTP of the Philippines.

#### **PS-222-257 Implementation of the quality assurance program in bacterioscopy laboratories**

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**Setting:** The purpose of the 'Quality Assurance Program' implementation is to improve reliability and effectiveness of laboratory services.

**Material and methods:** Quarterly reports of pilot sites and Reference Laboratory of the National TB Research Institute of Uzbekistan for 2002–2003. During analysis of the quarterly reports of 2002 we paid attention to the low quality of bacterioscopy examination in laboratories of pilot sites. Based on that, at the end of 2002 a 'Quality Assurance Program' implementation started. The quality assurance program is a system to continuously improve reliability and effectiveness of laboratory services, which includes: 1) internal quality control; 2) external quality assessment, 3) quality improvement.

**Research results:** 'Quality Assurance Program' implementation in bacterioscopy laboratories of Project HOPE/Uzbekistan pilot sites resulted in improvement of the following indicators. 'Sensitivity' of bacterioscopy examination has improved: in the 4th quarter of 2003 it increased by 17.2%, compared to the 1st quarter (76.7%), and reached 93.9%. 'Reliability' has also improved: In the 4th quarter 2003 it comprised 95.7%, compared to 91.9% in the 1st quarter 2003. The percentage of false positive smears decreased by 2.2% in the 4th quarter of 2003 and reached 6.1%, as compared to 8.3% in the 1st quarter. The rate of false negative smears also decreased in the 4th quarter, 2003 and reached 3.4%, 4.6 percentage points lower than in the 1st quarter (8.0%). The 'specificity' remained at 97.4% in 2003.

**Conclusion:** Implementation of 'Quality Assurance Program' in bacterioscopy laboratories of Project HOPE/Uzbekistan pilot sites contributed to the increase of reliability and effectiveness of laboratory services.

#### **PS-233-271 Sensibilité et spécificité des examens microscopiques dans le diagnostic de la tuberculose**

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**Cadre :** La mise en évidence des bacilles acido-alcoolrésistants (BAAR) à l'examen microscopique,

grâce à la coloration de Ziehl-Neelsen (ZN) et à l'auramine est à la base du dépistage des cas de tuberculose pulmonaire bacillifère.

**Objectif :** Préciser la sensibilité et la spécificité de chacune des techniques de colorations dans le diagnostic de la tuberculose pulmonaire et extra pulmonaire.

**Méthode :** 1354 échantillons de crachats et 876 prélèvements extra pulmonaires ont été traités par auramine et Ziehl-Neelsen.

**Résultats :** Dans notre étude la coloration de ZN montre une spécificité de 100%. La coloration à l'auramine est plus sensible mais moins spécifique.

**Conclusion :** Les frottis faiblement positifs en auramine doivent être confirmés par ZN, les prélèvements extrapulmonaires seront colorés par ZN.

#### **PS-281-303 Evaluation of two methods for preparation of panel test slides using NaOH or NALC**

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**Introduction:** Two methods to prepare panel test slide with known acid-fast bacilli using NaOH or NALC were introduced in External Quality Assessment for AFB Smear Microscopy (EQAASM) published by Association of Public Health Laboratories (APHL).

**Objectives:** To evaluate the preparation procedures of panel slides and the quality of the slides produced with these methods.

**Methods:** AFB positive and negative sputa were collected from several hospitals. Panel test slides were made according to both NaOH and NALC method described in EQAASM.

**Results:** The tested procedures were simple and easy and nearly 100 slides could be made in a day. However, some special expensive reagents were required. It seemed to be relatively easy for AFB detection comparing with actual specimens because the slides were very clear with less cell debris and fibers. Most obstacle problem was how to collect a large amount of AFB negative sputa for dilution of heavily positive sputa to make slides of different positivity.

**Conclusion:** The procedures were satisfactory, but they required expensive reagents and a large amount of AFB negative sputa which can be hardly obtained in TB prevalent countries. Therefore, artificial sputum should be made from ubiquitous cheap materials with avirulent mycobacteria to deliver standard panel test slides for QA.



**PS-488-536 TB reference labs in low income countries may need better support**

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**Introduction:** In Malawi, all previously treated smear positive TB cases submit 2 sputum specimens for TB culture and drug susceptibility testing (CDST) prior to starting retreatment. These specimens are sent to the Central Reference Laboratory (CRL), Lilongwe. An audit (published 2004) found only 36% of sets processed by CRL were successfully cultured and DST performed. Factors, such as excessive transit times, contributed to the poor isolation rate. Irregularities in laboratory processing of specimens may also have contributed.

**Objectives:** To determine whether practices within CRL were consistent with provision of a good quality CDST service.

**Methods:** CRL procedures were compared with standard practice recommended by WHO and IUATLD. Staffing levels, workload, availability of equipment, internal quality control (IQC) activities and external quality assessment (EQA) arrangements were assessed.

**Results:** CRL procedures sometimes differed significantly from standard practice. Staffing levels were adequate for current workload. Service and staff safety were compromised by deficiencies in equipment. IQC of activities was poor. The CRL was not actively participating in an EQA scheme for culture or drug susceptibility testing.

**Conclusion:** Practices at the CRL contributed to poor performance of the CDST service and could compromise drug resistance surveillance. CRL would benefit from technical and material support.

**PS-494-538 Quality management systems and the decentralisation of sputum smear microscopy services**

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**Introduction:** The Malawi NTP depends upon a national network of sputum smear microscopy centres. Central Reference Laboratory (CRL) is responsible, through Zonal TB Laboratory Coordinators (ZTLC), for quality of service provided. Decentralisation of sputum smear microscopy services is part of health sector reforms (HSR). However, quality management (QM) systems have retained their pre-HSR structure.

**Objectives:** To assess implications of service decentralisation for smear microscopy quality management systems.

**Methods:** Review of QM activities of CRL and ZTLC.

**Results:** Many people are screened for TB in the newly commissioned microscopy centers. Workload differed greatly between centres, as did the training of microscopists. Internal quality control procedures and reagent management practices also varied. The ZTLC is unable to conduct external quality assessment of all centres as scheduled, with some centres having no contact with the ZTLC. Criteria for triggering quality improvement activities are not defined. CRL does not assess quality of smear microscopy performed by ZTLC, nor does it provide a routine smear microscopy service, and it does not participate in an International EQA Scheme.

**Conclusion:** Decentralisation presents new challenges to the management of smear microscopy services. These new challenges may add to pre-existing ones. Quality management systems need to respond to changes in health service delivery.

**PS-828-899 Is there transfer of bacilli in batch staining of sputum smears?**

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**Introduction:** This study on batch against individual processing of sputum smears was done in Damien Foundation India Trust tuberculosis control project.

**Objective:** To document transfer of bacilli during restaining of sputum smears in batches in jar, in order to assess its suitability in the process of rechecking quality assurance.

**Design:** Routine samples from microscopy centers were randomly divided over batch and individual restaining prior to first rereading. Second level reader resolved discordant results.

**Results:** Of 2655 smears from 9 microscopy centers, almost equal numbers containing similar proportions of results were processed by either restaining method. Error rates among batch and individual restaining respectively were 0.5%/0.6% high false positive, 16.4%/7.1% low false positive (LFP), 0.6%/1.1% high false negative, and 2.9%/4.1% low false negative. Only the LFP difference attained borderline statistical significance ( $P = 0.05$ ), and total false negative (FN) came close ( $P = 0.08$ ).

**Conclusions:** If at all these differences in error rates correlated with restaining method used, they can not be explained by transfer of bacilli from positive to negative smears during batch staining, which would

have resulted in more FN. These results suggest that restaining smears in batches before rechecking does not introduce serious bias.

### PS-852-925 The TB laboratory network for sputum smear microscopy examination in Cambodia

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**Introduction:** The TB laboratory network in Cambodia has been playing an essential role in DOTS expansion. Support to basic TB lab network is one of the unique characteristics of JICA's assistance to NTPs in developing countries.

#### Achievements:

- 1 TB laboratories have increased from 118 to 180, namely 70 000 population covered with one laboratory, since DOTS was introduced through integrated health service at public hospitals in 1994.
- 2 The number of smears increased from 82 329 (700/lab/year) in 1994 to 145 105 (1200/lab/year) in 1998 when DOTS reached most hospitals. It increased more rapidly after DOTS expansion to health centers started in 2001, and it has reached 361 349 (2000/lab/year) in 2003.
- 3 The appropriate quality assurance activities including training were implemented by JICA TB Project that started in August 1999. As a result, smear positive rate among suspected patients decreased from over 30% in 1990s to 19% in 2003.
- 4 LQAS was adapted as a new sampling technique for blinded rechecking in 2002.
- 5 Systematic monitoring, evaluation and training for smear making have made it possible to expand DOTS to primary health care level where health workers such as nurses make sputum smear slides and transport them to the laboratory.

### PS-378-405 TPMo and sputum culture

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**Background:** The diagnosis of TPMo is often delayed. Our study evaluated the contribution of sputum culture (Lowenstein) to the diagnosis of this disease.

**Material and method:** All TPMo registered at the 'Laboratoire National de Référence' in 2002 and 2003. We have included all Ziehl-Neelsen negative cases and performed culture on Lowenstein-Jensen (LW).

**Results:** Only 7/123 (5.69%) cultures in 2002 and 7/130 (5.38%) in 2003 were positive. These results suggest the weakness of sputum culture to the diagnosis of TPMo and emphasize the relevance of other clinical markers.

### PS-384-410 Diagnostic evaluation of PCR, ADA and TNF- $\alpha$ assays for tuberculous pleuritis

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Diagnosing tuberculous pleuritis presents a problem as the patients fail to elicit typical symptoms of pulmonary tuberculosis. The conventional methodology to detect its causative pathogen, *M. tuberculosis*, is time consuming and low in sensitivity. In this paper an attempt has been made to validate additional diagnostic parameters like polymerase chain reaction test for tuberculosis, Adenosine deaminase (ADA) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels in pleural effusion from 65 suspected tuberculosis patients visiting Sri Guru Ram Das Institute of Medical Education and Research, Amritsar. The tests were compared with patients' response to anti tuberculosis treatment. It was observed that the specificity of the PCR test, ADA and TNF- $\alpha$  levels were 79, 85 and 93% respectively. Our results indicate that in countries with high prevalence of tuberculosis, determination of ADA and TNF- $\alpha$  level in pleural effusion provide a better criteria for initiating anti tuberculosis treatment as compared to the PCR test.

This work was supported by a research grant from University Grants Commission, New Delhi.

### PS-456-493 Rapid, sensitive detection of *Mycobacterium tuberculosis* in sputum: MODS (microscopic observation drug susceptibility assay) outperforms Löwenstein-Jensen and MBbAct culture

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**Introduction:** The global smear-positive case detection rate of 37% demands strengthening of the DOTS strategy and ignores the considerably lower smear-negative case detection and the 20% of transmission attributable to smear-negative disease. Rapid, sensitive detection of *M. tuberculosis* with the microscopic observation drug susceptibility assay (MODS) has been demonstrated in selected populations.

**Objectives:** To undertake a prospective head-to-head comparison amongst TB suspects of the performance (sensitivity of detection and time to culture-positivity) of MODS vs the twin gold-standards of culture in Löwenstein-Jensen and automated MBBacT culture.

**Methods:** In an operational evaluation in urban Lima, sputum samples of consenting patients are retrieved from the National TB Programme laboratories after performance of routine sputum smear, decontaminated and cultured in parallel in MODS, Löwenstein-Jensen and MBBacT.

**Results:** 102 of 1146 sputum samples were culture-positive for *M. tuberculosis* by at least one method. The sensitivities of detection (denominator = total number of positive cultures) were 79.5%, 87% and 95% for LJ, MBBacT and MODS respectively ( $P < 0.01$ ). The median times to culture-positivity were 16, 12 and 8 days respectively ( $P < 0.01$ ).

**Conclusions:** For detection of *M. tuberculosis* from the same clinical samples MODS has markedly superior sensitivity and is significantly quicker than LJ or MBBacT culture.

#### **PS-525-583 Sensitivity of a whole blood interferon- $\gamma$ release assay (IGRA) using ESAT-6 and CFP-10 compared to sputum smear in South African patients with sputum culture positive pulmonary tuberculosis**

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**Introduction:** South Africa (SA) ranks 9th worldwide in number of tuberculosis (TB) cases. The 2002 TB incidence was 558 cases/100 000. Despite expanding DOT coverage, the TB epidemic continues to grow, partly due to HIV co-epidemic. Up to 60% of adult TB cases in SA are HIV+ with associated high rates of acid fast bacilli (AFB) smear negativity.

**Objective:** To compare the sensitivity of a whole blood IGRA to that of sputum AFB smear for the rapid diagnosis of TB in the setting of a community TB clinic.

**Methods:** Preliminary analysis of results from 33 adults with positive sputum cultures for *Mycobacterium tuberculosis* but without a prior TB history from the Gugulethu TB Clinic in Cape Town, SA. Whole blood interferon- $\gamma$  responses to TB-specific antigens (ESAT-6 and CFP-10) were measured using an IGRA developed by Cellestis Ltd. of Australia.

**Results:** The sensitivity of sputum AFB smear and IGRA were 69.7% (23/33) and 87.9% (29/33), respectively. Of 9 patients known to be HIV+, 3 had negative smears, 1 had a negative IGRA.

**Conclusion:** This new whole blood IGRA offers higher sensitivity than sputum AFB smear for the

rapid diagnosis of pulmonary TB. Further data are needed to assess its specificity for this application.

#### **PS-685-758 Rapid diagnosis of multidrug-resistant tuberculosis using a novel, in-house, reverse line blot hybridisation method**

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**Introduction:** Tuberculosis remains the leading infectious cause of death in India, with more disease burden than any other country in the world. In the dilemma of diagnosing MDR, use of a rapid molecular assay would obviate the longer turnaround times with traditional drug susceptibility testing methods.

**Objective:** Using rifampicin resistance as a surrogate marker of MDR, we developed a rapid and highly sensitive reverse line blot technique for detection of mutations in the *rpoB* gene.

**Method:** Amine labelled oligonucleotide probes were designed (5 wild type and 10 mutant type) based on sequencing data of over 79 resistant isolates. These probes, covalently immobilized on the negatively charged membrane, were hybridized to *rpoB* gene PCR product from test samples and read by Electro Chemiluminescence.

**Results:** The results were seen as loss of signal in the corresponding wild type probe and gain of the signal in the respective mutant probe. Application of the method to a panel of 81 MDR-TB isolates with known mutations and 29 unknown isolates, showed 100% concordance with the sequencing results.

**Conclusion:** This rapid and economical method would give a breakthrough in the diagnosis of MDR-TB for individual patients and for the community at large and hence would also help reflect on the performance of the TB control programs. The method has been extended to direct detection from the patient samples and Ziehl-Neelsen stained slides, without the need for a viable culture.

#### **PS-727-801 Urine excretion study of rifampicin in patients with tuberculosis co-infected with HIV**

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**Background:** Reports have shown that very good correlation exists between the level of rifampicin in plasma and urine.

**Objectives:** 1) To determine the frequency and magnitude of below normal level of urine rifampicin in TB-AIDS patients. (2) Whether increment in dosage of Rifampicin achieves desired level?

**Materials & methods:** 63 patients with Pul.TB, with or without HIV-Infection were enrolled. After 2 weeks or more of anti-TB therapy urine was collected 2 hours and four hours after observed dose of rifampicin. Reading was reported as positive, trace or negative. Terminally ill patients and patients with diarrhea were excluded from the study.

**Results:** Low 2-hour and 4-hour urine concentration of rifampicin was common, compared to control group. Increment in the dose of Rifampicin had achieved desired level.

**Discussion:** Bio equivalence of rifampicin through urine excretion method proved to be simple, rapid, non-invasive and conclusive.

**Conclusion:** The result of the present study indicate that reduced rifampicin levels in TB-AIDS patients seems to be common phenomena and may be related to malabsorption in patients with HIV-infection. High doses of rifampicin may achieve the desired serum concentration.

#### **PS-749-823 Detection of culture positive tuberculosis by ligase chain reaction**

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**Objective:** The ligase chain reaction (LCx) *Mycobacterium tuberculosis* (MTB) complex assay uses LCx technology to detect tuberculosis DNA sequences in clinical specimen. This study was undertaken to determine usefulness of LCx, as a primary screening tool for the detection of culture positive tuberculosis.

**Methods:** The study was conducted on 8242 patient's clinical specimens, submitted for primary screening for MTB. Specimens were tested in parallel with smear, LCx, and culture. Positive culture was considered as the gold standard for diagnosis of tuberculosis.

**Results:** Total 176 patients were mycobacterium culture positive out of these 141 were LCx positive for MTB complex and 112 were smear positive for mycobacterium. Smear alone failed to detect 64 (36%) cases, where as, LCx alone failed in 35 (19.88%) cases, combined smear with LCx also failed to detect 32 (18.18%) case of culture positive tuberculosis. Smear has relatively low sensitivity (63.63%) but is highly specific (99.88%). LCx has high sensitivity (80.11%) and it is also highly specific (99.88%). Combining these two tests did not improve the detection rate.

**Conclusion:** We conclude that the LCx is a useful, primary screening test for tuberculosis, offering speed and discrimination in the early stages of diagnosis and complementing traditional smear and culture techniques.

#### **PS-764-838 Rapid BD Bactec MGIT 960 system vs standard methods for primary isolation and drug susceptibility testing of mycobacteria**

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**Introduction:** The Czech Republic is a small country in central Europe with 10 million inhabitants; it has a low incidence of TB (<18). However, poorly controlled migration and social unrest may change this situation.

**Objective:** To compare classical and rapid procedures for the investigation of mycobacteria.

**Materials and methods:** A total of 67 747 samples [59 558 (87.93%) sputum, and 8189 (12.09%) from other sources] decontaminated according to the NALC-NaOH method. Each sample was examined by Bactec, microscopy and culture on LJ. 345 strains were tested in S, H, R and E and 619 strains in S, H, R, E + PZA. Susceptibility to AT was determined by standardised methods of the Czech Health Care Service.

**Results:** The mean value for detection of all mycobacterial strains ( $n = 3608$ , 5.32%) was 13.76 days by Bactec, 28.27 days on LJ; for the *M. tuberculosis* complex ( $n = 3082$ , 4.55%) it was 12.67 days by Bactec, and 20.45 on LJ; for *M. avium*, ( $n = 130$ , 0.19%) 7.68, 30.56, respectively. Susceptibility to AT was performed on LJ medium and Bactec results were ready in 3–6 weeks, and 7.5 days, respectively, with identical results. The Bactec system is a better and advantageous than classical methods (LJ).

**Conclusions:** These results indicate that Bactec is rapid, more effective and sensitive, and is a valid alternative to primary isolation of mycobacteria and drug susceptibility testing.

#### **PS-794-867 Diagnosis of pulmonary tuberculosis by bronchoalveolar lavage and Mycobacteria Growth Indicator Tube (MGIT)**

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**Objective:** This study was conducted with aim to estimate the diagnostic ability of Mycobacterial Growth Indicator Tube and bronchoalveolar lavage as a methods for diagnosing mycobacteria in patients with smear-negative pulmonary tuberculosis.

**Methods:** Retrospectively were analysed the clinical records of 40 patients (15 females). The mean age of patients was 47.8 years. The main clinical symptoms were cough, fever and bloody sputum. Most prominent X-ray changes were small bilateral opacities.

**Results:** Mycobacterial Growth Indicator Tube was positive in 12 cases at 13.1 (4–20) day vs. 8 cases positivity in Lowenstein-Jensen at 32.5 (24–47) day and a smear for acid-fast bacilli was positive in 3 cases.

**Conclusion:** Bronchoalveolar lavage and Mycobacterial Growth Indicator Tube are more accurate and fast.

**PS-839-909 Direct diagnosis of MTB complex by the genetic technique TMA of the AMTD-Gen Probe system in patients suspect of tuberculosis, HIV and lung tumor**

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**Setting:** During 2003, we examined 8811 biological specimens by the TMA of Gen Probe (Bio-Merieux), 19 577 by LJ, 22 417 by ZN and 4926 by the MGIT (BD). Of the 8811 specimens, 37 were from 8 HIV patients and 61 BAL specimens, from 61 patients with lung tumor.

**Objective:** Evaluation of the AMTD Gen Probe system, LJ and ZN.

**Results:** We diagnosed 225 TB patients with >30 000 RLU, TMA Gen Probe. We found 9 patients with TB, under treatment with anti-tubercular drugs with <30 000 RLU. We found 14 resistant patients with RLU >535 005. We found 5 patients with L-J (+) for TB and (124 300, 72 244, 70 005, 54 028, 55 032) RLU each.

**Conclusion:** RNA is more sensitive than DNA. The cut off is specified in the double of the every day negative control. The observation is based on the generation time, with the reinforcement of the mycobacterium enzyme. Gen probe comes up with a result in 4, 5 hrs and has specificity 95–100% and sensitivity 96–100%. (LJ = 75% and ZN = 55–65%). An important reason for using the Gen Probe method is that there was no cross reaction neither among the 8 HIV patients nor in the 61 patients suffering from lung tumor.

**PS-918-993 Association of a course of pulmonary tuberculosis with genetic background**

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**Introduction:** Studying clinical course of destructive tuberculosis of the lungs (DTL) in patients with different genetic course that gives an earlier possibility to predict a course of process.

**Objectives:** To determine genetic markers in the patients with DTL in association with clinical course.

**Methods:** Three hundred and thirty three DTL patients have been examined. Haptoglobin (Hp) pheno-

type, inactivation type GINK, activity of glucose-6-phosphate dehydrogenase (G-6-PDA) enzyme were determined.

**Results:** It was established that Hp 2-2 phenotype, a weak type of GINK inactivation, a lack of G-6-PDA in  $9.7 \pm 2.1\%$  of patients were determined. A course of tuberculosis in these patients is grave, advances. Low indices of effectiveness were found. Hp 2-1 phenotype, a strong type of GINK inactivation, normal activity of G-6-PDA in  $7.7 \pm 1.8\%$  of patients was determined. A course of tuberculosis was low expressed, low symptoms. The patients with intermittent combinations of genetic markers formed  $56.4 \pm 2.7\%$  and  $26 \pm 2.4\%$ .

**Conclusion:** A range of genetic marker combinations associated with a course, outcome of pulmonary tuberculosis has been marked out.

**PS-344-368 L'apport de dépistage des sujets contacts sur la détection de la tuberculose Maroc 1993-2002**

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Au Maroc, l'incidence moyenne de la tuberculose est de 95 nouveaux cas pour 100 000 habitants. Depuis la restructuration du Programme National de Lutte Antituberculeuse en 1991, la priorité est portée sur le dépistage-traitement des cas de Tuberculose pulmonaire contagieuse (TPM+). Le dépistage est mené de façon passive chez les suspects et de façon active chez les sujets contacts. Ce dernier est réalisé dans l'entourage des cas de TPM+ et de primo-infection (PI). L'identification des personnes contacts est assurée à domicile, par le personnel de santé. Toutefois, depuis 1993 la collecte routinière des données montre que parmi les patients contacts recensés, chaque année, environ 80% sont examinés. Le diagnostic de tuberculose est retenu chez 2 à 4% des sujets examinés. La TPM+ et la PI sont dépistés dans environ 2% des cas. Ce qui représente respectivement 5 à 10% et 15 à 30% de toutes les TPM+ et les PI déclarés annuellement au Maroc. D'où l'impact sur l'amélioration du taux de détection de la tuberculose dépassant actuellement 85%.

**PS-743-817 A internet laboratory-based system for monitoring tuberculosis case-finding and diagnostic**

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São Paulo State, Brazil, has now more than 38 million inhabitants, living at more than 600 municipalities. Tuberculosis case-finding intensity is difficult to mea-

sure in a populous region with so many public and private laboratory facilities. Although the data were sent to tuberculosis program coordination, it were extremely difficult to be consolidated at state level. As case-finding is one of the main strategies for tuberculosis control, we developed a laboratory-based system, so named LAB-TB, to epidemiological surveillance of tuberculosis laboratory-related activities. From October 2002, all the laboratories involved with tuberculosis bacteriology were asked to inform monthly data about the number of suspects examined by smear examination, as well as the number of samples processed for diagnostic, smear-positive cases found and treatment control, and the number of cultures done. Until January 2004, a total 207 public and private laboratories participates, from 280 known to make tuberculosis bacteriology. They informed that 220 419 smear and 74 550 cultures were done in the year 2003, examining 122 695 suspects. The data are informed on-line, allowing evaluation at any time by all the involved personnel, detailed by laboratory and patient's residence. The LAB-TB system provides an easy and timely way for obtaining useful data for opportune interventions.

#### **PS-845-917 Results of contact investigations after identification of active tuberculosis in a pediatric case**

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**Introduction:** Children are seldom thought to be important transmitters of infection but spread of tuberculosis can occur from pediatric index cases.

**Objectives:** To determine the transmission of TB in a public school after identification of INH resistant pulmonary TB (PTB) in a 13-year-old female immigrant.

**Methods:** A descriptive review of investigations, chemoprophylaxis prescribed, and the rates of compliance in identified pediatric contacts.

**Results:** 313/318 contacts from school staff and students received a tuberculin skin test (TST). Of the pediatric patients, 17 were TST positive with another 13 converters were later identified after 2-step screening. 87% of patients were immigrants. All chest radiographs were normal. Two chest CT scans were performed. Chemoprophylaxis with Rifampin either self-administered daily or DOPT 3×/week was the standard prescription. Two patients refused prophylaxis, 70% agreed to daily therapy. Only one patient had poor compliance.

**Conclusion:** Transmission of infection occurred in 10% of exposed children. The number of converters among immigrant schoolchildren is high as is the possibility of infection from land of origin. There is a potential for possible transmission of infection from a pediatric case and disease progression and/or reactivation in the immigrant pediatric population.

#### **PS-933-1008 The magnitude of tuberculosis in children living with smear positive relatives**

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**Background:** Diagnosis of tuberculosis (TB) in children especially below 5 years is not easy. A study on children who were TB contacts was done using auramine-phenol method and culture. Sputum and gastric lavage specimens from clinically ill children were examined

**Method:** Between May and October 1999 we carried out an active specimen collection from children between 0–14 years who were clinically ill. Three hundred and six sputum and 322 gastric lavage specimens were collected from 312 children in University Teaching Hospital. Direct smears and smears from sediment were made and stained by auramine-phenol method examined by fluorescent microscope. All specimens were cultured on Lownstein-Jensen method. Parents or guardians were interviewed to find out if they were smear positive cases in the family.

**Findings:** A total of 95 (30.4%) children had smear and culture positive pulmonary tuberculosis. Three (1%) of these had smear negative but culture positive. Seventy one (22.6%) smear positive cases were involving children between 1–5 years while 24 (7.7%) were between 6–14 years and 60 (19.2%) were tuberculosis contacts.

**Interpretation:** The study showed that young TB contact children (0–5 years) were more at risk of contracting TB than the older children. Only 24 children (6–14 years) out of 95 smear positive cases were positive for acid-fast bacilli (AFB).

#### **TUBERCULOSIS IN LOW-BURDEN COUNTRIES**

##### **PS-197-240 Delay of diagnosis, drug resistance and treatment of TB in Germany 2001–2003: preliminary results of an epidemiological DNA-fingerprinting study**

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**Aims:** Description of preliminary data on initial tuberculosis (TB) treatment and drug resistance in 6 German regions.

**Methods:** Since October 2001, epidemiological data on TB patients have been collected and evaluated by the DZK in co-operation with 4 laboratories (Berlin, Borstel, Gauting, Regensburg) and regional public health services of 6 German regions: 4 cities (Berlin, Hamburg, Hanover, Munich) and 2 counties (Upper Palatinate, Lower Franconia). The data of 1329 patients were available by January 2004.

**Results:** 62% of patients were initially treated with four or five drugs, 33.8% with three drugs. 82.3% received a treatment regimen containing isoniazid, rifampicin and pyrazinamide. The time between suspicion of TB and diagnosis was less than one month in 61.2% of patients. In 28.7% the diagnosis was made 1–2 months after suspicion, in 7.9% after 2–5 months and in 2.2% a delay of more than 5 months was observed (mean delay 0.96 months; 95% Confidence Interval 0.57/1.35;  $n = 1145$ ). Resistance to any first-line drug (HRES) was observed in 11.7% of patients and multidrug resistance (MDR-TB) in 1.1%. Drug resistance was more frequent in the foreign-born with 16.4% (HRES) and 1.8% (MDR-TB), than in the German-born (7.5% and 0.4% respectively).

**Conclusion:** The diagnosis of TB is often delayed and the national TB guidelines are not adequately followed. Initial treatment should comprise four, in case of suspected drug resistance five drugs. The great variety of initial treatment regimens indicates the need for greater efforts in education and training.

#### PS-224-258 HIV-prevalence amongst tuberculosis patients in the Netherlands in the period 1993–2001

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**Objective:** To estimate prevalence of human immunodeficiency virus (HIV) infection among tuberculosis patients in the Netherlands and analyse the pattern of HIV infection according to demographic factors over time.

**Methods:** Data were obtained from the national surveillance register of notified tuberculosis (all forms) patients in the period 1993–2001.

**Results:** Of 13 942 patients diagnosed with tuberculosis, 542 patients were found to be HIV positive (overall prevalence 3.9%). Prevalence was 3.9% in 1993–1995, 3.7% in 1996–1998 and 4.1% in 1999–2001. The highest prevalence was observed among drug users (29%), homeless patients (20%) and patients residing illegally in the country (9%). Compared with the period 1993–1995, the relative risk of HIV-infection in the periods 1996–1998 and 1999–2001 decreased significantly for patients with drug or alcohol abuse, whereas it significantly increased for foreign-born patients, particularly refugees.

**Conclusion:** Although the prevalence of HIV infection amongst tuberculosis patients in the Netherlands remained stable over the period 1993–2001, the distribution of risk groups changed over this period.

#### PS-247-275 Tuberculosis among children in Florida, 1997–2003

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**Objective:** Identify trends in pediatric tuberculosis in Florida.

**Methods:** A retrospective review of tuberculosis cases, less than 15 years of age, reported to the state registry between 1997 and 2003.

**Results:** 261 cases were identified. This represented 3.1% of the total number of cases in Florida in 1997–2003. None were listed as contacts to active cases. The incidence rates per 100 000 individuals were as follows, less than 5 years 2.2, age 5–9 years 0.8, and age 10–14 years 0.6. There were no differences between incidence in boys and girls for any of the age groups. There were 7(2.7%) cases among children with HIV with a downward trend seen. There were 15(5.7%) cases of military or meningeal TB. Culture confirmation was obtained in 86(33.0%) and 7(8.1%) of these cases were resistant to isoniazid. There was one case of multidrug resistance. 18.4% were foreign-born in 1997 as opposed to 52.9% in 2003.

**Conclusions:** Rates of tuberculosis among children in Florida are stable. HIV has become less important and drug resistance is not an obvious problem. Trends in foreign-born children are reflective of trends in adults. Steps to improve identification of contacts are necessary to reduce the morbidity of TB in Florida's children.

#### PS-433-471 Gender, ethnic origin, and age and the risk of progression from infection to disease

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Tuberculosis is a two-step process—acquisition of infection and progression to disease. Different factors may contribute to each step. Identifying groups at risk for developing TB following infection is an important consideration for TB Control programs where treatment of LTBI is available. The study objective was to quantify the risk of progression to TB disease for gender, age, and ethnic origin. All Canadian-born nonaboriginal and aboriginal individuals registered in the Saskatchewan TB Control database with a newly documented positive tuberculin skin test (TST) between 1 January 1986 and 31 January 2002 were reviewed. A positive TST was defined as >5mm. Individuals who received BCG or LTBI treatment were

excluded. Results from 7588 individuals, 338 TB cases, were analyzed using Cox proportional hazards method. Males and females developed TB equally. All individuals <19 years of age were 10.6 times more likely to develop TB (95%CI 4.2–26.6) compared to those >19 years. Aboriginal Canadians were 6.2 (95%CI 3.1–10.2) times more likely to develop TB than non-aboriginal Canadians. Younger individuals regardless of ethnic origin and aboriginals regardless of age have a significantly higher risk of developing TB following infection.

**PS-533-591 Recurrent tuberculosis analyzed by DNA-fingerprinting: exogenous reinfection versus relapse tuberculosis.**

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Recurrent tuberculosis is a subsequent episode of tuberculosis occurring after a previous episode has been considered cured. Exogenous reinfection is a recurrent episode of tuberculosis, caused by a new strain of *Mycobacterium tuberculosis*. Relapse tuberculosis is a recurrent episode of tuberculosis, caused by the original strain. The possibility that a person previously infected can be exogenously reinfected has been debated for decades. Few studies have addressed this issue, and they include a limited number of observations, thus the reported proportion of recurrences due to exogenous reinfection has varied from 0% to 100%. Most often, a recurrent episode of tuberculosis is referred to as a relapse, not taking into account the significance of exogenous reinfection. If a patient, however, suffers from a recurrent episode of tuberculosis, the origin of infection has potentially important implications for tuberculosis control. Relapse tuberculosis can often be related to problems with treatment compliance, whereas exogenous reinfection, among others, can be related to the risk of infection, and thus transmission control efforts in a given area. This poster will describe 10 years nationwide data on more than 60 cases of recurrent tuberculosis, where both the initial and the subsequent episode of tuberculosis have been analyzed by IS6110 DNA fingerprinting.

**PS-569-638 Suivi de la tuberculose dans les centres médico-sociaux de la ville de Paris en 2002**

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Alors que l'incidence globale de la tuberculose a baissé en France en 2002, elle reste élevée à Paris et

touche plus particulièrement certains groupes de population. Cette étude décrit les caractéristiques démographiques, médicales et les résultats de traitement de 137 patients suivis pour tuberculose dans les Centres Médico-Sociaux (CMS) de Paris. Le recueil et l'analyse des caractéristiques de cette cohorte de patients est faite grâce à l'utilisation en routine d'un logiciel spécifique (TB INFO). Sur ces 137 patients, 89,8% étaient de sexe masculin, 88% étaient nés à l'étranger, 55,5% vivaient en collectivité, 41,7% n'avaient aucune protection sociale. Les formes thoraciques représentaient 96%. L'examen direct était positif dans 28% des cas et la culture positive dans 55%. Pour 68 antibiogrammes réalisés, 92,6% des souches étaient normosensibles et aucune n'était multirésistante. 75,9% des patients ont terminé leur traitement, 10,9% sont perdus et 10,9% transférés. Les patients suivis dans les CMS sont le plus souvent en situation de précarité. Dans ce contexte, le suivi informatisé a permis d'améliorer la surveillance du traitement.

**PS-590-660 Surveillance of drug resistance in Tuberculosis cases reported in England and Wales, 1998–2001**

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**Introduction:** The level of resistant TB is reported to be low in England and Wales but the increase in TB incidence over the last 10 years requires continued close monitoring of resistance trends.

**Method:** Drug susceptibility results reported through laboratories were matched to the 24230 cases reported to the National surveillance system in England and Wales for years 1998–2001 and analysed by standard statistical methods.

**Results:** Overall, during the 4 years, 735 cases were resistant at start of treatment to isoniazid (6%) and 95 were multi drug resistant (MDR) (0.8%). From 1998 to 2001 the proportion of isoniazid resistance significantly increased (5% in 1998 to 6.7% in 2001) while the proportion of MDR TB remained relatively stable. Persons born abroad had significantly higher levels of resistance for isoniazid and MDR but trend analysis of these population groups over time showed a significant increase in the UK born population only ( $P = 0.0016$ ) for isoniazid.

**Conclusions:** Levels of MDR resistance in England and Wales remained low and stable while the proportion of isoniazid resistant isolates have increased significantly. This is likely to be due to an ongoing outbreak of isoniazid resistance first identified in London in 1999.



### PS-596-666 New entrant TB screening to promote active case finding in the London Borough of Redbridge

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Since the mid 1980s the Rate of Tuberculosis in the London borough of Redbridge has nearly doubled. This increase has been partly attributed to increased migration to the area by individuals born outside of the UK; in 2002 only 16% of Redbridge patients were UK born ( $n = 20$ ). All new entrants to the borough are reported to the TB nursing team, those not screened at port of entry are offered screening at the chest clinic. Between January 2003 and December 2003 the TB nurses received 2388 notifications of new entrants to the borough. The predominant groups were immigrants (25.9%,  $n = 618$ ) and individuals entering under a student visa (36.9%,  $n = 881$ ). 677 patients were offered appointments. 43.1% attended ( $n = 292$ ), 33.1% had a chest X-ray performed ( $n = 224$ ) and 9.4% had a BCG scar check ( $n = 64$ ). Only 0.6% ( $n = 4$ ) had a tuberculin test performed. 4 patients (0.6% of all notifications of new entrants) were referred directly from the airport. There were no recorded cases of TB or chemoprophylaxis in the 292 patients attending the chest clinic. Routine chest X-ray screening of new entrants does not appear to identify cases of TB, different approaches should be introduced to increase active case finding amongst new entrants.

### PS-653-727 Epidemiological and clinical aspects of genitourinary tuberculosis in Siberia

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**Introduction:** Urogenital tuberculosis is on second place in a sick rate of tuberculosis. Complicated forms of disease predominate in the new-revealed patients.

**Material & methods:** We have analyzed epidemiology of extrathoracal tuberculosis in Siberia. The comparative analysis of clinical picture was conducted for 327 patients with nephrotuberculosis: 195 were observed in 1992 and 132 in 2002.

**Results:** In 2002 in Siberia 968 persons fell ill with extrathoracal tuberculosis (incidence 4.4 per 100 000). The share of genitourinary tuberculosis was 42.9%. Women were 69.8%, men—30.2%. In 2002 latent clinical picture was in 95.1%; though in 1992 34.5% patients had an acute beginning of nephrotuberculosis. Statistically more often the pain and hematuria were marked in 2002. Pyuria, dysuria and renal colic had approximately equal frequency in 1992 and 2002, but mycobacteriuria in 1992 was in 84.5%, and in 2002 only in 44.0%.

**Conclusions:** The main reason for the late diagnosis of urogenital tuberculosis probably is poor knowl-

edge of the doctors and the populations about this disease. The clinical picture was changed for the last year that makes timely diagnosis difficult.

### PS-654-728 Unnecessary anti-TB treatment in a liver transplant patient curtailed as a result of rapid genotyping of a suspected false-positive *Mycobacterium tuberculosis* (MTB) culture

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**Background:** Genotyping for suspected false-MTB+ isolates has taken 2–4 months from the 1st positive culture report.

**Patient history:** In January 2004, Patient A received a liver transplant and was placed on immuno-suppressant drugs. A small pleural effusion was seen; January bronchial washings were acid fast bacilli (AFB) smear-negative. On March 1, BactecR bottles were AFB+, and MTB+ by DNA probe 2 days later. Patient A was asymptomatic and tuberculin skin test negative. The pleural effusion had cleared. A false-positive culture was suspected. Caught between fear of 'fulminant' TB and drug hepatotoxicity, the physician prescribed anti-TB treatment on March 6. Laboratory staff reported that an MTB+ specimen from a known TB patient (Patient B) was collected 1 day before Patient A's specimen. **Methods:** On March 10, original BactecR bottles from both patient-specimens were submitted to the CDC genotyping laboratory for rapid (PCR) genotyping.

**Results:** Patient A and B's isolates had identical spoligotype and MIRU patterns. On March 15, anti-TB medications were discontinued. Patient A was treated for 9 days.

**Conclusion:** Rapid genotyping, clinical judgment, and prompt public/private communication significantly shortened the time from 1st culture false-positivity to genotype results (12 days vs. 2–4 months), resulting in cessation of unnecessary anti-TB therapy in a patient at high risk for hepatotoxicity.

### PS-660-734 Tuberculosis in London: results of the 2003 TB case load profile

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**Background:** London is the largest and most culturally and ethnically diverse city in Western Europe.

Rates of tuberculosis have doubled overall in the last ten years. This study aimed to describe factors affecting tuberculosis control and prevalence of disease in London.

**Methods:** Cross sectional survey including 2010 of 2080 patients with tuberculosis in London on 1 July 2003 (97%). Analysis of factors related to risk of disease, poor compliance, relapse and drug resistance and factors associated with patient management including access to services and DOT.

**Findings:** Very high prevalence of disease were demonstrated in people who were sleeping rough or using direct access hostels, prisoners, problem drug users and patients diagnosed HIV positive. A high proportion of patients have drug resistant disease (11.9% isoniazid resistant, 5.7% MDR-TB). 17% of prisoners with TB have MDR-TB and 10% of poorly compliant patients have MDR-TB. History of imprisonment in the UK and previous tuberculosis are strongly associated with isoniazid and MDR-TB on multivariate analysis. 10% of patients had ever been homeless and 4% were currently living on the streets or in hostels where more than half took tuberculosis treatment intermittently.

**Conclusion:** Tuberculosis in London is no longer under control.

#### **PS-719-793 Determinants of success in 9 European countries, 2000–2001: a multivariable analysis**

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**Objective:** To study determinants of tuberculosis treatment success.

**Method:** Individual tuberculosis notifications made by Austria, Belgium, Czech Republic, Estonia, Germany, Netherlands, Norway, Slovakia and Slovenia between 2000–2001 were pooled ( $n = 9808$ ). Outcome was determined by 12 months. A model with 19 explanatory variables and a binary response variable (success, yes/no), was analyzed using logistic regression.

**Results:** Success occurred in 74% of cases, death in 9%, unknown outcome in 9%, and other outcomes in 8%. At multivariable analysis, success was associated with young age (reference  $>74$  years): 55–74 years: OR 2.0, 95%CI 1.7–2.3]; 35–54 years 3.0, 95%CI 2.6–3.5; 15–34 years 3.6, 95%CI 3.1–4.3;  $<15$  years 4.2, 95%CI 2.8–6.3; absence of polyresistance (13.5, 95%CI 0.6–17.1); female gender (1.4, 95%CI 1.3–1.6) and being native or citizen of the reporting country (1.1, 95%CI 1.0–1.3). Compared to Estonia, odds ratios of success were significantly greater in the Netherlands (OR = 2.2), Slovakia (OR = 2.0), Norway (OR = 1.7), and Slovenia (OR = 1.5).

**Conclusions:** Poor success in the elderly should be addressed by improving detection in this risk group.

The low levels of success in polyresistant cases indicate that observation should be longer than 12 months in such cases. Differences in success between countries reflect variations in data completeness, residual confounding from other key determinants (comorbidity) and differences in the effectiveness of national control programmes.

#### **PS-791-865 Morbidity of pulmonary diseases registered by dispensaries of pulmonary diseases in AP Vojvodina and at the Institute for Pulmonary Diseases, Sremska Kamenica from 1992–2002: concerning tuberculosis**

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**Introduction:** There is a thick network of dispensaries for pulmonary diseases and tuberculosis throughout the region of Vojvodina. Of 44 municipalities in total, 42 have a pulmonary dispensary. Good cooperation is maintained between the dispensaries and the Institute for Pulmonary Diseases in Sremska Kamenica as their referential coordinating centre.

**Objectives and methods:** The analysis of the morbidity of the population in Vojvodina and the most common diseases has revealed the top position of pulmonary disorders in recent years, making 25–72% of the total of the diseases registered at certain health centres. Among pulmonary diseases, the acute respiratory ones have been taking the lead.

**Results:** Although tuberculosis has been exhibiting a decreasing incidence rate, the number of MT patients requiring hospitalization has been slightly increasing. This points to the fact tuberculosis has nowadays been taking severe forms.

**Conclusion:** The social and medical relevance of acute infectious respiratory diseases is due to the fact they affect a large number of people and spread rapidly, causing frequent absence from school and work. The increasing number of MT patients requiring hospital treatment indicates expansion of severe forms of this disease. Good prevention, timely diagnosis and therapy based on the most up-to-date achievements are therefore required to reduce the incidence of tuberculosis.

#### **PS-820-892 Treatment outcome in a large national cohort of pulmonary tuberculosis cases**

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**Introduction:** Population-based two-year cohort of all culture-verified pulmonary tuberculosis cases in

Finland was analysed for outcome, problems in applying the treatment outcome monitoring recommendations, and the feasibility of reaching the target level for successful outcome set by WHO.

**Methods:** WHO/IUATLD classification for treatment outcome evaluation was used. The treatments were divided in seven categories; A (2RHZ + 4RH), B (2RHS or 2RHE + 6RH), C (2RH + Z/E/S [ $>2$  of these] + 6-8RH + any other), D ( $<2$ RH + Z/E/S + 6-8RH + any other), E (non-standard combinations excluding previous), F (ineffective treatment), G (no treatment).

**Results:** The cohort included 693 culture-verified pulmonary tuberculosis cases. Mean age of the patients was 63 years. The outcome was favourable (cured/treatment completed) in 71% in A (total 333 in group), 47% in B (43), 68% in C (136), 73% in D (59), 69% in E (51), 61% in F (38), 0% in G (33), and overall 65%. There were no failures, and total proportion of defaulters and transfers out was low. Death rate was 20%, including also cases found at autopsy.

**Conclusion:** Treatment protocols varied both in combination and duration. The outcome monitoring recommendations were difficult to apply in a low-incidence country. Setting targets for favourable outcome proportions should take into consideration the age distribution of the population with tuberculosis.

#### PS-844-916 A review of pediatric tuberculosis in Manitoba, Canada

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**Introduction:** Canada is a low burden country, but there are at-risk groups for tuberculosis (TB), specifically the aboriginal (AB) and immigrant (IM) populations. Pediatric cases reflect transmission of infection in these groups.

**Objectives:** To review the epidemiology and distribution of pediatric TB in Manitoba.

**Methods:** A descriptive review of out-patient and in-patient profiles of children seen for evaluation of TB in a Respiratory Clinic between 2000 and 2003.

**Results:** Records of 208 (109 males) out-patients and 23 (7 males) in-patients were examined. Patients were 2 months-18 years old, 2/3  $<10$  years. Fifty-three per cent of the children were AB, with IM (38%). BCG rate was 53%. A diagnosis of TB infection was made in 58%, pulmonary TB 22%, and extrapulmonary TB in 2%. Two IM children were HIV seropositive.

**Conclusion:** TB continues to be disproportionately represented in AB and IM groups. Improved contact tracing and initiation of chemoprophylaxis and treatment for AB, with consistent pre-arrival screening and post-arrival surveillance for IM may change the incidence of TB in these groups.

#### PS-848-921 TB among aboriginal children in Manitoba

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**Introduction:** The incidence of tuberculosis (TB) in Canada remains 7-10 $\times$  higher in the aboriginal (AB) population compared to the Canadian-born non-AB.

**Objectives:** To determine the incidence of tuberculous infection and disease in AB children in Manitoba.

**Methods:** A descriptive review of pediatric TB seen in the aboriginal population.

**Results:** 114 AB (11/114 Inuit) were seen for evaluation of TB (2001-2003). 59 patients were male. 58/114 definitely had the BCG vaccine. The index case was a close household member in 77% of the cases. 51% had latent infection. One 5-year old patient had miliary TB. Majority of primary disease occurred in children  $\leq 5$  years old, 4/5 pleural effusions occurred in patients  $\geq 15$  years of age. Treatment was commonly self-administered until late 2001 when DOPT/DOT became more regularly enforced.

**Conclusion:** AB children generally acquire TB infection from the adults in their households. Younger children are at risk for progression to primary disease especially when the diagnosis of active TB in the adult is delayed. Improved contact tracing and investigations followed by prompt institution of chemoprophylaxis or treatment should reduce the incidence of disease in this high-risk population.

#### PS-897-971 The changing face of tuberculosis in a large North American city: a review of the last 500 consecutive admissions to a specialized TB service

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**Introduction:** We reviewed the last 500 consecutive admissions to the TB service at West Park Healthcare Centre, Toronto's only remaining in-patient unit for the treatment of complex cases of TB.

**Objectives:** To document the observed changes in both the clinical presentation and the demographic characteristics of the most complex TB cases in a large urban centre in North America.

**Methods:** We retrospectively reviewed all the charts of the last 500 consecutive admissions to our service.

**Results:** There has been a demographic shift in the complex TB cases, with 95% of cases occurring in foreign born patients, in Toronto for less than 5 years. We have seen a dramatic increase in the percentage of drug resistant and multidrug-resistant TB, with the latter increasing from 1% to 10% of all admissions.

We have also observed the emergence of dual infection with HIV/TB.

**Conclusions:** The world-wide TB epidemic with increasing drug resistance and HIV/TB co-infection, combined with ongoing complex emergencies and displaced populations moving from endemic to non-endemic countries will ensure that TB continues to be a major public health challenge and has changed clinical characteristics of the disease in our environment.

#### PS-898-973 Collaboration between welfare and health sectors for TB treatment of the homeless in Japan

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**Objective:** Poor adherence to drug treatment is a major problem among the homeless TB patients, which is major population of TB patients in Japan. Although the Japanese TB Protection law provides them of treatment service as national duty, the patient are not willing to be treated and not a few patients escaped from hospitals to stop treatment. To investigate its reasons and implement an effective measures, operational studies has been conducted.

**Methods:** In Tokyo and Osaka, which were ranked highest national notification rates of TB among the homeless, coordination between the welfare and health sectors beyond routine meetings, such as exchange roles in simulation exercise to learn other roles, has implemented. In addition, welfare activities were strengthened by private sectors including NPOs. Action plans were integrated welfare segments with TB care under the guidelines of the New TB Protection Law and the Livelihood Protection Law.

**Results:** Better linkage between welfare and health sectors contributes to improvement of treatment completion of TB among homeless people.

**Conclusion:** The study shows work division of central and local governments, and NGOs also should be clearly identified for creation of effective cooperation of two sectors. The collaborative action plan in local government with financial commitment of central government with support of NPOs is important for TB control among the homeless.

#### PS-929-1004 Comparative patient control during the years 2001–2003 compared to the years 1991–2000 at the MBTB Reference Centre, Greece

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**Objective:** TB diagnosis and the study of incoming suspect TB patients, during the years 2001–2003 in comparison to the years 1991–2000 at the MBTB) reference center of the Aristotle University Pneumonological Clinic.

**Material and methods:** During the years 2001–2003 we examined 24 957 suspected TB patients, 81 046 biological specimens and we performed 155 279 laboratory tests (69 186 of sputum, 11 860 of other biological specimens); 33 499 were examined by the Lowenstein-Jensen, 14 627 by Gen-Probe, 35 389 by Ziehl-Neelsen and 11 246 by the MGIT method.

**Results:** We isolated 557 new *M. tuberculosis* strains out of an equal number of patients (460 Greeks and 97 immigrants) which later on were inoculated in dilutions of anti-tuberculosis drugs for susceptibility testing. We used the following drugs: NSM, INH, RMP, EMB, PAS, PZ (Canetti method).

Year	Percentage <i>M. tuberculosis</i>	Biological specimens	Strains
1991–2000	3.22%	56 585	1820
2001–2003	0.68%	81 046	557

Table: The results show: 1) An increase of TB in 2001–2003 in comparison to 1991–2000; 2) a reduction of the virulence of the biological specimens; 3) An increase in *M. tuberculosis* strains.

#### EPIDEMIOLOGY OF TB: SPECIAL POPULATIONS AND INSTITUTIONS (MIGRANTS, HOSPITALS, PRISONS)–2

##### PS-566-634 Improving case-detection by including prisoners in reported notifications to WHO

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**Introduction:** In the European Region, prisoners are a high risk group for TB, particularly in the Newly Independent States. However, the inclusion of prisoners with notification data is not routine for some countries.

**Methods:** We evaluated which countries in the Euro-

pean region did not include prisoners with national data submitted to WHO over the last two years (2002–2003). We used estimated numbers of prisoners to calculate the estimated number of prisoners with TB. We added these estimates to the reported notifications and recalculated the case-detection rates. Lower and upper ranges were estimated.

**Results:** Three countries have not routinely included prisoners in their reported notifications (Table):

Estimates	No. of prisoners	No. of prisoners with TB	Increase in detection rate: all cases	Increase in detection rate: new, pulmonary, smear-positive
Serbia and Montenegro	7 241	29–145	0–2%	1–4%
Ukraine	202 943	6 088–12 177	3–13%	7–29%
Uzbekistan	47 297	1 419–2 838	1–5%	3–12%

**Conclusions:** Inclusion of prisoners in national data reported to WHO could significantly improve the case-detection rates in two countries in the Newly Independent States, but is unlikely to make a significant impact in case-detection in Serbia and Montenegro.

### PS-567-633 Modelling the effect of new entrant screening in England and Wales

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The efficacy of new entrant screening was assessed with the use of a mathematical transmission model that simulates the epidemiology of tuberculosis within England and Wales. In order to assess the efficacy of new entrants screening in this way it is necessary to first define a suitable outcome variable, a control baseline and the set of service models to be investigated, including the status quo. The outcome variable is the number of tuberculosis cases attributable in a 5 year period to chains of transmission initiated by new entrants. This has been evaluated by running a simulation in which no screening of any kind was carried out, thus defining a baseline. The difference in outcome between baseline and the number of cases of tuberculosis predicted to occur over a similar period under conditions chosen to mimic the status quo provides a quantitative measure of the benefit of current

control measures. The benefits of alternative screening scenarios, similarly calculated, were then compared with the current system and any advantage or disadvantage quantified. Estimated costs of different approaches have been entered into the model to estimate their cost effectiveness.

### PS-579-649 TBSCAN: understanding the results of screening immigrants for tuberculosis

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**Introduction:** Evaluation of tuberculosis screening programmes for immigrants is not straightforward due to poorly understood aspects of tuberculosis epidemiology. **Objectives:** To identify key factors that determine the impact of screening on transmission, to capture these factors in the micro-simulation model TBSCAN, and to analyse results of screening programmes.

**Methods:** Concepts from existing models of tuberculosis transmission and screening theory serve as inspiration. TBSCAN is being developed, quantified and validated using immigration pattern data and epidemiological databases of tuberculosis, including the Netherlands Tuberculosis Register.

**Results:** Identified key questions currently under investigation are: what is the infection prevalence in immigrants?, what are the reactivation rates in infected immigrants?, what are the transmission rates?, how fast is progression to various stages of pulmonary tuberculosis (e.g., sputum smear-positive)?, what is the gain in detection delay due to screening (lead-time)?, and how long is the period without complaints during which tuberculosis can be diagnosed by x-ray? The TBSCAN model captures these factors and will be presented together with tentative quantifications of model parameters and exploratory simulations of effects of the Dutch screening programme.

**Conclusion:** We envisage that TBSCAN will be a valuable tool to investigate the effectiveness of screening programmes.

### PS-584-656 Comparison of immigrant tuberculosis patients detected by screening and passively: unexpected findings

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**Introduction:** Immigrants are screened by X-ray in the first 2.5 years of residence in the Netherlands.

**Objectives:** To investigate how screening interferes with tuberculosis transmission.

**Methods:** For immigrants with pulmonary tuberculosis detected during 1996–2002, either passively or by screening and within 2.5 years after immigration, detection delay, risk to be the first detected patient of a DNA-fingerprint cluster, and sputum smear (ZN) results were analyzed.

**Results:** The study population included 777 patients. The risk to be first of a cluster did not substantially differ between patients detected passively and by screening, although the average detection delay was clearly shorter for the latter group. The delay was shorter in first patients of clusters compared to unclustered patients for those passively detected, but not for those detected by screening. Patients detected by screening were significantly more often ZN-negative (58% vs. 32%). Still, about half of those detected by screening who were the first of a cluster, were ZN-negative.

**Conclusion:** The risk that patients detected by screening are the first of a cluster is not negligible, even if they are ZN-negative. The detection delay reduction by screening increases the risk to be detected first in clusters. Consequences of this lead-time bias are investigated.

#### **PS-622-690 Long-term risk of tuberculosis among foreign-born residents in Norway**

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**Objective:** To examine the long-term risk of TB among foreign-born.

**Methods:** Data on 384 868 of foreign-born (except those from Nordic countries) aged five and above who arrived in Norway from 01.01.1986 to 31.12.2002 were received by the Directorate of Immigration. Of these, 1514 persons were subsequently reported as having TB at the National TB Register. Observation period for TB cases was calculated from date of arrival to TB registration. For persons without TB (the denominator), it was calculated from date of arrival to date of leaving the country, date of death or to end of follow-up (31.12.2002).

**Results:** For persons born in Africa and Asia, the TB rates were 190 and 80 per 100 000 person-years respectively 7 years after arrival in Norway. For persons born in former Yugoslavia, Somalia, Pakistan and Vietnam, the TB rates were 40, 520, 160, 210 per 100 000 person-years respectively in that period. These rates are 7 to 90 times higher than the annual TB incidence for Norway. This increased risk applies also for both men and women and for pulmonary and extra-pulmonary TB sites.

**Conclusion:** There is a need of awareness among health personnel that foreign-born residents remain at significant risk for TB many years after arrival.

#### **PS-774-848 Tuberculosis in marginal groups in the Slovak Republic**

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In Slovakia, a small country in Central Europe, with the incidence of tuberculosis 18.4/100 000 population (990 new cases in 2003), there are marginal groups, such as migrants, asylum seekers, refugees and gypsies. These represent a problem for national tuberculosis program management. Gypsy population represents about 6% of the Slovak population. The process of assimilation of this ethnic group is indisputable. However, there are numerous factors, such as different age structure, socioeconomic and cultural factors, as well as mentality of this population that contribute to the process of the disease transmission. In the years 1990–2003 there were 1348 cases of tuberculosis in this ethnic group reported. It is 9.3% of all newly detected cases. The regional distribution of the incidence show great differences. In Eastern Slovakia, with 65% of gypsy population 88% of TB cases were reported. This is also the area with the highest unemployment rate, where gypsies live in poor social and economical conditions. In 2003, 72.3% of total childhood TB cases were observed in gypsy children. The main problem seems to be a difficult control of treatment under DOTS according to their mentality and a great proportion of childhood TB. There were new groups-at-risk in Slovakia created in the past four years. These are migrants, asylum seekers and refugees, mainly from India, Afganistan and NIS. These groups of patients were responsible for 50% of drug resistant cases in Slovakia. Is very difficult to obtain the treatment outcomes, these patients do not remain in the Slovak territory for the whole period of their treatment. It is necessary to establish the compatibility among the National TB registers of EU member states with respect to these groups at-risk, and create a unified system compatible with the majority of EU countries.

### PS-817-889 Linking structured interviews with the United States tuberculosis registry to identify missed opportunities for tuberculosis prevention among the foreign-born

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**Introduction:** Tuberculosis cases among foreign-born residents in the United States (U.S.) exceeded 50% of reported cases in 2003, a phenomenon that occurred years earlier in other established market countries. Mandatory public health reporting of newly diagnosed cases provides surveillance data including country of birth and length of U.S. residence, but does not address the potential for prevention.

**Objectives:** 1) To describe hypotheses regarding the efficacy of immigrant and refugee screening, hypotheses that have been generated by published analyses of national surveillance data. 2) To show how surveillance data can be enhanced through the use of a structured questionnaire.

**Methods:** We review published analyses of national surveillance data of tuberculosis cases among the foreign-born in the US Pilot data collected for a study supplementing national surveillance data with structured interviews is analyzed.

**Results:** Current surveillance can only generate hypotheses regarding the efficacy of immigrant and refugee screening but cannot substantiate them. Pilot interview data for >100 subjects, most interviewed in Chinese, French, Haitian Creole, Hindi, Korean, Spanish, Tagalog, or Vietnamese, shows that TB cases occur in screened and unscreened foreign-born residents alike.

**Conclusion:** Changes in public health reporting may be required to define opportunities for prevention of tuberculosis among the foreign-born.

### PS-832-903 Effect of migration on epidemic of tuberculosis in Beijing, China

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**Introduction:** With opening policy implemented, tuberculosis situation changed and tuberculosis cases increased in the migration in Beijing, China.

**Objectives:** A study of the effect of migration on the epidemic of tuberculosis in Beijing, China.

**Methods:** Trends of newly registered active and smear-positive pulmonary tuberculosis cases were compared and evaluated in census and migration in Beijing.

**Results:** Number of newly registered active and smear-positive pulmonary tuberculosis cases decreased

from 2347 and 764 in 1993 to 2204 and 703 in 2002 in census register population of Beijing, which only went down by 6% and 8% respectively during the 10 years. In the contrary, number of newly registered active and smear-positive pulmonary tuberculosis in migration increased from 242 and 90 cases in 1993 to 1075 and 304 cases in 2002, which increased by 344.2% and 237.8% respectively. If the number of active and smear-positive cases in census register added the cases in migration were 3279 and 1007 cases in 2002, which corresponded to the levels of number of active and smear-positive cases in 1989 and 1992 respectively.

**Conclusion:** The trends of increasing tuberculosis cases in migration were gradually effect on epidemic of tuberculosis in Beijing, which should pay great attention and have to take effective control measures.

### PS-842-915 TB resistance in the Republic of Moldova before and after DOTS implementation

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**Settings:** Drug shortage in 1996–2000 resulted in an eruption of high level of morbidity and TB resistance in Moldova. In 2001 the DOTS strategy was implemented.

**Objective:** To evaluate the level of TB resistance of Moldova in 2003, comparing with previously data (1996–2001).

**Design:** The method of absolute concentrations on L-J media was used for drug-susceptibility-testing (DST). Were recorded: DST results, previous treatment, age, sex.

**Results:** The TB drug resistance in Moldova was increasing during five years (1996–2001) and was estimated to grow up to 31.6% any resistance and 6.6% MDR. For last two years, after DOTS implementation, the increase of TB resistance is not marked. In 2003 any resistance of patients never treated was 20.4% and the level of MDR was 6.0%.

**Conclusion:** The level of TB drug resistance in Moldova is in still high. Inadequate treatment has led to increasing prevalence of drug-resistance. The implementation of the DOTS programme has resulted in some decrease in TB resistance. It is important to establish prospective anti-TB drug resistance surveillance on a national level.

**PS-846-919 TB among foreign-born children in Manitoba**

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**Introduction:** Canada accepts >250 000 immigrants/year, mostly from countries with high tuberculosis (TB) prevalence rates with 35% of new arrivals <25 years of age. Current immigration screening focuses on high-risk groups but excludes the pediatric population as being at risk for progressive disease.

**Objectives:** To determine the incidence of pediatric TB in immigrant population seen at a pediatric clinic in Manitoba.

**Methods:** A descriptive review of TB seen in foreign-born (FB) children.

**Results:** 73 FB children were referred for contact investigations (2001–2003). 24% were from the Philippines and 51% were from the African continent. 38 were male. 50% definitely had the BCG vaccine. 69% had latent TB infection, 5% had primary disease, 1% reactivation TB, 3% with extrapulmonary disease (cervical lymphadenopathy and miliary disease). 16% were tuberculin skin test negative with normal chest X-rays. Most of the patients went on self-administered chemoprophylaxis or treatment. There was good adherence to therapy.

**Conclusion:** Over a third of patients seen in a pediatric TB clinic originate from countries with high incidence of TB. Current immigration medical examination of children does not screen for latent infection, which is likely acquired in their home countries.

**PS-855-928 Tuberculosis: a real challenge for general hospital**

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**Introduction:** Tuberculosis (TB) is a major health problem in Brazil. The general hospital plays an important role in tuberculosis epidemiology as a risk place for transmission. Currently, difficulties of access to basic health care means that patients with active TB are admitted to hospital for any conditions, and not have TB as their main diagnosis.

**Objectives:** To determine the epidemiological situation of tuberculosis at Cardoso Fontes Hospital.

**Methods:** In this retrospective study, 87 patients with TB cases were analysed, notified to epidemiology service from January to October 2003.

**Results:** 87 in-patients were analysed. Seventy per cent were males, aged between 9 and 84 years; 50% were diagnosed at emergency room. Pulmonary tuberculosis was present in 45%, with positive sputum in 44%. The others forms were pleural (35.2%), mil-

iary (9.1%) bone (1.1%) and ocular (1.1%). New cases were diagnosed in 82%. Respiratory isolation occurred in 85.7% within first 24 hours of admission. Cachexia was the main reason for hospitalization. Death occurred in two patients.

**Conclusion:** Knowledge of tuberculosis outline in the general hospital allows staff and health managers to cope with treatment and administrative challenges, fighting together against spread of this disease.

**PS-856-929 Presentation of pulmonary tuberculosis in cannabis and/or opiate drug abusers**

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**Introduction:** Drug abuse is one of the possible factors for TB. Presentation of pulmonary TB may differ in this hidden population group.

**Objectives:** 1) To determine the clinical and radiological presentations and susceptibility pattern in new PTB patients who smoked either cannabis or opiates or both. 2) To compare the difference/s, if any, between drug abusers and non abusers.

**Methodology:** This was a comparative hospital based study conducted among new culture positive PTB patients who either smoked cannabis or opiates or both and who never abused drugs. Patients were recruited from two major health facilities—Jinnah Postgraduate Medical Center Karachi and Ojha Institute of Chest Diseases, Karachi.

**Results:** Dyspnoea was the presenting symptom in significant proportion of the PTB patients who smoked drugs (43.6% vs. 7.4%) (OR 9.68, 95%CI 3.69–27.11,  $P < 0.01$ ). Mean durations of most of the symptoms were significantly longer ( $P < 0.05$ ) in drug abusers. More than 70% of PTB patients abusing drugs presented with bilateral extensive lesion on chest X-ray ( $P < 0.05$ ). 3% of PTB patients abusing drugs presented with primary MDR TB ( $P > 0.05$ ).

**Conclusion:** New PTB patients with drug abuse differ in clinical and radiological presentations from those who never abused drugs.

**PS-891-966 Pathologists have the shortest interval between graduation and respiratory tuberculosis**

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**Methods:** 75 cases were registered as physicians with active tuberculosis in the National Register of Occupational Diseases within years 1966–2000 in Finland. Data was combined with the register of physicians



and with the information of patient records when available. The information included age, sex, diagnosis, date of registration of tuberculosis and year of graduation, possibly work history and specialization. Nine cases were excluded (not physician, not respiratory tuberculosis). 65 cases were analysed (39 men, 26 women). Grouping was based on risk fields: 19 (29.2%) had worked in the field of pathology or legal medicine, 11 (16.9%) in pulmonary medicine, 3 (4.6%) in laboratory, 3 (4.6%) in developing countries, 24 (36.9%) in other fields, and for 5 cases (7.7%) work history was not known.

**Results:** In the field of pathology or legal medicine the interval between graduation and disease was short, mean 4.9 years, in other groups it was 9.4 years, 15.7 years, 14.3 years and 11.1 years respectively. Those with no work history had the mean of only 1.6 years, this included the cases with the shortest disease onset after graduation or even as a student. Further analysis and discussion is presented.

#### PS-893-967 Improvement of TB control program in a hard to reach area of Nepal

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**Introduction:** After the implementation of DOTS strategy in 1996 Nepal has been able to expand DOTS throughout the country, achieve and sustained the global target in case finding and cure rate. Still TB control in hard to reach area is a challenge. To address this issue a pilot program was initiated in a mountain district.

**Objective:** Increase the no of TB symptomatic visit to the health facilities, increase case finding and cure rate and produce hard to reach TB control model in Nepal

**Methods:** Expansion of microscopic services and DOTS center to increase accessibility; intensive IEC activities to increase public awareness; community mobilization to improve compliance and development of a courier system for smear transfer.

**Conclusion:** Increase public awareness by mobilization of community together with increase accessibility to quality services will improve TB control program.

#### PS-928-1003 MDR-TB prevalence and its influence on treatment outcomes in East Kazakhstan prisons

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**Objective:** To identify the reasons of failure and MDR TB prevalence among patients in prisons.

**Methods:** Review of case histories. DST results were retrieved from the regional TB laboratory; treatment outcomes were identified through the TB register.

**Results:** In 2002 failure makes 19% among NC smear+ and 29.3% among relapses. Failure patients were tested for DST by the end of 2nd–3rd month of treatment. 82.8% NC smear+ and 70.6% relapses had MDR. In the 2003, 1 quarter, 25 NC smear+ were notified. 20 out of 25 had been tested for DST (Table).

#### Treatment outcomes of NC smear+ registered in 2003, 1 quarter

Cured	11 (44%)
Failure*	10 (40%)
Defaulted	1 (4%)
Transferred out	3 (12%)
Total	25 (100%)

\* All 10 failures had MDR–100%.

#### DST results of NC smear+ 2003, 1 quarter

	Tested in 1st month	Tested after 1 month	Total
Underwent DST, total	12 (48%)	8 (32%)	20 (80%)
MDR	5 (20%)	6 (24%)	11 (44%)
Poly-resistant (H <sub>s</sub> S <sub>s</sub> E)	1 (4%)	0	1 (4%)
Completely susceptible	4 (16%)	0	4 (16%)
No culture growth	2 (8%)	2 (8%)	4 (16%)

**Conclusion:** Prevalence of MDR TB in East-Kazakhstan Region prisons is very high. MDR is the main reason for failures.

## DOTS EXPANSION

#### PS-145-181 The incorporation of symptomatic respiratory active search for tuberculosis control in community health agents practice in the municipal health department of Ribeirão Preto-SP, 2002

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**Aim:** To analyze the incorporation of the active search for respiratory symptoms in TB control into daily activities, from the perspective of the Community Health Agent (CHA), in the context of basic care reorganization.

**Methods:** This study was structured in two phases: 1st: Monitor sputum smear records in municipal reference laboratories. 2nd: Analyze the incorporation of the active search for RSs in a Ribeirão Preto district from the perspective of 81 CHA.

**Results:** Initially, the number of requested smear (BK) increased, but decreased over time.

**Conclusion:** With a view to its development, the fam-

ily approach demands CHAs to master other kinds of knowledge and requires the integration among different care points in the health service system.

**PS-203-246 Incorporating the active search for breathing symptoms for tuberculosis control into the practice of community health agents from the perception of nursing supervisors: a challenge for primary health care**

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**Aim:** To analyze the incorporation of the active search for respiratory symptoms (ASFRS) for Tuberculosis Control at a Municipal Health District in Ribeirão Preto-SP, Brazil, according to the perception of nursing supervisors in the Community Health Agent Program (CHAP).

**Population:** 8 nurses, responsible for supervising 81 Community Health Agents (CHA).

**Methodology:** A qualitative approach and semi-structured interviews were used as a data collection instrument. Data were analyzed by means of the thematic content analysis technique.

**Results:** the 2 thematic units were: 1. Strengths and Weaknesses in inserting the CHAP into Health Units. The decentralization of the active search for respiratory symptoms revealed to be a strong point. The weak points indicated were: nursing supervisor's accumulation of functions; insufficient CHA training process; absence of discussion about inserting the CHAs into the health team; absence of CHAP leadership or coordination in the municipal sphere. 2. Relation between the CHAP and the Health Unit in APS actions. The organization of the health service system and the relationships and commitment between health professionals and users came up as difficulties.

**Conclusion:** In order to incorporate the ASFRS into the CHAP, we have to rethink the organization of health services and assume a set of actions that go beyond the internal environment, so as to move towards a new work logic.

**PS-250-278 Diagnostic and treatment delays of TB and their determinants in Pakistan**

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Delay in diagnosis and treatment of tuberculosis results in increased infectivity of contacts. A multicountry study was conducted in 7 countries of EMRO with the objective of studying diagnostic and treatment delays of tuberculosis and their determinants.

This was a cross-sectional study of newly diagnosed TB cases conducted in Pakistan. 844 cases of TB were enrolled. Self-medication was tried by 59% of patients. Nearly 56% of patients consulted at least five local HCPs before reaching the Chest Clinic. Nearly 85.4% were diagnosed with TB, between two to four months after first consultation with HCP (diagnostic delay) with a mean of 86.6 days. On the contrary, the patient delay was only 9 days (mean). In the Chest Clinics Treatment Delay was 3 days in 71.4% of cases and nearly 10 days in the case of private HCPs. Multiple regression indicated diagnostic delay to be more strongly correlated with stigma's associated with TB, as opposed to treatment delay being affected by availability of services. In Pakistan, consultation with several private HCPs results in long diagnostic and treatment delay for TB patients. Stigma associated with TB and services at the health facilities contributes towards this.

**PS-289-324 Integration of TB-DOTS in the services range in urban NGO clinics in Bangladesh: a situation analysis**

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**Introduction:** Bangladesh is the 4th highest burden country, with 300 000 new cases annually. This poses a challenge, especially for case detection and treatment compliance among urban populations.

**Objectives:** To assess scope and extent of integration of TB-DOTS in primary health care, quality of drug dispensing and follow up in urban areas.

**Methods:** Providers' knowledge and skills, and records studied in 15 primary health care NGO clinics.

**Results:** Overall TB caseload was low; mode of DOTS was through family members (60%), direct patient attendance (60%) and provider home visits (53%). All clinics had TB-related BCC activities, which were not integrated with overall BCC. Though immunization and ANC were available, there was no integration between these and TB. Only 13% of dispensers were fully trained in anti-TB drugs; record keeping was inadequate; advice on DOTS, especially importance of regular treatment and follow up was inappropriate in majority cases.

**Conclusion:** Ensuring successful urban TB-DOTS implementation calls for focus on

- TB-DOTS integration with primary health care, especially through missed opportunities among maternal and child health clients;
- Enhancing community involvement in urban DOTS.
- Quality of drug dispensing, focusing on ensuring compliance through intensive counseling and follow-up.

### PS-310-341 Prise en charge communautaire des tuberculeux pulmonaires positifs (TPM+) à Yopougon

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**Introduction :** Le (CDT) de Yopougon a bénéficié d'un projet pilote sur le traitement directement observé (DOT) à travers les visites à domicile (VAD) des TPM+ par 10 volontaires de l'ONG SidAlerte-CI.

**Objectif :** Amener tous les malades à la guérison.

**Méthodes :** Collaboration entre le Programme National de Lutte contre la Tuberculose, le CDT et SidAlerte-CI, formation, cartographie, identification des TPM+, distribution des médicaments, information-éducation-communication aux malades et à la communauté, deux VAD/semaine/volontaire/malade.

**Résultats :** juillet à décembre (tableau)

	Avant (2001)	Après (2002)
TPM+	114	171
Guérison	35,96%	71,92%
Traitement complété	18,42%	8,18%
Echec	7,89%	3,50%
Transfert	10,52%	4,67%
Abandon	24,56%	4,67%
Décès	2,63%	7,01%

**Conclusion :** Succès, acceptation de la tuberculose par la communauté. Les fausses adresses, l'insuffisance des volontaires, l'étendue de Yopougon sont des difficultés majeures. La décentralisation du projet est en cours.

### PS-336-363 Community participation in DOTS expansion in Kenya

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Kenya is one of the 22 high tuberculosis burden countries. The drastic increase in the TB burden over the past decade has greatly increased pressure on existing government health services prompting fresh interest in evaluating the potential contribution of communities to TB care. The number of new TB cases reported by the National TB Program (NTP) for 2003 was 82 000 with a case detection rate of 47%. In Kenya a study done in Machakos in 1998–1999 showed that the intervention was effective. As part of the first phase of DOTS expansion strategy in Kenya, a workshop was held where 45 regional trainers of trainers (TOTs) were trained. These will in turn train district TOTs, who will be responsible for training community TB treatment supporters. Capacity building on the new tasks assigned is greatly emphasized. The implementation will be phased in approach to allow les-

sons to be learned and adjustments made as implementation proceeds. The strategy aims to increase accessibility to TB care services in the community and improved treatment outcomes.

### PS-374-400 DOTS implementation through community health workers in a poor community (Rocinha) in Rio de Janeiro city

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**Introduction:** Rio de Janeiro has a high incidence of TB and several poor communities (slums) heavily affected by the disease. This project aims to strengthen TB control in Rio de Janeiro promoting the integration of DOTS activities into the Family health and Community health workers program (PSF/PACS). Rocinha has 100 000 inhabitants and reports 320 TB cases annually.

**Objectives:** To establish a DOTS program relying mainly on community health workers (CHW) in large urban center.

**Methods:** Forty CHW were selected from their own community and trained by the health department. Each HW covers about 150 to 250 households and performs an average of 8 household visits per day. Each team has 20 CHWs supervised by a nurse.

**Results:** From July 2003 to January 2004, 234 TB cases were identified in the community and treated under DOTS. The cure rate was 92.9% for those who already completed treatment. No defaults were observed. During this same period different educational activities were developed in schools, NGOs, and community based organizations reaching 97 teachers, 365 students and 695 inhabitants.

**Conclusion:** This experience shows that CHWs can be a good strategy for DOTS implementation in a slum in a large urban city.

### PS-551-614 Directly Observed Therapy at patients' homes: analysis of care delivered by health professionals in a Tuberculosis Control Program by the Ribeirão Preto Municipal Health Secretariat, São Paulo, Brazil, 2004

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This exploratory study aimed to analyze the use of Directly Observed Therapy (DOT) with respect to the

domestic patient care delivered by health professionals, in the framework of a Tuberculosis Control Program (TCP). A specific form was applied on a daily basis through systematic observation at patients' homes. Descriptive statistics was used for data analysis, resulting in 140 activities carried out during DOT, 62 (44.3%) of which corresponded to medication intake observation; 28 (20%) were other activities (PPD, test material delivery, search for breathing symptoms, among others); 26 (18.6%) were related to the delivery of benefits (basic food products and milk); 14 (10%) referred to guidance (related to the disease, hygiene customs, among others) and 10 (7.1%) to marking medical appointments at the TCP. We conclude that the main DOT activity is medication intake observation, although the health professional realizes other activities with a view to creating the necessary conditions for co-responsibilization in treatment and a more integral care, so as to attend to the specific needs of patients and families.

Sponsored by PROCAD/CAPEs, CNPq and Brazilian Tuberculosis Network.

#### **PS-549-619 Measuring programme performance: early indicators of detection and treatment success**

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**Introduction:** CARE Zambia in collaboration with the Central Board of Health and District Health Management Boards with World Food Programme has been running an Operations Research and TB control project in seven districts of Zambia namely Tuberculosis Integrated Project in Eastern and Central provinces (TIPEC).

**Objective:** To test the impact of strengthened health and community support systems to TB detection, treatment progression and treatment outcomes.

**Methods:** A shared health and community support system (capacity building) to TB detection, management, treatment support, follow up, recording and reporting is being tested on how it can strengthen DOTS implementation.

**Results:** Following one and half years of effective DOTS implementation, TB detection increased from 33% to 50%; sputum conversion increased from 76% to 80%; defaulter rate reduced from 17% to 1%; whilst cure rate at 8 months improved from 29% to 57%. Further, community and health support system has been established with 95% DOT plan, suspect registers and community treatment registers.

**Conclusion:** Effective DOTS implementation is possible in a resource poor setting like rural Zambia where TIPEC operates, however communities and health workers need to be strengthened to build a strong partnership of shared responsibility.

#### **PS-555-623 Occurrences during domestic treatment supervision in a tuberculosis control program, Ribeirão Preto-SP, Brazil (2003)**

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This exploratory study aimed to analyze occurrences during domestic treatment supervision (TS) in a Tuberculosis Control Program (TCP) by the Ribeirão Preto Municipal Health Secretariat (2003). Study participants were 18 patients under domestic TS and the persons responsible for supervision (health professional and driver). Data were collected through the Systematic Observation Technique, by accompanying daily supervisions during one month. Occurrences were organized into categories and divided into health service, patient, family and community. Results demonstrate the presence of occurrences throughout TS, which are related to the health service (delay of the TS car, great demand by patients at the service, need for domestic visits not related to TS, etc.) as well as to the patient, family and/or community (patient absent at the time of the visit, patient took medication before the health professional's visit, etc.). These occurrences may affect the availability of human and material resources to realize programmed TS activities and observe medication intake. We conclude that the identification of these occurrences will contribute to the planning and systematic organization of domestic TS activities, with a view to improving the TCP.

Sponsored by PROCAD/CAPEs, CNPq and Brazilian Tuberculosis Network.

#### **PS-691-765 DOTS Strategy Expansion for TB control at Dominican Republic**

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**Introduction:** Dominican Republic is included between the 10 countries in America with higher load of TB, its control is priority for health authorities. In 2000, 9% of the population were covered with DOTS; in the 2002 DOTS strategy expansion begins, with a percentage of treatment 60%, detecting 48% of waited cases, and in 2003 66% (791) of health establishments applied DOTS with 71% population coverage.

**Objectives:** To measure advances obtained for DOTS expansion.

**Methods:** Data provided by the NTP information system was compared by after and before strategy DOTS expansion.

**Results:** 71% of the population in 2003 were covered with DOTS; the respiratory symptomatic ones identified increased of 27 856 (2002) to 54 695 (2003)

examining to 67% (2002) and 86% (2003), detecting 61% of the awaited cases. The percentage of cured of new cases increase of 60% (2002) in 68% in the first semester of the 2003.

**Conclusion:** With DOTS expansion it is hoped to reach for 2005 WHO goals: curing 85% of new cases and detecting 70% of awaited ones.

#### **PS-697-772 Registry and information system of the NTP in the Dominican Republic**

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**Introduction:** The information registry is one of the components on DOTS. In 2003, the Dominican Republic NTP implemented the Operational and Epidemiologist Information system in the health establishments of the country.

**Objectives:** To systematize quality information through a system that allows suitable and opportune data collection and processing.

**Methods:** The components of the system were designed and validated: recording tools, information, and indicators. Qualification courses to equipment of intermediate and local level in the compilation and filing of records were made.

**Results:** In 2003 the Operational and Epidemiologist Information system was implemented; health establishments with DOTS used the recording tools. Every trimester compilation and information revision courses are given in health establishments in the country; we are increasing health establishments, which reported information of 678 (58%) in first 2003 trimester to 881 (75%) in the fourth trimester. Filing errors and sending late information was corrected with the courses.

**Conclusion:** We have implemented a registry and information system in local level to the power station, which allows the decision-making.

#### **PS-704-779 Suivi communautaire des malades tuberculeux dans la commune de Yopougon, Abidjan**

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**Objectif:** Améliorer l'observance du traitement anti-tuberculeux par la mise en œuvre du traitement directement observé dans la communauté et sensibiliser les tuberculeux au dépistage volontaire de l'infection à VIH.

**Méthodes:** A travers un partenariat entre le pro-

gramme national de lutte contre la tuberculose et l'ONG SIDALERTE CI, le suivi communautaire des patients tuberculeux a été initié en juillet 2002 dans la commune de Yopougon. Les tuberculeux sont suivis à domicile par des conseillers de l'ONG. Le test VIH est proposé aux malades par les conseillers et réalisé à la Formation sanitaire en cas d'accord du malade.

**Résultats:** Au cours de la période de juillet 2002 à décembre 2003, 465 malades ont été enregistrés et suivis par 10 conseillers formés. Au 31 décembre 2003, 340 avaient terminé leur traitement. Le résultat du traitement met en évidence 80% de guérison, contre 69% avant l'intervention des conseillers communautaires et 5% d'abandon contre 15%. Le Taux de décès est de 9% contre 1% une année auparavant. Les cas de transfert représentent 4% contre 11%. 84 malades ont bénéficié de conseils prétest pour le dépistage du VIH. Le nombre de refus est de 27 (32.14%). Sur les 57 malades testés, 10 (17.54%) ont refusé de connaître le résultat. Parmi les 47 qui ont accepté le post-test, 36 se sont révélés VIH-positifs (76.6%). Les malades positifs au VIH ont bénéficié d'une assistance psychologique de la part des conseillers et ont été référés vers les autres structures de prise en charge (Projet COTRIMO, USAC, etc).

**Conclusion:** L'intervention de relais communautaires a permis d'accroître le taux de guérison. Elle fournit des informations supplémentaires sur les cas d'abandon qui sont pour la plupart des cas de décès. La sensibilisation sur le dépistage du VIH a permis de dépister des cas d'infection à VIH référés dans les centres de suivi de VIH. Il est important de renforcer cette activité et de procéder à l'extension du suivi des tuberculeux par des relais communautaires.

#### **PS-723-797 La tuberculose dans la région du fromager en Côte d'Ivoire**

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**Introduction:** La tuberculose demeure un problème de santé préoccupant dans notre région. Depuis ces dernières années, des réformes ont été apportées dans la prise en charge des malades : quadrithérapie, décentralisation, DOTS.

**Objectifs:** Mesurer l'impact des réformes sur la qualité de la prise en charge des malades tuberculeux dans la région du fromager.

**Méthodes:** Revue des dossiers et des rapports d'activités, analyse des données sur le dépistage et le traitement.

**Résultats:** Le nombre de cas dépistés est passé de 534 en 2001 à 611 en 2003. Les cas de tuberculose à frottis positifs représentent 80% des tuberculeux. La séroprévalence de l'infection à VIH est passé de 33 à 35%. Le taux de succès est passé de 50 de 61% de

2000 à 2002. Le taux d'échec thérapeutique après une envolée en 3 1999 s'est établi à 1%.

**Conclusion :** Malgré la crise sociale que connaît la Côte d'Ivoire, la mise en œuvre du programme anti-tuberculeux dans la Région du fromager permet d'améliorer les résultats du dépistage et du traitement. Il est nécessaire de maintenir les acquis et d'améliorer le suivi communautaire des tuberculeux ainsi que les activités de supervision.

#### **PS-811-883 Reducing the distance in Kenya**

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In Kenya, TB remains a major public health problem with a 75% cure rate (10% off the WHO mark). Long distances to health facilities (HFs), TB social stigma and the high TB/HIV co-infection rates have restrained our success. To buffer the distance effect, some health workers (HWs) have been giving a month stock to patients. Some places, we have registered high treatment completion and low levels of defaulting, yet we could be grooming multidrug resistance. Occasionally, some nomadic patients have used the 'large' supplies to treat their livestock. The TB program in Eastern South province is modifying the DOTS strategy to include DOTS Supporters (DOTS-S) in order to cut on the distance that the patients have to travel. These are trained and provided with a bicycle for transporting drugs and conducting home visits. Every new patient is given drugs for one week and referred to the nearest DOTS-S who observes the patient taking drugs during regular home visits. On a weekly basis, DOTS-S brings progress briefs and collects more drugs. For every patient who completes intensive treatment, DOTS-S is given 2.5 USD. DOTS-S own the bicycle if no patients from their batch defaults for one year.

#### **PS-807-879 Forging partnership to achieve NTP targets: lessons learned from leprosy elimination, Bangladesh**

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**Introduction:** With 99% DOTS geographical coverage, case detection rate is only 38%, requiring increased population coverage and improving quality of services.

**Objectives:** Discuss challenges ahead to achieve national targets of TB control through strengthening partnership.

**Methods:** Increase DOTS population coverage targeting health services providers, special situation and hard to reach areas involving NGOS, Private providers and others.

**Results:** Bangladesh achieved leprosy elimination at national level 2 years ahead of the target date. Key factors that contributed this success are strong political commitment, integration of leprosy into the general health services, model partnership with NGOS, uninterrupted supply of drugs and other logistics, involvement of other key players, e.g., private practitioners, scouts, religious leaders, etc., will be presented.  
**Conclusion:** To achieve the national target the case finding has to be doubled, which is a gigantic task that can only be possible through forging partnership with all key players. Particular challenge is coordinating and sustaining partnership based on mutual trust and respect.

#### **PS-880-957 Impact of Women's Self Help Groups on tuberculosis case-finding in Coimbatore District, Tamil Nadu, India.**

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**Objective:** To assess the impact of community mobilisation on tuberculosis case-finding.

**Setting:** Coimbatore District, Tamil Nadu, India (population 4.5 million), involving community women's self help groups (SHGs) in the tuberculosis programme.

**Methods:** For 2 days, 2617 SHGs in all six rural Tuberculosis Units were trained, covering key concepts of tuberculosis control, the referral method for diagnosis, and the supervision of treatment. The change in the number of notifications of sputum smear-positive tuberculosis cases before and after the intervention was assessed to ascertain its impact.

**Results:** Before the intervention in 2002, the number of cases decreased from 251 to 232 from the third to the fourth quarter. 324 cases were reported in the third quarter of 2003. The activities of the SHGs started in the fourth quarter, during which 366 cases were notified, an increase of 13.0%.

**Conclusions:** In contrast to the observed decrease from the third to the fourth quarter in the year before the intervention, involving SHGs resulted in an increase in case-detection during the same period in the intervention year. Follow-up will show whether their involvement will also result in improved treatment results.

#### **PS-888-963 DOTS advances in Guayas Province, Ecuador**

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**Background:** Although DOTS activities started in the year of 1997 year in Guayas Province, because of logistic elements and poor governmental support, it

did not produce the expected results. From 2001, TB control activities were strengthened with the support of Canada (ACDI): training, registration system and information, and creation of local laboratories and a continuous monitoring.

Actual situation:

- BCG vaccination covers in children aged under 1 year—year 2002 (> to 100%).
- Early detection BK (+) new cases.
- Epidemiological impact: 35% increase in new cases (first term data 2002 and 2003).
- Greater percentage of new case detection in regard to the notified cases around the country (53%).
- Increase in DOTS coverage:
  - Strengthened health areas 32 (100%)
  - Urban areas 13 (41%) and rural 19 (59%).
  - Operative Units 200 (100%)
  - Covering population 3'483.362 (100%)
- Cured leaving conditions 74%.
- Treatment efficiency, cured + completed treatment (78.3%).
- Treatment efficacy, cured + completed treatment (98%).
- Tendency to abandon treatment 2001 (11.3%), 2002 (9%).
- Implementation of tuberculosis provincial laboratory.
- Diagnostic capacity, new cases BK (+) 89%.
- Concordance, bacterioscopic quality control (99.5%).

**Conclusions:** Optimal BCG Vaccination covers. Bacterioscopy, method to detect lung tuberculosis UTIL. Detection of BK(+) new cases with the ascending tendency. Treatment efficiency and efficacy with a significant increase in cured persons. Evidence of decrease in default.

#### PS-913-988 Experience of introducing fixed dose combinations (FDCs) in a programme

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**Introduction:** Fixed dose combination drugs were introduced in TB Control Programme Pakistan in early 2003. The change in program policy from individual to FDCs required interventions at policy and implementation level. Thus it became imperative to assess the experience of managing FDCs at the programme, district and community level.

**Objectives:** To review the process of translating policy into feasible implementation decisions; to review the early implementation experience of introducing FDCs; and to assess the experiences of the managers, health care providers and patients with FDCs.

**Method:** A qualitative review has been designed to conduct an assessment of the process and experience

of introducing FDCs. The review would be carried out in four districts two from each province by documenting the process, record/report review and by interviews with managers, care providers and patients.

**Result:** The results of the review would be available by September and would help the TB control programme in making evidence based decisions for further expansion of FDCs in the remaining districts of Pakistan.

**Conclusion:** The review would help the programme to comments on FDCs whether significantly (or not) increase treatment success rate and will be in the context of routine programme implementation in typical districts within Pakistan.

#### PS-930-1005 First results of smear conversion and treatment success in DOTS areas of Donetsk oblast, Ukraine

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**Introduction:** In 2001–2004, with assistance of the WHO Project office for TB control, DOTS strategy has been implemented in Donetsk oblast—first pilot area in Ukraine. Practical implementation started in January 2002 in 5 small areas. Gradually it was expanded and embraced all Donetsk oblast, and by January 2004 DOTS implementation was completed. 100% of the 4.8 million Donetsk oblast population was covered by DOTS.

**Objectives:** To estimate smear conversion rate and success of TB treatment in DOTS implemented areas.

**Methods:** Analysis of quarterly 2002 TB reports and those available for 2003.

**Results:** The following results were observed in DOTS areas of Donetsk (Table).

	2002		2003	
	New cases	Re-treatment cases	New cases	Re-treatment cases
Smear conversion rate % after initial phase of treatment	81.9	63.6	79.6 (1st and 2nd quarters)	64.4 (1st and 2nd quarters)
Treatment success % (cured and treatment completed)	79.5	68.0	Not available yet	Not available yet

**Conclusion:** Taking into account high TB resistance rate in Ukraine, first results of smear conversion and treatment success in Donetsk oblast could be considered as satisfactory.

### PS-931-1006 Treatment outcome of patients with tuberculosis in three district hospitals of Uganda

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**Introduction:** The performance of a National Tuberculosis Control Program must be continuously evaluated.

**Objective:** To assess the outcome of treatment of the patients diagnosed with tuberculosis during 2002 in three district hospitals in Southeast Uganda.

**Results:** The population covered is about 1.5 million. St Francis Hospital diagnosed 100% of the patients in its district; Jinja Hospital 70%; and Iganga Hospital 85% (Table).

Outcome/ Hospital	St Francis H. <i>n</i> = 215 <i>n</i> (%)	Jinja H. <i>n</i> = 880 <i>n</i> (%)	Iganga H. <i>n</i> = 437 <i>n</i> (%)	Total <i>n</i> = 1532 <i>n</i> (%)
Cured	45 (21)	63 (7)	87 (18)	195 (13)
TC	53 (25)	277 (31)	149 (31)	479 (31)
Dead	27 (13)	71 (8)	84 (18)	182 (12)
Defaulted	86 (40)	467 (53)	117 (35)	670 (44)
Failed	4 (2)	2	—	6
Not recorded	34 (8)	239 (21)	38 (8)	311 (16)

Patients transferred were excluded.  
TC = treatment completed.

**Conclusions:** Treatment success is low. The number of unrecorded outcomes reveals deficient supervision. It is unlikely that higher success rates will be achieved without a stricter supervision and unless patients

### PS-943-1018 Economic analysis of scaling up DOTS in Mexico

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**Background:** Although there is a broad consensus that DOTS is the most effective approach for national TB control programmes. DOTS implementation on a national scale has not undergone formal economic analysis. The impact on TB incidence and mortality of the status quo approach were compared with scaling up DOTS to achieve national coverage in Mexico. **Methods:** Markov modeling was performed using DATA (version 4.0) over 20 year interval. Key inputs included: Current TB incidence, HIV sero-prevalence, ARI, and drug resistance—from WHO estimates and published literature; Outcomes of treatment and mortality for different HIV, and TB disease states, and drug resistance—from published literature; Costs of scaling up DOTS nationally—from Ecuador national programme; Treatment outcomes and TB incidence

after DOTS implementation—from Peru Programme, Patient and Health care system costs were extrapolated from directly gathered data in the Dominican Republic.

**Results:** Cumulative probabilities and costs over 20 years—total population of Mexico (of 105 million) (Table)

	Status quo	Scale-up
Smear positive TB cases (cumulative)		
Probability of TB	0.0014	0.0013
Number of TB cases	147 000	136 500
Probability of TB mortality	0.00053	0.00039
Number of TB deaths	52 500	41 475
TB related costs		
Cost per person	\$525	\$369
Total costs	\$55.2 billion	\$38.8 billion

**Conclusions:** Scaling up DOTS to achieve national coverage, and WHO targets, would result in modest reduction in TB cases, but substantial reduction in mortality and costs.

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## TUBERCULOSIS EDUCATION AND TRAINING

### PS-110-152 Youth involvement in TB control: lessons from Youth Forum, Zambia

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**Introduction:** TB is one of the most serious opportunistic infections associated with HIV/AIDS. TB is preventable and curable. Therefore, youth involvement in its prevention and treatment is not only desirable but critically needed.

**Youth response:** Some of the good practices of youth involvement in TB control include:

- 1 Use of peer educators: in the past peer education focused on HIV/AIDS. Open discussions with young people on transmission and prevention efforts of TB has proved useful in the awareness and reduction of stigma against TB patients. Young people can play a vital role provided they receive adequate support, motivation and incentives. What needs to be done is identify and train young people and supervise them in supporting TB patients and directly observing treatment.
- 2 The integration of TB messages in education through sport has helped reduce stigma against TB patients.
- 3 Youth participation in home based care: as parents, friends and relatives fall sick from TB, young people become care givers.



**Conclusion:** Youths ought to learn how to administer DOTS. Enhancing good systems of supervising young people by TB programme staff can do this.

#### **PS-147-179 Training activities for tuberculosis (TB) control in the WHO European Region**

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Effective TB control in the WHO European Region cannot be achieved without strengthened human resource development. WHO EURO supports training for TB control at the regional, subregional and country levels, organized in cooperation with national TB programmes and international partners. In 1995–2003, 284 participants from 25 countries of eastern and central Europe and the former USSR were trained at the WHO/KNCV regional workshops on TB control management, Warsaw. 86 participants from 20 countries improved their knowledge at the WHO European workshops for TB laboratory managers, Warsaw, 2000–2003. WHO EURO assistance to the Member States has been strengthened through the WHO training course for TB consultants, Sondalo, since 2001. Since 2000, eight meetings of the Collaborative for Training and Education for TB control in Russia, the Baltic States and the NIS have allowed representatives of 16 partner organizations to exchange experience and coordinate international support for training activities in the Region. WHO EURO activities facilitate the training of qualified TB specialists and consultants at national and international levels and the strengthening of TB control in the Region. Special attention is needed for the problems of multidrug-resistant TB, TB/HIV co-infection and the TB control global targets.

#### **PS-178-214 Utilization of rural doctors for DOTS expansion: whether as an alternative or supplementary to existing health workers**

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**Introduction:** NTP, Bangladesh is expanding DOTS strategy to achieve targets of 70% case detection and 85% cure rates. In addition to resources like health workers available at field level, using rural doctors is considered to have potential impact on DOTS expansion.

**Objectives:** 1) Assess capability of rural doctors to increase case detection/provide DOT services. 2) Determine effectiveness of training curriculum/methodology, follow-up/supervision procedure for quality services. 3) Identify their role in integration of TB

control activities with other health services. 4) Determine whether they can replace or supplement activities of existing health workers.

**Methods:** Information of rural doctors regarding age, educational background, working experience, acceptability/popularity, distance of residence from working area, and attitude towards community in the working area will be analyzed. Training curriculum/methodology will be investigated to assess appropriateness of contents, in relation to the task/responsibility assigned to rural doctors

**Results:** Results will be extracted from findings of investigation to decide whether rural doctors have capability to provide quality services for case detection/DOT, replace or supplement existing health workers.

**Conclusion:** Results of the analysis will be presented and recommendations be given about whether or not rural doctors may contribute to DOTS expansion and which should be their major tasks.

#### **PS-221-256 Interaction between monitoring and health education**

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Interaction between monitoring and health education during DOTS implementation is aimed at creation of sustainable system able to detect and cure TB patients. Project HOPE in Uzbekistan studied interaction between monitoring and education during DOTS implementation in 5 pilot sites for 2000–2003. The analysis of 101 trainings and 72 monitoring visits was carried out. During monitorings we determined target groups for trainings, weak and strong points, priorities for educational directions. These data were used for planning trainings, designing new curriculum, development questionnaires and training techniques, and determination of practical skills for specific groups of specialists. Close interaction between monitoring and education contributed to the quality of education. The result was the correct application of WHO recommended algorithm for TB detection and increase in detection of SS+ patients. Instability of cohort indicators in 2000–2001 revealed the need to train all specialists involved in TB program implementation. By the end of 2003, 97.8% of TB and PHC doctors and nurses were trained. As a result of strengthening the control during all treatment phases, indicators of cohort analysis increased. Number of cured SS+ patients reached 79.4% in 2002 compared to 70.1% in 2001. Other treatment outcomes of this cohort for the year 2002 reached WHO standards: treatment completed – 3.9%, died – 4.4%, failed – 4.9%, treatment interrupted – 4.4%, transferred – 2.9% compared to the year 2001 when treatment completed was 9.3%, died – 6.5%, failed – 8.9%, treatment interrupted – 3.3%, transferred – 1.9%.

Project HOPE experience proves for the important role of interaction between monitoring and education to establish actively functioning TB control system.

### **PS-259-285 Training of nurses on DOTS: the first experience in Turkmenistan**

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**Background:** The educational program on DOTS is being implemented in Turkmenistan since 1999. It involves TB specialist, family doctors, health care managers, epidemiologists and nurses. Nurses' training on DOTS is a new trend of the health educational program in Turkmenistan, which was initiated by Project HOPE Turkmenistan and TB Faculty of the Turkmen State Medical Institute.

**Objective:** To develop highly professional human resources for the National Tuberculosis Program of Turkmenistan.

**Methods:** Nurses training needs assessment, module and curriculum development, nurses training by means of lectures, group discussions, pre- and post- testing, exercises and interactive teaching methods.

**Results:** The first training course on DOTS for family nurses started in July 2002 in the city of Turkmenbashi. To date, 59 family nurses and 9 Red Crescent Society patronage nurses were trained on DOTS in the city of Turkmenbashi. Training courses were focused on the basic elements of DOTS strategy: treatment observation technique, sputum collection technique, patients' education and on the skills which are important in the nurses' daily activity. To create a sustainable educational program on DOTS, the local team of trainers, including one nurse, was trained on TOT.

**Conclusions:** Training on DOTS is an important chain in the nurses' proficiency improvement. The educational program on DOTS for nurses ought to be sustainable, comprehensive and involve family nurses, nurses of TB facilities, Red Crescent Society patronage nurses and students of Medical Colleges.

### **PS-364-390 Selective neonatal BCG immunization: uptake is poor among Caucasian infants**

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**Introduction:** Selective neonatal BCG (Bacille Calmette-Guerin) vaccination is recommended for a group of infants at risk of TB. Neonatal BCG is safe and effective,

with an overall protective value of 75% especially against disseminated TB.

**Objectives:** To assess the coverage of neonatal BCG vaccination in Cardiff for the year 2003.

**Methods:** A list of eligible infants was generated from computerised antenatal records. Vaccination details were obtained from the hospital's TB database.

**Results:** 5308 infants were born in 2003. Those 'at risk' for TB were 514 (9.6%). Of these 390 (75.8%) received the vaccine; 91 infants were not referred postnatally (17.7%). 19 infants failed to attend appointments (3.6%). Nine infants are due for vaccination soon (1.8%); 5 infants could not be traced (0.9%). The vaccination uptake rate among White British infants at risk was 34%, while it was greater than 80% for Asian and Black African infants.

**Conclusions:** Selective neonatal BCG uptake in Cardiff is 76%. Vaccine uptake is poor among Caucasian infants compared to those from other ethnic groups. Education of health professionals and parents to recognise the need for vaccinating Caucasian children 'at risk' is necessary to improve BCG uptake.

### **PS-401-435 The client-oriented aspect of responding to TB: the BEHAVE Framework**

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**Introduction:** AED's BEHAVE Framework identifies commonalities and differences among groups who are impacted by TB, and identifies barriers that prevent successful treatment and prevention, and what it takes to remove these barriers.

**Objectives:** To introduce the BEHAVE Framework as a tool that empowers stakeholders by listening to their audiences and increasing dialogue.

**Methods:** The framework focuses on four key questions: Who is the target audience? What do we want them to do? What perceptions guide their action(s)? What interventions might affect those determinants and action?

**Results:** Stakeholders will better understand why people behave as they do, what their rewards are, and what influences them. They will uncover why initially people choose not to take advice. For those affected by TB, exasperation comes from not understanding what motivates people in their daily life. This exasperation is a sign to listen more closely to clients and families.

**Conclusion:** AED understands that TB prevention and treatment require an understanding of the most complex and intimate human behaviors, and have developed the BEHAVE Framework to assist in understanding these behaviors. The Framework provides users with proven, research-based tools for designing, implementing and evaluating interventions leading to large-scale behavior change.

### PS-451-489 Knowledge of TB control guidelines among medical students at Cairo University

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**Introduction:** Teaching of TB in medical schools in Egypt is solely dependent on a series of academic lectures that is insufficient in many aspects.

**Objective:** To reveal the gap in relation to TB control as regards knowledge among medical students.

**Methods:** A cross-sectional survey included those in the 4th and 5th year. A systematic random sample of 190 and 170 respectively with self administered questionnaire.

**Results:** About 80% of those included did not recognise the existence of the National TB Control Program or the proper guidelines for the proper diagnosis and treatment of TB patients. More than 75% gave a wrong response as regards the advantages of DOTs. Over 60% of the responders revealed a stigmatized attitude in dealing with TB patients.

**Conclusion:** TB curriculum should be evaluated to cope with and integrate recent standards as regards diagnosis, treatment and care of TB patients in Egyptian Medical schools.

### PS-452-491 Do medical students have better knowledge about tuberculosis than community people? Results of an activity in the 2004 World TB Day in Phnom Penh, Cambodia

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**Methods:** Thirty medical students participated in World-TB-Day in an urban community. They visit the houses and interviewed 331 people by using a structured questionnaire, which investigated TB knowledge of the respondents. Before the community survey, we evaluated TB knowledge of these students by using the same questionnaire. A focus group discussion (FGD) with medical students was conducted.

**Results:** The medical students had significant better knowledge about TB than community people (means scores were 6.9/10 and 5.1/10 respectively;  $P$ -value < 0.001). Half of the community respondents heard about TB. They had misperception about TB transmission and prevention. About 82.5% reported that TB is not curable. Although 17.5% reported that TB is a curable disease, they did not know treatment duration. The FGD show that the students had good knowledge about TB etiology, transmission and diag-

nosis. Most students did not know names of TB medicine and they did not know TB treatment duration. Some students reported that BCG was the best way to prevent TB. Most students were aware of the problem of TB stigma.

**Conclusion:** Medical students had significantly better knowledge about TB than community people. Involvement of medical students and the community in World TB Day improved TB knowledge of both parties.

### PS-460-503 Knowledge, attitudes and practices of public school teachers in Ilocos Sur regarding tuberculosis

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**Background:** Philippines is one of the 22 countries accounting for 80% of world's TB cases. Public school setting favors transmission of TB putting teachers at risk. 25% of 269 112 teachers in the Philippines are positive for TB but only 33% were treated.

**Objective:** To determine level of knowledge, attitudes and practices (KAP) of public school teachers on etiology, signs, symptoms, treatment and prevention of TB.

**Methods:** Descriptive study of KAP of randomly selected 573 public school teachers in Ilocos Sur, Philippines utilizing questionnaires. Data were analyzed using Epi-Info Statistical Analysis Program.

**Results:** Scores reveal that 46% of teachers have average, 38% have good and 16% have poor level of KAP. Most teachers believe TB is hereditary, 63% think treatment lasts from 1 week to 6 months depending on severity of the illness, 81% believe TB is prevented by sterilizing kitchen utensils, and 71% believe amulets can protect one from TB.

**Conclusion:** Public school teachers lack sufficient knowledge of TB and harbor misconceptions but have positive attitudes and practices regarding the disease. These data can serve as baseline information to monitor influences of ongoing health education programs, and from which future policies on TB prevention and control will be based.

### PS-534-597 Survey on tuberculosis in Brazilian nursing schools, 2003-2004: a multicentric study

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**Setting:** UNION meetings highlighted the need to identify how Nursing Education Institutions approach

TB teaching in their curricula. This study is a joint project between the University of São Paulo; FAPESP and UNION.

**Objectives:** To identify the approach to tuberculosis adopted in the undergraduate curricula of Nursing Schools in Brazil and to estimate the time dedicated to tuberculosis teaching, verifying the theoretical content, training in health institutions, involving operational and epidemiological aspects of the Brazilian TB Control Program (TCP) through a questionnaire.

**Methods:** Survey; November/2003 to September/2004; Study population: 377 Nursing Schools, distributed throughout the 5 regions of Brazil: (17) North, (48) Northeast, (71) South, (195) Southeast, (16) Central-West; 90 of which were public schools and 257 private.

**Preliminary results:** The 15 pilot questionnaires were analyzed in a database (Excel) and summarized using the Statistical Package for Social Sciences (SPSS).

**Results:** 26.7% of the schools are public and 73.3% private; 33.3% are Schools and 66.7% Universities. 100% of the schools dedicate time to TB teaching; the theoretical hour load ranges from 4 to 8h in 40% of the schools and 10 to 20h of practical training in 36%, in the framework of primary and predominantly secondary care levels.

Sponsored by FAPESP and Brazilian Tuberculosis Network.

#### **PS-572-637 Tuberculosis higher education in Brazil: what is wrong, how to change?**

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**Introduction:** Training health science students on tuberculosis issues has been a major concern among educators in Brazil.

**Objectives:** To diagnose main tuberculosis educational problems and to propose appropriate solutions.

**Methods:** A workshop on TB higher education was performed in Rio de Janeiro in April 2004, including 18 educational institutions from eight states, 11 TB health services, one TB-NGO and the Ministries of Health (MOH) and Education (MOE).

**Results:** The main problems identified were training in hospitals instead of out-patient units, professor-oriented teaching, focus on biological issues with little approach to humanistic and sociological issues, insufficient field experience. Proposed solutions included innovative experiences such as the Gama Filho students' Tuberculosis Scientific League, straight interaction between Governmental Healthcare Services, Universities and NGOs, operational research efforts within Universities. Standardized didactic material

was considered less important. Curricular changes related to local health problems and active participation of students and faculty are essential. The Permanent Education Poles strategy, proposed by MOH/MOE should involve undergraduate and graduate students training. Multidisciplinary TB teams should be created in educational institutions to perform evaluation of TB educational programs.

**Conclusion:** The mobilization of society, educational institutions and health services is fundamental in order to implement effective educational changes towards TB control.

Sponsored by UNESCO/DECIT-MS and Brazilian Tuberculosis Network/Instituto do Milenio-MCT.

#### **PS-588-655 Perception and practices among health providers toward tuberculosis (TB) and continuation phase treatment compliance in Romania**

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**Objective:** To identify perceptions and practices toward TB treatment and patient's compliance among general practitioners and family medicine nurses in Romania, which has the region's highest TB burden.

**Materials and methods:** Quantitative research consisting of 207 questionnaires (approximately 100 each) with providers during January 2004 in Ilfov county, Neamt county and Sector 5 of Bucharest city in Romania (approximately 1 million population coverage or 4.6% of the Romanian population).

**Results:** Providers felt more monitoring and education were necessary for treating TB patients as most patients and families are little informed about TB. According to providers, patients feel fear and shame upon learning they have TB. Significant numbers of doctors and nurses recommend patients with TB to isolate themselves and their belongings. Half of the doctors had patients who accept the treatment regimen but do not adhere to the entire course. Lack of understanding of the necessity of TB treatment completion was the most common reason perceived for treatment non-compliance. Over two-thirds of doctors surveyed said that an educational program on TB would be useful. Doctors and nurses noted lack of information materials as a barrier to educating patients but felt their own role was very important.

**Conclusions:** General practitioners and nurses need support, including appropriate health education training and materials, in order to carry out effective DOTS education and implementation. Along with increasing provider skills and materials to improve patient knowledge, provider attitudes and knowledge should also be the focus of an intervention.

**PS-651-720 Creating usable education materials for a diverse audience: a brief guide on tuberculosis control for primary health care providers**

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**Introduction:** NJMS National Tuberculosis Center and the WHO Regional Office for Europe used a systematic health education approach in creating a Brief Guide on Tuberculosis Control for Primary Health Care Providers for Countries of the WHO European Region with a High and Intermediate Burden of Tuberculosis. Creating a material for a diverse group of primary health care (PHC) workers in many countries presented challenges.

**Objectives:** To produce a usable and acceptable material by utilizing an intensive process of stakeholder involvement and feedback.

**Methods:** The guide was created based on extensive needs assessment and field-testing. Flexibility to the specific situations in each country was used during field-testing, and in creating the final guide.

**Results:** Though elements of the material development process were unfamiliar to some stakeholders, the extensive stakeholder involvement and flexibility led to positive and useful feedback. Overall, the policies and recommendations were similar, though some differences by country and field of specialty (TB control versus PHC) existed.

**Conclusion:** Care was used to make the final content specific enough to be useful, yet general enough to be applicable in different countries in the region. The flexible approach and stakeholder involvement allowed for the creation of a useful and acceptable material.

**PS-657-731 Educational program on DOTS as an essential component of National Tuberculosis program of Turkmenistan**

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**Background:** Educational program on DOTS in Turkmenistan involves Medical Institute students, family doctors and nurses, TB specialists, health care managers, epidemiologists. Educational program on DOTS is integrated into the state system of medical education.

**Objective:** To develop sustainable educational program on DOTS in Turkmenistan.

**Methods:** Training needs assessment, curricula development, target groups training by means of lectures, group discussions, role plays, pre-and post-testing

**Results:** Regular trainings on DOTS were imple-

mented into the Medical Institute curricula in 2002. To date: averagely 300 students and 100 family doctors and TB specialists participate DOTS trainings annually. Training courses are focused on TB detection algorithm, TB treatment regimens, sputum collection and treatment observation technique, and situation analysis and solutions development.

**Conclusion:** Sustainable educational program is the basis for efficient DOTS implementation in the country.

**PS-671-744 Strengthening the network of National TB Laboratories in Peru through training**

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Developing an increased capacity for TB testing requires extensive training for laboratorians. A training program for TB Laboratory Network, which is designed by the National Reference Mycobacteriology Laboratory (LNRN) at the Peruvian National Institute of Health (INS) is currently underway. The Program includes bench training provided by the LNRN and annual workshops, which take place at the INS and have both didactic and practical components. Two international workshops have covered updates in TB bacteriology, clinical and epidemiological aspects of TB, advances in new diagnostic methods, biosafety and QA/QC issues. Representatives from Regional and Intermediate laboratories, LNRN and other sites have participated in a course, Evaluation and Certification of Biosafety Cabinets. Courses have been developed as a collaborative effort among national, as well as international instructors from the INS, Ministry of Health (MINSA), World Health Organization (WHO), Partners in Health (PIH)-Socios en Salud, Massachusetts State Laboratory Institute (MSLI) and Eagleson Institute. Financial support was received from the INS, Proyecto Vigía, PIH, MSLI and WHO. This training Program implemented by the Peruvian LNRN shows the importance and feasibility of a proactive approach to advanced training of TB laboratorians in a country with limited resources.

**PS-695-770 Health human resources qualification program for DOTS expansion**

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**Introduction:** NTP began in 2002 DOTS strategy expansion; it established a qualification plan; it elabo-

rated and valued the qualification modules, enabling the health personnel in DOTS application.

**Objectives:** To qualify personnel responsible for the TB control at intermediate and local level.

**Methods:** The personnel responsible for the TB control at intermediate and local level participated in four days qualification course for DOTS implementation; subjects treated are content in four modules: Management, Prevention, Detection, Diagnose, Treatment, TB patients Attention, Contacts Study and Quimioprofilaxis, Operational Information and Epidemiologist System, Programming, Supervision. All participants received test of evaluation at beginning and ending course.

**Results:** 25 qualify courses were made since June 2002 to October 2003, when were enabled 933 people of 334 establishments of health at national level. The average obtained by the participants after qualification course increase from 5.5 to 8.9 based on 10 points. These qualifications course have contributed to DOTS expansion from less 10% to 66% in the health establishments in Dominican Republic.

**Conclusion:** To count with qualify human resources is very important for DOTS expansion.

#### **PS-712-790 Impact of integrated approach of IEC on leprosy & tuberculosis**

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**Introduction:** Since PR in leprosy was drastically reduced after the introduction of MDT, some major leprosy projects started a tuberculosis program with community and patient education as the mainstay of case detection and case-holding. The impact of 5 years of IEC activities in urban and slums of 2 projects in Kolkata have been analysed and reported.

**Objectives:** To provide the significance and efficacy of integrated approach of IEC, its cost effectivity, appropriation of total resources and ultimate contribution in quality enhancement of the program.

**Methods:** The combined IEC programmes included coverage of mainly organised and institutional groups through group-talk and lectures, audio-visuals, printed material distribution backed by media support and sound clinical services.

**Results:** Gradual and substantial improvement in case detection rate as per the ARI of the city, improved self-reporting in early stage, treatment compliance and cure rate were documented. Familial, social cooperation and personal productivity enhanced.

**Conclusion:** The combined IEC accelerated the pace, quality and cost effectiveness of the program. Infrastructure and resources were judiciously appropriated, contributed to reduce stigma for the diseases

and ensured community acceptance. A definite and feasible plan of action on IEC should be formulated as an integral part of program. Combination of tuberculosis with low prevalence leprosy projects should be encouraged.

#### **PS-755-829 New approaches to health education policies implementing in the programme on tuberculosis in Kazakhstan**

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**Introduction:** Health education work is a necessary but few noticeable component of anti-TB Programme. Enhancement of the informativity among population can certainly influence on the decrease of the main epidemiological TB indices.

**Objective:** The health education activity improvement among different strata of population in Kazakhstan.

**Methods:** Coordination of counsel formation for strategic design of health education policies, training courses and course organization.

**Results:** As a basis of health education activity in Kazakhstan activity of the Coordination Council for strategic design of health education policies the activity of the Coordination Counsel on strategic design of health education policies is taken including the representatives of 4 organizations: National Center for TB Problems, National Center for healthy lifestyle formation, Project HOPE, Society of Red Crescent. Members of Coordination Council jointly elaborate the health education policies covering all strata of population: children, adolescents, students, patients with TB. Main means to improve the informativity on TB are the information companies organization involving the mass media, training courses on TB problems among journalists of all mass media species, teachers, course organization with incentives for winners among journalists, students, pupils, leaflet production issue. New approaches to evaluate results of health education policies and scientifically based approaches for their implementation are planned.

#### **PS-895-969 Training of professionals in tuberculosis contact tracing**

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**Background:** With an incidence of 8/100 000, The Netherlands is a low incidence country. Therefore it is difficult to obtain experience in methods of contact tracing. To guarantee high-qualified contact tracing (CT), KNCV Tuberculosis Foundation (KNCVTF) has developed a training for nurses and doctors in

Tuberculosis control. The first training was held in February–March 2004.

**Aim:** To guarantee high-qualified CT by upgrading the knowledge of and skills in the methods of CT using the input of experts.

**Methods:** The training consultant of KNCVTF has convened a reference group of experts in tuberculosis control. The special qualifications for CT were explored by interviewing these experts. A study book on CT was written using CDC material. The National TB-Policy Committee (CPT) approved the book. The written instructions were tested among experts followed by a pilot training of 3 days. The training dealt with the stone-in-the-pond principle and interview methods in small discussion groups, using cases. Communication and evaluation about various issues in CT was learned, including RFLP.

**Results:** Although it was difficult to train CT issues, participants were very satisfied afterwards. The evaluation forms show that the objectives for the training were reached.

**Conclusion:** The input of experts and exchanging experiences in discussion groups proved to be an efficient method to make training on contact tracing effective.

## DRUG RESISTANCE/MDR-TB MANAGEMENT-3

### PS-186-230 Resistance a la rifampicine et a l'INH des souches de *Mycobacterium tuberculosis* isolées au laboratoire

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**Cadre :** La rifampicine et l'isoniazide sont deux anti-tuberculeux majeurs qui constituent la clé des schémas thérapeutiques dans la tuberculose. La résistance à INH et/ou à la rifampicine définit la multirésistance. **Objectif :** Nous avons étudié les souches provenant de patients positifs par bacilloscopie au 5<sup>ème</sup> et 6<sup>ème</sup> mois du traitement de première ligne.

**Méthode :** 51 cultures positives sur Löwenstein-Jensen ont permis la pratique des tests de sensibilité, selon la méthode des proportions.

**Résultats :** Toutes nos souches sont trouvées multi-résistantes, par résistance acquise et par résistance primaire.

**Conclusion :** La multirésistance de *Mycobacterium tuberculosis* est importante à connaître, la résistance à la rifampicine et l'isoniazide peut compromettre le schéma thérapeutique et la vie même du malade.

### PS-407-447 Detection of resistance to isoniazid and rifampicin in *Mycobacterium tuberculosis* by Lowenstein-Jensen proportion and BACTEC system methods

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**Introduction:** Recommendations for drug susceptibility testing (DST) of *Mycobacterium tuberculosis* were formulated in the early 1960's by WHO. Although the advantage of rapid drug susceptibility testing was recognized early on, the Lowenstein-Jensen (L-J) proportion method has remained the most common procedure in resource poor countries.

**Methods:** Of *M. tuberculosis* strains sent to non-US participants enrolled in the CDC's *M. tuberculosis* DST Performance Evaluation Program from 2001 through 2003, test methods and susceptibility results were assessed for each biannual shipment.

**Results:** Of the laboratories submitting DST results for isoniazid and rifampicin on *M. tuberculosis* strains tested in 2003, those performing rapid methods (BACTEC 460/MGIT) were more likely to detect resistance than laboratories performing L-J method. However, good results were achieved by both methods in 2002 on a stable low-level INH-resistant strain which may be used to monitor quality control. Laboratories performing rapid DST methods were consistent in using recommended drug concentrations based on the method while laboratories using L-J proportion were not.

**Conclusion:** Laboratories should continue to focus on quality control, testing recommended concentrations of drugs, and on maintaining a high level of proficiency in *M. tuberculosis* drug susceptibility testing.

### PS-456-496 Rapid, reliable detection of MDR-TB direct from sputum using MODS (microscopic observation drug susceptibility assay)

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**Introduction:** The emergence of MDR-TB across the globe demands the development of affordable, rapid methods for detection of MDR disease in order that transmission of MDR strains can be interrupted at the earliest opportunity and inappropriate empirical first-line therapy avoided. MODS (the microscopic observation drug susceptibility assay) is inexpensive (<\$2) and rapid. Further data on reliability is needed.

**Objectives:** To determine the concordance of direct drug susceptibility testing in MODS with the indirect colorimetric MIC assays MABA and TEMA.

**Methods:** Retrospective analysis of data from 2 large prospective epidemiological field studies in which sputum samples were cultured in parallel in MODS and Löwenstein-Jensen media with colorimetric indirect susceptibility testing using MABA or TEMA.

**Results:** 276 culture-positive sputum samples (207 pre-treatment, 69 on-treatment) had susceptibility data available for MODS and MABA/TEMA. Concordance of results for detection of isoniazid, rifampicin and multidrug resistance was excellent (95%, 98% and 94% agreement; kappa values 0.8, 0.7 and 0.7 respectively). Concordance of susceptibility results for ethambutol and streptomycin were poor (kappa 0.35 and 0.48 respectively).

**Conclusion:** MODS is a reliable tool for the rapid detection of MDR-TB. Further prospective evaluation in appropriate target groups and subgroups is now needed to optimize operational utility.

#### PS-529-590 Rifampicin resistance screening directly from sputum in 2 days using the FASTPlaque-Response test

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Susceptibility to rifampicin is critical to the success of short-course chemotherapy for tuberculosis. Moreover, in most settings rifampicin resistance in TB is a good predictor of multidrug resistance, and thus of treatment outcome in short course regimens. Target groups and subgroups are now needed to optimize operational utility. This is the first report of preliminary data from a study evaluating the ability of a 2 day bacteriophage-based screening test, FASTPlaque-Response, to detect rifampicin resistance directly from smear positive sputum specimens from re-treatment patients in the Port Elizabeth metropolitan area, South Africa. The performance of FASTPlaque-Response is being compared with conventional susceptibility testing using Löwenstein-Jensen and 7H11 media. Analysis of *rpoB* mutations is used to resolve discrepant results. Preliminary data show 100% agreement between FASTPlaque-Response and the conventional method. All rifampicin resistant strains exhibited multidrug resistance. FASTPlaque-Response may provide a rapid means for screening patients to identify those likely to fail treatment with standard short course regimens. In settings where alternative treatment strategies are available, this could substantially improve treatment outcome for individual patients and reduce the spread of multidrug-resistant disease.

#### PS-613-678 Drug-resistant tuberculosis in Cuba, 1997–2002

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**Introduction:** The resurgence of tuberculosis in the world has been accompanied by rising drug resistance. Prevention of the occurrence and spreads of MDR is therefore a major priority of all TB control programmes.

**Objectives:** To determine the prevalence of antituberculosis drug resistance in Cuba in patients who had not received prior treatment and in those who had.

**Methods:** Drug resistance was determined using the proportion method in 1883 *Mycobacterium tuberculosis* strains to first line antituberculosis drugs during the period 1997–2002.

**Results:** The results included in this study are part of the second and third Global Project on Antituberculosis Drug Resistance Surveillance. Resistance was identified in 109 of 1774 patients (6.14%) who had had no prior treatment. Resistance was 0.62% to isoniazid, 4.18% to streptomycin, 0% to rifampicin and ethambutol and 0.39% to MDR. Among 187 patients who had received prior treatment, 54 (28.87%) were resistant and 12 (6.41%) showed MDR.

**Conclusions:** The contributed data through Cuba demonstrated that our country is relatively free of MDR strains, recognizing it to world level the good tuberculosis-control programs and the success of the application in our country of the DOT strategy from the year 1971.

#### PS-617-681 New techniques for drug susceptibility testing of *Mycobacterium tuberculosis*

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**Introduction:** The spread of multidrug-resistant tuberculosis in the world remains a major public health problem. Early detection of drug resistance is an urgent priority to identify patients who are not responding to the standard treatment and to avoid dissemination of resistant strains.

**Methods:** The susceptibility study to the first line antituberculous drugs was carried out, using the colorimetric assay MTT, Resazurin (REMA) and Nitrate Reduction Assay (NRA) in 100 strains of *Mycobacterium tuberculosis*. The results were compared with the gold standard (Proportion Method).

**Results:** The cut off value obtained by the ROC curve analyze was >0.25, >1, >4 and >0.25 for iso-



niazid, streptomycin, ethambutol and rifampicin, respectively. Sensibility and specificity were more than 96% and 87.0% respectively, for the three methods; the accuracy was 97.3%, 83.0% and 88.2% by NRA, MTT and REMA, respectively. The majority of results were available at 10 days of incubation.

**Conclusion:** The three low cost methods do not need any sophisticated equipment, are simple to perform, reduce the time of results compared to the Proportion Method and could be implemented in laboratories with limited resources.

#### **PS-673-746 Proficiency testing program for drug susceptibility testing of *Mycobacterium tuberculosis* in Serbia**

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Drug susceptibility testing (DST) of *M. tuberculosis* is performed in 11 laboratories in Serbia. The National Reference Laboratory (NRL) in cooperation with the Supranational Reference Laboratory from Borstel (Germany) introduced external quality control for DST in 2001. In order to determine the accuracy of DST in 5 local laboratories, NRL carried out quality assurance program in 2002 and 2003. Batches of 10 strains were tested for susceptibility to isoniazid (INH), rifampicin (RMP), ethambutol (EMB), and streptomycin (SM). The efficiency, sensitivity and specificity of DST in 2002 and 2003 were compared. In 2002 the overall efficiency, sensitivity and specificity were 83.6%, 87.1%, and 82.5%, respectively. In 2003 the obtained results were higher than in the first testing (the overall efficiency, sensitivity and specificity were 88.9%, 91.9%, and 93.3%, respectively). All laboratories reached 100% agreement with NRL for RMP. At least 90% agreement with NRL for INH has been achieved in 4 out of 5 tested laboratories. The technical failures in the DST procedure in some of the local laboratories have been revealed, and corrective measures have already been undertaken. The quality improvement of DST in one laboratory is still not satisfactory, and additional intervention measures should be introduced.

#### **PS-746-820 Degré de sensibilité de *Mycobacterium tuberculosis* au traitement anti-tuberculeux à l'hôpital IME/Kimpese (RDC)**

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**Introduction :** La surveillance de la résistance au traitement anti-tuberculeux est une des priorités de la lutte contre la tuberculose.

**Objectifs :** Déterminer le degré de réponse de *Mycobacterium tuberculosis* au traitement anti-tuberculeux en vigueur.

**Méthodologie :** Durant une période de 8 ans (de 1996 à 2003), tous les patients tuberculeux avec test positif de Ziehl-Nielsen(ZN) sur crachat sont repris dans l'étude. Les tests de contrôle sont faits systématiquement au 2ème mois (C2), 5ème mois (C5) et au 7ème mois (C7).

**Résultats :** Nous avons eu au total 988 patients. Ce nombre a évolué en diminuant chaque année, de 161 en 1996 à 61 en 2003. Les contrôles successifs ont révélé 56 cas positifs au C2 (5,7%), 18 au C5 (1,8%) et 5 au C7 (0,5%).

**Discussion :** L'étude montre que le nombre de nouveaux cas ZN positifs diminue chaque année. 5,7% des cas restent positifs au C2, 1,8% au C5 et seulement 0,5% au C7. Ces résultats sont justifiés par la prise irrégulière des médicaments ou par l'abandon du traitement.

**Conclusion :** La surveillance du traitement est capitale pour minimiser l'apparition de la résistance aux médicaments.

#### **PS-859-932 Model system for strengthening national surveillance of MDR-TB**

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**Introduction:** From 1996 to 2003 Brazil notified 1472 cases of multidrug-resistant tuberculosis (MDR-TB). Monitoring these cases, to control this important public health problem required greater effort to harmonize, field test and decentralize appropriate diagnostic and therapeutic mechanisms.

**Objectives:** Develop and implement methods for decentralizing control of MDR-TB to reference units in Brazil's 27 states. Qualify MDR-TB reference units on how to use the decentralized information system for managing diagnostics, treatment, notification and surveillance of MDR-TB cases.

**Methods:** Evaluation, harmonization and validation of current control procedures, preparation of a procedural manual for epidemiological surveillance of MDR-TB, preparation of training materials, conducting trainings, implementation and supervision of new procedures in reference units, managing pharmaceutical assistance activities and evaluation of new procedures.

**Results:** A model management system for controlling MDR-TB developed and implemented in the southern and southeastern regions of the country in 2004 with focus on the role of a multidisciplinary team, the DOTS scheme and information management.

**Conclusion:** The model management system will demonstrate methods for improving notification of cases, analysis of cohort data, more rapid access to medicines, better adherence to treatment schemes and harmonization of control procedures.

### PS-885-961 Plasmatheresis for patients with MDR pulmonary TB at treatment with second-line anti-TB drugs

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Treatment of patients with MDR pulmonary TB with second-line anti-TB drugs is accompanied with different drug complication right up the lethal outcome. Plasmatheresis implementing with prophylactic and medical target is the effective method to cut off the drug complications. As a preventive method, plasmatheresis is implemented for patients with pulmonary MDR-TB at the indices changes in alkaline phosphatase ( $>90$ ) and lactatdehydrogenase ( $>280$ ). Plasmatheresis implementing allowed anti-TB chemotherapy to continue without interruption of drugs in 83.3%, in one case hemoperfusion was needed. While in the control group in 96.7% there were needed the durable and repeated courses of the hematotropic and infusion therapy and interruptions in the chemotherapy that was not useful for stabilization of the specific process. In this group in one case (3.1%) anti-TB therapy was complicated with lethal outcome. Thus, plasmatheresis is the effective method to cut off the beginning and developed drug complications among patients with pulmonary MDR-TB form at the treatment with second-line drugs.

### PS-932-1007 Evolution de la résistance aux antibiotiques (ATB) de *Streptococcus pneumoniae* (Spn) et d'*Haemophilus influenzae* b (Hib) agents d'infections graves

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Le traitement des infections à Spn et à Hib pose des problèmes bien recensés à cause de l'existence de résistance aux bêta lactamines. De plus, on relève des résistances associées aux autres familles d'ATB. La connaissance de la fréquence des résistances améliore le traitement probabiliste. Nous testons systématiquement toutes les souches isolées de sang et de LCR par la méthode des disques pour tous les ATB (antibiogramme standard) et par l'étude de la CMI en E test (AB Biodisk) pour les principales bêta lactamines. Les résistances des Spn et Hib à la pénicilline G (Péni G) et à l'ampicilline (Ampi) atteignent (tableau):

### Taux de résistance de Spn et Hib

	1989 à 1992	1994 à 1999	2001 à 2002	2003 à 2004 (1 Avril)
Spn	<i>n</i> = 94	<i>n</i> = 89	<i>n</i> = 23	<i>n</i> = 18
Péni G (I+R)	12,5%	32,5%	43%	35%
Hib	<i>n</i> = 25		<i>n</i> = 25	
Ampi R (Pénicillinase)	60%		20%	

I = Intermédiaire (sensibilité diminuée) ; R = résistant.

Ces mêmes souches présentent des résistances associées aux tétracyclines, cotrimoxazole, chloramphénicol et érythromycine. L'émergence puis la dissémination des Spn et Hib résistants d'une part et la gravité des infections causées d'autre part, justifient notre étroite surveillance.

### PS-708-782 Nurses supporting nurses: nurses supporting other nurses by writing a manual on DOT. A report from The Netherlands

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**Introduction/background:** In The Netherlands a report on DOT was accepted in 2000 by the National TB Policy Committee (CPT), an authoritative policy forum with representatives of Municipal Health Services, Ministry of Health and Pulmonologists. The report recommends implementing DOT in the Netherlands for patients risking to become non-compliant. In 2002 a questionnaire on DOT was sent to every Public Health Nurse (PHN) working in TB control. The results showed that many nurses, for various reasons, were reluctant to use DOT as an intervention. Therefore, in 2002 a DOT working group was set up by the National Association of Public Health Nurses. This working group aims to support PHNs in TB control to implement, practise and evaluate DOT. The working group developed different tools to achieve its goal. This poster focuses on the development of a manual on DOT.

**Objective:** By using the manual PHNs will be supported to implement, practise and evaluate DOT in The Netherlands, a low tuberculosis prevalence country.

**Methods:** A questionnaire was sent to PHNs to investigate the use of DOT. The evaluation of the results showed that many PHNs do not use DOT as an intervention. A concept manual on how to implement, practise and evaluate DOT was developed. After initial use the concept was evaluated. The final manual will be sent to the CPT for authorisation after which it will be implemented.

**Preliminary results:** The concept manual is presently used by many PHNs in TB control and is seen as a useful tool in implementing, practising and evaluating DOT.

### PS-291-327 The strategy of MDR-TB control in Lithuania

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**Setting:** In March 1998 the Ministry of Health had presented the National Tuberculosis programme, where the WHO-recommended DOTS strategy is implemented in whole country.

**Objectives and methods:** In 2002 the project of MDR-TB in Lithuania was carried out cooperation with CDC (USA, Atlanta).

**Results:** It was estimated that primary initial MDR-TB - 9%, acquired - 54%. As MDR-TB is threatening, special TB control strategy of MDR-TB has been prepared. There are five tools approved for MDR-TB strategy: the commitment of the Government of Lithuania for the MDR-TB control; possibility to carry out the susceptibility tests of tuberculosis to the second-line antituberculosis drugs in the special laboratory; the coordination of activities in the municipal, governmental, international levels; the central procurement of the second-line antituberculosis drugs; the guarantee of the directly observed treatment with the second-line antituberculosis medicine; the improvement of monitoring system: observation, treatment outcome and management of data in drug resistance and MDR-TB patients.

**Conclusion:** The aim of MDR-TB control strategy is to reduce the spread of MDR-TB, to improve TB rates, to protect the society from the spread of resistance TB, to implement the means of TB control, to make the treatment according WHO recommendation.

### PS-561-625 Cost and cost-effectiveness of DOTS-plus: evidence from the Philippines

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**Background:** Increasing numbers of developing countries are implementing 'DOTS-plus' projects that use second-line drugs for multidrug-resistant tuberculosis (MDR-TB). However, evidence about their feasibility, effectiveness, cost and cost-effectiveness is limited. Data are required for global and national policy development.

**Methods:** We evaluated the effectiveness, cost and cost-effectiveness of a pilot DOTS-plus project established in 1999 at Makati Medical Center, Manila. Individualised regimens tailored to the drug susceptibility pattern of isolates were utilized. We considered the cohort enrolled between April 1999 and March 2002. Costs (in year 2002 US\$) and effects (DALYs averted)

were estimated as the additional (incremental) costs and effects compared with a situation in which DOTS-plus is not implemented.

**Results:** 71 patients (61%) were cured, 12 (10%) failed, 18 (15%) defaulted, and 16 (14%) died. The average cost per patient treated was US\$ 3346 from the perspective of the health system, of which US\$ 1557 was for drugs, and US\$ 837 from the perspective of patients. The mean cost per DALY averted was US\$ 242 (range 85 to 426).

**Conclusions:** DOTS-plus for MDR-TB using individualised regimens can be feasible, effective and cost-effective in low and middle-income countries.

### PS-739-814 Policy recommendations on economic aspects of managing multidrug-resistant TB cases in the Russian Federation

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**Objective:** To develop policy recommendations on economic aspects of the management of multidrug-resistant (MDR) TB cases in the Russian Federation.

**Methods:** Assessment of the cost and cost-effectiveness of the DOTS-plus programme in Tomsk, comparison with the results from similar studies in other countries, and discussions with key policy makers, public health and TB experts at federal and regional levels. Costs were assessed using standard methods, and the effectiveness was measured using a) the treatment outcome definitions recommended by the WHO Working Group on MDR-TB for cohort analysis and b) a generic measure (DALYs averted).

**Results:** Data related to the costs, effectiveness and cost-effectiveness were collected during the first quarter of 2004. The final results of the analysis and policy recommendations will be presented at the 35th IUATLD Congress.

**Discussion:** The data will be used to assess the affordability and cost-effectiveness of treatment of MDR TB cases with individualized regimens including second-line anti-TB drugs in the Russian Federation. Policy recommendations concerning the justification of DOTS Plus projects in middle-income countries with a high prevalence of MDR TB from an economic perspective will be presented.

### PS-352-382 The growth rates of in vitro-generated rifampicin-resistant mutants of *Mycobacterium tuberculosis*

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**Introduction:** Studies carried out on different bacterial species have shown an association between drug resistance and decreased growth rates. However, there are very few such studies concerning *M. tuberculosis*.

**Objectives:** To study the relationship between level of rifampicin resistance and type and frequency of mutation with bacterial fitness relative to the wild-type parent strain.

**Methods:** Growth rates (in vitro fitness) of different rifampicin-resistant mutants derived from *M. tuberculosis* (strain Harlingen) were assessed in single, competition and macrophage cultures.

**Results:** Three types of *rpoB* mutants with high level resistance to rifampicin were isolated. These were at codons 522 (TCG to TTG, 4 isolates), 526 (CAC to TAC, 11 isolates) and 531 (TCG to TGG, 2 isolates). All mutants were less fit than the wild-type parent in all culture systems. In single cultures, the 522 mutants grew fastest. In both competition and macrophage cultures the 526 mutants exhibited the highest growth rate.

**Conclusion:** All rifampicin resistance mutations examined carried a biological fitness cost. This cost was most pronounced in macrophage cultures. There appears to be a positive correlation between frequency of mutation and fitness in competitive environments.

## PATIENT TREATMENT ADHERENCE/MANAGEMENT-2

### PS-700-775 Les effets secondaires au cours du traitement chez les patients tuberculeux au Centre Antituberculeux d'Adjame en 2002

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**Introduction :** Etude prospective chez 2066 patients tuberculeux toutes formes confondues suivis au cours de leur traitement antituberculeux et ayant présenté des effets secondaires vis-à-vis des médicaments antituberculeux

**Objectifs :** Décrire les caractéristiques socio – démographiques des patients ayant présenté des effets secondaires. Préciser les type d'effets secondaires. Evaluer les résultats du traitement antituberculeux.

**Méthodologie :** Etude prospective chez 2066 patients >15 ans tuberculeux toutes formes confondues dépistés au Centre Antituberculeux d'Adjamé du 02 Janvier au 31 Décembre 2002 et mis sous traitement

antituberculeux standard (2 RHZE/4RH) chez lesquels il est apparu des signes liés aux effets secondaires du traitement antituberculeux.

**Résultats :** Sur 2066 patients 178 ont présenté des effets secondaires (8,6%), sexe ratio = 1,02, age moyen = 32 ans, 98 patients sont des manœuvres (55%). Selon la forme de tuberculose : pulmonaires = 130 (73%) dont 112 bacillifères et 18 non bacillifères ; extrapulmonaires = 48 (27%) à majorité pleurale et ganglionnaire. Les effets secondaires sont d'abord mineurs = 157 (88%) avec arthralgie/myalgie(69), prurit(53), paresthésie(14), troubles digestifs(11), autres (10 dont pâleur, syndrome grippal. Puis des effets secondaires majeurs = 21(12%) avec oedèmes des membres inférieurs (16), ictère (4) et 1 trouble neuropsychique.

**Résultats du traitement :** succès thérapeutique = 120(67%), Echec = 4(2%), Transférés = 14(8%), Perdus de vue = 37(21%), décédés = 3(2%).

**Conclusion :** Parmi les patients sous traitement antituberculeux 8,6% présentent des effets secondaires. Les effets secondaires mineurs sont les plus importants 88% avec une prédominance des arthralgies/myalgies et des prurits. Les patients sont perdus de vue dans 21% des cas.

### PS-747-821 Analysis of treatment outcome in patients with pulmonary tuberculosis in 2001, in Belgrade

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**Introduction:** Monitoring of treatment outcome is considered a key indicator of the success of health services.

**Objective:** To determine treatment outcome in patients with pulmonary bacteriologically confirmed tuberculosis.

**Methods:** We analyzed patients notified in the TB register of our Institute. Of total 601 registered patients, 534 had pulmonary tuberculosis, out of whom 288 were smear positive (M+) and 372 culture positive (C+).

**Results:** Of 262 new M+ patients, 77% were cured, 14% completed, 5.4% died, 1.9% defaulted, 0.4% still on treatment, 1.1% transferred, and 0.4% with unknown treatment outcome. Of 26 M+ relapses, 54%, 4%, 31%, 11%, 0%, 0%, 0%, respectively. In new C+ 335 patients, the results were: 76% cured, 13% treatment completed, 5.6% died, 0.5% failed, 4% defaulted, 0.2% still on treatment, 0.2% transferred, and 0.5% unknown. In 37 C+ relapses: 57% cured, 10.5% completed, 22% died, 0% failed, 10.4% defaulted, 0% still on treatment, transferred, and unknown.

**Conclusion:** Our results confirmed that 87% of the patients with bacteriologically confirmed tuberculosis completed treatment with success. However, when new and relapse cases are studied separately, success

treatment outcome seemed to be incomparably more unfavourable in relapses (58% and 67%), with high percentage of both died and defaulted patients.

#### **PS-835-906 Factors affecting patient compliance with directly observed treatment, short course in urban Kathmandu, Nepal**

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**Introduction:** The Kathmandu urban area has a population of one million with high rate of TB transmission (ARI~ 4.0%). It is estimated that up to 200 people default from treatment in Kathmandu annually, a defaulter rate of 10%.

**Objectives:** This study identifies socioeconomic and behavioral factors affecting patients' compliance with DOTS, (and to make recommendations to the NTP regarding those factors that might be amenable to intervention.)

**Methods:** Structured face to face questionnaire of random sample of 571 new smear-positive TB patients currently under treatment (or defaulted). Analysis of socio-demographic, psycho-social factors, availability, accessibility of DOTS services and social support. Sub-analysis of non-compliant (missed >7 consecutive treatment days) v compliant using SpSS data analysis package.

**Results:** Reasons given by non-compliant patients included 61% reporting insufficient knowledge on need to take daily treatment, especially after feeling better. Directly observed treatment, younger age groups, knowledge of TB and availability of daily health education were associated with increased compliance. Daily health education was independently associated with compliance in logistic regression analysis with an odds ratio of 6.27.

**Conclusion:** Daily health education delivered in DOTS centres is strongly associated with improved compliance in urban Kathmandu DOTS centres. Full course compliance needs emphasis.

#### **PS-902-977 Organization of the Mexican Tuberculosis Nursing Net**

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**Background:** By December 2002, IUATLD and WHO launched the recommendation for integrating a Latin-American tuberculosis (TB) nursing and allied professionals net, to strengthen the tuberculosis combat in the region, improve the treatment, cure and patient attention quality, to increment the expansion of DOTS

strategy. Mexico's TB National Program initiated this allied integration in 2003, with the main objective of consolidate a Mexican Nursing Net (MNN) and team of over 300 TB trainers nurses, based in three action lines: Community Organisation, 2) Components of the DOTS strategy 3) Sensibility Ability Development with humanitarian content, besides expansion of such training to faculties and nursing schools.

**Method:** The beginning of the MNN was possible through the selection of over sixty nurses from state levels in a national announcing, integrating with them the state net. For the beginning of the activities, didactic material was elaborated and a formation course in tuberculosis was realised in which the nature of the components where: 1) Humanistic, 2) Technical, 3) Community Organisation, integrating in this National Course the Mexican Tuberculosis Nursing Net National Committee with six nurses from all the participants. When back in their respective states each capacitated nurse reproduced the didactic material, with aid from the health authorities, realised one state course, and integrated a jurisdictional net.

**Advances and results:** The 32 Mexican states already count with over 60 state capacitated nurses in the national net: in 25 states the course was been replicated for all nurses and other allied professionals. In three states (Sinaloa, Chiapas and Baja California) it has been realised only partially. Four states have not capacitated the nursing personnel (Zacatecas, Hidalgo, Sonora and Campeche). 52 courses have been realised in 164 sanitary jurisdictions involving around 2980 nurses and allied professionals, besides with 52 courses have been realised in 164 sanitary jurisdictions involving around 2980 nurses and allied professionals, besides with participation of the national level personnel. The great majority of the states have integrated a directory of the nursing net including allied from other institutions like nursing schools. The integration of advances has been given through diverse ways, as the monthly chats, electronic-mail, telephone, and fax. The evaluation of actions impact for this program will be done through national workshops for interchange of experiences. The development of stimuli and knowledge is in process.

**Conclusions:** Viewing the nurse as a sensible element and with high community impact, the National Tuberculosis Program has been strengthened with participation of the enthusiastic nurses, besides the community, making possible the increment of detection actions. It is desirable that cure rates may be impacted in the middle term, and concretise the DOTS strategy expansion, walking to a 'Mexico Free of Tuberculosis'.

### PS-915-990 Inpatient care utilization in three Russian Regions

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**Background:** There are around 80 000 TB beds in Russia, and in-patient care accounts for the majority of TB control costs. Evidence about how the use of in-patient care could be reduced, and the efficiency of case management improved, is limited.

**Methods:** A one-day bed census survey in all TB in-patient facilities in three Russian regions.

**Results:** 2726 beds and 2067 patients were surveyed. 657 (24%) beds were unoccupied, 1322 (49%) beds were occupied by patients with active TB, 701 (26%) beds were occupied by patients with non-active TB and non-TB, 44 (1.6%) beds were occupied by patients awaiting diagnosis. Patients that met one or more criteria that could justify in-patient care {a) surgery b) general clinical condition requires admission c) MDR TB d) currently sputum smear positive} represented 1412 (68%) patients and 52% of available beds. If social problems are added (e.g., homeless), 1815 (88%) patients required admission and 67% of available beds are needed.

**Conclusion:** There is a considerable scope for reducing use of in-patient care in three Russian Regions. If these results apply elsewhere, and new lower-cost approaches to care are developed and implemented to address social issues, large improvements in the efficiency of case management could be achieved.

### PS-122-156 La place de la courbe des déterminants de la couverture comme outils de monitoring des activités de lutte contre la tuberculose dans une zone de santé

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**Introduction :** Les équipes des bureaux Centraux (BCZ) des Zones de Santé (ZS) collectent les données des Centres de Diagnostic et Traitement (CDT) et les expédient au niveau des Coordinations Provinciales Lèpre-Tuberculose (CPLT) sans suivre le niveau de performance. Ainsi, nous mettons des outils, particulièrement la courbe des déterminants, pour suivre le niveau de performance.

**Objectifs :** L'étude montre comment le suivi graphique peut aider à améliorer le niveau de performance d'une ZS.

**Méthodes :** Nous avons procédé par une étude prospective en comparant des cohortes mis en traitement

au cours de 4 trimestres de l'an 2002 dans la ZS de MASA dans la Province du Bas-Congo en RD-Congo.

**Résultats :** Les courbes trimestrielles de détection et de guérison ont montré une bonne performance de la ZS, tandis que la courbe des déterminants a révélé précocement des faiblesses de processus dans le programme de lutte contre la TBC dans la ZS. Les goulots d'étranglement ont été identifiés, des solutions opérationnelles ont été microplanifiées et exécutées, ce qui a permis d'améliorer le niveau de performance au 4<sup>e</sup> trimestre.

**Conclusion :** Les courbes de détection trimestrielle et de guérison trimestrielle sont pratiques, mais la courbe des déterminants, inspirée de la courbe de Tanachie du Programme Elargi de Vaccination (PEV), présente un léger avantage de présenter synoptiquement la situation de l'ensemble du programme dans la ZS et permet de détecter à temps les faiblesses de processus.

### PS-330-360 Tuberculosis and Primary Health Care (PHC) workload: a district performance management system

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**Introduction:** Regular district performance management reviews that assess PHC facility workload and TB management outcomes provide an effective model for service improvement.

**Objectives:** To ascertain the effect of staff deployment and workload on TB control in health districts through the development and provision of a district rapid appraisal tool (DRAT) that can be implemented across South Africa.

**Method:** Quarterly Reviews of PHC facilities using the rapid appraisal tool with a scored set of indicators (staff, logistics and TB outcomes) and qualitative targets for service improvement, including staff development.

**Results:** The DRAT showed significant sustained improvements in TB control for >75% of facilities reviewed, including those with higher than average workloads. It also highlights inappropriate deployment of staff by District Management Teams.

**Conclusions:** Quarterly reviews in partnership with facility staff allow management and practitioners to discuss PHC workload and the logistical requirements and interventions needed for improving TB outcomes. The use of a simple scoring tool ensures consistency in assessment of outcomes. The identification of mutually agreed qualitative and quantitative performance targets between management and facility practitioners ensures consistent improvement.

### PS-661-735 Impact of socio-demographic factors on treatment compliance among TB patients in Bishkek City, Kyrgyzstan

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**Setting:** Treatment non-compliance is one of serious problems for TB treatment in Bishkek City, Kyrgyzstan. Data analysis for the last three years shows that defaulter rate has steadily increased 1999 (4.78%), 2000 (6.60%), 2001 (13.17%). Project HOPE Kyrgyzstan conducted research to detect possible reasons of treatment defaulting in Bishkek TB Dispensary in September 2003.

**Goal:** To determine impact of socio-demographic factors on treatment compliance.

**Methodology:** A retrospective comparative analysis of socio-demographic characteristics of 80 defaulters with control group of 342 patients who completed treatment was carried out.

**Outcomes:** Based on research outcomes, socio-demographic profile of defaulter was identified: male, age 30–40, has prison experience, lives alone or homeless, alcoholic or drug addict. An impact of other factors and characteristics like education, employment, drug side effects in data obtained are not statistically important.

**Conclusion:** To increase attention of a medical staff to the patients possessing socio-demographic characteristics contributing to treatment non-compliance and improving work with this group of patients.

### PS-670-743 A comparative synthetic indicator to evaluate municipalities' performance in tuberculosis control

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To adapt tuberculosis program's evaluation in the new health sector context, we developed a scalar comparative indicator of 57 municipalities from São Paulo State, Brazil. Based on routine collected data, we tested the reliability of variables related to case finding, diagnostic and treatment performance. The method to test reliability of the variables was Cronbach's Alpha statistic. We then constructed partial indicators for diagnostic and treatment performance, and a comparative scalar synthetic indicator. It was then applied Cluster Analysis to distribute the municipalities according to similarities and plotted them graphically. From a set of 23 variables, we selected 6 that were compatible each other, with a Cronbach's Alpha value 0,6753. These variables were related to diagnostic and treatment quality. It was impossible, with this methodology, to include case-finding related variables, indicating that the determinants of these activities are possibly other than the ones that were

selected. More than evaluating municipalities' scale of performance, this methodology allowed to design common strategies fitted to each group's particularities and necessities. This analysis permits to use routine surveillance data to monitoring for evaluating comparatively the municipalities' performance in tuberculosis control, as well as detecting their differences and similarities.

### PS-909-984 L'impact de soins à domicile dans le suivi des PVV par le personnel qualifié

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**Introduction :** Dans la plupart des pays africains subsahariens, la République Démocratique du Congo se trouve être très touchée par l'épidémie du VIH/Sida. Les structures étatiques étant débordées, l'impréparation du personnel infirmier sur la prise en charge de PVV entraîne la stigmatisation et l'exclusion des malades et ceci a comme facteurs la dégradation de l'état de malade et de mort précoce, il a fallu mettre en place des stratégies permettant de rendre partenaire l'équipe médicale, le patient et sa famille.

**Objectifs :** Faire le suivi des patients de l'hôpital et à domicile.

**Méthodes :** Sensibilisation du personnel soignant par des séminaires de formation.

**Activités :** Création d'un point focal du RIGIAC-SIDA/SANNAM dans des différentes institutions, Enquête sur le niveau de connaissance des infirmiers (ères) sur le VIH/SIDA et la prise en charge des PVV.

**Résultat :** Nombre de patients suivis à domicile 39, Visite effectuée 312, Implication familiale 47%, Malade soulagé et intégré, Expérience de vie augmentée, Réduction de la stigmatisation.

**Conclusion :** Vu ces résultats, nous constatons que les soins administrés par un personnel qualifié constitue un élément très important dans la prise en charge communautaire de PVV c'est à dire en préconisant la formation des volontaires communautaire et personnel de santé dans l'exécution de soins à domicile entraîne l'observance d'une réduction de perte de vue précoce de PVV/VIH et réduit la stigmatisation.

### PS-890-965 Nurses contribution to TB control at facility level

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**Issues:** TB and HIV/AIDS remains a challenge to program managers globally. Participation of Nurses in TB control had been limited at policy making level. Nurses have the obligation to control TB and HIV especially at facility level as 85% make up the health sector work force.

**Description:** In 2003 the National Leprosy and Tu-

berculosis program decided to have a nurse at its national level to look in to matters for Nurses. Nurses were mobilized and this was achieved through sensitizing senior nurses to win their political and administrative support. Latter, TOTS were trained and expectation to cascade training activities in collaboration with provincial TB coordinators.

**Lessons learned:** Extensive networking following trainings changed nurse's attitudes and practices in handling TB patients at facility level. Health facilities are meeting patient's needs from variety of approaches. It has been seen such initiatives are imperative prerequisite to scale up TB control in the country.

**Recommendations:** Greater support to continued education would be ideal to deal with misconception on TB and HIV diseases among health workers at facility level.

#### **PS-850-923 Strategies applied for the prevention of the abandonment and the transferred in Lima, Peru, between 1991 and 2000**

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**Introduction:** To know the experience carried out in Lima City, for the prevention of abandonment and transfers.

**Objective:** The personnel of health know the warning signal in the patients with risk of abandoning treatment.

**Results:**

- The profile of patients who abandons treatment: don't have fixed home, unoccupied or with eventual work, family boss, feels shame, irregular during its treatment in the first phase, social problems like addicted, alcoholism, delinquency and prostitution.
- Used strategies of prevention: interviews, domiciliary visits, education and information to the patient and family about the importance of the supervised treatment, flexibility in the schedule of attention of the centers of health, better relationship between the personnel of health and the patient.
- The abandonment decrease of 12.3% to 2.7% and the transferred decrease from 3.2% to 0%, while the cure rates increase from 79% in 1991 to 92.9% in 2000.

**Conclusions:** The committed participation and not simply of other professionals' support (Social Workers and Psychologists) and promoters of health and the development an effective DOTS have allowed the implementation of strategies to increase the adherence to the TB treatment; and prevention of abandons and transfers.

#### **PS-597-667 Introducing nurse led TB follow up clinics to streamline services and enhance patient care**

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The rate of tuberculosis in Waltham Forest has more than doubled since the early 1980's; this has been accompanied by an increasingly complex patient case-load. To cope with this change TB services need to demonstrate greater flexibility to meet the clients' needs. It is estimated that in 2002, TB patients accounted for over 700 appointment slots. At Whipps Cross University Hospital the clinic structure has been revised with the aim of streamlining patient care, prioritising complicated cases, reducing waiting times and improving the patient experience of TB care. After diagnosis the consultant reviews the patient at start of treatment and 2 months, with the TB nurse seeing the patient at all other times liberating over 500 consultant appointment slots. By liberating these sessions, waiting list times at the chest clinic are reduced. This results in fewer delays for suspected cases of TB as the TB nurse fast tracks them to see the consultant. In addition more consultant time can be spent reviewing the complex TB cases. Introducing nurse led clinics provides an extended role for the TB nurse, reduces TB consultant waiting times and streamlines nursing services allowing increased community based and outreach work whilst providing patient centred TB care.

#### **PS-286-317 A paper tiger as a costless, but effective, treatment adherence tool in the control of tuberculosis among the poor of Jakarta, 1978-2003**

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As long as TB treatment still lasts at least 6 months (DOTS), Treatment Adherence (TA) will always be a co-determinant of a successful TB control program. Numerous TA tools have been tried so far. The TB Control Clinic of PPTI-Jakarta (PPTI-J) has used a Paper Tiger since its opening in 1978, 25 years by now. Year after year the defaulter rate has always been below the 5% level of an ever-increasing patient load, from only 46 in 1978 to 1598 in 2003. It is a one-piece contract-paper where the patient agrees to come regularly to complete his treatment, which PPTI-J will provide free-of-charge. In case of default he agrees to refund the entire medicines token. The patient must sign this paper, which subsequently need to be co-signed by a treatment supervisor, two community elders, the local Governmental Official and the PPTI-J doctor. No stand-ins are allowed and return of empty blisters have been added lately. As it



will be impossible to pursue a defaulted patient, in reality this contract-paper is not more than just a Paper Tiger. Nevertheless, time (25 years) has proven that it is highly effective in securing a satisfactory treatment adherence and at no cost!

### PS-286-320 What is the greatest incentive for a poor TB patient?

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A poor TB patient is fully aware of his worsening health and that without proper treatment he soon cannot work anymore followed with a miserable premature death. He will frantically seek an affordable treatment leading to a cure. Is an incentive needed in this respect? In fact, for him the greatest incentive is to find it, for which he will thank God endlessly. Any incentive system intervening with this spontaneous course of events, however noble its purpose, might subvert the patient's way of thinking. Therefore, PPTI-J never uses incentives to entice poor TB patients to come for diagnosis and treatment. On the other hand an all-out effort has been done to minimize their expenses, e.g., free sputum microscopy and medical examination, free weekly DOTS (fortified), free drug delivery to remote areas, etc. As if to justify this approach, during its life-time (25 years) this Clinic has been visited by an ever-increasing number of new-comers, from 1485 in 1978 to 4000 in 2003; with more and more TB cases detected, from 171 smear positives in 1978 to 653 in 2003. Subsequently the number of TB cases treated also increases from 46 smear positives in 1978 to 1598 (smear positives and negatives) in 2003.

### PS-936-1011 Recherche des patients tuberculeux irréguliers au traitement au cours de la prise en charge au CNHP-P de Cotonou

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**Introduction :** L'intérêt de la mise en place d'une stratégie de recherche des patients tuberculeux irréguliers au traitement, en pratique de routine, dans le cadre du Programme National contre la Tuberculose, est diversement apprécié. Au Bénin, la relance des patients irréguliers est surtout ciblée sur des cas ponctuels et n'a jamais été l'objet de directives nationales obligatoires.

**Objectif de l'étude :** Apprécier la contribution éventuelle de cette activité à l'amélioration de la prise en charge des patients.

**Méthode :** Les responsables du PNT ont entrepris une expérience de recherche systématique des patients tuberculeux irréguliers au traitement, au CNHPP de Cotonou, le centre de référence du pays. Cette mé-

thode de recherche active, démarrée en Novembre 2001 comporte les étapes suivantes :

- Recensement des malades n'ayant pas fait de contrôle bactériologique du 5ème mois à partir du registre de la tuberculose.
- Identification de l'adresse précise à partir des fiches de traitement conservées au niveau des dossiers des malades.
- Récapitulation dans un cahier des malades et de leurs adresses pour mieux organiser les déplacements de l'agent chargé de cette activité.

**Résultats :** Les résultats préliminaires de cette étude sont présentés dans la présente communication, ainsi que les difficultés de sa mise en œuvre. Le tableau ci-dessous résume les résultats préliminaires de cette expérience en cours.

Répartition par période des malades TPM1 irréguliers, de ceux qui ont pu être relancés ainsi que le pourcentage des relancés par rapport aux irréguliers de la même période

	27 au déc.01 5ème mois	2002 5ème mois	1 <sup>er</sup> juin au déc.03 5ème mois	1 <sup>er</sup> janvier au 31 mars 04 5ème mois	8ème mois
Irréguliers	15	9	42	38	25
Relancés	11	6	25	25 dont 2 DCD	13 dont 1 DCD
% de relancés	73.3	54	60	66	52

**Difficultés :**

- Identités imprécises : changement de noms
- Adresses imprécises des patients
- Mobilité des patients (recherche d'emploi de survivance)
- Ressources financières insuffisantes pour une telle activité.

**Conclusion :** Les problèmes liés à la relance des patients irréguliers sont nombreux et variés notamment l'imprécision d'adresse des patients (problème d'état civil). Les résultats en dernière analyse ne sont pas à la mesure des ressources investies si cette activité doit viser un grand nombre de patients irréguliers. D'où l'intérêt de la prise en charge correcte au départ afin de minimiser le nombre de patients susceptibles d'être relancés.

### PS-938-1013 Knowledge of disease and treatment among tuberculosis patients in Yaounde, Cameroon

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**Objectives:** Determine patients' general knowledge and identity factors associated with satisfactory level of knowledge of tuberculosis and its management.

**Methods:** 184 previously untreated patients aged = 15 years with smear positive pulmonary TB, consec-

utively diagnosed from July to November 2003 in the tuberculosis centre of Hôpital Jamot in Yaounde were included. Information was obtained from the patients using a structured questionnaire. Questions were based on Cameroon's National TB Control Programme (NTCP) treatment guidelines for teaching TB patients. **Results:** Seventy-four (40.2%) of the 184 patients knew at least one symptom of TB. 25.5% knew the cause of the disease. The question on transmission was correctly answered by 34.8% of them. 87.5% of the 70.7% believed it could be prevented. The correct duration of treatment was known by 76.6% of the 184 patients. Correct knowledge of at least one side effect was obtained from 19 (10.3%) patients. 29.9% of the study population had satisfactory knowledge when correct answers to 4 out of the 7 questions asked was considered as satisfactory. Persons of a younger age (OR 0.71; 95%CI 0.52–0.97) and those with an education level higher than primary school (OR = 3.61; 95%CI: 2.15–6.05) were more likely to have a satisfactory level of knowledge about the disease.

**Conclusion:** Using NTCP treatment guidelines as reference, the majority of TB patients in Yaounde had an unsatisfactory level of knowledge about the disease and its management. Younger age and education level higher than primary school appear to be factors associated with satisfactory level of knowledge.

#### **PS-944-1019 The prevalence of tuberculosis in Central Division, Wajir District in North Eastern Province of Kenya**

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A study was carried out in the Central Division of Wajir District between July and October 2002. The study aimed at establishing the level of undiagnosed tuberculosis (TB) in the community and to quantify the disease prevalence in the area. Persons above 10 yrs and children of 0–5yrs with no BCG scar were targeted. Information was gathered using structured questionnaires and laboratory results of sputum, especially from acid-fast bacilli (AFB) Mantoux Test. From the results, 94% of the studied population had knowledge of tuberculosis while 91.7% sought treatment in hospital for the disease. 9.2% of the respondents tested smear positive whilst 8.6% of children tested positive to the Mantoux test. This infection rate increased with age. Despite the high level of awareness, TB remains one of the most important diseases in the area in terms of mortality. Results from this study demonstrated a significant relationship ( $P < 0.05$ ) between the level of education and the duration of illness with TB. From these results, it is suggested that there may be need to boost the level of literacy

alongside control measures. This could help increase awareness and the overall quality of knowledge about TB among community members and positively influence seeking early treatment.

## **TOBACCO AND AIR POLLUTION-2**

#### **PS-390-415 Tabagisme en milieu scolaire secondaire dans la commune de Cocody, Abidjan**

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Il s'agit d'une étude transversale sur le tabagisme en milieu scolaire dans les établissements secondaires de la commune de Cocody. Elle s'est déroulée du 18 mars au 04 mai 2003 à l'aide d'un questionnaire individuel anonyme, auprès de 1000 élèves. Au terme de cette étude, nous pouvons retenir les faits suivants : L'initiation tabagique était précoce avec un âge moyen de 13,93 ans. La prévalence du tabagisme était de 15,9% avec une forte proportion de fumeuses (10,59% des filles). Les établissements privés et internationaux étaient les plus concernés par le tabagisme et 37,74% des élèves de Cocody ont affirmé que leurs enseignants fumaient au sein de l'école en leur présence. Seulement 13,79% des parents savaient que leurs enfants fument. Comme facteur favorisant nous pouvons souligner l'influence du tabagisme parental (26,47%) mais surtout celui des pairs (67,65%) ; ces influences ont été entretenues par deux motivations principales : la curiosité et le désir d'imitation. L'acquisition de cigarette se faisait par l'usage de l'argent de poche (62,71%). La majorité des fumeurs fumait plus dans les boîtes de nuits et les maquis (74,36%) et consommait de l'alcool (69%). Les connaissances des élèves sur le tabac et ses conséquences étaient d'un niveau appréciable mais incomplètes : elles concernaient essentiellement les pathologies pulmonaires (62,88%) plus précisément le cancer broncho-pulmonaire (63,01%). La nicotine était le constituant de la fumée de tabac le plus connu par les élèves (52,88%). Il en résulte de ce qui précède qu'une stratégie de sensibilisation efficace s'impose pour réduire la progression de ce fléau.

#### **PS-437-476 The impact of smoking on the spread of tuberculosis**

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Research shows that smokers are more likely to contract tuberculosis. This risk increases the longer or more a person smokes. Smoking also increases cough-

ing, which spreads the disease and delays diagnosis by masking symptoms. I study the impact of smoking on the spread of tuberculosis using agent-based modeling. This approach allows simulation of a population of heterogeneous individuals whose characteristics and behaviors adapt over time to changes in their environment. I incorporate the social networks through which both contagious diseases (like tuberculosis) and behavior (like smoking) spread. These networks are critical since peers have a substantial impact on a person's behavior and, in large part, define an individual's environment. The experiences of acquaintances, for example, influences whether a person starts or stops smoking, whether they are exposed to tuberculosis, or whether a person visits a doctor for a persistent cough.

Such a model will allow me to answer several key questions:

- Does smoking impact the size of tuberculosis epidemics?
- Perhaps an effect exists only beyond some threshold of smoking prevalence. If so, what determines this threshold?
- How much more likely are smokers to spread tuberculosis?
- What factors confound how smoking impacts the spread of tuberculosis?

#### **PS-679-752 Smoking behaviour among health care professionals in 'Novi sad' primary health care center**

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**Introduction:** The prevalence of smoking behaviour, the risk factor of non-communicable diseases, is very high in population of Serbia and Montenegro.

**Objectives:** To evaluate the prevalence of smoking behaviour among primary health care professionals.

**Methodology:** Survey was conducted among all of 2000 employees in Primary Health Care Center 'Novi Sad' by self administrated questionnaire.

**Results:** There were 14.6% men and 83.6% women, mostly aged between 40 and 49 years. Among them were 29.4% doctors, 52.6% nurses and 18% others. According to smoking rate there were 41% smokers, 50% nonsmokers and 9% ex-smokers. There is statistically significant difference in smoking habit between men and women who smoked less ( $\chi^2 = 8.773$ ,  $df = 2$ ). The onset of smoking was at the age of 19.9 years. The reasons for smoking were habit, pleasure and stress. The average number of daily smoking dose was about 20 cigarettes. About half of the smokers would like to quit smoking, mostly due to health related reasons. They would do it with assistance

of their children, health care professionals or by themselves.

**Conclusion:** The smoking rate among health care professionals as potential health educators gives us the justification to create and implement program for reduction of smoking prevalence which could influence smoking rates in the general population.

#### **PS-688-760 The association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area**

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**Introduction:** Associations between smoking and tuberculosis disease as well as death from tuberculosis have been reported, but there is little data on the influence of smoking on the risk of developing *M. tuberculosis* infection.

**Objectives:** To determine the association between smoking and tuberculin skin test result.

**Methods:** In a population survey, data on smoking and tuberculin skin test of 2443 adults were compared.

**Results:** 1866 (76%) adults had a positive tuberculin skin test and 1345 (55%) were current smokers or ex-smokers. There was a significant association between a positive tuberculin skin test and smoking (unadjusted OR 1.94, 95%CI 1.60–2.34). A positive dose-response relationship with the average number of cigarettes smoked per day was shown, with 10–19 cigarettes per day having the highest risk (unadjusted OR 2.63, 95%CI 1.84–3.76).

**Conclusion:** This association suggests that smoking increases the risk of *M. tuberculosis* infection.

#### **PS-804-877 Statut socio-économique des fumeurs consultants d'un Centre de Diagnostic au Maroc**

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**Objectif :** Décrire le profil socio-économique des fumeurs consultant au Centre de Diagnostic (CD) du CHU de Fès (Maroc).

**Méthodes :** Les données de 303 consultants ont été recueillies lors d'un entretien à l'aide d'un questionnaire anonyme.

**Résultats :** Les 2/3 des répondants 287 (95%) sont des hommes. Parmi eux, 144 (50%) sont non-fumeurs (âge moyen de  $39 \pm 17$  ans), 61 (21%) anciens fumeurs (âge moyen de  $48 \pm 15$  ans) et 81 (29%) fumeurs actuels (âge moyen de  $35.6 \pm 13$  ans). 91% des fumeurs ont fumé au moins 100 cigarettes au cours de leur vie. L'âge moyen du début du tabagisme est de  $19 \pm 6.5$  ans. Tous les fumeurs et ex-fumeurs (sauf une personne), sont de sexe masculin. Parmi eux, 32% sont illettrés et 38.5% ont un niveau d'étude  $\leq$  au niveau primaire. Le revenu mensuel de 56% des fumeurs est  $\leq 2000$  DH (soit  $< 190$  euros) et 79% n'ont pas d'assurance maladie. Les fumeurs quotidiens fument en moyenne  $15 \pm 8$  cigarettes/jour et dépensent en moyenne 483 DH/mois pour leurs cigarettes soit pour 56% d'entre eux au moins le quart de leur revenu mensuel.

**Conclusion :** Ces résultats montrent le bas niveau socio-économique des consultants fumeurs du CD de Fès et justifient de se servir de ces CD pour l'éducation de ces patients et leur aide au sevrage tabagique.

#### **PS-805-878 Comportements tabagiques des consultants du Centre de Diagnostic du CHU de Fès, Maroc, et leurs connaissances des risques liés au tabac**

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**Objectif :** Décrire le comportement tabagique et la connaissance des risques des patients suivis en ambulatoire au Maroc.

**Méthodes :** Les données ont été collectées à l'aide d'un questionnaire anonyme rempli par 303 consultants du Centre de Diagnostic (CD) du CHU de Fès.

**Résultats :** Parmi les 287 répondants, 50% (144) avaient déjà fumé. Ces fumeurs se répartissaient comme suit : 50% (71) de fumeurs quotidiens, 7% (10) de fumeurs occasionnels et 43% (60) d'ex-fumeurs. La quantité de nicotine et de goudrons des cigarettes habituellement consommées n'était connue que par 16% des fumeurs actuels. 91% des fumeurs voulaient arrêter complètement de fumer et 78% avaient fait au moins une tentative de sevrage. Le motif le plus évoqué pour l'arrêt était la protection de la santé (98.7%). Les risques du tabagisme les plus cités par les patients étaient les maladies respiratoires (62%), les cancers (43%) et les maladies cardio-vasculaires (31%). Ces risques étaient mieux connus par les fumeurs que par les non fumeurs (69% vs. 58% pour les maladies respiratoires ( $P < 0.05$ ), 46% vs. 41% pour les cancers et 39% vs. 26% pour les maladies cardiaques ( $P < 0.05$ ).

**Conclusion :** Les résultats de cette étude montrent la nécessité d'améliorer l'information sur les risques liés

au tabac dans les CD et l'aide au sevrage tabagique des patients fumeurs.

#### **PS-132-164 The etiologic profile and determinant factors of hemoptysis**

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**Objective:** To study the etiologic profile and determinant factors of hemoptysis in hospitalized patients.

**Design:** We study the charts of patients admitted with diagnosis of hemoptysis or other diagnosis with hemoptysis as a symptom. We study the chart of control group patients without hemoptysis to find out determinant factors of hemoptysis.

**Results:** There were 441 patients with hemoptysis. The number of control group without hemoptysis was 341 patients. The male patients with hemoptysis made up 76% of cases. The patients older than 50 years old made up 69% of cases. Thirty four per cent of patients were smokers. There was significant difference between cases and control group in appearing of hemoptysis during months of year. August, September, October, November and December were the months with more cases than controls. Lung cancer made up 46% of all cases followed by tuberculosis which made up 14% of cases. Bronchial diseases made up 12% of cases and thrombembolia 10%.

**Conclusion:** In Albania the etiologic profile of hemoptysis has changed. Lung cancer is the main cause of hemoptysis followed by TB and bronchial diseases. The determinant factors of hemoptysis were gender, smoking and seasons.

#### **PS-132-165 The predictable diagnostic value of socio-economic and risk factors in hemoptysis**

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**Objective:** To estimate the predictable diagnostic value of socio-economic and risk factors in hemoptysis.

**Design:** The socio-economic and risk factors have been analyzed by multinomial logistic regression test.

**Results:** The age, itself, has not any predictive diagnostic value. The males with hemoptysis have highest probability for having lung cancer. The patients with hemoptysis who didn't smoke had a chance of 80% less than smokers to be diagnosed of lung cancer. The patients with hemoptysis without radiologic data had a chance of 60% less to be diagnosed of lung cancer. Patients with duration period of hemoptysis less than 8 days have the chance of 55% less to be diagnosed with lung cancer. The patients with negative data of fibrobronchoscopy have 90% less chance to be diagnosed of lung cancer.

**Conclusion:** There are different variables which have predictable diagnostic value in patients with hemoptysis. The following variable: gender, smoking, X-ray examination, duration period of hemoptysis and fibrobronchoscopy are important variables in diagnosis of lung cancer of patients with hemoptysis.

### PS-350-375 Chronic lung disease in indigenous Australian populations: parallels and insights into developing world disease

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**Setting:** Indigenous Australians continue to die from chronic lung disease at a rate up to 14 times that of non-Indigenous Australians. It is likely that such a dramatic disparity in mortality from COPD in Indigenous compared with non-Indigenous Australians is due to more than tobacco consumption alone.

**Methods:** Cross-sectional, retrospective cohort and prospective cohort studies of several remote Indigenous Australian communities in the north of Australia were conducted to elucidate risk factors associated with the attainment of optimal adult lung function and COPD.

**Results:** Whilst lung function was lower than that of non-Indigenous Australians this difference and airflow obstruction could be partially attributed to social disadvantage including household crowding and lower levels of education. Optimal lung function was also associated with growth in early life. Acute exacerbations were associated with the concentration of bacteria though not with specific species or strains of bacteria as seen in developed world populations.

**Conclusions:** COPD in this setting is a disease of poverty. Indigenous Australians have disease more comparable to that of developing world populations. Successful interventions in this and developing world populations are likely to be transferable and synergistic research partnerships should be encouraged.

### PS-394-420 Enquête sur les allergies respiratoires aux Cliniques Universitaires de Kinshasa (CUK)

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**Introduction :** Les manifestations allergiques respiratoires sont polymorphes. Cette enquête évalue la connaissance et les tests objectifs dans une population des patients admis aux CUK.

**Patients, matériel et méthode :** 33 sujets (19 H et 14 F, âge moyen 31 ans) sont concernés. Un question-

naire est soumis reprenant les principales manifestations, les antécédents, les tests cutanés, un kit d'allergènes (chat, pollens, poussières).

#### Résultats :

- 27 sujets (81,8%) se reconnaissent allergiques contre 6 (18,2%).

#### Symptômes

Eternuement	29/33	88,7%
Rhinorrhée	18	54,5%
Nez bouché	25	75,7%
Larmoiements	17	51,5%
Démangeaisons	16	48,5%

- Exacerbations : avril (15%), mai (21%), juin (17%), juillet (13%), autres ( $\leq 9\%$ ).

#### Facteurs déclenchants

Poussières	49	87,5%
Fumée	8	24,2%
Froid	8	24,2%
Animaux	3	9%
Pollens	1	9%

- Antécédents atopie familiale : 12 (36,4%) vs 21 (63,6%).

#### Prick tests

	Diamètre 0-4mm	5-9	>9mm
Poussières	3(9%)	12(36,3%)	6(18%)
Chat	1(3%)	6(18%)	3(9%)

**Conclusion :** L'allergie respiratoire est une réalité chez nous. La connaissance de ses manifestations est moyenne. La saison sèche (Mai-Août) est la plus propice. Les acariens représentant le principal facteur déclenchant.

### PS-728-802 HIV infection and smoking in an urban workforce in Zimbabwe: a cross-sectional survey in adult factory workers

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**Introduction:** HIV infection and cigarette smoking strong risk factors for common respiratory tract illnesses. In developed countries a disproportionate number of HIV-infected adults smoke.

**Objectives:** To investigate association between HIV and smoking.

**Methods:** Demographic and smoking data collected plus blood for HIV testing.

**Results:** 4902 workers consented to HIV testing, 88% male, median age 34 years. HIV prevalence was 19%, current smokers 17%, and 7% former smokers. Significantly more of the HIV-positives were smokers (33%) than the HIV-negatives (22%) at  $P < 0.001$ . Potential for confounding with age shown, as both smokers (median age 44 years) and HIV-positive (median age 38 years), older than average. HIV infection, male sex, older age and being married, shown as independent risk factors for being a smoker. Previous history of TB treatment (adjusted OR 0.7; 95% CI) and higher level of education (adjusted OR, 0.9; 95% CI) associated with low risk of being a current smoker

**Conclusion:** Shared risk factors for being both a smoker and being HIV-positive. Possibly reflects 'risky' personality traits associated with multiple risk taking behaviours plus age and sex. With 33% of HIV-positives being smokers, smoking maybe an important and preventable co-factor increasing the risk of respiratory illnesses among HIV-positives.

#### **PS-810-882 Profile of smokers attending a smoking cessation program**

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**Objective:** The aim of the study was to establish the profile of smokers opting for a smoking cessation treatment. The study followed a strong mass-media antitobacco campaign.

**Material and methods:** We studied 96 patients, aged between 19 and 68, smoking for more than 5 years. Each filled-in a simple questionnaire on tobacco habits, clinical signs, social status and motifs for smoking cessation. Also, the Fagerstrom test was performed. The patients received antitobacco counseling together with two booklets, on how to quit smoking. They agreed with smoking cessation after being explained the risks smoking implies. Most of them had pulmonary or cardiovascular problems and knew their habit represents a danger for their health. The medication proposed being expensive, only 57 patients accepted anti-tobacco treatment (bupropion hydrochloride) and the rest of 39 agreed with psychological support.

**Conclusions:** There is a high disponibility of smokers for quitting smoking, after adequate explanations, but there is a lack of health education on smoking cessation, which does not face the aggressive concurrence of the tobacco advertising. PG together with pneumologists must increase their efforts in smoking cessation among their patients. Addressability to the doctor would increase in case of a well conducted educational programme at national level.

#### **PS-229-268 Patterns of tobacco use among school teachers**

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Indulgence in tobacco is known to be health risk. The example of school teachers is likely to have influence on their pupils. This study refers to 300 school teachers (150 from town schools, the other from village schools). The smoker's proportion is still high, as 32% of males and 14.3% of females smoke in village schools, rather than in town schools. In village schools 8% of the teachers smoked more than 20 cigarettes daily, in comparison to 35 of the teachers in town schools. An interview among teachers suggested a high interest in the organization of health education programs and antismoking courses. However, both smoking and non-smoking teachers had similar views regarding methods to control the smoking habit which included banning the sale of cigarettes, putting a halt to the tobacco industries and banning cigarette advertisements. Regarding the female teachers in village schools, it came out a percentage of 8% more than female teachers in town schools (1.33%). The lack of information and of programs for health education in village schools explains the greater number of smoking teachers in village schools, which has also impact upon the pupils.

# Index

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## A

Abbassi, F S196  
Abbebe, M S141  
Abdukarimov, Kh S222  
Abrego, M S117  
Abu Laban, R S7  
Abulkasimov, S A S58  
Abzharkenova, E S113, S139  
Acencio, M S124  
Achmetgaliyeva, S S S92  
Ackah, A N S72, S209  
Acosta, I S74, S91, S158, S208, S209, S217  
Adama, B S72  
Adewole, O S156  
Adhikari, J R S168  
Adja, M S72, S97, S116  
Afanasyev, N S112  
Agboatwalla, M S206  
Agbroko, S S147  
Aghaji, M S153  
Aghi, M S20  
Agizaw, T S131  
Agrawal, S S48, S62  
Agzamova, R A S121, S170, S171, S172  
Ahamed, N S S217  
Ahmed, F S98, S117, S170  
Ahmed, J S77  
Ahmed, J U S184, S210, S213  
Ahmed, N S211  
Ahmed, S U S96, S97, S206  
Ahui, B S59  
Ahui, B J M S67, S151  
Ait-Belghiti, F S158  
Aitkaka, B S219  
Ait Kaki, B S188  
Ait Khaled, N S8, S102  
Aka-Danguy, E S59, S156, S230  
Aka Danguy, E A S151  
Aka Danguy, E K S60  
Aka Danguy, K E S67  
Akamatsu, Y S63, S64  
Akarasewi, P S84  
Akhmetgalieva, S S S76, S218  
Akhmetgalievna, S S S62  
Akhmetov, M S172  
Akiko, F S188  
Akram, M S133  
Akramul Islam, Md S77  
Alam, A S98, S117, S170  
Alarcón Arrascue, E S32  
Albalak, R S60  
Albert, H S220  
Aldiguireyeva, L Kh S62  
Aldulaymi, A M S95, S105

Alfaham, M S142, S214  
Ali, A A K S96  
Aliko, A S232  
Alimbekova, B S179, S188, S213  
Aljafari, A S A S61  
Alkhodzhaev, S S133  
Allaby, M S47  
Allamuratova, S S77  
Alleg, H S222  
Allen, S S12  
Almeida, A S S43, S49  
Almeida, M M B S227  
Alonso, P S156  
Alonso, V S80  
Al Qubaysi, W A S105  
Altinöz, H S104  
Aman, K S65  
Amanzholova, L S133  
Amaya, A S117  
Ameer, A S76  
Amin, L H S43  
Amirkanova, Z S139  
Amougou, G S88  
An, Y-s S203  
Anagonou, S S229  
Andersen, A B S149, S196  
Andersson, D I S224  
Andreev, E G S69  
Andreev, V S192  
Andreev, Y G S68, S70, S138  
Andrew, P S70, S111  
Andrianarisoa, A C F S103, S147  
Anilkumar, P S162  
Anouan, J S209  
ANRS 1260 Study Group S75, S76  
Anstey, N S131  
Antic, S M S152, S231  
Antoine, D S52, S196  
Antonangelo, L S124  
Antonios, V S127  
Antonova, N S157  
Antoun, F S196  
Aoki, T S51  
Appleton, S C S112  
Aptsiauri, N S167  
Aquino, G S112  
Arabiti, M A S223  
Araújo, M C C S207  
Arbeit, R D S51  
Arcêncio, R A S185  
Arda, H S104  
Ardian, M S131  
Arguin, P S112  
Arias, M S S98, S99, S115, S169, S172  
Arifeen, S E S77  
Arnisto, N M S223

Arnold, G S228  
Arora, S S29  
Arosi, Z A S45  
Aroyan, A S S129  
Arrascue, E A S215  
Arslan, Z S61  
Arya, A S192  
Asamidinov, U S188  
Aselbor, V S72  
Asencios, L S120, S217  
Ashokraj, Y S48  
Ashtekar, C S S142  
Assi, Y S67  
Atek, M S20, S101  
Atitalla, S A S105  
Attab, S S188, S219  
Au, B S42  
Au, K F S166  
Austin, J S164, S191  
Avena, A S225  
Avendaño, M S199  
Awases, M S1, S32  
Ayache, B S196  
Ayle, H S75  
Ayles, H S54  
Azevedo, V S31  
Aziz, M S157  
Azzam, E S86, S151

## B

Bacalso, D S55  
Badoum, G S91  
Bafende, A E S127  
Bafende, E A S221  
Baggi, F S154  
Baghdadi, S S185  
Bagno, N S112  
Bahadir, A S60, S122  
Bahati S233  
Bahati, E S56, S78, S190  
Bai, G H S82  
Baig, M S89  
Baismukhanova, K Kh S76  
Bajaj, L S71  
Bakayoko, A S116  
Bako, S S58  
Bakolitiana, R P S103  
Balandin, A S85  
Balasubramanian, R S137  
Bam, D S S45, S47, S57, S99, S114, S159, S160, S168, S176, S184, S205, S225  
Bam, T S S47, S160, S176, S184, S225  
Bamba, M S97, S116  
Bambara, M S91  
Bamber, S S141  
Bamgboye, P S147  
Bana, M S144  
Banavaliker, J N S187

Banda, H T M S189  
Banda, J S57, S75  
Banda, R S189  
Banda, R P S115  
Bandyopadhyay, S S218  
Banu, S S77  
Bañuelos, M S117  
Baough, L S20, S101, S144  
Baqi, A H S77  
Baradzina, G L S127  
Baradzina, H S150  
Baraka, O S105  
Baral, S S47, S99  
Barer, M S70, S111  
Barnashov, A V S68, S69, S70  
Barreira, D S49  
Barrera, L S80  
Barreto, M L S177  
Barreto Conde, M S216  
Barry, D S67, S223  
Barua, M K S98, S117, S170  
Baruch, N S197  
Basaraba, R S42  
Bashir, A A S154  
Bass, C S15  
Basse, K S116  
Bastos, L G V S221  
Bateman, E D S231  
Batkhuayag, B S50  
Baumanis, V S72  
Baussano, I S84  
Bayona, J S66, S94, S112, S116, S128, S136, S217  
Bayriyeva, N S96  
Becerra, M C S112  
Becx, M S213  
Becx-Bleumink, M S83, S96, S166, S184, S210  
Béguinot, E S15  
Begum, V S96, S166, S184, S213  
Behets, F S56, S180  
Behr, M A S128  
Beith, A S23  
Bekieva, A S92, S96, S214  
Bekot, S S88  
Belaïba, M S100  
Belen, V A S223  
Belghiti, F S198  
Belí, J S123, S125  
Bell, A S87, S201  
Bellis, K S226  
Belo, C S89, S93, S182  
Belo, M T S89, S93, S182  
Belo, M T C T S85  
Belova, E S S137  
Belova, Y S218  
Belova, Y S S62, S92

- Benator, D S52  
 Bencharif, L S188  
 Bencheikh, N S193  
 Benger, N S233  
 Benjamin, N S123  
 Ben Jerad, I S147  
 Benkolli, S S125  
 Benlabed, K S222  
 Bennett, J S42  
 Bentchouala, C S222  
 Berggren Palme, I S2  
 Bergstrom, K S31  
 Berikova, E S85, S113, S139, S140  
 Beringhs, E M S102  
 Bernal, M S118  
 Berraho, M S100, S231, S232  
 Bethlem, E S85  
 Beyers, N S113, S143, S162, S180, S231  
 Bhade, S S62  
 Bhade, S R S48  
 Bhatta, P P S168  
 Bhattarai, P C S149  
 Bhutani, H S94  
 Bialas, B S50  
 Bibikova, S S139  
 Bidaybaev, N S133  
 Billo, N E S176  
 Biondi, E S167  
 Bisaglia, J B S204  
 Bishai, D S149  
 Bishai, W S43, S44  
 Bismilda, V L S121  
 Bisuta S80  
 Bjune, G S105, S202  
 Black, R E S77  
 Blackwood, K S S104  
 Blagodetelev, G S83, S203  
 Blok, L S77, S114  
 Bloss, E S173  
 Blythe, D S197  
 Boccia, D S52  
 Bock, N S37  
 Bodika, S S131  
 Bodika, S N S142  
 Bodon, A S121  
 Bogale, M S141  
 Boktor, M S86  
 Bond, V S54  
 Bonilla, G S117  
 Boom, H S123  
 Booth, H S167  
 Booyen, C S113  
 Borgdorff, M A W S201  
 Borgdorff, M W S14, S79, S82, S162, S177, S231  
 Borisov, S S60, S112  
 Boschiroli, M L S118  
 Boskovska, K S141  
 Botha, E S162  
 Boughedaoui, M S20, S101  
 Boujemaa, W S100  
 Boulahbal, F S35, S219  
 Bousnina, S S70, S147, S151, S163  
 Bouzin, M S89, S93, S182  
 Braga, J U S177, S221  
 Branigan, E S169  
 Brant, R S90  
 Brassard, P S108, S109, S110, S128, S177  
 Bredin, C P S192  
 Breiman, R F S77  
 Brito, R S90  
 Britton, S S176  
 Bugiani, M S84  
 Bukhman, G S113  
 Bukli, J S232  
 Burinschi, V S83, S203  
 Burman, W S52  
 Burney, P S7, S9  
 Bushati, J S123, S125  
 Butterworth, A E S233  
 Buu, T N S82  
 Byelotseva-Bobro, M G S58  
 Byrazeri, G S232
- C**  
 Cabello, C S228  
 Cadieux, L S110  
 Cadikovska, N S141  
 Çağlar, E S60, S122  
 Calisir, H S130  
 Çalisir, H C S104  
 Callens, S S71  
 Camacho de Colque, M M S34  
 Camara, L M S47  
 Cameron, N S45  
 Campbell, M S104  
 Campbell, P S182  
 Campean, I S58  
 Campean, I M S58, S59, S234  
 Campean, M S58, S59, S234  
 Campell, I A S142  
 Canales, R S112, S118  
 Candia, N S80  
 Cao, J P S22  
 Capone, D S167  
 Capone, S S131  
 Cardoso-Gonzales, R I S205  
 Cardozo-Gonzales, R I S11, S77, S185, S206, S207, S208  
 Carosi, G S131  
 Carvalho, A C C S131  
 Casalini, C S131  
 Casanova, J-L S28  
 Casinillo, N S82  
 Castagnini, L S108  
 Castellanos, M S118, S165, S225  
 Castello Branco, M M S85  
 Cauchoix, B S114  
 Caugant, D A S87  
 Cavalcante, B S89, S93, S182  
 Cavalcante, S C S168, S207  
 Cavalcanti, A S157  
 Caviedes, L S119, S190, S219  
 Cegielski, P S112, S164  
 Çetintas, G S104  
 Chabbou, A S70, S100, S147, S151, S163  
 Chaisson, R S9, S85  
 Chaisson, R E S53, S207  
 Chakaya, J S227  
 Chakraborti, A K S94  
 Chalachala, J-L S S221  
 Chalchala, S J L S127  
 Chalco, K S94, S116  
 Chalmers-Nixon, T S182  
 Chamroonsawasdi, K S225  
 Chan, C K S166  
 Chan, S K S132  
 Chan, S S75, S76  
 Chandrasekaran, V S137  
 Chandiwana, S K S233  
 Chang, L S108  
 Changelucha, J S149  
 Chapau, B S92  
 Chatzidimitriou, D S193, S200  
 Chaudhary, R D S171  
 Chauhan, L S S39, S106  
 Chea, Y S S75, S76  
 Checchi, F S70, S111  
 Cheikh Rouhou, S S151  
 Chen, C S21  
 Chen, Y S S111  
 Chen, Z W S124  
 Cheng, H F S22  
 Cheng, S M S21, S22, S185  
 Chengeta, B S142  
 Chenhall, R S88  
 Cherri, D I S85  
 Chhavian, T S190  
 Chhenglay, L S215  
 Chiaravalloti, F N S79  
 Chilikwela, L S54  
 Chimzizi, R S38  
 Chin, D P S107, S185, S187  
 Chisamba, W S189  
 Chisanga, Q S57  
 Chitanondh, H S1  
 Chiunda, A S127  
 Ch'ng, K I S132  
 Choi, S P S66  
 Chorgoliani, D S167, S168  
 Choudhary, K R S192  
 Chow, F S142  
 Chryssanthou, E S122  
 Chukova, N V S69  
 Chukwu, J S99  
 Chukwu, J N S46  
 Cisse, F S47  
 Cobelens, F G S177  
 Cobelens, F G J S79, S82, S195  
 Coetzee, D S164, S191  
 Coetzee, D J S18  
 Coggin, W S160  
 Coker, R J S87, S201  
 Cole, B S51  
 Cole, R A S126  
 Colreavy, M S197  
 Colvin, C S173  
 Comstock, G S85  
 Consunji-Araneta, R S194, S199, S204  
 Cook, S S197  
 Corbett, E L S14, S233  
 Corlateanu, A S83  
 Coronado, M S228  
 Coronel, J S190  
 Corrigan, C B S73  
 Costa, M V S94  
 Costa, P A S168  
 Costa, W S167  
 Costa-Junior, M L S80  
 Coulibaly, G S116, S224  
 Coulibaly, I S224  
 Cowan, L S197  
 Cox, H S77, S114  
 Craig, G M S167  
 Creac'h, P S3, S167, S168  
 Creswell, J S118  
 Cristea-Fernström, M S122  
 Crofts, J S196  
 Cronin, W S197  
 Crudu, V S83, S203  
 Cruz, A S165  
 Cryan, B S192  
 Cukic, V S59  
 Cunha, A J L A S85, S180, S181  
 Cunningham, J S19, S108, S155  
 Cunningham, J A S178  
 Curcic, R S224  
 Currie, B S233  
 Cury, M R C O S79
- D**  
 Dacevski, D S141  
 Dadié, E A S151  
 Dahle, U R S87  
 Daix, T S116  
 Dakic, I S221  
 Dalcolmo, M P S221  
 Dalla Costa, E R S136  
 Daly, L S100  
 Dametov, U S S76  
 Danilova, I S56, S106, S164  
 Danilovits, M S155  
 Danusantoso, H S228, S229  
 Darge, K S141  
 Daru, P S76  
 Dauby, C S92  
 Daukiene, L S223  
 Dautova, O S140  
 Dauya, E S233  
 Davidaviciene, E S223  
 Davidow, A L S203  
 Davidson, P T S111  
 Davies, M S115  
 Davies, P D O S84, S161  
 Davletmuratova, Z S77  
 Dayal, A S S86  
 de Bérard, C S15  
 DeBoer, M S117



- Declercq, E S76, S179  
de Escobar, A S117  
Degeffie, T S141  
De Iaco, G S131  
de Kantor, I S16  
del Castillo, H S135  
Del Granado, M S26  
Delikatzi, D S193, S200  
Delpech, V S52  
DeLuca, N S118  
Dembele, M S91  
Demiröz, Ö S61  
Demkow, U S50  
Demsienne, I S223  
den Boon, S S231  
de Negri, B S214  
Dennis, A M S142  
Derouineau, J S196  
Déry, S S177  
Design Workgroup S165  
Dev, A S173, S216  
Devi, T S S81  
de Vlas, S J S155  
Diallo, M B S47  
Dias, E S89, S93, S182  
Díaz, R S143  
Dick, J S12  
Diclo, J S74, S91, S158,  
S208, S209, S217  
Diem, L S197  
Diethelm, P S33  
Di Giulio, A S121  
Diguimbaye, C S16, S154  
Dilberovska, M S141  
Dimiti, A I S142  
Dinda, M S91  
Dinda, M K S91  
Dizdarevic, Z S59, S129  
Djemli, O S125  
Do, H T S55  
Doi, N S63, S64  
Domki, A S206  
Domoua, K S72, S116,  
S209  
Donald, P R S140  
Doornenbal, G S222  
Dorcas, N S154  
Dorsinville, M S26  
Doshetov, D S77, S114  
Douvelle-Fradet, M S177  
Drabo, Y J S91  
Driscoll, J S51, S86  
Driver, C R S86  
Drost, A S218  
Du, G Z S124  
Du, X S187  
Dubey, G S71  
Dubrovina, I S211  
Dufour, H S15  
Duisenova, R S85  
Dujardin, B S92  
Duncan, H S134  
Dunda, K B S127  
Durdyeva, M S132, S214,  
S217  
Durovni, B S10, S168,  
S207  
Dussembaev, A S133  
Dussembaev, K S133  
Dutta, P S82  
Dwivedi, A S190  
Dye, C S105  
**E**  
Eang, M T S79, S110,  
S182, S190, S215  
Echemendía, M S143,  
S220  
Edwards, D S180  
Edwards, D A S151  
Egger, F B S94  
Egos, G E S82  
Egwaga, S M S79, S177  
Eilers, P S82  
El Aila, N A S78  
El Fakir, S S100  
Elfakir, S S231, S232  
El Hag, I A S61  
El-Hassan, A M S61  
Elias, D S176  
Elias, R S74, S91, S158,  
S208, S209, S217  
Eligan, A D S99  
Elkadir, I M S61  
Elmoghazy, E S86, S151  
Elmuradova, G S188  
Elnour, A A S61  
El Rhazi, K S100  
Elrhazi, K S231, S232  
El-Sadr, W S164, S191  
Elsafi, M E M O S61  
EL Sharif, N S8  
Elsiddig, K E S61  
El Sony, A S37  
Elsony, A S102  
El-Sony, A I S105  
Eltegan, M S102  
Emge-Koen, E S141  
Enarson, D A S105, S231  
Enarson, P S2  
Endo, S S55, S187  
Eng, P S181  
Erhabor, G S110  
Erhabor, G E S147, S156  
Erokhin, V S157  
Espasa, M S156  
Espinola, A B S167  
Espiritu, N S142  
Evaluation Design  
Workgroup S165  
Evans, B S52  
Evans, C A S190  
Eyongeta, L A S78  
**F**  
Fall, A S S186  
Falzon, D S114, S158,  
S198  
Fanning, A S182  
Farah, M G S202  
Farias, R S89, S93, S182  
Farmer, P S113  
Farmer, P E S67  
Fattorini, L S70, S81,  
S111  
Fatty, U S141  
Fawzi, M K S113  
Fehd, R S219  
Feit, M S83  
Fela, C S78  
Feldmann, K S114  
Ferjac, F S43  
Ferreira, E S118, S165,  
S212, S225  
Ferreira-Filho, M S53  
Ferroussier, O S118, S165  
Feshchenko, Y I S83  
Fiegel, J S151  
Filho, J P S153  
Filleul, L S101  
Filleul, L S20, S100  
Finlay, A S155  
Firsova, N S217  
Fiser, Z M S152, S231  
Fissah, A S144  
FitzGerald, J M S7  
Floyd, K S105, S223, S226  
Fonseca, Z S207  
Fonseca-Costa, J S43, S49  
Fonseca Nobre, F S177  
Forde, J S52  
FORESA Project S92  
Forleo, M A S131  
Franco, R S143  
Franke, M S112  
Freceirova, K S202  
Freire, R S89, S93, S182  
Frieden, T R S81  
Friedland, J S S190  
Friis, H S149  
Frolova, O S72  
Fry, R S173  
Fujikawa, T S163  
Fujiki, A S55, S187  
Furin, J S66, S67, S94,  
S116, S136  
**G**  
Gabos, S S182  
Gacheri, S S207  
Gad, M S151  
Galal, A S86  
Galesi, V M N S169, S193  
Gallo, P R S102  
Galvão, M G A S180, S181  
Gao, J S183  
Garay, J S117  
García, L S119  
Garrett, D S49  
GASP Study Group S7  
Gazetta, C E S79  
Gelmanova, I E S67  
Gelmanova, I Y S67,  
S135, S138  
Gençoğlu, A S122  
Gengiah, T N S71  
Gerdes, N S141  
Gerhardt, G S167  
Germany, Y S76  
Gevorkyan, A S140  
Gheorghiu-Branaru, M C E  
S159, S160, S234  
Gheorghiu-Branaru, M I  
S159, S160, S234  
Ghimire, S R S176  
Giampaglia, C M S S119  
Giang, D C S82  
Giang, C B S187  
Gibbs, F S90  
Gie, R S131  
Gie, R P S143, S180  
Gilman, R H S119, S142,  
S190, S219  
Glaziou, P S75  
Glotova, G G S69  
Gnim, S S215  
Gninafon, M S229  
Gocmen, S S130  
Godfrey-Faussett, P S10,  
S233  
Goldfeld, A E S54, S175  
Goliscsev, O S83, S203  
Golubchikov, P N S163  
Golubchikova, V T S69,  
S135, S138, S163  
Golyshevskaya, V S157  
Gong, Y S183  
González, J S156  
Goodburn, A S167  
Gopi, P G S81, S137  
Goranov, E P S137  
Gore, R P S131  
Goria, M S16  
Goron, M A S130  
Gotuzzo, E S108  
Gough, J S50  
Gouya, M M S178  
Grace, J S88  
Graham, S S22  
Graham, S M S37  
Granskaya, J S173  
Gray, A L S71  
Grazhdanov, N S74  
Gregori, D S84  
Grésely, L S210  
Grewal, H M S S87  
Grimaldo, E R S82  
Grimard, F S212  
Grinchenko, S Y S67  
Grosset, J S43, S44, S152  
Guardia, C S228  
Guda, D R S96, S97, S206  
Guerra, D S66, S94, S116,  
S136  
Guerra, J S219  
Guesnon, M S S196  
Guevara, R S117  
Guillebaud, C S S142  
Gunneberg, C S47, S99,  
S114, S160, S176, S184,  
S225  
Gupta, H G S168  
Gupta, R S223  
Gutierrez, R S142  
Gwanzura, L S233  
**H**  
Haar, C H S195  
Haas, W H S141  
Habbema, J D F S201  
Habeenzu, C H S95, S194  
Hai, L T S82  
Hall, J S167  
Hamid, S M A S76, S179  
Hamzaoui, A S100  
Han, S K S163  
Hane, F S186  
Hanh, L Q S111  
Hanson, C S89, S93, S182  
Haque, K E S213

- Haque, S A S218  
 Harada, N S107, S119  
 Harcourt, R L S126  
 Haroutunyan, D S140  
 Harries, A D S17  
 Harry, J L S126  
 Harton, M S42  
 Hassane, M H S154  
 Hassine, E S70, S100, S151  
 Hassmiller, K M S230  
 Hattori, S S63, S64  
 Hauer, B S194  
 Haves, S S37  
 Hay, D S104  
 Hayward, A S87, S167, S197, S201  
 Hazir, T S144  
 He, G X S22  
 Heldal, E S24, S87, S202  
 Hénault, S S118  
 Heng, P S S190  
 Henry, K S109  
 Heredia, J S74, S91, S158, S208, S209, S217  
 Herman, C S78  
 Hernandez, A S171  
 Hesseling, A C S140, S180  
 Hewinson, G S50  
 Heydari, G S108  
 Hiebert, G S170  
 Higuchi, K S107, S119  
 Hijjar, M A S221  
 Hilty, M S154  
 Hino, P S77, S207  
 Hiramatsu, K S51  
 Hiroyuki, Y S188  
 Hoang Thi Phuong S144  
 Hoepfner, V H S195  
 Hoffner, S S49  
 Hoffner, S E S224  
 Hohmuth, B A S86  
 Hökerberg, Y H M S134  
 Holakoi, K S178  
 Hollemans, D W S140  
 Hollm Delgado, M-G S219  
 Hollo, V S155  
 Holmström, P S198  
 Holtz, T S109, S154, S155  
 Holtz, T H S30  
 Hong, C S119  
 Hopley, M S174  
 Horo, K S59, S60, S67, S151, S156, S230  
 Horsburgh, C R S51  
 Hoshino, H S65  
 Hossain, S S77  
 Hovan-Somborac, J V S95, S152, S198, S231  
 Hoyal, D S47  
 Huamán, M E S228  
 Huang, D S124  
 Huitric, E S49  
 Huseynova, S S227  
 Hussain, S F S89, S120, S144  
 Hussein, A M S61  
 Hutubessy, R S105, S223, S226
- Hwang, S H S66  
 Hyder, K A S83, S96, S166, S213  
 Hyder, M K A S44, S184
- I
- Ibafidon, L S110  
 Ibrahim, M E S61  
 Idema, C S160  
 Idrissova, M S56, S117, S132  
 Igarashi, M S63, S64  
 Ihsan, M S133  
 Imperiale, B S121  
 Inaba, H S200  
 Indrati, K S98  
 Infuso, A S158, S198  
 Irawati, S R S98, S99, S172  
 Irfan, M S89, S120, S144  
 Irgashev, A A S58  
 Isakov, A M S68, S70  
 Iseman, M S14  
 Ishepe, M C N S230  
 Ishikawa, N S200  
 Islam, A S44  
 Islam, M S120  
 Islam, M A S98, S117, S170  
 Islamov, T S133  
 Ismailov, G S77, S114  
 Ismailov, Sh S85, S76, S113, S133, S138, S139, S140  
 Isola, D S70, S111  
 Isteljeva, M B S66  
 Itchy, N M V S67, S151  
 Ito, M S125, S163  
 Iversen, K S148
- J
- Jabeen, K S120  
 Jaggarajamma, K S137  
 Jahan, K S210  
 Jaisankar, R S189  
 Jakubowiak, W S24, S46, S56, S72, S106, S112, S157, S164, S223, S226  
 Jalal, U A S83, S96, S166  
 Jamal, L S49  
 Jamieson, S J S84, S161  
 Jamsheed, M S133  
 Janiyarov, R S205  
 Janjgava, M S S81  
 Janson, C S102  
 Jansone, I S72  
 Jarosz, T S70, S111  
 Jarret, N S56  
 Jassor, A O S102  
 Jayavanth, P S215  
 Jeon, D H S66  
 Jha, K K S47, S99, S176  
 Ji, B S152  
 Jiang, S W S20, S107, S187  
 Jibril, H S142  
 Jibuti, T M S81  
 Jindal, K C S94  
 Jit Kaur, K S62  
 Jittimane, S S3
- Jittimane, S X S174, S184  
 Johnson, L S50  
 Johnson, S S75  
 Johnston, L S134  
 Jones, B S52  
 Jones, J S196  
 Jones, M P S84, S161  
 Joshi, V S62  
 Jun, B Y S66  
 Junqueira-Kipnis, A P S42  
 Juréen, P S49  
 Jurkuvenas, V S85  
 Juskiewicz, K S92  
 Jutla, J S110
- K
- Kabani, A M S104  
 Kabuya, G S56, S78, S190  
 Kachtanova, L F S135  
 Kafle, K K S149  
 Kafuma, T S54  
 Kafwabulula, L S54, S75  
 Kaing, S S75, S76  
 Kaisermann, M C S126  
 Kalafati-Tzimaka, E S193, S200  
 Kalisvaart, N S79  
 Kalisvaart, N A S195  
 Källenius, G S122  
 Kam, K M S12, S42, S166  
 Kamal, H S179  
 Kamaté, M S72, S97, S116, S209, S224  
 Kama, N S210  
 Kamenov, B S146, S148  
 Kamenov, S S124, S146  
 Kammerer, S S154  
 Kandaker, E H S83  
 Kandulu, J S189  
 Kao, C H S111  
 Kapalata, N S73  
 Kapisyzi, P S232  
 Karatayev, O S113, S211  
 Karcheva, A S192  
 Karecki, A E S214  
 Kariev, T M S58, S129  
 Karkee, S B S171  
 Karkee, Y B S171  
 Karoui, C S118  
 Karpeichik, Y P S67, S68  
 Karrach, R S47  
 Kartashova, L V S170  
 Kartoshova, L S172  
 Kashamuka, M S78  
 Kasimova, D S117  
 Kasland, O S225  
 Kassa, F S229  
 Kassi, A S116  
 Kassi, O S230  
 Kassu, A S57  
 Kassymova, B S133  
 Kassymova, G S133  
 Kato, J S47  
 Kato, S S55, S187  
 Katovich, I L S127  
 Katunina, L S164  
 Katz, D J S203  
 Kaul, C L S48  
 Kaur, K J S48
- Kawuma, H J S S212  
 Kayembe, J M S80, S190, S233  
 Kayukova, L A S121  
 Kazakov, A S157  
 Kazeonny, B S112, S226  
 Kazi, G N S206  
 Kazykhanova, B S222  
 KC, K N S205  
 Keba, S P S59  
 Kedebe, Y S77, S114  
 Keita, B S97, S116  
 Keith, J S136  
 Keizer, S S218  
 Kelly, P S88  
 Kelly, P M S131  
 Kemp, J S183  
 Kenangalem, E S131  
 Kenzhebaev, S S133  
 Keravec, J S221  
 Keshavjee, S S67, S138  
 Ketenci, A S60, S122  
 Khachatryan, D G S65  
 Khadka, D K S114  
 Khalakdina, A S108  
 Khalil, E A G S61  
 Khamar, B M S62  
 Khamis, A H S37, S105  
 Khan, A S52, S179  
 Khan, J A S89, S120  
 Khan, M A S211  
 Khan, N S144  
 Khan, S S144  
 Khandaker, I U S96, S97, S206  
 Khatri, G R S24  
 Khauadamova, G S133  
 Khechinashvili, G N S81  
 Khodjikanov, M S179, S213  
 Kholi, G S48  
 Khondoker, H A S179  
 Khoo, S K S145  
 Khorosheva, T S112  
 Khoshnood, K S173  
 Khourieva, N S223  
 Khurieva, N S105, S226  
 Kilmarx, P H S131, S142  
 Kim, B J S66  
 Kim, D Y S66  
 Kim, S J S6, S82  
 Kim, Y W S163  
 Kimerling, M S85  
 Kimerling, M E S98, S99, S115, S169, S172  
 Kimsam, K S79  
 Kimsan, K S182, S215  
 Kinyanjui, G S210  
 Kipnis, A S42  
 Kirianova, E S112  
 Kitada, S S125  
 Kitetele, F S71, S180  
 Kitoh, T S107  
 Kjoller, E S148  
 Klarenbach, S S182  
 Kliiman, K S155  
 Kluge, H S106, S112, S164  
 Kochumov, B S92, S96, S214

- Koffi, G S116  
 Koffi, N S59, S60, S67, S151, S230  
 Koivula, T S122  
 Kok-Jensen, A S134  
 Kokki, M S198  
 Kokkozov, T S139  
 Kolappan, C S81  
 Kolk, A H J S123  
 Komena, K E A S60  
 Konan, Y S S156  
 Koné, M S S151  
 Korobitsyn, A S72, S226  
 Kosinova, O S74  
 Kostornoi, O S S67  
 Kotovich, I S150  
 Kouakou, J S72, S209  
 Kouanda, S S91  
 Kouassi, B S59  
 Kouassi, B A S60, S151, S156, S230  
 Kouassi, B E S67  
 Kovalyova, A S74, S113  
 Kozhamkulov, U A S121  
 Kozlov, A S173  
 Krasnov, V S197  
 Kreiswirth, B S51, S86  
 Kremer, K S42, S80  
 Krishnamurthy, P S65, S189  
 Kritski, A S119, S216  
 Kritski, A L S43, S49, S53, S85, S126, S136, S168  
 Kritski, R M P A S168  
 Krook, S S140  
 Kropsch, L S90  
 Kuaban, C S88, S153, S229  
 Kubasu, S S S227, S230  
 Kubota, A H S53  
 Kuijper, S S123  
 Kulchavenya, E S197  
 Kulsharova, A S218  
 Kulsharova, A D S92  
 Kumar, P S197  
 Kuntz, T S79  
 Kuramoto, L S7  
 Kurbanova, R S213  
 Kurup, S S142  
 Kus, J S50  
 Kuyumjian, F G S79  
 Kuyvenhoven, V S25  
 Kuzin, L S112
- L**  
 Lacerda, A P M S53  
 Lagahid, J S75, S186  
 Laid, Y S20, S101  
 Lal, S S S39  
 Lal Kaul, C S62  
 Lalvani, A S23  
 Lam, T K S42  
 Lambregts, K S S82  
 Lan, N T N S82  
 Lands, L C S110  
 Laouar, H S222  
 Lapa e Silva, J R S43, S49, S153, S216  
 Laraque, F S164  
 Larouze, B S167
- Laserson, K S49, S109, S117, S118, S154, S155, S165  
 Laszlo, A S57  
 Laticevski, D S83  
 Laticevski, V S83  
 Laureillard, D S75, S76  
 Lauzardo, M S134, S195  
 Lavigne, M S108  
 Lavryentjeva, V I S76  
 Lawrence, K S143  
 Lawton, E S30  
 Lazaryan, A N S129  
 Lazovic, N S103  
 Le Brun, F S196  
 Lee, S M S163  
 Lee, S S S111  
 Lee, S W S163  
 Leiderman, J S165  
 Leimane, V S109, S154  
 Lemus, D S120, S143, S220  
 Leng, C S75, S76  
 Leo, E S120, S217  
 Leon, R S118  
 Leonardo, N D B S94, S134  
 Leorati, M B M S193  
 Leroy Terquem, E S75  
 Lesley, L S233  
 Lessa, F S108  
 Le Strat, Y S198  
 Letvin, N L S124  
 Leung, C C S166  
 Leung, S M S166  
 Le Van Duc S175  
 Levi, B M S221  
 Lezzar, A S222  
 L'Her, P S75, S76  
 Lienhardt, C S186  
 Liippo, K S198  
 Lillabaek, T S196, S134  
 Lins, D S93  
 Litvinov, V I S91  
 Liu, E Y S21, S185  
 Liu, J J S20, S21, S22, S107, S185, S187  
 Liu, X Q S20, S187  
 Liu, Y C S111  
 Lixia, W S13  
 Llanes, M J S220  
 Llanos, F S128  
 Llaro, K S94, S112, S116  
 Llubani, S S232  
 Lo, C S181  
 Loch, C S78  
 Lodenkemper, R S194  
 Logan, M S219  
 Loh, L C S132, S145  
 Lombard, C J S231  
 London Tuberculosis Nurses Network S11, S197  
 LONG DRUG Study Group S81  
 Lonnroth, K S39  
 Lopes, I M S204  
 Lopez, S S142  
 Lored, C C S S43, S49  
 Lounis, N S152
- Lourenço, M C S168  
 Love, E J S168  
 Loveday, M S226  
 Lowe, P S174  
 Lozhkin, V S172  
 Lu Q S20  
 Lubasi, D S194  
 Lubemba, M S212  
 Luhadia, S K S62  
 Lui, X S183  
 Luiz, R R S85, S89, S93, S182  
 Lukiana S80, S233  
 Luna, A L S89, S93, S182  
 Luna, O S89, S93, S182  
 Lungjina, S S215  
 Luo, R F S119  
 Lutete Nkayilu, A S227  
 Luzze, H S123  
 Lyepshyna, S S74, S113  
 Lynch, L S197
- M**  
 Macalintal, L A S223  
 Macaraig, M S86  
 Machado, F S153  
 Macintyre, K S173  
 Macq, J S89, S92  
 Madansein, R S69  
 Madigan, E A S184  
 Madison, B S219  
 Madjdzadeh, S R S178  
 Maekura, R S125, S163  
 Maestre, J L S143  
 Magnussen, P S149  
 Maguire, G S131, S233  
 Maguire, G P S178  
 Maharjan, B S114  
 Mahmood, Y S62  
 Maia, S F S85  
 Makarov, V A S48  
 Makasa, M S57  
 Makhmatov, M S171, S172  
 Makhmatov, M M S170  
 Maksuda, A N S210  
 Maksumova, Z S56, S117, S132  
 Malakhov, K S46, S56, S106  
 Male, R S114  
 Malenganisho, W S149  
 Malinovskaya, T Z S67  
 Malla, P S47, S99, S114, S160, S176, S184  
 Mallet, H P S196  
 Mambo, M S95  
 Man, M A S130  
 Mancuso, A S16  
 Mandke, A N S191  
 Manfrin, M S131  
 Mangan, J M S4, S115  
 Mangubat, N V S223  
 Mangura, B T S217  
 Mannsaaker, T S87  
 Manzenigo, C S226  
 Mapara, K S144  
 Marais, B J S143, S180  
 Marandino, R Z S85
- Marcelino, B S74, S91, S158, S208, S209, S217  
 Marciniuk, D D S195  
 Mariam, D H S224  
 Marks, G B S87  
 Marniche, K S70, S147, S151, S163  
 Martin, A S120, S220  
 Martinez, G S89  
 Martinova, L P S48  
 Martins, A M S89, S93, S182  
 Martins, M C S119  
 Martiny, P S89  
 Maschmann, R A S136  
 Maseeh, A S62  
 Masjedi, M R S108  
 Mason, P S233  
 Masuda, T S63, S64  
 Masunge, J S142  
 Matambo, R S233  
 Matee, M S51  
 Matiru, R S5  
 Matteelli, A S131  
 Matuskevich, V G S83  
 Maug, A K J S76, S179  
 Maung, W S46  
 Maus, C E S42  
 Mayanja, H S123  
 Mayaud, C S75, S76  
 McArthur, A S156  
 McDonald, S S233  
 McIlleron, H S62  
 McIntyre, D S15  
 McKinstry, L S182  
 Mdivani, N G S81  
 Meacci, F S70, S111  
 Medvedeva, O S164, S226  
 Megdiche, M L S147  
 Megumi, H S200  
 Meheni, Z S222  
 Mehic, B S59  
 Mehra, R K S187  
 Meima, A S201  
 Mein, J K S178  
 Meirelles, E B S79  
 Meless, T S60, S67, S151, S156  
 Mello, F C Q S43, S49, S53  
 Melnyk, V M S83  
 Melo, H S43, S49  
 Memon, S S144  
 Mendoza, D S219  
 Mengistu, G S176  
 Menon, L S214  
 Menzies, D S85, S128, S212  
 Merletti, F S84  
 Messele, T S52  
 Mestanza, L S66, S94, S116, S136  
 Méyé Offossé, D S207  
 Meyer, H E S202  
 Mezzabotta, G P S185  
 M'Gbo, A S72  
 Mhlope, E S226  
 Michalowska, D S50  
 Michongwe, J S189  
 Miller, M D S124

- Min, D S75, S76  
 Minassian, G R S129  
 Mira, N R C S223  
 Miranda, A S49  
 Miranda, A G S117  
 Mireya, D S127  
 Miskinis, K S211  
 Mitarai, S S65, S162, S194  
 Mitchison, D S30  
 Mitimingi, P S54  
 Mitnick, C D S112  
 Mittar, D S190  
 Miura, T S79, S110, S190  
 Miyake, T S63, S64  
 Mizoguchi, K S162  
 Mizuno, S S51  
 Mogri, M S144  
 Moh, I S72  
 Mohamed, D S215  
 Mohamed Ahamed, O S102  
 Mohammad, K S178  
 Mohamud, A M S230  
 Mohan, S S103  
 Mohr, T S56, S117, S132, S181  
 Moldakhmetova, K S85  
 Moldovan, M S58  
 Mole, R J S220  
 Molina, J S228  
 Molla, A S15  
 Molyneux, E M S37  
 Monchy, D S76  
 Mondoka, D S95  
 Monroe, A A S11, S77, S185, S205, S206, S207  
 Montéiro, G S229  
 Montero Valencia, C S32  
 Montoro, E S120, S143, S220  
 Moodley, T S69  
 Moore, D A J S119, S142, S190, S219  
 Moore, T S221  
 Morcillo, N S121  
 Mori, T S107, S119  
 Morkve, O S73  
 Morris, S S142  
 Moulding, T S111  
 Moumeni, A S125  
 Mtei, L S51  
 Mugerwa, R D S123  
 Mugenyi, P S75  
 Muhajarine, N S195  
 Muhwa, C S40  
 Mukherjee, J S67  
 Mukushev, N S85, S222  
 Muller, G S196  
 Müllerova, M S192  
 Mulu, A S57  
 Mundy, C J F S75, S186  
 Muniz, J N S205, S206  
 Muñoz, M S94, S116  
 Munsanje, J S S208  
 Munsiff, S S86, S164  
 Munyati, S S S233  
 Mupere, E S127  
 Murray, J S109, S174  
 Musa, O A S102, S154  
 Musabaike, W S233  
 Musialike, T S95  
 Mussabekova, G S138, S139  
 Muwinge, H S79, S177  
 Muzy de Souza, G R S216  
 Mvusi, L S160  
 Mwale, A S54  
 Mwale, F S194  
 Mwale, M S208  
 Mwasekaga, M J S142  
 Myasnikova, G S133
- N**  
 N'Gom, A S59, S230  
 N'gom, S A S60, S67, S151  
 Nagelkerke, N J D S155  
 Nahoua, I S72  
 Naidoo, K S125  
 Naidoo, O S228  
 Nakagawa, N S63, S64  
 Nakajima, Y S119  
 Namba, Y S125  
 Nandili, M C I S227  
 Naranbat, N S50  
 Narayanan, P R S81, S137  
 Nardell, E S86  
 Narimanidze, R S168  
 Nascantes, R S153  
 Nasehi, M S178  
 Nasir, H A S95  
 Nasir, M S233  
 Natal, S S94, S134, S167  
 Naujokaite, A S223  
 Ñavincopa, M S119  
 Ndongosieme, A S5  
 Nejjari, C S100, S231, S232  
 Nelson, G S109  
 Nelson, L S131  
 Nelson, L J S135, S142  
 Nemtsova, E S112  
 Neves, A C S94  
 Ng, J S166  
 Ngamtrairai, N S174  
 Ngamvithayapong-Yanai, J S215  
 Ngandolo, R S154  
 Nguyen, D S109, S128  
 Nguyen, L N S87  
 Nguyen Thi Bic Ngoc S144  
 Nhlema-Simwaka, B M S183  
 Ni, Z S179, S213  
 Niazi, A D S95  
 Niemann, S S70, S81, S111, S114, S194  
 Niessen, L S148, S149  
 Nimba, J S209  
 Nisar, Y B S144  
 Njiru, H S210  
 Nkamsse, P S153  
 Nkiligi, E S177  
 Nkoghe, D S73  
 Nnaji, I R N S54  
 Nnogue, S S73  
 Nodieva, A S72  
 Noe, P S46
- Noeske, J S88, S153  
 Nordtvedt, S S87  
 Nordvall, L S102  
 Notshe, Y S45  
 Nouaigui, H S100  
 Nuermberger, E S29, S43, S44  
 Nurzhanov, G K S64  
 Nyblade, L S54  
 Nyirenda, S S131  
 Nyirenda, S T S142
- O**  
 Obihara, C C S180  
 Obioh, I B S110  
 O'Brien, R S19  
 O'Brien, R J S60  
 O'Connor, T M S192  
 Oedraougo, N S231, S232  
 Oey, L S218  
 Ogata, H A65, S162  
 Oggioni, M R S70, S81, S111  
 Ogretensoy, M S130  
 Ogundele, O S156  
 Okada, K A79, S110, S182, S190, S215  
 Okumura, M S65  
 Okwera, A S123  
 Oliveira, I S156  
 Oliveira, M M S43, S49  
 Ollé-Goig, J E S212  
 Olson, S S109  
 Omonova, M S188  
 Omurzakov, M S227  
 Ong, T H S181  
 Öngel, A S104  
 Onozaki, I S13, S79, S110, S158, S182, S215  
 Orefici, G S70, S81, S111  
 Orejel Juárez, R I S27  
 Orillaza, R S127  
 Orillaza, R B S223  
 Orme, I M S42  
 Orrù, G S70, S111  
 Ortaköylü, G S60, S122  
 Ortiz, J S219  
 Oruç, Ö S61  
 Osakwe, C S99  
 Osakwe, P C S46  
 Osuga, K S45, S47  
 Otete, F S190  
 Otgontsetseg, D S50  
 Otomo, K S65  
 Ouattara, N S209  
 Ouchfoun, A S101  
 Oudjehane, R S20, S101  
 Ouedraogo, G S91  
 Ouedraogo, M S91  
 Ouédraogo, S M S91  
 Ouedraougo, N S100  
 Ovsyannikova, T N S69  
 Oxlade, O S212  
 Ozere, I S135  
 Özgül, G S122  
 Özişik, N S61  
 Öztin, A A S104
- P**  
 Pacheco, A G F S53  
 Pacheco, A G S S49  
 Padayatchi, N A69, S141  
 Pahwa, P S195  
 Pai, M S108  
 Pak, S S4  
 Palaci, M S119  
 Palacios, E S94, S116  
 Palha, P F S205, S206  
 Pallangyo, K S51  
 Palomino, J C S80, S120, S220  
 Pana, B S173, S216  
 Panchagnula, R S48  
 Pande, J N S191  
 Pande, S B S99  
 Panic, E S93, S107  
 Panic, I S107  
 Pant, R S47, S205  
 Pant, R P S176  
 Panta, R S99  
 Parajuli, B K S171  
 Parajuli, R S171  
 Paralija, B S129  
 Paramasivan, C N S36  
 Pardini, M S70, S81, S111  
 Park, S K S66  
 Park, Y K S82  
 Parveen, S D S96, S97, S206  
 Pasechnikov, A D S67, S68, S70, S135, S138, S163  
 Pashkevich, D S112  
 Passos, S R L S134  
 Patakas, D S193, S200  
 Pavlik, I S17  
 Pavlova, V E S69  
 Paz de Zavala, N S115  
 Pedersen, S K S126  
 Peloquin, C S52  
 Perdigão, P S156  
 Pereira, S M S177  
 Perelman, M S157  
 Peremitin, G G S67, S69, S135, S138, S163, S223  
 Perkins, M S18, S155  
 Perkins, M D S178  
 Perumal, M S210  
 Peters, A S27  
 Petterskaite, A S223  
 Petrov, D B S137  
 Phadungchai, G S197  
 Phillips, R S123  
 Piatek, A S164  
 Pibello, A S88  
 Pillay, M S125  
 Piller, R V B S168  
 Pimentel, R S74, S91, S158, S208, S209, S217  
 Piñeda, D S117  
 Pinheiro, M C C M S204  
 Pinheiro Rodrigues, N C S177  
 Pinto, D S53  
 Pires, J S167  
 Piryani, R M S57, S159, S204  
 Pitman, R S87, S201

- Plikaytis, B B S42  
 Pljaskic-Kamenov, S S146, S148  
 Plochev, M Ph S137  
 Polivakho, V V S69  
 Pontino, M S121  
 Pool, I S218  
 Pop, C M S130  
 Popov, S S157  
 Portaels, F S6, S78, S120, S220  
 Portilla, S S136  
 Power, R S167  
 Prasai, M K S176  
 Pravdina, I I S67  
 Prignot, J S33  
 Procopio, M J S221  
 Proulx, M S128  
 Pulatova, L M S56, S132  
 Punga, V S106  
 Putova, E S56  
 Puzanov, V S157
- Q**  
 Qazi, S S144  
 Qiu, L S124  
 Quah, S Y S145  
 Qualls, M S117  
 Quantrill, S S228  
 Queiroz Mello, F S216  
 Quelapio, M I D S127, S223  
 Quilala, D D S215  
 Quispe, N S120, S217  
 Quy, H T S82  
 Quy, N C S82
- R**  
 Rabahi, M S43, S49  
 Racil, H S70, S147, S151, S163  
 Radhakrishna, S S81  
 Rahim, Z S77  
 Rahman, M S57, S159  
 Rai, C S171  
 Raikenova, R S113  
 Raimbek, S S133  
 Raitio, M J S204  
 Rajnoveanu, R M S130  
 Rajobov, O S181  
 Rakishev, G S85, S222  
 Rakishev, G B S76, S121, S137  
 Rakotoarisaonina, A S114  
 Rakotoarivelo, N H S103  
 Rakotoherisoa, A S114  
 Rakotondramarina, D S114  
 Rakotondravelo, S J B S103  
 Rakotonirina, V S114  
 Rakotosihanaka, F S147  
 Ralamboson, M S114  
 Ramachandran, R S137  
 Ramarokoto, H S114  
 Ramjee, A S69  
 Ramon, P S171  
 Ramon-Pardo, P S169  
 Ramos, L S117
- Ramsay, A R C S189  
 Randriantahiry, M S147  
 Range, N S S149  
 Ranjan, R S71  
 Rao, N A S78  
 Rasolofo Razanamparany, V S114  
 Rasolonalavona, T S114  
 Ratanavijit, L S84  
 Ratsirahonana, O S114  
 Ratte, S S15  
 Raveendranathan, T S169  
 Raykenova, R S139  
 Raykhert, I S74, S211  
 Reeder, B A S195  
 Reichman, L B S217  
 Reis, A O A S102  
 Rekhis, O S70, S147, S163  
 Rekhiss, O S151  
 Reyes, R S203  
 Reyes, L S74, S91, S158, S208, S209, S217  
 Reza, R S96, S97, S206  
 Riabova, O B S48  
 Ribeiro, E C S216  
 Ribeiro, M O S136  
 Ribeiro Lopes Filho, D S89, S93, S182  
 Rich, M L S67, S112, S138  
 Ridderhof, J S219  
 Ridzon, R S11, S18  
 Riekstina, V S72, S109, S154  
 Rielle, J-C S33  
 Rienthong, D S84  
 Rienthong, S S84  
 Rifles, G S73  
 Rigouts, L S78  
 Rijal, B P S57, S159  
 Rikleen, D S111  
 Rimm, A A S127  
 Rinder, H S70, S111  
 Rintiswati, N S98  
 Rios, M S94, S116  
 Ristevski, D S126  
 Ritacco, V S80, S143  
 Rivest, P S165, S177  
 Rizvi, N S204  
 Robbie, B S115  
 Roberts, W S197  
 Roberts, W G S197, S228  
 Robinson, P S219  
 Rocha, L F S204  
 Rocher, I S108  
 Rodrigues Junior, A L S185  
 Rodriguez, A S74, S91, S158, S208, S209, S217  
 Rodriguez, R S117, S169, S171  
 Rolla, V C S53, S134  
 Romero, N S80  
 Rompel, O S41  
 Rossetti, M L R S136  
 Rouvier, J S196  
 Rowinska-Zakrzewska, E S50  
 Roy, B S98, S117, S170  
 Rozemberg, B S94
- Ruesch-Gerdes, S S77, S114  
 Ruffino-Netto, A S32, S53, S85, S185, S205, S206, S207, S208, S215, S216  
 Rusakaniko, S J S233  
 Rüsck-Gerdes, S S48, S70, S81, S111  
 Russomando, G S80  
 Ruutu, P S198  
 Rybka, L S46  
 Ryder, R S78  
 Ryu, S W S82
- S**  
 Saad Eldien, O S102  
 Sabera, S S44  
 Sabirin, S W S181  
 Sabirov, S Y S129  
 Sabirov, Sh Y S58  
 Sacarlal, J S156  
 Sadacharan, K S81  
 Saddiq, H S211  
 Sadykov, S S139  
 Saeed, S S206  
 Safaryan, M S140  
 Safaryan, M D S65, S129  
 Safdar, N S179, S211  
 Sagebiel, D S194  
 Sagintaeva, G S130  
 Saha, G S218  
 Sahu, S S39, S106  
 Saidaliev, S M S56  
 Saini, A S71  
 Saint, S S182  
 Saito, Y S162  
 Sajeena Beevi, A S162  
 Saka, D S130  
 Salananiponi, F S183  
 Salaniponi, F S189  
 Salaniponi, F M S115, S189  
 Salazar, J S86  
 Saleri, N S131  
 Salgado Cruz, A S212  
 Salih, A M S37  
 Salim, A H S78  
 Salim, M S213  
 Salman, D H S105  
 Saly, S S79, S215  
 Samandari, T S131, S142  
 Samantaray, J C S191  
 Samaratunga, R M S159  
 Samatov, E V S129  
 Samir, K C S148, S149  
 Samson, K S44  
 Samungole, G K S57  
 San, K S97, S209  
 San, K-M S72  
 Sanchez, A S167  
 Sandven, P S87  
 Sani-Gwarzo, N S44  
 Sanjay, J S97  
 Sankara Sarma, P S103  
 San Koffi, M S116  
 Sant'Anna, C C S143  
 Santha Devi, T S137  
 Santos, A R S43, S49  
 Santos, C B S77
- Santos, J S49  
 Santos, L A R S193, S227  
 Santos, M S143  
 Santos, M A R C S180, S181  
 Sapag, R S94, S116, S118, S136  
 Sar, B S75, S76  
 Saraç, S S61  
 Saravia, J C S112, S190  
 Sarin, B C S190  
 Sarna, S S198  
 Sarsamaliyev, R V S66  
 Sarsembaev, S S139  
 Sarsembayev, S S113  
 Sassaki, C M S77, S80  
 Satha, P S79, S110  
 Satheesh, S S65  
 Satoshi, M S188  
 Satyajit, N S76  
 Saugat, R S62  
 Savic, B S221  
 Sazhin, V S173  
 Scalvini, A S131  
 Scano, F S38  
 Schaaf, H S S22, S131, S135, S140, S143  
 Schaap, A S52  
 Schelling, E S154  
 Schelokova, I S92, S96, S214  
 Schmid, L S167, S168  
 Scholten, J N S186, S200  
 Schreurs, I S222  
 Schwartzman, K S128, S212  
 Seaman, T S220  
 Sebek, M S218  
 Sebsebe, Y S141  
 Segura, B S108  
 Sehajpal, P K S190  
 Sehgal, P S124  
 Seiscento, M S124  
 Seita, A S106, S185  
 Sekiya, Y S107, S119  
 Selig, L S89, S90, S93, S182  
 Selmer, R S202  
 Seltsovsky, P P S91  
 Selvakumar, N S137  
 Semra, S S188  
 Semra, Z S219  
 Şenel, F Ç S60  
 Serikbaeva, K S S137  
 Serpa, J S219  
 Seth, P S191  
 Sethi, A S123  
 Seung, K S66  
 Seung, K J S136  
 Shah, K S179, S206  
 Shah, S K S211  
 Shajmuratov, Sh S130  
 Shamputa, I C S78  
 Shanaube, K S75  
 Shanmuganandan, S S89, S145  
 Shapiro, A E S175  
 Sharafeldein, G S61  
 Sharashidze, L S167, S168

- Sharma, U S114  
 Shashkina, E S51  
 Shean, K P S113  
 Sheehan, S S192  
 Shegertsov, D Y S67  
 Shemyakin, I S60  
 Shen Y S124  
 Shen, L S124  
 Shim, Y-S S163  
 Shimanovich, S V S70  
 Shin, S S66, S94, S116, S136  
 Shin, S S S67, S138  
 Shinnick, T S60  
 Shinnick, T M S42  
 Shiomi, M S65  
 Shirahama, T S55, S187  
 Shishido, S S55, S187  
 Shitara, T S64  
 Shivakumar, M S65  
 Shpakovskaya, L S173  
 Shrestha, B S114  
 Shrestha, G B S114  
 Shrestha, N S148, S149  
 Shuja, Z A S133  
 Sia, I S127  
 Siddiqi, K S179  
 Siddiqi, S S7  
 Sigande, L M S57  
 Sigaud, M A S221  
 Silva, E C S94  
 Silva, F G S94, S134  
 Silva, G S49  
 Silva, M S N S136  
 Silva, V S153, S157  
 Simbayi, L C S78  
 Simpson, S E S87  
 Sinfield, R S37  
 Singh, I S48, S62  
 Singh, S S94  
 Singh, U B S191  
 Sinkala, A S57  
 Sirojiddinova, U Y S56, S132  
 Sirotkina, O B S69, S135  
 Sitdhirasdr, A S84  
 Sitienei, J K S166  
 Sitthi-Amorn, C S168  
 Skenders, G S72  
 Skhiri, N S147  
 Skolnik, R S39  
 Skopinska, E S50  
 Slama, K S152  
 Slogotskaya, L V S91  
 Sloutsky, A S217  
 Slutsky, A S69  
 Smailova, A S140  
 Smailova, G S130  
 Smailova, G A S64  
 Smaoui, M S70, S163  
 Smati, F S188, S222  
 Smith, K R S108  
 Smith, L L S45  
 Smith, P S62  
 Smith Fawzi, M S86  
 Smithtikarn, S S84  
 Soares, E C C S168, S207  
 Soares, L C P S85  
 Sohtome, H S64  
 Sok, T S54, S175  
 Sokolo, L S116  
 Soliman, S S151  
 Solis, A S89  
 Solovic, I S202  
 Somasekhara Reddy, Y S65  
 Somborac, S J S95, S198  
 Somocursio, J S66, S136  
 Sondrini, M A S128  
 Sopiyeu, B S96  
 Sopyev, B S132, S217  
 Sosnovskaja, A S223  
 Soto, G S219  
 Soto, M S117  
 Sotomayor, A S66, S136  
 Soukhov, V M S58  
 Soukhova, E V S58  
 Souza, C T V S94, S134  
 Sow, O Y S47  
 Soza Pineda, N I S177  
 Spencer, Y S50  
 Spradling, P S38  
 Squire, S B S183, S189  
 Sredkova, M S192  
 Sreelatha, P R S161, S162  
 Srefanova, D I S137  
 Srinivasan, R S214  
 Stallworthy, G S41  
 Stamboltsyan, Ye S140  
 Stanley, M S154  
 Steensma, C S108, S110  
 Stefanova, D I S90  
 Stefanovic, B S59  
 Stefanovic, G S221  
 Steigviliene, R S223  
 Stein, Z S164, S191  
 Stevens, P S214  
 Stinson, K W S135  
 Story, A S11, S52, S167, S196, S197  
 Stowell, M S128, S217  
 Strelis, A A S69  
 Strelis, A K S69, S135  
 St. Sauver, J S127  
 Study Group of  
 Laboratories and Public  
 Health Offices S194  
 Sturm, A W S125  
 Suarez, P G S75, S186  
 Subedi, S K S171  
 Subramani, R S81, S137  
 Sudan EPILAB S152  
 Sudhakara, K S S65  
 Sugawara, I S51  
 Sughis, M S62  
 Sugiyama S205  
 Sugiyama, T S45, S47  
 Suleiman, G S61  
 Suluburic, D M S103, S146  
 Suluburic, T T S103, S146  
 Sung, J S151  
 Supply, P S78  
 Suresh, N S191  
 Svenson, L S182  
 Svetlichnaya, S S74  
 Swan, S S199  
 Syrtanova, A S140  
 Syty, V S150  
 Szilard, I S25  
 T  
 Tabala, M S56  
 Tacconi, E S185  
 Tafradijska, M S192  
 Taganovich, A S150  
 Tahanovich, A D S127  
 Tai, L M S166  
 Takahashi, Y S63, S64  
 Talbot, E A S142  
 Taleb, A M S179  
 Talevski, S S56, S132  
 Tam, C M S166  
 Tamashakina, G S150  
 Tan, L Z S132  
 Tang, S S183  
 Tannenbaum, T N S165, S177  
 Tanner, M S154  
 Tapia Conyer, R S212  
 Tarimo, E S73  
 Tashpulatova, F S193  
 Távora, E S90  
 Tawfik, L S186  
 Tawfik, T S215  
 Tchapau, B S96  
 Tchapu, B S214  
 Tchieche, K C S67, S151  
 Teixeira, E S89, S93, S182  
 Teixeira, E G S85  
 Teixeira, L S124  
 Tejada, D S74, S91, S158, S208, S209, S217  
 Telles, M A S S119  
 Ten Asbroek, A H A S149  
 Tenorio, A S171  
 Terlikbaeva, A S133  
 Terquem, E L S76  
 Tessier, J F S20, S100, S101, S231, S232  
 Thanasi, N S123, S125  
 Thankappan, K R S103  
 Thayaparan, T S132, S145  
 Thiam, S S186  
 Thibert, L S128  
 Thomas, A S137  
 Thomsen, V O S134, S196  
 Thomson, R S183  
 Thorel, M F S118  
 Thornley, C N S104  
 Thorpe, L S109, S154  
 Thresiamma, T P S161, S162  
 Ticona, E S119, S219  
 Tippu, M S62  
 Tiwari, S K S168  
 Tjandra, H S131  
 Tjitra, E S131  
 Toksanbayeva, B S172  
 Toktabayanov, A S171  
 Toktabayanov, A K S170  
 Toktabaynov, A S172  
 Tomic, Lj S221  
 Tong Chau Man S26, S150  
 Tonkel, T P S67, S69, S135, S138  
 Toro, P S164, S191  
 Torres, R S228  
 Tounes, M M S73  
 Touré, K S72  
 Touré, N S207  
 Tracevska, T S72  
 Trajman, A S85, S89, S93, S126, S182, S216  
 Traoré, M S72  
 Trappetti, C S70, S111  
 Trébucq, A S116  
 Trenchard-Mabere, E S228  
 Trenkler, J S202  
 Trollip, A P S220  
 Truffot-Pernot, C S152  
 Truong Huyen Truong S150  
 Trusov, A S170, S171, S172  
 Tsai, H T S111  
 Tse, L W S42  
 Tsiouris, S J S191  
 Tu, D-H S203  
 Tuberculosis Trials Consortium S52  
 Tuberculosis Working Group in Perú S219  
 Tupasi, T E S82, S127, S223  
 Tutkysbayev, S O S170  
 Tyagi, S S43, S44  
 Tzimaka, M S193, S200  
 U  
 Udagawa, T S51  
 Umarova, Zh S139  
 Uplekar, M S39  
 Urakov, S S179  
 Urbanczik, R S35  
 Usarova, S S179  
 Usembayeva, S S85, S113, S139  
 Ustamujic, A S59  
 V  
 Valcárcel, M S136  
 Valência, C M S215  
 van den Hombergh, J S52  
 Van der Have, J J S195  
 Van Deun, A S6, S12, S34, S76, S78, S189  
 Van Gerven, P J H J S195  
 Van Ginkel, T S177  
 van Helden, P S113  
 van Lill, S W P S231  
 Vanna, T S S110  
 Vanrie, A S78  
 Van Rie, A S56, S71, S180  
 van Sooling, D S28, S42, S80, S143, S201  
 van Zyl, S S143  
 Varaine, F S70, S81, S111  
 Vargas, D S119, S219  
 Vargas, F S S124  
 Vargas, P S89, S93, S182  
 Varma, M V S S48  
 Vasankari, T S198  
 Vasilieva, I S112  
 Vásquez, L S120, S217  
 Vasquez, L S80, S128

- Vdovichenko, E S173  
 Velazquez Monroy, O S212  
 Vendramini, S H F S79  
 Venugopal, K S161, S162  
 Verdonck, K S108  
 Verhage, C S79  
 Verhagen, M S218  
 Verhoek, T S222  
 Verma, S C S45, S176  
 Vermaak, E S45  
 Vernilho, B C S207  
 Vernon, A S52  
 Verver, S S162, S201, S231  
 Vesna, S S129  
 Vezhnina, N S5  
 Viazon, R S75, S186  
 Vidal, L S186  
 Videnovic-Ivanov, J S129  
 Vieira, G S119  
 Vieira, M A M S S53  
 Vieira Amim, L H L S49  
 Vijayakumaran, P S65, S189  
 Vijayasingham, P S132, S145  
 Vikarunnessa, B S83  
 Vikas, I S97  
 Villa, T C S S11, S32, S77, S79, S80, S185, S205, S206, S207, S208, S215, S216  
 Villar, M S73  
 Villatoro, M H S171  
 Vingadio, E S95  
 Vinhas, S A S119  
 Vink, K S155  
 Vinokur, A S105  
 Vitek, E S164  
 Vlada, Z S129  
 Vlasov, V I S137  
 Volchenkov, G S56, S226  
 von Reyn, C F S51  
 Vordermeier, M S50  
 Vos, A M S201  
 Voskens, J S98, S99, S172  
 Vu Thi Khanh S144  
 Vu Thi Loan S144  
 Vucinic, V S129  
 Vukovic, D S221  
**W**  
 Wada, M S65, S162  
 Walley, J S179  
 Walley, J D S211  
 Walley, R S114  
 Wallis, R S28  
 Waltenburg, R S164  
 Walton, W S32  
 Wandwalo, E S73  
 Wang, H D S20, S107  
 Wang, L S107  
 Wang, L X S107, S185, S187  
 Wang, X J S20  
 Wang, Y S183  
 Wangoo, A S50  
 Wann, S R S111  
 Wanneh, E S229  
 Wansbrough-Jones, M S123  
 Waramori, G S131  
 Ward, H A S195  
 Wares, F S39, S106  
 Warren, R M S140  
 Waterman, S S165  
 Watson, J S52, S87, S201  
 Watson, J M S196  
 Weil, D S89, S93, S182  
 Weiner, M S52  
 Weir, S S78  
 Weis, S S52  
 Wells, C S49, S109, S112, S117, S131, S154, S155  
 Wells, C D S135, S142  
 Werneck, A S167  
 Werneck, G L S177  
 Werneck-Barroso, E S53  
 Wernersbach Pinto, L S177  
 Werngren, J S49  
 Wesley, T S166  
 Westley, J S128  
 Whalen, C C S123, S127  
 Whalen, C M S75, S186  
 Wiegandt, A S99  
 Wieland-Alter, W S51  
 Wilce, M S165  
 Wilcke, J T R S148  
 Wilks, M S123  
 Willcox, P A S113  
 Willekens, F S148  
 Willery, E S78  
 Willetts, A S183  
 William, G S215  
 Williams, C D S S84, S161  
 Williams, G S32  
 Williams, K S43, S44  
 Wilson, N S210  
 Winfrey, W S178  
 Winje, B A S87  
 Wiratunga, B S84, S161  
 Wolfe, J N S104  
 Wolter, S S99  
 Wonderling, D S201  
 Wong, K L S42  
 Wong, M S174  
 Wright, A S114  
**X**  
 Xu, H C S20  
**Y**  
 Yaalaoui, S S70, S163  
 Yagui, M S128, S217  
 Yala, D S219  
 Yamada, H S51  
 Yamada, N S110, S158  
 Yamakami, K S190  
 Yamanija, J S86  
 Yann, Y S113  
 Yanova, G V S69  
 Yao, H Y S21, S185  
 Yao, K S72  
 Yaogho, M G S91  
 Yapi, A S116  
 Yarosh, O A S138  
 Yasin, M S189  
 Yatudo, P B S89, S93, S182  
 Yedilbaev, A S138  
 Yedilbayev, A S113, S135  
 Yedilbayev, A B S67  
 Yesilkaya, H S70, S111  
 Yew, W W S166  
 Yim, J-J S163  
 Yip, C W S42  
 Yoo, C-G S163  
 Yoshimatsu, T S44  
 Yoshimatsu, Y S43  
 Yoshiyama, T S47, S65, S200  
 Yu, C S40  
 Yu, L S22  
 Yunus, Md S77  
 Yurasova, Y S213, S217  
 Yurteri, G S61  
 Yushkevich, K S218  
**Z**  
 Zaharov, T S146, S148  
 Zaki, A S89  
 Zaleskis, R S186, S200, S213, S217  
 Zaman, K S77  
 Zamani, G S178  
 Zamora, C D S130  
 Zanetti, G S85  
 Zaric, D V S95, S152, S198, S231  
 Zarovska, E S109, S154  
 Zellweger, J-P S33  
 Zendah, I S151  
 Zhanabaeva, A S140  
 Zhandauletova, Z S172  
 Zhandauletova, Zh S170, S171, S172  
 Zhang, H M S22  
 Zhang, L Y S22  
 Zhang, L-x S203  
 Zhao, B S86  
 Zhao, X S183  
 Zhao, Z S52  
 Zhaparkulova, M S139  
 Zhemkov, V S173  
 Zhemkova, M S173  
 Zhuri, G S173, S216  
 Zidouni, N S20, S101, S144  
 Zinsstag, J S154  
 Zintl, P S128  
 Ziolkowski, J S50  
 Zivadinovic, D S103, S146  
 Zou, J Q S21  
 Zuim, R S90  
 Zulu, F S95  
 Zumla, A S167  
 Zungu, I S189  
 Zutic, H S59  
 Zwang, J S155, S183  
 Zwolska, Z S50

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## **Green Light Committee: 2004 Application Review Cycle**

### **WHAT IS THE GREEN LIGHT COMMITTEE?**

Current global tuberculosis (TB) efforts are threatened by high levels of multidrug-resistant TB (MDR-TB) in some parts of the world. DOTS-Plus, currently under development, is designed to address MDR-TB in DOTS settings. The World Health Organization (WHO) and its international partners have established the Working Group on DOTS-Plus for MDR-TB (Working Group) in order to address MDR-TB effectively. Members of the Working Group have successfully reduced the price of second-line anti-TB drugs by up to 99% of their original prices. A process has been established to foster access to these concessionally-priced second-line drugs and access to technical assistance via members of the Working Group.

The Green Light Committee is a multi-institutional partnership that reviews project applications to determine if they are in accordance with current international recommendations for establishing DOTS-Plus pilot projects.

### **HOW CAN YOU APPLY?**

Applications to the Green Light Committee should be submitted to the WHO Secretariat. Specific instructions for the application are available from WHO.

The application review cycle for 2004 is as follows:

*Deadline for receiving applications*

CYCLE 1: 20 JANUARY  
CYCLE 2: 19 MARCH  
CYCLE 3: 20 MAY  
CYCLE 4: 20 JULY  
CYCLE 5: 20 SEPTEMBER  
CYCLE 6: 19 NOVEMBER

For further information on DOTS-Plus for MDR-TB and the Green Light Committee, please contact:

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# Scaling up and sustaining effective tuberculosis, HIV and asthma prevention and control

Paris, Palais des Congrès,  
**18–22 October 2005**

#### **Important Dates**

Deadline for  
submission of abstracts:  
2 April 2005

Early-bird registration:  
20 July 2005

#### **Venue**

Palais des Congrès,  
Paris, France

#### **Official languages:**

English and French  
(with simultaneous  
translation)

#### **For more information**

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