



**International Union Against
Tuberculosis & Lung Disease
Asia Pacific Region (IUATLD-APR)**
1st Asia Pacific Region Conference 2007
2nd - 5th August 2007 Shangri-La Hotel, Kuala Lumpur, Malaysia
*Overcoming An Old Scenario With A New Face
(HIV/TB Co-Infection)*

Kuala Lumpur
2007



Abstracts for Day 3 (4th August 2007)



ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

P2

THE CONTRIBUTION OF THE UNION TO GLOBAL LUNG HEALTH

NILS E. BILLO

International Union Against Tuberculosis and Lung Disease (The Union)

The International Union Against Tuberculosis and Lung Disease (The Union) is one of the oldest Non Governmental Organizations founded in Paris in 1920 when tuberculosis was still a major public health problem in Europe and in industrialized countries. Over almost 70 years tuberculosis was the only disease that The Union dealt with and it is mainly known for the development of the DOTS strategy under the leadership of Drs Karel Styblo and Annik Rouillon. The organization expanded its mandate in the mid 1980s to include other lung diseases such as asthma, pneumonia in children under 5 years of age, HIV/AIDS, tobacco control and prevention etc. The Union's mission "improving lung health in low- and middle income countries drives all activities in all regions of the world with the aim to contribute to the Millennium Development Goals.

The work of The Union is carried out by three entities, (1) the Constituent and Organizational members which work mostly at country level, (2) individual members who are presently collaborating in several sections to prepare the World Conference of The Union and develop projects within time limited working groups and (3) The Union Secretariat which fulfills an Institute like function staffed with over 120 collaborators throughout the world working in the areas mentioned above.

The Union Institute is currently involved in three main areas of work, i.e. technical assistance, education and operational research. The organization is present with its activities in all continents with the aim to improve access to good health services, offering models which use the experience of the successful TB model. Currently, The Union is offering its support to millions of affected populations to tackle tuberculosis, HIV, the tobacco epidemic, asthma and pneumonia in children. World and Regional Conferences are an instrument to present newest findings to a large audience of colleagues interested in the same goals as The Union. In a recent independent evaluation completed in 2006 The Union World Conference has been judged by many to be a very appropriate networking opportunity in which new ideas and projects are developed. The Union's Journal offered to more than 6,000 colleagues worldwide offers up to date review and original articles to keep all interested colleagues informed. The network of courses of The Union offering more than 50 courses touching upon technical but also on management issues are well received by hundreds of participants every year.

The network of clinical trials has been developed over the last 10 years and has now nearly 20 sites all over the world. A first trial was recently completed comparing the 6 month rifampicin containing regimen with an 8 month regimen containing EH in the continuation phase. Currently one of the largest clinical trials ever conducted in tuberculosis is comparing regimens using single tablets with a regimen containing 4 Fixed Dose Combination tablets. A recently concluded operational research project led to a change of diagnostic procedures with smear microscopy adopted by the WHO. This will reduce the work load of health services considerably.

The Union is in an important expansion phase with regional offices in India, China, Uganda, Mexico, Egypt and others to follow. With a decentralized structure and with its Members it will hopefully continue to contribute substantially in reducing suffering from tuberculosis and lung diseases worldwide.

S13-1

TREATMENT OF LATENT TUBERCULOSIS INFECTION AND VACCINATION

NITIPATANA CHIERAKUL

*Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok, Thailand.*

Latent tuberculosis infection (LTBI) is defined as a clinical condition characterized by a positive tuberculin skin test (TST) in the absence of clinical or radiological signs of active tuberculosis (TB) disease. The bacilli can exist lifelong in a dormant state inside persons with LTBI, with a potential to reactivate and cause active disease at anytime.

The majority of TB cases results from the reactivation of LTBI, identification and treatment of infected persons at risk for developing disease may be an effective tool for TB control. However, careful consideration of the risk to benefit ratio should be warranted before offer treatment for LTBI to an individual. Development of drug resistant strains during treatment is unlikely if we appropriately exclude persons with active disease and ensure regimen adherence. Bacillus Calmette-Guérin (BCG) is a life attenuated vaccine first use in 1921. It can protect against overall TB incidence and mortality, and also severe childhood forms of disease including miliary and extrapulmonary TB especially the often fatal TB meningitis. BCG is an inexpensive vaccine and has long-established safety profile. It also has outstanding adjuvant activity and can elicit effective both humoral and cell-mediated immune responses. A single dose of BCG vaccine given at birth can produce long-lasting immunity for nearly 60 years thereafter. Recent study from Turkey demonstrated the protective effect of BCG vaccination against TB infection in house hold contact children (OR 0.60, 95% CI 0.43-0.83, $p = 0.003$). Although the efficacy of the BCG vaccine continue to be discussed, it is still the only vaccine in use for prevention of TB in humans. Influential factors determining its effectiveness include: 1) different BCG strains for vaccine preparation, 2) route and number of vaccinations, 3) quality control of vaccine, and 4) protective against TB from environmental mycobacteria.

New potential candidate vaccines use different strategies: prime boost, recombinant BCG, or fusion protein. Factors that should be determined are timing, adjuvants, and deliver methods. Surrogate markers for specific resistance should also be considered. Safety considerations and interference from exposure to environmental mycobacteria are the ultimate concern for most investigators.

Major problems encounter in new TB vaccine development is our lack of understanding of what happens when *Mtb* enter our body. Most individuals do not get disease because their immediate innate immune mechanisms, while in the minority specific resistance must be generated. The biomarkers determined in acquired rather than natural resistance should be use as a guide for novel vaccine design. In addition, development of a therapeutic vaccine against LTBI is also necessary to make TB eradication possible.

Recent development of interferon-gamma assays for detection of LBTI may have advantages over TST, in terms of higher specificity, better correlation with exposure to *Mtb*, and less cross-reactivity due to BCG vaccination and non-tuberculous mycobacterial infection. This may enhance an insight into vaccine development and cost-effectiveness analyses for testing and treatment of LTBI in diverse populations. A critical factor for the determination of this new tool in global application is its rather high cost and the necessity to have certain instruments for performing the assays.

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

S13-2

PREVENTION OF TB - WHO AND HOW TO SCREEN?

CYNTHIA CHEE BIN ENG

Tan Tock Seng Hospital, Singapore

Treatment of latent TB infection (LTBI) in selected high-risk groups is a key TB control strategy in many low TB incidence countries. This strategy is however not widely used in high TB burden countries where resources are more appropriately directed towards the detection and treatment of active TB cases, which is the top priority in TB control.

Until very recently, the century-old tuberculin skin test (TST) has been the only practical means to identify persons with LTBI. Almost all the information in the scientific literature regarding progression of LTBI to active disease in the various risk groups is based on experience with the TST. Candidates for LTBI treatment comprise those at risk for progression to active disease, namely, those recently infected (within two years) or those with certain medical conditions.

The American Thoracic Society (ATS) / Communicable Disease Centre (CDC) guidelines have based their recommendation for LTBI treatment using different TST cut-off readings stratified according to various levels of risk. The highest risk groups are close contacts of infectious cases, HIV-infected persons and those with radiographic evidence of fibronodular scarring. Other risk groups include persons with recent TST conversion (eg. in serially tested healthcare workers), those with immunosuppressive medical conditions (eg. haematological malignancy, end-stage renal failure, diabetics, persons on long-term oral steroids), and persons from high TB incidence countries.

Although LTBI treatment in high-risk groups has been proven to be efficacious and effective, its implementation is fraught with inefficiencies and poses many challenges eg. the labour-intensive TST screening process and difficulties in its interpretation, and the candidate's acceptance of and adherence to the relatively long duration of LTBI treatment. As the risk-benefit ratio of LTBI treatment may not be favourable in low-risk persons with LTBI, screening for LTBI should only be targeted at those who, if infected, are at high risk for progression to disease, and who will be likely to adhere to and complete their course of treatment.

Newer, more accurate methods of LTBI detection – the QuantIFERON-GOLD® and T-SPOT. TB® - which measure the T-cell interferon-gamma response to *M. tuberculosis*-specific antigens should overcome the non-specificity and operational difficulties associated with the TST. Although these blood tests are expected to eventually replace the TST, the experience with these tests is still limited, and their present high cost relative to the TST may be a major limiting factor to their widespread use for LTBI testing.

S13-3

TUBERCULOSIS OUTBREAK IN HIGH SCHOOL STUDENTS

LEW WOOJIN, HEEJIN KIM, JEONGYM BAI, SOOYOON OH,

YOUNGKIL PARK

Korean Institute of Tuberculosis, Seoul, Korea

- Setting** : 89 cases of active TB occurred in a high school during 1 year in Korea.
- Objectives** : The aim is to investigate an outbreak in a high school students.
- Methods** : The investigation included interviews, tuberculin skin test (TST), Interferon gamma release assay (IGRA) among TST positives, chest radiography, and chest C-T. *Mycobacterium tuberculosis*

isolates from the students with TB were submitted to restriction fragment length polymorphism typing to find clustering of strains with identical fingerprints.

- Results** : An epidemiological outbreak investigation was performed several times after the first case emerged, but not followed by preventive control measures. All of students were considered close contacts since TB cases emerged from every class and grade. TST responses $>$ or $=$ 10mm of induration of size was regarded as positive. TST was performed in 1029 (93.2%). TST positive rate was 37.6% (18% in control group). IGRA positive rate was 7.5% among TST positives. Preventive treatments were given to 31 who were positive on both TST and IGRA. DNA fingerprints of *Mycobacterium tuberculosis* isolates from 12 sputum specimens available showed clustering.
- Conclusions** : Tuberculosis (TB) outbreaks among high school students is a public health challenge in Korea. The reason of having a large outbreak of 89 cases in a high school was a delay of 1 year in implementation of preventive control measures mainly due to no standardized guidelines for contact investigation, less capability of local health departments, and no leading technical body.

S14-1

MANAGEMENT OF COMMUNITY-ACQUIRED PNEUMONIA IN THE ASIA PACIFIC REGION

LIAM CHONG KIN

University of Malaya

Community acquired pneumonia (CAP) is a common illness which is potentially life-threatening especially in older adults and those with co-morbid disease. Although many microorganisms can cause CAP, it is a small number of key pathogens that are the causative agents most cases. *Streptococcus pneumoniae* is the most frequently identified pathogen, with the highest incidence of this organism reported in studies that used urinary antigen detection. *Haemophilus influenzae*, atypical pathogens (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella pneumophila*), and respiratory viruses (influenza A and B, adenovirus, respiratory syncytial virus and parainfluenza virus) are the other commonly identified pathogens of CAP.^{1,2} Gram-negative bacilli (*Enterobacteriaceae* and *Pseudomonas aeruginosa*) are the causes in patients who have had previous antimicrobial treatment or who have underlying lung diseases such as bronchiectasis or chronic obstructive pulmonary disease. Even when carefully sought for in prospective studies, the causative organism remains elusive in about half of the cases. Reasons for failure to identify the microbial aetiology include prior antibiotic therapy, unusual pathogens that are not recognised, viral infections and organisms that are currently unrecognised.

Aetiologies of community-acquired pneumonia in the Asia Pacific region

Studies conducted in Japan, Korea and Thailand, showed that the aetiologies of CAP are similar to that reported in the West except that *Legionella pneumophila* is infrequently identified.³⁻⁶ The low incidence of *Legionella* infection, also reported in the other Asian countries, could have been due to limitations of laboratory tests used. In a surveillance study conducted in 12 urban tertiary medical centres in Asia involving ambulatory and hospitalized patients, the overall infection rate for atypical pathogens based on $>$ 4-fold rise in antibody titres between acute and convalescent sera was 23.5%.⁷ The

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

infection rates were 12.2% for *Mycoplasma pneumoniae*, 4.7% for *Chlamydomphila pneumoniae* and 6.6% for *Legionella pneumophila*.⁷ In a recent study on inpatients, *Legionella pneumophila* was identified in 5.8% of the cases.⁸ *Mycoplasma pneumoniae* and *Chlamydomphila pneumoniae* often cause a mild clinical disease, therefore patients are more likely to be seen as outpatients. Similar to reports from the West, *Chlamydomphila pneumoniae*, *Mycoplasma pneumoniae* and *Streptococcus pneumoniae* were identified to be the most common aetiologies in outpatients in a Thai study, accounting for 37%, 30% and 13% of the cases, respectively.⁶ Similar findings were demonstrated by a study in Japan.⁹

The prevalence of tuberculosis is high in the Asia Pacific region and several studies performed in this region showed that *Mycobacterium tuberculosis* infection can frequently present as CAP.^{8,10-12} *Burkholderia pseudomallei* is a possible causative organism in rural Southeast Asia and northern Australia particularly if the patient has diabetes mellitus.¹³ This organism was identified in 15.4% of hospitalised CAP patients in Khon Kaen in northeastern Thailand.¹³ In urban parts of Thailand⁶ and Malaysia,^{12,14} melioidosis is less common. However, studies in Singapore and Khon Kaen showed that *Burkholderia pseudomallei* is a common causative organism in patients admitted with severe CAP in Southeast Asia, especially if the patients are diabetic.¹⁵⁻¹⁷ In the Asia Pacific region, Gram-negative bacilli other than *Haemophilus influenzae* such as *Klebsiella pneumoniae* are frequently isolated.^{3,5,6,8,12-14} It was not too long ago that the Asia Pacific region was badly affected by the severe acute respiratory syndrome (SARS) and the region like the rest of the world is vigilant on possible outbreaks of highly pathogenic H5N1 avian influenza.¹⁸

Severity assessment and initial site of care

Clinical practice guidelines categorise CAP patients based on the initial site of treatment (outpatient, general ward, or intensive care unit), the presence of co-morbidity and the presence of modifying factors such as risk for penicillin-resistant *Streptococcus pneumoniae*.^{19,20} Each category group of patients is assigned a list of likely pathogens and recommended antimicrobial therapy that covers both the likely pathogens and resistant strains.

The use of severity-of-illness scores such as the CURB-65 score (confusion, elevated blood urea nitrogen, elevated respiratory rate, low systolic or diastolic BP, and age >65 years)²¹ and prognostic models such as the pneumonia severity index (PSI)²² for initial risk assessment of severity is endorsed by the Infectious Disease Society of America, the American Thoracic Society, the Canadian Infectious Disease Society and Canadian Thoracic Society, and Australia therapeutic guidelines.^{19,20,23} The PSI score is based on 20 variables of patient demographics (sex, age), residence, co-morbidities, presenting vital signs and investigation results. A clear correlation between mortality and risk class exists. The risk of mortality is low for risk classes I-III (0.1-2.8%), intermediate for class IV (8.2-9.3%), and high for class V (27-31%).²² However, the PSI may not be practical for routine use in busy hospital emergency departments or primary care settings because of its complicated calculation. Furthermore, since the PSI gives high weighting to patient age and past history but lower weighting to clinical features such as hypoxia, young and previously well patients may be classified as having mild CAP (PSI classes I-III), despite being hypoxaemic and having clinically severe pneumonia. The PSI is more useful for identifying low-risk patients who may be safely treated as outpatients rather than those with severe CAP. The CURB-65 score is a simpler alternative severity assessment tool.²¹ Patients are stratified into 3 groups according to

increasing risk of death or need for intensive care unit admission. CURB-65 places more emphasis on the severity of the episode of CAP rather than the patient's past history. The recently revised Japanese Respiratory Society guidelines recommend the use of a modified version of the CURB-65 score which include oxygen saturation by pulse oximetry as an additional parameter.²⁴ However, this new severity scoring system needs prospective validation. Neither the PSI nor CURB-65 appears particularly useful for predicting accurately whether an individual patient will require intensive care unit admission. Furthermore, the PSI, CURB criteria and the earlier American Thoracic Society definition of severe CAP²⁵ have not been prospectively validated for ICU admission. A recent Australian study²⁶ suggests a modified version of CURB-65 as being more accurate for this purpose, again this needs validation

Increasing resistance of *Streptococcus pneumoniae* to antimicrobials in the Asia Pacific region

In recent years, the proportion of penicillin non-susceptible strains of *Streptococcus pneumoniae* and the level of penicillin resistance have increased in many Asian Pacific countries.²⁷ Resistance of *Streptococcus pneumoniae* to other b-lactams and macrolide is also prevalent. In fact, in several Asian Pacific countries, the prevalence rates of erythromycin resistance exceed 70%.²⁷ After controlling for comorbid illness, patients infected with antibiotic-resistant *Streptococcus pneumoniae* have not been found to have increased mortality in most studies. Patients infected by resistant organisms, however, may have more severe disease and suppurative complications as well as a longer length of hospital stay.²⁸⁻³⁰ In spite of the widespread emergence of in vitro resistance, current antimicrobial regimens are mostly effective in the treatment of *Streptococcus pneumoniae* CAP.

References:

- 1) File TM. Community-acquired pneumonia. *Lancet* 2003; 362:1991-2001.
- 2) British Thoracic Society. Guidelines for the management of community-acquired pneumonia in adults. *Thorax* 2001; 56 (suppl 4): iv1-64.
- 3) Ishida T, Hashimoto T, Arita M, Ito I, Osawa M. Etiology of community-acquired pneumonia in hospitalized patients: a 3-year prospective study in Japan. *Chest* 1998; 114:1588-93.
- 4) Miyashita N, Fukano H, Niki Y, Matsushima T, Okimoto N. Etiology of community-acquired pneumonia requiring hospitalization in Japan. *Chest* 2000; 119:1295-6.
- 5) Woo JH, Kang JM, Kim YS *et al*. A prospective multicenter study of community-acquired pneumonia in adults with emphasis on bacterial etiology. *Korean. J Infect Dis* 2001; 33:1-7.
- 6) Wattanathum A, Chaoprasong C, Nunthapisud P *et al*. Community-acquired pneumonia in Southeast Asia. *Chest* 2003; 123:1512-9.
- 7) Ngeow YF, Suwanjutha S, Chantarojanasri T *et al*. An Asian study on the prevalence of atypical respiratory pathogens in community-acquired pneumonia. *Int J Infect Dis* 2005; 9:144-53.
- 8) Liam CK, Pang YK, Poosparajah S. Pulmonary tuberculosis presenting as community-acquired pneumonia. *Respirology* 2006; 11:786-92.
- 9) Miyashita N, Fukano H, Mouri K *et al*. Community-acquired pneumonia in Japan: a prospective ambulatory and hospitalized patient study. *J Med Microbiol* 2005; 54:395-400.
- 10) Chan CH, Cohen M, Pang J. A prospective study of community-acquired pneumonia in Hong Kong. *Chest* 1992; 101:442-6.
- 11) Hui KP, Chin NK, Chow K *et al*. Prospective study of the aetiology of adult community acquired bacterial pneumonia needing hospitalisation in Singapore. *Singapore Med J* 1993; 34:329-34.
- 12) Hooi LN, Looi I, Ng AJ. A study on community acquired pneumonia

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

- in adults requiring hospital admission in Penang. *Med J Malaysia* 2001; 56:275-83.
- 13) Reechaipichitkul W, Tantiwong P. Clinical features of community-acquired pneumonia treated at Srinagarind Hospital, Khon Kaen, Thailand. *Southeast Asian J Trop Med Public Health* 2002; 33:355-61.
 - 14) Liam CK, Lim KH, Wong CMM. Community acquired pneumonia in patients requiring hospitalisation. *Respirology* 2001; 6:259-64.
 - 15) Lee KH, Hui KP, Tan WC, Lim TK. Severe community-acquired pneumonia in Singapore. *Singapore Med J* 1996; 37:374-7.
 - 16) Tan YK, Khoo KL, Chin SP, Ong YY. Aetiology and outcome of severe community-acquired pneumonia in Singapore. *Eur. Respir. J.* 1998; 12:113-5.
 - 17) Reechaipichitkul W, Pisprasert V. Severe community-acquired pneumonia (CAP) treated at Srinagarind Hospital, Khon Kaen, Thailand. *Southeast Asian J Trop Med Public Health* 2004; 35:430-3.
 - 18) Tsang KW, Eng P, Liam CK, Shim YS, Lam WK. H5N1 influenza pandemic: contingency plans. *Lancet* 2005; 366:533-4.
 - 19) Mandell LA, Wunderlink RG, Anzeuto A, *et al.* Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007; 44:S27-72.
 - 20) Mandell LA, Marrie TJ, Grossman RF, Chow AW, Hyland RH. Canadian guidelines for the initial management of community-acquired pneumonia: an evidence-based update by the Canadian Infectious Diseases Society and the Canadian Thoracic Society. *Clin Infect Dis* 2000; 31:383-421.
 - 21) Lim WS, van der Eerden MM, Laing R *et al.* Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003; 58:377-382.
 - 22) Fine MJ, Auble TE, Yealy DM *et al.* A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997; 336:243-50.
 - 23) Antibiotic Writing Group. Therapeutic guidelines: antibiotic. Version 12. Melbourne: Therapeutic Guidelines Limited, 2003.
 - 24) Kohno S, Matsushima T, Saito A *et al.* The Japanese Respiratory Society guidelines for the management of community-acquired pneumonia in adults. *Respirology* 2006; 11: S84-5.
 - 25) Niederman MS, Bass JB, Campbell GD, *et al.* Guidelines for the initial management of adults with community-acquired pneumonia: diagnosis, assessment of severity, and initial antimicrobial therapy. *Am Rev Respir Dis* 1993; 148:1418-26.
 - 26) Buising KL, Thursky KA, Black JF *et al.* A prospective comparison of severity scores for identifying patients with severe community acquired pneumonia: reconsidering what is meant by severe pneumonia. *Thorax* 2006; 61:419-24.
 - 27) Song JH, Jung SI, Ko KS *et al.* High prevalence of antimicrobial resistance among clinical *Streptococcus pneumoniae* isolates in Asia (an ANSORP study). *Antimicrob Agents Chemother* 2004; 48: 2101-7.
 - 28) Pallares R, Linares J, Vadillo M *et al.* Resistance to penicillin and cephalosporin and mortality from severe pneumococcal pneumonia in Barcelona, Spain. *N Engl J Med* 1995; 333:474-80.
 - 29) Song JH, Jung SI, Ki HK *et al.* Clinical outcomes of pneumococcal pneumonia caused by antibiotic-resistant strains in Asian countries: a study by the Asian Network for Surveillance of Resistant Pathogens. *Clin Infect Dis* 2004; 38:1570-8.
 - 30) Metlay JP, Hofmann J, Cetron MS *et al.* Impact of penicillin susceptibility on medical outcomes for adult patients with bacteremic pneumococcal pneumonia. *Clin Infect Dis* 2000; 30:520-8.

S14-2

TREATMENT OF HOSPITAL-ACQUIRED PNEUMONIA AND HEALTHCARE-ASSOCIATED PNEUMONIA

JAE HOON SONG

Samsung Medical Center, Sungkyunkwan University, Seoul, Korea

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are often difficult to treat in clinical practice, resulting in high rates of morbidity and mortality worldwide. Presently, guidelines for diagnosis and treatment of HAP have been proposed by various organizations and societies. Initial empiric approach to antibiotic therapy is based on clinical onset of pneumonia, likely pathogens, risk factors for resistant pathogens, antimicrobial resistance in major pathogens, host factors and antibiotic issues. Early onset HAP within the first 4 days of hospitalization are usually caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, methicillin-sensitive *Staphylococcus aureus*, and antibiotic-susceptible enteric gram-negative bacilli (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* species, *Proteus* species or *Serratia marcescens*). Recommended treatment for this group is limited-spectrum antimicrobial therapy with either ceftriaxone, fluoroquinolone (levofloxacin, moxifloxacin or ciprofloxacin), ampicillin-sulbactam or ertapenem. Late-onset HAP or VAP or risk factors for MDR pathogens, requires broad-spectrum therapy. Late-onset HAP occurring 5 days or more after hospitalization, is more likely to be caused by multidrug-resistant pathogens and is associated with increased morbidity and mortality. Risk factors for resistant pathogens include antimicrobial therapy within the preceding 90 days, current hospitalization of 5 days or more, high frequency of antibiotic resistance in the community or specific hospital unit, admission from a healthcare-associated facility, and immunosuppressive disease or immunosuppressant therapy. This group of patients is more likely to be infected by MDR pathogens (*Pseudomonas aeruginosa*, ESBL⁺ *Klebsiella pneumoniae*, *Acinetobacter* species, methicillin-resistant *S. aureus* and *Legionella pneumophila*). Antimicrobial options for this situation are combination regimens consisting of either antipseudomonal cephalosporin (cefepime, ceftazidime) or antipseudomonal carbapenem (imipenem or meropenem) or beta-lactam/beta-lactamase inhibitor (piperacillin-tazobactam) plus either antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or aminoglycoside (amikacin, gentamicin, or tobramycin). If MRSA is suspected, linezolid or vancomycin is added to the other two drugs. If ESBL⁺ *K. pneumoniae*, or an *Acinetobacter* species is suspected, carbapenem is considered a reliable choice. If *L. pneumophila* is suspected, the combination regimen should include macrolide (e.g., azithromycin) or fluoroquinolone (ciprofloxacin or levofloxacin) should be used rather than aminoglycoside. Local microbiology data and the circumstances of the individual patient should always be considered when selecting antimicrobial agents.

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

S15-1

ESTABLISHING PUBLIC PRIVATE MIX DOTS IN THE PHILIPPINES

ANNA MARIE CELINA G. GARFIN

National Center for Disease Prevention and Control, Manila, Philippines

Tuberculosis (TB) in the Philippines remains to be a major public health problem. TB is the sixth leading cause of deaths and illness. Globally, Philippines is one of the twenty-two high burdened countries under the World Health Organization.

In 1996, the National Tuberculosis Control Program of the Department of Health implemented DOTS strategy to control tuberculosis and reached 100 percent coverage in 2003. However despite the 100% coverage in the public sector the Case Detection Rate (CDR) of 70% was not reached.

The 1997 National Prevalence Survey showed that only few cases are seeking treatment at the government health centers and are reported and about 10% are seeking treatment with private physicians but are not reported.

Because of remarkable expansion and coverage of DOTS in the public sector and the large and well-developed private health sector in the Philippines, Public-Private Mix DOTS (PPMD) was started. This initiative was undertaken in collaboration with the Philippine Coalition Against Tuberculosis (PhilCAT). The objectives of the PPMD initiative were to increase case detection rate and to synchronize management of TB cases.

PPMD is an initiative or collaboration involving the public and the private sector in TB control. In the Philippines, the private sector can be involved in TB control by referring their patients to the public DOTS facilities or their private clinics will provide DOTS services. These are the two approaches of PPMD in the Philippines. The Public initiated PPMD unit and the Private Initiated PPMD unit.

The following components were put into place before the PPMD units were established: supporting policies and structures, sustainability mechanisms and guidelines on technical operations (referral mechanisms, recording and reporting, monitoring, supervision and evaluation).

The installation process includes: preparatory visits, planning workshop, initial publicity, DOTS advocacy symposium, DOTS training, Meetings for the memorandum of Understanding/agreements, launching, implementation and the monitoring.

The case detection rate of 70% was reached by the Philippines after a year of PPMD implementation. To date, a total of 129 PPMD units have been established and they have contributed 2 percent to the national case detection rate.

In conclusion the involvement of the private sector can increase case detection rate.

S15-2

INVOLVING THE PRIVATE SECTOR IN TB CONTROL

SEIYA KATO, AKIHIRO OKADO, NOBUKATSU ISHIKAWA

Research Institute of Tuberculosis, Japan

Anti-Tuberculosis Association, Tokyo, Japan

Public private partnership is one of the challenges in TB control. We review the history and current TB control in Japan to show issue and challenges on it.

Tuberculosis burden in Japan was extremely high in the middle of 20th Century. The government, academe, Medical Association, as well as NGO including JATA, patients alliance etc. all joined to make social movement for control of the disease. Tuberculosis Prevention Law enacted in 1951

adopted comprehensive policy including involvement of private sector, because of heavy burden of the disease.

TB advisory committee, which was set up in the public health center and composed of specialist and general practitioner, supervise the diagnosis and treatment of each patient on the application for medical cost benefit. It was important to maintain quality of the service

In 2003, we started DOTS strategy version Japan. Smear positive patients who are hospitalized during infectious period are treated under "In-hospital DOTS". After discharged, drug is prescribed by hospital/clinic, while case management is responsibility of health center. DOTS service is provided by health center, clinic, prescribed drug store, care provider for the aged, social welfare section etc. Health center hold regular meeting with DOTS provider, because close coordination between medical institution and health center is important for the successful implementation of the strategy.

Government initiative for involving private sector, regulatory mechanism for the quality of the service and coordination between government and private sectors are important for successful implementation of public private partnership.

S15-3

COLLABORATION BETWEEN THE GENERAL HOSPITAL AND TB DISPENSARY IN CHINA

LIU XIAOQIU

National Center for TB Control and Prevention, China Center for Disease Control, Beijing, China

Objective:

To increase case detection rate of TB by strengthening the collaboration between the general hospital and the TB dispensary.

Method:

To issue the document of strengthening collaboration from MOH, all pulmonary TB cases and suspects detected in general hospital should be reported through the Internet Based Communicable Disease Reporting System (IBCDRS) and referred to TB dispensaries. The cases that were referred unsuccessfully should be traced by TB dispensaries. Central governmental funds and the round 4th Global Fund of TB control project would support the implementation of referring and tracing.

Result:

There were 813,522 TB patients and suspects identified and reported by general hospitals through IBCDRS in 2006, and reported rate was 62/100,000. Among the cases reported, 353,249 cases were referred successfully to TB dispensaries. TB dispensaries had traced 401,709 cases, and 223,649 cases were traced available and identified in TB dispensaries. The tracing rate and the arrival tracing rate was 87% and 56% respectively. By reporting, referring and tracing, there were 575,898 cases available to TB registration system from general hospitals in 2006, the overall arrival rate was 71%. By evaluation, the approach of referring and tracing TB cases would contribute 29% SS+ patients to case finding in 2006. Compared with in 2005, all the indicators of PPMD activities were enhanced obviously in 2006, excluding the arrival referring rate.

Conclusion:

The Collaboration was significantly effective to increase case finding. There is potential to improve the reporting, referring and tracing approaches for increasing case finding and accessibility of DOTS service for the patients.

Key words: Case-detection, PPMD, Referring, Tracing, Tuberculosis.

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

S16-1

TB IN HEALTHCARE WORKERS

JAMALUL AZIZI BIN ABDUL RAHAMAN

Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia.

Nearly one-third of the global population is infected with *Mycobacterium tuberculosis* and at risk of developing the disease. More than 90 percent of global TB cases and deaths occur in the developing world, where 75 percent of cases are in the most economically productive age group (15-54 years). An increasing trend of TB cases among health care workers has also been observed in developing countries.

In Malaysia, the number of TB cases among health care workers has increased steadily from 31 cases in 2002 to 123 cases in 2006. Most of the cases were predominantly smear positive (i.e. infectious) pulmonary TB. Of note, TB cases were higher among health care workers who had frequent direct contact with infectious pulmonary TB patients such as nurses, attendants and medical officers. Almost 60 percent of TB cases among healthcare workers in Malaysia were in the very economically productive age group (20 to-34 years).

Although it can be argued that the number is small and some health care workers may have contracted TB from outside the healthcare facilities they work in, the current data from the Malaysian Ministry of Health suggest the majority of them have contracted TB while working in their healthcare facilities.

It is therefore imperative to create a safer working environment for healthcare workers in order to reduce the number of TB cases among healthcare workers. However, it must be emphasised that complete elimination of TB among healthcare workers is not a realistic goal.

With these goals in mind, the Malaysian Ministry of Health has initiated a project this year to produce guidelines to prevent TB among healthcare workers. A historical meeting attended by respiratory physicians and public health specialists was held on March 13-15 this year in Malacca to produce the said guidelines. Further meetings have been planned to finalise the guidelines. The contents of the guidelines that cover administrative control measures, engineering control and personal respiratory protection equipment will be discussed.

Keywords: *Mycobacterium tuberculosis*, healthcare workers, guidelines.

S16-2

TB IN SPECIAL GROUPS – TB IN INMATES OF CORRECTIONAL FACILITIES

CYNTHIA CHEE BIN ENG

Tan Tock Seng Hospital, Singapore

The TB incidence among inmates of correctional facilities (eg. prisons and drug rehabilitation centres) has been shown to be much higher than that of the general population. Correctional and detention facilities are recognized amplifiers of TB transmission due to several factors: the presence of disproportionately higher number of persons with risk factors for TB (eg. intravenous drug use, HIV infection, the socially disadvantaged and medically underserved); the often crowded and inadequately ventilated physical environment and the frequent transfer of inmates within and between these facilities. TB control in correctional facilities therefore poses an important challenge. As the consequences of poor TB control measures among this vulnerable population will ultimately have a spill-over effect on the general population and community, TB control in these facilities should be a priority of, and integrated into civilian TB control programmes.

Early detection and prompt treatment of the infectious TB case is the

most effective means of preventing transmission. Screening for active disease prior to entry into correctional facilities is essential. The preferred method for pre-entry screening would depend on the available resources, the prevalence of TB in the inmates' community and the prevalence of risk factors for TB (eg HIV infection) in the incarcerated population. Prison staff should have a high index of suspicion for active TB among inmates with suggestive symptoms, and these persons should be evaluated with sputum examination, isolated and appropriate treatment under directly observed therapy (DOT) instituted without delay.

In low TB incidence, resource-rich countries, latent TB infection (LTBI) screening especially in high-risk groups (eg. close contacts, HIV-infected) for LTBI treatment is an important TB control strategy in correctional facilities. However, in high TB burden settings, this activity might divert attention and resources away from the priority of early identification and treatment of the infectious case and is not recommended.

Correctional facilities provide a valuable opportunity for active TB case finding, the use of DOT to ensure good treatment outcomes, and, where appropriate, LTBI screening and treatment in high-risk persons who might otherwise not have access to proper medical services outside of these settings. The importance of collaboration between the prison administration and public health service / civilian TB control programme cannot be overemphasized.

S16-3

TB IN CHILDREN

NORZILA MOHAMED ZAINUDIN

Paediatric Institute, Hospital Kuala Lumpur

Paediatric tuberculosis is increasing in many parts of the world. Children accounts for a major proportion of global tuberculosis disease burden especially in endemic area. However, the treatment of tuberculosis is not considered as a priority as they rarely transmit the disease and does not contribute to the tuberculosis epidemic. In the year 2000, 884,019 (11%) of the 8.4 million newly diagnosed new cases of TB were children.

The natural history and clinical manifestations of tuberculosis differs significantly from adults. The diagnosis of tuberculosis in children may be difficult. Children particularly the young are rarely smear positive for acid fast bacilli on routine smear microscopy. In young children gastric aspirates are taken as sample. However they are positive only in 20% of smear and 5% on culture. This is due to the paucibacillary nature of the disease.

However the yield may be higher in children with adult type of tuberculosis and sputum smear may have a definite diagnostic value in older children. In view of the difficulty in bacteriologic confirmation, the diagnosis is usually based on known contact with an adult index case usually within the household, positive tuberculin test and suggestive signs on the chest radiograph. The diagnostic problem may be more obvious in HIV infected children.

The aims of antituberculosis treatment are to cure the individuals and prevent the emergence of drug resistant organism. Chemoprophylaxis is the preventive treatment given in children after exposure (without proof of infection) or in children with latent tuberculosis which is indicated by positive tuberculin test.

Isoniazid monotherapy for six to nine months is the best studied chemoprophylactic regimen. It reduces the tuberculosis risk in exposed children by two thirds. Contact tracing is important in detecting children with high likelihood of developing infection.



ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

This includes children with TB disease, latent TB and children with evidence of recent exposure.

BCG vaccination is the most widely used preventive measure. However the efficacy remains controversial. The efficacy varies from 0-80% in the prevention of adult pulmonary TB. Its protective effect was greatest in preventing serious forms of TB that occur in young children, TB meningitis, miliary or disseminated TB. Due to these reasons WHO continue to recommend BCG vaccination in young infants.

In conclusion, children contribute a significant proportion of the disease burden and may suffer severe tuberculosis related morbidity and mortality particularly in endemic area. Preventive measures such as BCG vaccination, chemoprophylaxis, early and more efficient diagnostic tools and early treatment may reduce these.

S18-1

COMMUNITY DOTS IN CAMBODIA

KHLOEUNG PHALLY, SAR SOKUN, MAO TAN EANG

National Centre for Control of Tuberculosis & Leprosy, Phnom Penh, Cambodia

Introduction:

The DOTS strategy was introduced in Cambodia in 1994. Till 1999, DOTS was implemented at the hospital level only, with a treatment success rate of over 85%. However, the case detection rate remained low, around 50%, till 1998. Decentralization of DOTS to health center (HC) level was piloted in 9 HCs from late 1999. Encouraged by the increase in TB case detection, DOTS expansion to HCs was accelerated from 2001 and by the end of 2004, 100% DOTS coverage at health centre level was achieved. In an attempt to further increase the case detection, Community DOTS (C-DOTS) was piloted in 2003 to improve the accessibility to DOTS services for disadvantaged groups.

Process:

In the beginning, TB services at HCs focused mainly on providing DOT to all ambulatory TB patients. But, it was found later that not all patients diagnosed with TB could access the daily DOT at HCs. This was due to a number of factors, that included those who were elderly or disabled, those living far away from HC, or unable to afford the travel cost. To address this issue, Community DOTS was piloted in 2003 in four provinces in collaboration with NGOs.

Lessons learnt from these pilot projects provided the basis for developing the Guidelines on Community DOTS Implementation, which was officially published in December 2004. This facilitated the steady expansion of C-DOTS; by the end of 2006, the coverage areas under 380 HCs (out of 950 functioning HCs) had C-DOTS. It was observed that case finding and treatment outcomes were better in areas under C-DOTS than in areas without C-DOTS. It is planned to expand and scale-up C-DOTS to cover 80% of HCs by 2010. As C-DOTS requires partnership with NGOs, the cost related to expansion and sustainability of C-DOTS is of great concern to the National TB Programme (NTP).

Conclusion:

Although the implementation of C-DOTS has significantly contributed to an increase in TB case finding, better treatment services and outcomes, the additional resources needed to sustain and expand C-DOTS is a major challenge to the NTP in Cambodia.

Key words: Community DOTS, Cambodia

S18-2

Public - Private Mix (PPM) for TB control in Vietnam

NGUYEN DING TUAN

National Hospital of Tuberculosis and Respiratory Diseases, Hanoi, Vietnam

In the last years, Viet Nam National Tuberculosis Control Program (NTP) have been interested in Public-Private Mix (PPM) filed of action, but actually this is new approach, so we are working and learning.

Viet Nam NTP have implemented PPM pilot in some provinces and achieved encouraging outcomes. (about 20% of TB patients referred to public health facilities by private healthcare sectors) In my presentation here, I would like showing PPM activities have done in Vietnam as pilot activity but haven't got guideline of NTP.

With my purpose is share information about PPM activities to other countries in the region and desire to receive implemented experiences from all of you in order to Viet Nam NTP can conduct strategy as well as guideline for this in next time.

S19-1

TB IN SPECIAL SITUATIONS (LIVER DISEASE, RENAL DISEASE, PREGNANCY AND EPILEPSY)

GEORGE KUTTY SIMON

Hospital Sultanah Bahiyah, Alor Star

Tuberculosis management has to be modified in situations where there is liver impairment.

In patients with no evidence of chronic liver disease (eg Hep B carrier, previous history of acute hepatitis and alcoholics) the treatment can be carried out with the usual regimens.

However, treatment has to be modified in patients with established chronic liver disease and acute hepatitis. In such cases, it is often necessary to exclude pyrazinamide and the duration of the altered regimen would be longer. In acute hepatitis, it may be possible to defer treatment till the acute episode resolves.

In renal impairment, the drugs that require modification or monitoring are streptomycin and ethambutol. It is necessary to closely monitor renal function in such instances. Lengthening the interval between conventional doses is often recommended as a safe method to achieve adequate but safe serum drug levels. An alternative and safe regimen to use would be 2RHZ/6RH.

In pregnancy, streptomycin should be avoided because of the risk of ototoxicity and possible teratogenic effects on the foetus. Other drugs such as rifampicin, isoniazid, pyrazinamide and ethambutol can be safely administered although the effect of pyrazinamide on the foetus has not been well established. Lactation can also be safely carried out as the amount of drug ingested by the nursing infant is minimal. Rifampicin interacts with the oral contraceptive pill and there will be decreased protective efficacy against pregnancy.

Drug interactions are the main problems in the presence of epilepsy and may pose a major challenge in the optimal management of either condition. Ten to fifteen percent of people are genetically slow acetylators of isoniazid (INH). INH is an inhibitor of the 2C9 and 2C19 cytochrome P-450 isoenzyme systems, of which the antiepileptic phenytoin is a substrate. If these people are given the two drugs concurrently, phenytoin will significantly accumulate. Conversely, seizures are a well-documented complication of INH overdose.

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

S19-2

HANDLING ADVERSE DRUG REACTIONS AND OTHER COMPLICATIONS

YEW WING WAI

Grantham Hospital, Hong Kong, China

Although 25 – 60% of a sizeable number of patients with tuberculosis in clinical studies have reported at least one type of adverse drug reaction, most of these were mild and required no modification of treatment regimens. The most common reactions were gastrointestinal and cutaneous in nature. Adverse reactions usually occur in the first three months of antituberculosis treatment. HIV-infected subjects on the whole experience adverse reactions more commonly. Second-line drugs are generally more likely to incur toxicity than conventional first-line agents. For some severe drug reactions like haematological, circulatory, or renal ones, often linked with rifampicin administration, the drug should be withdrawn and never given again. For cutaneous hypersensitivity, the incriminated drug should be identified by careful rechallenge. Desensitisation would be appropriate for most subjects, except those HIV-infected. Hepatotoxicity and drug-drug interactions constitute the two rather special areas of complications due to treatment with antituberculosis drugs. Both reactions require prudent approach in their management to curtail undesirable aftermath. Paradoxical reactions during antituberculosis treatment, while not caused by the drugs, really represent an immune reconstitution inflammatory syndrome.

S20-1

THE TOBACCO EPIDEMIC, A NEGLECTED PUBLIC HEALTH PROBLEM

KAREN SLAMA

International Union Against Tuberculosis and Lung Disease (The Union)

Tobacco is a product on the market which kills almost 5 million people per year and it remains a legal consumer good. We are still drawing up the list of diseases tobacco use causes, and know that it takes approximately 15 years for these diseases to appear after a population starts using tobacco. People have been informed for some time about health consequences of smoking. In 1957, a survey of 154 people in the UK found that only one person (0.6%) had not heard of the association between tobacco smoking and lung cancer. People in tobacco control note that countries destroy entire stocks of chickens or sheep or beef cattle to avoid human disease epidemics that have not yet started, and governments of rich countries invest billions of dollars in fundamental research to find treatments for the diseases that occur as a result of tobacco use, but put smaller investment into health promotion and lifestyle change. We see that tobacco use is growing in the world, and that the already huge death toll is rising. Despite recent events that have put tobacco control more in the spotlight, notably the world's first public health treaty, the WHO Framework Convention on Tobacco Control (FCTC), the tobacco epidemic is a neglected public health problem. Why is it neglected?

There are many possible explanations for this neglect but I will focus on the following.

First, the tobacco companies make tremendous profits from selling tobacco products and they use their money and power to subvert tobacco control. Second, pro-tobacco interests act to reinforce the idea that smoking is an individual choice like any other. This in

turn feeds into number three, the lay perception that smokers are responsible for what happens to them because of smoking, despite addiction, and despite court cases that show industry deception and exploitation of their own customers. All of the above allow governments to focus on the money coming in from taxes and other "benefits" from tobacco consumption, such as new employment opportunities when, say, a tobacco company opens a new factory. With over one third of all adults in the world smoking tobacco, it is difficult to say that smokers are using their knowledge of the effects of tobacco on health to influence their choices. Finally, despite the growing sophistication of cessation programmes, a dismal 15% successful long-term cessation rate is the usual result of assisted treatment of smokers motivated to stop.

The conclusion that we have to draw from these factors in the neglect of the tobacco epidemic in public health, is renewed effort to win over the population and demand government action. We know that it can be done, because various populations are abandoning tobacco and creating an environment that reduces the lure of tobacco for young people. We know that it must be done because others are not.

S20-2

IMPROVING ACCESS TO ASTHMA DRUGS: THE ASTHMA DRUG FACILITY

KAREN BISSELL

International Union Against Tuberculosis and Lung Disease (The Union)

Problem:

The majority of asthma and COPD cases live in developing countries. Yet, priority is still given to communicable diseases. Health services are not organised for long-term quality care of asthma or COPD. The Union studies demonstrate that most asthmatics cannot afford essential asthma medicines. So, people are not receiving care or being enabled to manage their own asthma. Also, costs increase when asthma is not treated or incorrectly treated: there are unnecessary expenses from emergency visits, hospitalisation, ineffective and inappropriate medicines, and indirect costs for patients, families, governments. Therefore, these countries cannot afford to not treat asthma.

Response:

The Union has established an Asthma Drug Facility (ADF) to allow countries to purchase good quality essential asthma medicines at low prices. ADF promotes a standardised approach to asthma management and offers The Union's technical package: Asthma Guide, training materials and information system.

Challenges:

Countries have different purchasing procedures and are at different stages of asthma policy-making and implementation.

Bringing about change:

Respiratory specialists among others must convince their governments to allocate budget for essential medicines and produce appropriate asthma guidelines. ADF's services should be accompanied by country efforts to strengthen health systems, improve quality assurance, and implement rational drug purchasing and distribution policies. Advocacy should aim to increase funding for chronic respiratory diseases, referring to Millennium Development Goal 8, and to recent projects by WHO (PAL, GARD), The Union and GINA.



ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

S21-1

THE PHILIPPINES ON PRIVATE PARTNERSHIP, ADVOCACY AND COALITION-BUILDING

ROSALIND GUERRA VIANZON

National Centre for Disease Prevention and Control, Manila, Philippines

The Philippine's National TB Control Program (NTP) still embraces the D.O.T.S. strategy as its overarching framework for TB control. Historically, DOTS expansion was carried out within the public sector, thereby achieving nationwide DOTS coverage between 2002 to 2003. With all the elements in place, the NTP was then gaining acceptable Treatment Success Rates but not on its Case Detection Rate (CDR).

The private sector in the country is a large sector of healthcare, and this includes TB care. A third of the country's TB cases are managed by different types of private physicians e.g. general practitioners, infectious disease experts, lung specialists. The NTP regards them as a fertile source in finding more TB cases that are missed within the public's infrastructure. As private referring physicians, the NTP has embarked on the Public-Private Mix D.O.T.S. (PPMD) strategy, in partnership with PhilCAT and international communities, particularly, the World Health Organization (W.H.O.).

The Philippine Coalition Against TB, or PhilCAT, is an organized alliance of concerned TB groups that works in a unified action. Most of its member groups are private agencies but are committed in supporting the policies of the NTP. As such, PhilCAT is now the strong ally of the NTP for engaging the private sector. Through a series of advocacy and strong leaderships, PhilCAT has now replicated itself to more localized coalitions and still maintaining its commitment to the NTP.

To heighten the awareness on TB amongst the various stakeholders, the NTP commemorates yearly two key advocacy activities: the World TB Day and a national version held every August, the National Lung Month. This advocacy strategy ensures the sustained support from political leaders and the dynamic participation of communities at the peripheral levels. These days also represent the strong partnerships that the NTP has initiated, as well as opportunities to gain additional TB partners.

The Philippine NTP has evolved into a deeper viewpoint of how TB can be controlled; promoting a multi-faceted perspective of disease management through strengthened partnerships – because, TB control is not the sole responsibility of the Government alone, but a synchronized effort of *all* those concerned and committed.

S21-2

TOBACCO CONTROL AND TUBERCULOSIS CONTROL: IS THERE AN ASSOCIATION?

CHIANG CHEN YUAN

International Union Against Tuberculosis and Lung Disease (The Union)

Tobacco use has been convincingly shown to be associated with a wide variety of cancers, cardiovascular diseases, deterioration of pulmonary function, and increased respiratory infections. The associations between cigarette smoking and tuberculosis have been investigated since 100 years ago and a substantial number of papers investigating cigarette smoking and tuberculosis have been published in past decades. Both passive and active exposure to tobacco smoke has been shown to be associated with tuberculous infection. The association between cigarette smoking and developing tuberculosis disease has been reported in more than 20 papers. It has been shown that ever smokers are more likely to have cough, chest radiograph appearances of upper zone involvement and cavity formation, and

positive sputum culture as compared with non-smokers. Smoking has also been found to be associated with relapse of tuberculosis. In the transition from exposure to developing tuberculosis disease, cigarette smoking facilitates the transition from being exposed to being infected, from being infected to developing tuberculosis disease, and from being cured to relapse. Cigarette smoking may facilitate transmission of tuberculosis as well because it is associated with cough, cavity formation and positive sputum culture. Although tobacco use is a serious public health concern, tobacco control has so far been neglected in terms of tuberculosis control. The potential contribution of tobacco control to the fight against tuberculosis needs to be investigated.

S22-1

LABORATORY DIAGNOSIS OF ATYPICAL MYCOBACTERIAL INFECTIONS

NGEOW YUN FONG

National Public Health Laboratory, Ministry of Health, Malaysia

A typical mycobacteria comprise a wide range of animal and human pathogens, and saprophytic species in the environment. These organisms are increasingly being isolated from a wide spectrum of clinical manifestations in predisposed as well as immunocompetent persons, in community and nosocomial settings. Few routine diagnostic laboratories have facilities for the characterisation of atypical mycobacteria, but species identification could help to define the clinical relevance of an isolate and the most appropriate therapeutic regimen.

Conventional speciation is based on biological properties such as colonial morphology, rate of growth, pigmentation, and limited biochemical tests. However, growth may take up to several months and biochemical tests are often difficult to interpret. Mycolic acid analysis by high-performance liquid chromatography allows complete speciation of mycobacteria but requires expensive instrumentation. The trend in mycobacteriology is towards the use of nucleic acid-based technology for rapid detection, species differentiation and genotyping.

A common strategy for the diagnosis of atypical mycobacterial infection is to use a multiplex PCR to detect *M. tuberculosis* and/or other mycobacteria. When the presence of mycobacteria other than *M. tuberculosis* is indicated, the amplicon is used for speciation by restriction enzyme digestion, probe hybridisation or DNA sequence analysis. Commercial systems such as the Accuprobe and Amplified *M. tuberculosis* Direct Test from Gen-Probe, Probe Tec ET system from Becton Dickinson and Inno-LiPa line immunoassay from Innogenetics, are available for identification of isolates or detection of mycobacteria in clinical specimens, either directly or after nucleic acid amplification. Real-time PCR assays are also available for the differentiation of atypical mycobacteria from *M. tuberculosis*.

Despite advances, however, there are still many limitations in current diagnostic methods. With molecular tests, there are well known problems with DNA extraction, specimen inhibition, cross contamination, lack of sensitivity for AFB-negative specimens, inability to distinguish dead from viable bacteria, and high cost. Hence, it is recommended that molecular tests be always performed in conjunction with microscopy and culture. Differentiation into species and subspecies is difficult among closely-related members. Commercial test systems focus on only a limited number of species. DNA sequence-based identification depends on gene bank information which is still limited for many species. Quite often, final identification is made by reference to clinical, histopathological and

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

epidemiological features.

The significance of a positive test for atypical mycobacteria is also often uncertain. For differentiation between invasive disease, colonization and contamination, there may be a need for repeated testing, quantitative cultures, identification in deep body fluids and tissues, and always, interpretation in light of clinical data.

S22-2

TREATMENT OF ATYPICAL MYCOBACTERIOSIS

YEW WING WAI

Grantham Hospital, Hong Kong, China

The prevalence of atypical mycobacteriosis (better known as nontuberculous mycobacterial disease: NTM disease) is on the rise in different parts of the world. The underlying reasons are multifactorial. Unlike extrapulmonary forms, NTM disease of lung has to be appropriately differentiated from the state of mycobacterial colonisation, as the latter can be observed without the need to render active treatment immediately. The American Thoracic Society has published official guidelines in 1997 on the diagnostic criteria of NTM lung disease including clinical, radiographic, and bacteriologic ones, the last being particularly stringent. These guidelines are currently updated in 2007 to enhance its scientific validity. The advent of macrolide therapy (in conjunction with use of rifampicin / rifabutin and ethambutol) has improved the treatment outcome of NTM disease like that due to *Mycobacterium avium-intracellulare* and some others due to slowly growing mycobacteria. *M. kansasii* disease can still be treated with a combination of rifampicin, isoniazid and ethambutol in the non-HIV setting. A number of antimicrobials are active *in vitro* against the rapidly growing mycobacteria, although relevant clinical experience is still limited. Examples include amikacin, tobramycin, macrolides and fluoroquinolones. New compounds like linezolid also appear to have potential in improving the treatment of some NTM disease.

S23-1

THE THREAT OF AN INFLUENZA PANDEMIC: REAL OR IMAGINED?

ONG BEE LEE

WHO Western Pacific Regional Office, Manila, Philippines

Concerns are mounting that the threat of another influenza pandemic will become a reality and that the epicentre of the outbreak could be the Asia Pacific Region. The presentation attempts to answer the question whether the threat of an influenza pandemic is real or imagined? Historically, influenza pandemics have been caused by viruses possessing avian-virus-derived HAs to which human populations lack immunity. This mechanism of emergence is likely to continue. Whether these viruses are introduced directly or indirectly into human population is uncertain. Pandemics in the previous centuries were caused by the introduction of a wholly avian virus or an avian-human reassortment virus. Avian influenza A (H5N1) virus has become firmly entrenched, particularly in Asia. Human infections of A (H5N1) continue to occur and limited person-to-person spread is suspected. There is continued antigenic and genetic evolution of influenza A (H5N1) virus which is a normal feature of influenza viruses. The virus in 1918 started as an avian influenza and likely circulated for many years before it is fully adapted to humans. Is the current influenza A (H5N1) showing the same threat? The evolution of the threat cannot

be accurately predicted. The next pandemic may cause severe disease or death in large populations, stressing health, social and economic systems. We have a window of opportunity to control the spread of the virus, reduce the risk of human infection, and prepare for a pandemic. The presentation shows the various strategies and actions taken by the World Health Organization in combating the influenza pandemic threat.

S23-2

ARE WE PREPARED FOR THE NEXT INFLUENZA PANDEMIC? LESSONS FROM THE SARS EPIDEMIC

DAVID HUI SHU CHEONG

The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong.

Recent development of highly pathogenic H5N1 avian influenza in Asia, the Middle East, Europe and Africa has increased the threat of the next influenza pandemic. As of 30 May 2007, 307 human cases of H5N1 have been confirmed in 12 countries with a fatality rate of 60%, which is much higher than the mortality of 10% due to SARS in 2003. Effective antiviral therapy was not available during the SARS epidemic as the aetiology and pathogenesis were unknown in the early outbreak in 2003. In contrast, oseltamivir is an effective treatment of choice for avian influenza. It is however important to diagnose and treat H5N1 disease as early as possible to ensure better clinical outcome (WHO Writing Committee, NEJM 2005).

A case control study involving 124 medical wards in 26 hospitals in Guangzhou and Hong Kong has identified 6 independent risk factors of super-spreading nosocomial outbreaks of SARS: minimum distance between beds < 1m, performance of resuscitation, staff working while experience symptoms, SARS patients requiring oxygen therapy or NPPV whereas availability of washing or changing facilities for staff was a protective factor (Yu IT et al. CID 2007). These data have important clinical implications for planning of infection control against avian influenza. It is important to note that substantial exposure to exhaled air occurs within 0.5m and 0.4m radius of patients receiving NPPV and oxygen via a simple mask respectively (Hui DS et al. Chest 2006 and 2007). Barrier precautions (including standard, contact, and airborne protection) are recommended by the WHO for frontline healthcare workers who are managing H5N1 patients, esp during aerosol-generating procedures. The laser mask confers less protection than the FFP2 respirator and only marginally more protective than the surgical mask. In addition, taping masks to the face only provides a small improvement in protection (Derrick JL et al. J Hosp Infect 2006). Multiple surgical masks filter ambient particles poorly and are not recommended as a substitute for N95 masks (Derrick JL et al. J Hosp Infect 2005).

Systemic steroid was given to patients with SARS with favorable response in many cases as there was evidence of BOOP radiologically (Wong KT. Radiol 2003) and pathologically (Tse GM et al. J Clin Pathol 2004). However, premature use of steroid may prolong viraemia (Lee N et al. J Clin Virol 2004) whereas high dose steroid may cause avascular necrosis of bones (Griffiths J et al. Radiol 2005). Diffuse alveolar damage is the main pathology in avian influenza (Ng WF et al. Human Pathol 2006) and the clinical response to steroid has been poor (WHO Writing Committee, NEJM 2005). It is recommended that high dose steroids not be given in avian influenza whereas low dose steroids may be considered in the treatment of refractory septic shock (Dellinger R, et al. Crit Care Med 2004; WHO recommendation 2007).

IVIG was used considerably in Singapore for SARS but there were



ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

thrombo-embolic events despite prophylactic LMW heparin (Lew TW et al. JAMA 2003). IVIG should be used with caution for haemo-phagocytic syndrome related to H5N1 infection whereas more data from animal models are needed before any cytotoxic can be recommended (Henter JI et al. Lancet 2006). Convalescent plasma was used as a rescue therapy in SARS and it has been used for avian influenza with seemingly favorable response (Kong LK. HKMJ 2006). Another important lesson learnt from SARS, which is applicable to an influenza pandemic, is the observation that good community hygiene in 2003 led to significant reduction of common respiratory viral infections in HK (Lo JY et al. EID 2005).

S24-1

TOBACCO CONTROL – AN OVERVIEW

LEKHRAJ RAMPAL

University Putra Malaysia

Smoking is the most preventable cause of death¹. It causes four million deaths per year worldwide. There are 1.1 billion smokers. Unless we take very action to change the trend, two hundred and fifty million children alive today eventually will die from tobacco use and about half a billion people alive today will die from smoking. As smoking rate decline in the wealthy nations, the tobacco pandemic has moved to the developing countries and 80 % of them live in low and middle-income countries.² Every day, thousands of young people around the world are trying their first cigarette and 80,000 – 100,000 are becoming regular smokers often precipitating a lifetime of addiction and untimely death. Most smokers start young. Tobacco must be seen as a drug and not as an agricultural product. Tobacco use is deadly in any form or disguise. All tobacco products are addictive, harmful and can cause death, regardless of the form, packaging, or name under which they are presented to the public.³ There are over 4 000 known chemicals in tobacco smoke; more than 50 of them are known to cause cancer in humans. The scientific evidence is sufficient to infer a causal relationship between smoking and cancers of the oral cavity, larynx, esophagus, stomach, bladder, renal pelvis, pancreas and cervix. There is also sufficient evidence to infer a causal relationship between smoking and cardiovascular diseases such as coronary heart disease, stroke, sub-clinical arteriosclerosis and abdominal aortic aneurysm and a causal relationship between active smoking and chronic obstructive pulmonary disease and mortality. Smoking is also associated with reduced fertility in women; between sudden infant death syndrome and maternal smoking during and after pregnancy and a causal relationship between maternal active smoking and premature rupture of the membranes, placenta previa and placenta abruption.⁴ Second hand smoke is a serious environmental hazard contributing heavily to the global burden of disease and one that is easily avoided. It causes and increases the risk of lung cancer^{5,6,7} and ischaemic heart disease.⁸ In Malaysia, the prevalence of smoking in 2004 among males was 47.2% and 2.7% in females⁹. Amongst the males, the prevalence of current smokers was highest in Malays (55.6%) followed Bumiputras from Sarawak (50.9%) and Sabah (50.2%) by Chinese (34.1%), and Indians (33.4%). There are more than three million current smokers in Malaysia. The highest prevalence of current smokers were found in Kelantan (30.1%), Trengganu (29.7%), Pahang (28.7%), Kedah (26.9%), Johor (26.3) and Negeri Sembilan (25.9%), while the lowest prevalence were in Wilayah Persekutuan Kuala Lumpur (20.4%) and Perak (21.4%). Majority (83%) of the current smokers started smoking either because their friends asked them to try or they were trying it for fun. More than

eighty five percent of current smokers started smoking before the age of twenty-five years old. The overall mean initiation age of current smokers was 19.2 years (95% CI = 19.1, 19.4 years). The difference between the mean initiation age for the males of 18.7 years as compared to 23 years for the females was statistically significant ($p < 0.001$). The results also show that the mean duration of smoking amongst the current-smokers was 18.6 (SE = 0.3) years. Majority (69%) of the current smokers had smoked for 10 years or more. Of the smokers about a quarter had smoked for 20 years or more. The mean duration of smoking amongst current smokers was significantly lower in males (18.3 years) as compared with 23.3 years in females ($p < 0.001$). The results show that once they started to smoke, overall only 22.3% were able to quit. The quit ratio for the females was 42.6% as compared with 20.6% for the males. The results show that the highest quit rate was amongst the ever smokers who had no formal education (31.1%).

There is an urgent need for a more comprehensive and integrated tobacco control program. There is definitely a need for Smart partnership between the government agencies involved, researchers and the community including NGO's to find the solutions to the problem. The tobacco control strategy must be broad and continuous and involve all levels. The tobacco control efforts should be focused on several fronts such as: preventing people from taking up tobacco consumption, promoting cessation, protecting non-smokers from the exposure to tobacco smoke, regulating tobacco products. These measures could be classified in various ways. WHO classifies interventions into two major groups. Firstly, those aimed at reducing the demand for tobacco, such as; price and tax measures, protection from exposure to second-hand tobacco smoke, regulation and disclosure of the contents of tobacco products, packaging and labeling, education, communication, training and public awareness-raising; comprehensive bans and restriction on tobacco advertising, promotion and sponsorship and tobacco-dependence cessation measures. Second those aimed at reducing the supply of tobacco. Control of smuggling has proven to be the key supply side measure.¹⁰ The youth should be one of the main target groups for the preventive measures. The paper highlights and defines the problem, factors associated with smoking in Malaysia and an overview of tobacco control.

S24-2

SMOKING CESSATION CLINIC

CHANCHAI SITTIPUNT

King Chulalongkorn Memorial Hospital,
Chulalongkorn University, Thailand

Nicotine addiction is now considered as a chronic disease and active smokers need proper treatments as same as other chronic illnesses in order to help them quit smoking. The effective interventions for active smokers that can increase success rate are counseling (behavior modification) and smoking cessation medications. Roles of physician and other health care providers are very important in motivating smokers to start quitting process and help them with appropriate approach. Large proportion of smokers may be able to quit with some suggestion or treatment from health care providers but some others may find it very difficult to quit and may need more intensive treatment program. The implementation of 5 A's model will improve smoker identification and quitting process. (Ask, Advise, Assess, Assist and Arrange follow up). All physicians must view tobacco addiction as a chronic disease and provide appropriate treatment for individual patient. Roles of general practitioner are identifying active smokers and provide motivation and giving

ABSTRACTS FOR DAY 3 (4TH AUGUST 2007)

advises to quit and also simple brief counseling to help patient with quit process. However, in difficult cases, the intensive counseling takes a long period of time and general practitioners are usually overwhelmed with large number of patients so smoking cessation specialists or smoking cessation clinic should be available to provide intensive treatment for smokers who can not quit by simple intervention.

Smoking cessation clinical has a major role as a referral center for active smokers seeking smoking cessation treatment. But smoking cessation clinic also has other important roles such as 1) conduction clinical research for treatment of tobacco dependency 2) setting up referral/intervention strategy in the health care institute such as implementation of 5 A's 3) educating physicians and other health care provides in smoking cessation treatment and being a resource for smoking cessation treatment including local smoking cessation guideline.

Setting up smoking cessation clinic depends on many important factors including health care policy, reimbursement methods for treatment and medications, intensive for physicians and health care specialist. There are many different models of smoking cessation clinic in different countries. The key success factors for smoking cessation clinic are multidisciplinary team approaches, appropriate reimbursement system for patients, incentive for staff and patient referral system.

References:

- 1) British Thoracic Society. Smoking cessation guidelines and their cost-effectiveness. *Thorax* 1998;53 (Suppl 5 part 1): S1-S38.
- 2) A Clinical Practice Guideline for Treating Tobacco Use and Dependency. A US public health service report. *JAMA* 2000; 283(24):3244-3254
- 3) A clinical practice guideline for treating tobacco use and dependence. *JAMA* 2000;283:3244-3254
- 4) Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. In: *The Cochrane Database of Systematic Reviews*, 2, 2005.

needs to recruit "replacement" smokers. Understanding of how the tobacco industry uses psychological data to profile and market cigarettes to specific target audiences, how the tobacco industry downplays the health risks associated with smoking and awareness of how advertisers use specific strategies to target youth is crucial in avoiding the addiction of this weed to the younger generation.

The country needs to act rapidly on the basis of a large body of existing knowledge. Malaysia should "leapfrog" over the standard regulatory route followed in developed countries. There is a need to introduce comprehensive tobacco control policies and strategies. We need experts to deal with industry arguments. and develop expert capacity within the tobacco control community on technical issues relating to product design, manufacture and technology. An international alert and response system linking media and experts should rapidly mount public responses to industry claims and critique. More effective use of the media should aim to reframe the debate away from tobacco industry claims.

Is there a role for doctors? A wider range of strategic partners should be involved in tobacco industry regulation development and implementation. This could include any group that is willing to advance public health goals. There is a role for all of us, the government, the media, the hospitals, the clinics, the doctors, the health allied professionals, associations and societies, housewives or the man on the street to confront the strategies of the tobacco industries.

S24-3

MEETING THE MARKETING STRATEGIES OF THE TOBACCO INDUSTRY

ABU BAKAR ABDUL MAJID

University Cyberjaya College of Medical Sciences

The tobacco industry is known to spend large amounts of money and exerts its influence through multiple channels. Examples are: lobbying; use of third parties; questioning the science and raising public doubt about health and addiction effects; warning governments about the cost of regulation; use of scientists with unproven ideas; dissemination and repackaging of legislative/regulatory problems from other countries; divide and conquer across bureaucracies, countries and public health groups; legal and media attacks on regulatory agencies; as well as constitutional challenges.

In some developing countries, weaker knowledge about health impacts, weak regulatory and scientific capacity and greater vulnerability of the media and politicians to the power of the industry meant that industry strategies were often more intense and successful. When the tobacco industry cannot prevent new laws and regulations, it finds ways, for example through voluntary agreements with governments and scientists, to ensure that regulations favor their interests.

We need to understand how the tobacco industry targets the needs, wishes and desires of young boys and girls in particular in order to sell their cigarettes and looking at the reasons why the tobacco industry