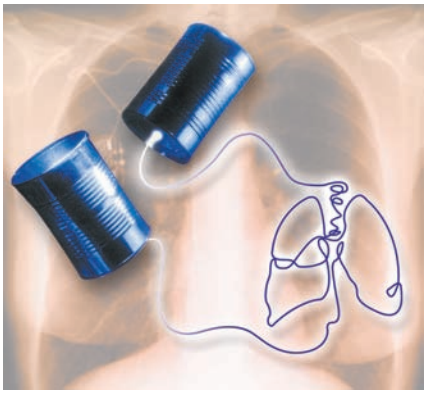
Malaysian Thoracic Society

4th Annual Congress

"Respiratory Infection - Challenges in the New Millennium"

29 June - 1 July 2001 • Hotel Istana, Kuala Lumpur

Souvenir Programme & Abstract Book



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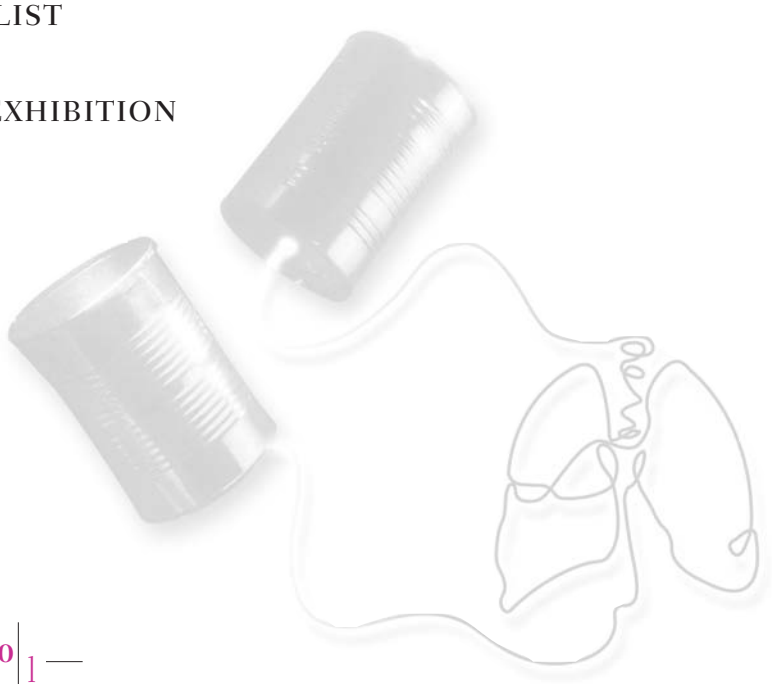

MESSAGE FROM THE PRESIDENT OF THE MALAYSIAN THORACIC SOCIETY

Dear Friends and Colleagues

It gives me great pleasure to welcome you to the 4th Annual Congress of the Malaysian Thoracic Society. As in the past, the Annual Congress this year will cover a wide spectrum of respiratory diseases to cater for the diverse interest of the delegates, but our main focus will be on respiratory infection. With the changing behaviour of micro-organism in particular the acquisition of antibiotic resistance the availability of many newer anti-microbial agents and the resurgence of tuberculosis in many countries, it is very appropriate that the highlight of this year's Congress is on respiratory infection. Besides the Scientific Symposia, there are Meet-The-Expert Sessions, Grand Rounds, Free Communications, Sponsored Symposia and a Pre-Congress Workshop which will provide opportunities for everyone to learn, interact and discuss issues pertaining to respiratory diseases. The Organising Committee has invited an eminent faculty of speakers from within and outside Malaysia to participate in the Congress. These speakers who are experts in their respective fields will update us on the latest understanding and management of certain common respiratory diseases. I also hope that you will visit the exhibition booths which will display some of the latest products of pharmaceutical and other medical related industries. Please do not forget our hospitality suites for some light refreshments and perhaps mysterious gifts.

To our overseas speakers and delegates from outside Kuala Lumpur, I hope you will have an enjoyable and exciting moment in Kuala Lumpur. I believe this Congress too will give everyone of us the opportunity to meet up with old friends and make new ones.

Dr Zainudin Md Zin
President
Malaysian Thoracic Society

MESSAGE FROM THE ORGANISING CHAIRMAN OF THE 4TH ANNUAL CONGRESS

Dear Friends and Colleagues

On behalf of the Organising Committee, I have the honour and pleasure to invite you to the 4th Annual Congress of the Malaysian Thoracic Society. Again we promise an outstanding scientific programme consisting of one Pre-Congress Workshop, 8 Scientific Symposia, Meet-The-Expert Sessions, Grand Round Sessions and Free Communications.

It is well known that pulmonary infections often influence the health and quality of life. For this year's meeting, we have chosen "Respiratory Infection - Challenges In The New Millennium" as the Congress theme. Comprehensive overview on tuberculosis will be covered during the pre-congress workshop. The meeting will focus on upper and lower respiratory infections, nosocomial pneumonia, pneumonia in immuno compromised host and management of parapneumonic effusion and empyema. The Scientific Programme will also cover the latest frontiers in asthma and COPD management, advances in the management of interstitial lung diseases and paediatric respiratory topics. Interesting clinical cases with important "take home messages" will be discussed in Grand Rounds. Selected topics covering a variety of current important problems of adult and paediatric pulmonology will also be discussed during the Meet-The-Expert sessions. Free communications, either poster or oral sessions, will provide a good opportunity for the researchers to present their research findings.

The Organising Committee has done its best to prepare an exciting programme with special highlights for everyone. In addition, it will be our pleasure to make your stay in Kuala Lumpur a most enjoyable and interesting one.

Assoc Prof Roslan Harun
Organising Chairman
4th Annual Congress 2001

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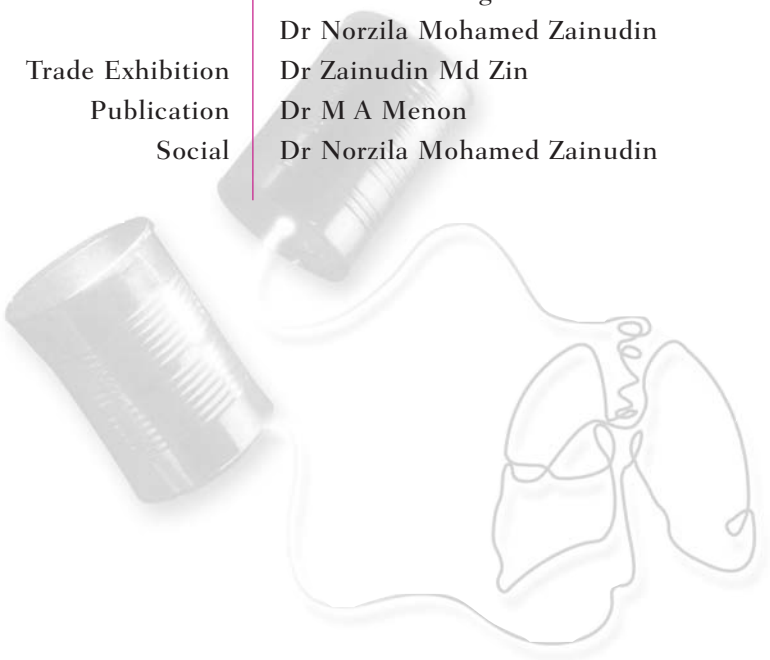

FACULTY OF SPEAKERS

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Dr Yew Wing Wai

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MALAYSIA

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Dr Lim Hong Liang

Assoc Prof Lim Tow Keang

Prof Tan Wan Cheng

SWEDEN

Prof Thomas Sandström

THAILAND

Asst Prof Chaicharn Pothirat

UK

Dr Lawford Hill

USA

Asst Prof Marilyn K Glassberg

PROGRAMME

Thursday 28 June 2001

1930 - 2230 hrs **Eli Lilly Satellite Symposium** — Mahkota II

Facilitators : Prof Liam Chong Kin
Dr Albert Lim Kok Hooi

Recent Advances in the Treatment of Non Small Cell Lung Cancer
Dr Lim Hong Liang (Singapore)

Friday 29 June 2001

PRE-CONGRESS WORKSHOP — Mahkota III

TB: Recent Advances for Primary Care Providers

0800 hrs		Registration
0830 - 0845 hrs		Introduction ***Dr Aziah Ahmad Mahayiddin (Malaysia)***
0845 - 0930 hrs	p20	Recent Advances in the Bacteriological Examinations of Tuberculosis ***Dr Chiyoji Abe (Japan)***
0930 - 1015 hrs	p21	Recent Advances in Tuberculosis Treatment ***Dr Yew Wing Wai (Hong Kong)***
1015 - 1030 hrs		COFFEE
		Chairperson : Dr George Kutty Simon
1030 - 1115 hrs	p22	ABC of National TB Control Programme ***Dr I Kuppusamy (Malaysia)***
1115 - 1200 hrs	p23	Management of Difficult Tuberculosis ***Dr Yew Wing Wai (Hong Kong)***
1200 - 1230 hrs		Discussion/Questions and Answers
1230 - 1430 hrs		LUNCH
1430 - 1445 hrs		Welcome Address by Dr Zainudin Md Zin, the President of MTS
1445 - 1645 hrs		**SYMPOSIUM 1** - Respiratory Emergencies **Chairperson: Assoc Prof Roslan Harun**
	p24	Acute Asthma ***Prof Liam Chong Kin***
	p25	Management of Massive Haemoptysis ***Dr Roslina Abdul Manap***
	p26	Management of Acute Upper Airway Obstruction in Children ***Dr Norrashidah Abdul Wahab***
1645 - 1715 hrs		TEA
1715 - 1845 hrs		**ANNUAL GENERAL MEETING OF THE MALAYSIAN THORACIC SOCIETY** — Baiduri & Berlian Courtroom
1930 - 2230 hrs		**Glaxo SmithKline Satellite Symposium** — Mahkota I
1930 hrs		Registration
2010 hrs		Welcome by Chairperson ***Dr Aziah Ahmad Mahayiddin***
2015 hrs		Malaysian AIRIAP Data ***Dr Zainudin Md Zin***
2035 hrs		Asthma Management : Control through Synergy ***Dr Lawford Hill***

Saturday 30 June 2001

0800 - 0900 hrs **MEET-THE-EXPERT**

Chairperson: Prof Liam Chong Kin

p27 1) Bronchoscopic Palliation of Lung Tumours — Mahkota III
Dr Alan Ng Wei Keong (Singapore)

NSCLC - Issues on Staging and Chemotherapy
Dr Ahmad Radzi (Malaysia)

Chairperson: Assoc Prof Jessie de Bruyne

2) Environmental Control in Asthma Management — Baiduri & Berlian Courtroom
Dr Phil Thompson (Australia)

0900 - 1100 hrs **SYMPOSIUM 2** - Respiratory Tract Infections

Chairperson: Dr M A Menon

p28 Aetiology and Antibiotic Resistance of Respiratory Tract Pathogens: Implications on Choice of Antibiotic Therapy
Prof N Parasakthi (Malaysia)

p29 Upper Respiratory Tract Infection
Prof Lokman Saim (Malaysia)

p30 Community Acquired Pneumonia: Severity Assessment and Treatment
Prof Kenneth Tsang (Hong Kong)

1100 - 1115 hrs COFFEE

1115 - 1230 hrs **SYMPOSIUM 3** - Pneumonia in Immunocompromised Host — Mahkota III

Chairperson: Dr Yap Boon Hung

p31 Pneumonia in HIV Infected Patients
Asst Prof Chaicharn Pothirat (Thailand)

p32 Pneumonia in Non-HIV Immunocompromised Host
Dr Zainudin Md Zin (Malaysia)

1230 - 1430 hrs **Merck Sharp & Dohme Satellite Symposium** — Mahkota III

1230 hrs Welcome Address by Chairperson ***Dr Aziah Ahmad Mahayiddin***

1240 hrs p33 Asthma Control : The Real World Effectiveness
Asst Prof Marilyn K Glassberg (USA)

1330 hrs LUNCH

1430 - 1615 hrs **SYMPOSIUM 4a** - COPD — Mahkota III

Chairperson: Dr Abdul Wahab Sufarlan

p34 Airway Inflammation in COPD Versus Asthma
Asst Prof Marilyn K Glassberg (USA)

p35 Global Initiative for Chronic Obstructive Lung Disease - The GOLD Guidelines
Prof Tan Wan Cheng (Singapore)

p38 Pulmonary Rehabilitation vs Lung Volume Reduction Surgery
Dr Percival Punzal (Philippines)

SYMPOSIUM 4b - Chronic Lung Disease in Children — Baiduri & Berlian Courtroom

Chairperson: Assoc Prof Patrick Chan

1615 - 1630 hrs — TEA

1630 - 1745 hrs — Clinical Grand Round / Radiology Grand Round
(Concurrent Sessions for Adults and Paediatrics)

1800 - 1900 hrs — **AstraZeneca Pharmaceuticals Satellite Symposium** — Fui Gui Restaurant

1800 hrs Registration
1810 hrs Welcome by Chairperson ***Dr Aziah Ahmad Mahayiddin***
1815 hrs The New Way of Looking at Beta2-Agonists -
A Clinical Perspective ***Prof Thomas Sandström***

1915 - 2000 hrs — Reception

2000 - 2230 hrs — **CONGRESS DINNER** — Fui Gui Restaurant

Sunday 1 July 2001

0800 - 0845 hrs

MEET-THE-EXPERT

Chairperson: Dr Hooi Lai Ngoh

1) Rare Insterstitial Lung Disease — Mahkota III
Asst Prof Marilyn K Glassberg (USA)

Chairperson: Dr Norzila Mohamed Zainudin

p43 2) Manifestations of Occult Hypoxaemia in Chronic Neonatal Lung Disease — Baiduri & Berlian Courtroom
Dr Dominic Fitzgerald (Australia)

0845 - 1015 hrs

SYMPOSIUM 5 - Severe Difficult Asthma — Mahkota III

Chairperson: Dr I Kuppusamy

0845 - 1015 hrs p44 Clinical Presentation of Severe Difficult Asthma: Phenotypes and Risk Factors
Dr Lawford Hill (UK)

p45 Management of Asthma in 2001
Asst Prof Marilyn K Glassberg (USA)

p46 Difficult Asthma in Children
Assoc Prof Jessie de Bruyne (Malaysia)

1015 - 1030 hrs COFFEE

1030 - 1130 hrs p54–58 **Oral Presentations of Selected Free Papers** — Mahkota III

Chairperson: Dr Zainudin Md Zin

1130 - 1320 hrs

SYMPOSIUM 6a - Pleural Disease — Mahkota III

Chairperson: Dr Wong Wing Keen

p47 Diagnostic Approach to Pleural Effusion
Assoc Prof Roslan Harun (Malaysia)

p48 Management of Parapneumonic Pleural Effussion (PPE)
Assoc Prof Lim Tow Keang (Singapore)

p49 Management of Pneumothorax
Dr Aziah Ahmad Mahayiddin (Malaysia)

p50 Role of Video-Assisted Thoracoscopy
Dato' Dr Ahmad Sallehuddin (Malaysia)

SYMPOSIUM 6b - Paediatrics — Baiduri & Berlian Courtroom

Chairperson: Dr Mazidah Abd Rashid

p51 Non-Cystic Fibrosis Bronchiectasis in Children
Dr Azizi Omar (Malaysia)

p52 Management of Parapneumonic Effusion and Empyema in Children
Assoc Prof Patrick Chan (Malaysia)

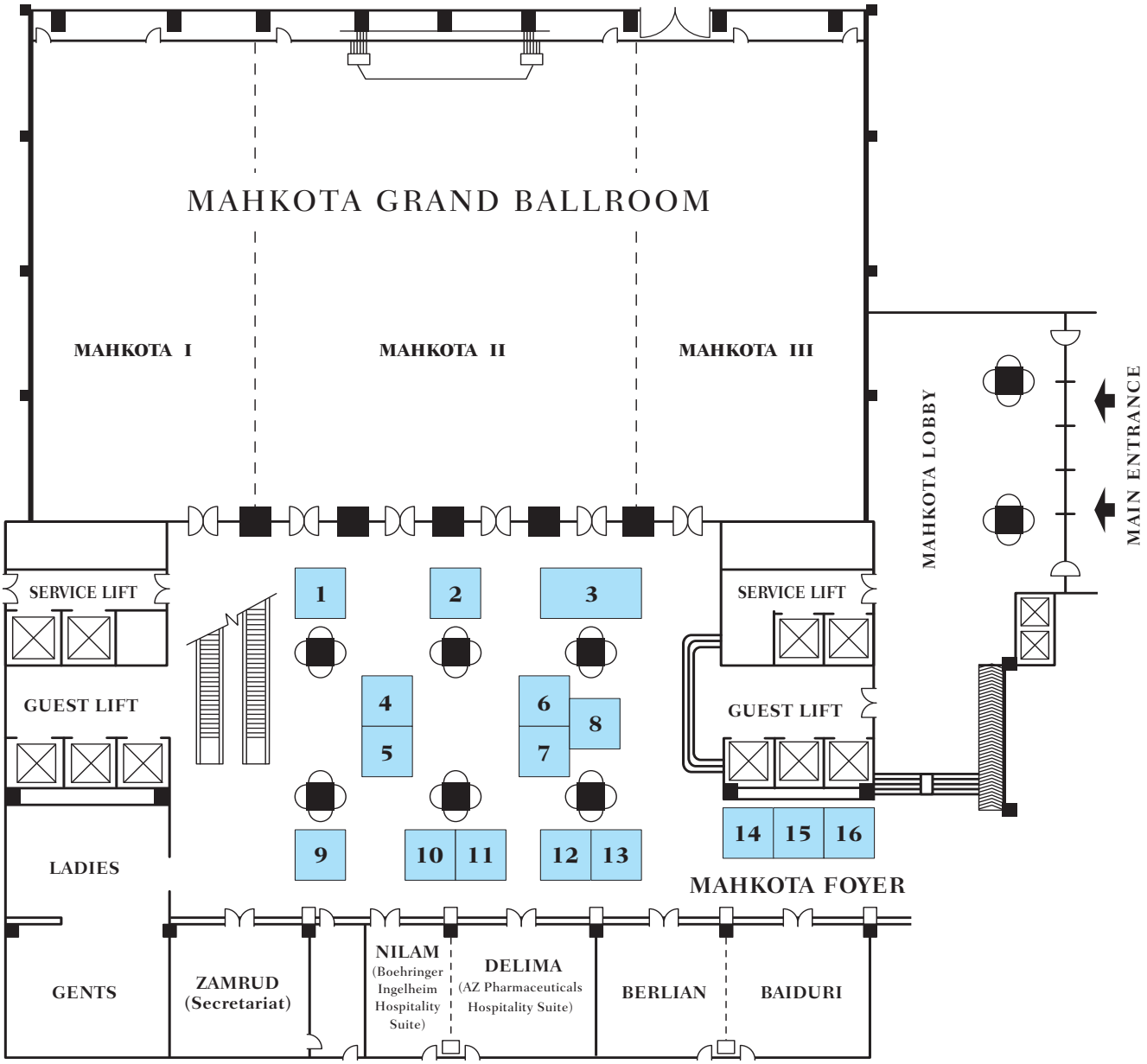
p53 Role of Bronchoscopy in Airway Disease
Dr Norzila Mohamed Zainudin (Malaysia)

1320-1330 hrs **Closing Remarks**

ORAL PRESENTATIONS

POSTER PRESENTATIONS

FLOOR PLAN
& TRADE EXHIBITION



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ACKNOWLEDGEMENTS

The Organising Committee of the 4th Annual Congress of the Malaysian Thoracic Society expresses its deep appreciation to

Ministry of Health Malaysia

AZ Pharmaceuticals (M) Sdn Bhd
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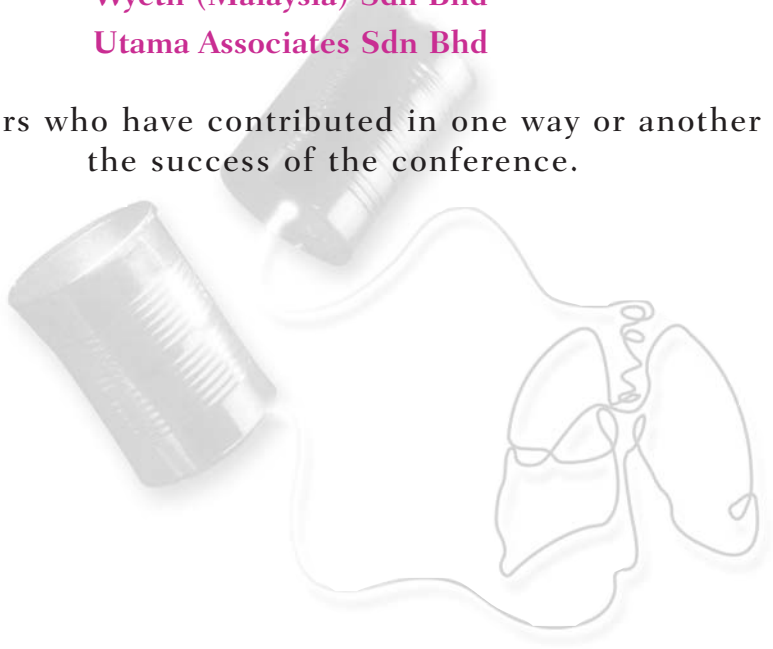
and others who have contributed in one way or another to the success of the conference.



ABSTRACTS

FROM p20 *to* p69

RECENT ADVANCES IN THE BACTERIOLOGICAL EXAMINATIONS OF TUBERCULOSIS

CHIYOJI ABE
Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan

In the last 10 years, there were many advances in the bacteriological examinations of tuberculosis. Six systems based on liquid media, MGIT, BacT/Alert, ESP, MB Redox, Septi-Chek AFB and BACTEC systems, proved to be significantly better than the egg-based media for the isolation of mycobacteria from clinical specimens. Isolation of the M. tuberculosis complex (TB) by these systems occurred 8 days previous to the isolation by the egg method. MPB64-ICA (Capilia TB) is the newly developed immunochromato-graphic assay for rapid discrimination between TB and MOTT bacilli. The kit can be easily used for rapid identification of TB bacilli in combination with the culture systems based on liquid media. PCR and other nucleic acid amplification methods are widely used for the detection of TB in clinical specimens. Although the sensitivities of these methods for the detection of TB appeared to be similar to that of the culture method using liquid-based culture systems, the two methods should be quite useful for rapid identification of TB infections. On the other hand, two cooperative blind studies revealed the necessity of good laboratory practice and development of reference reagents to monitor the performance of the whole assay. Considerable progress has been made in recent years toward understanding the molecular basis of the resistance to anti-tuberculosis drugs. Most cases of resistance are related usually to simple nucleotide substitutions rather than to acquisition of new genetic elements. Multidrug-resistant isolates of *M. tuberculosis* arise as a consequence of sequential accumulation of mutations conferring resistance to single therapeutic agents. The basis of resistance is not explained yet in a substantial percentage of strains (10-30%) for other anti-tuberculosis drugs than rifampin and pyrazinamide. Further studies are required to fully understand the molecular mechanisms of resistance.

RECENT ADVANCES IN TUBERCULOSIS TREATMENT

YEW WING WAI
Chief of Service, Tuberculosis & Chest Unit, Grantham Hospital, Hong Kong, P R China

The aims of antituberculosis chemotherapy are discussed. So is the scientific basis of short-course chemotherapy. The standard 6-month short-course chemotherapy regimen is currently recommended by the World Health Organization and the International Union Against Tuberculosis and Lung Disease (WHO/IUATLD) for treatment of smear-positive new cases. This comprises administration of 4 drugs - isoniazid (H), rifampicin (R), pyrazinamide (Z), plus ethambutol (E) or streptomycin (S) for 2 months, followed by the first 2 drugs for another 4 months. Controlled studies have not shown administration of Z for more than 2 months to be advantageous. However, for individual cases with extensive radiographic disease and slow sputum bacteriological conversion to negative especially in light of suspected unfavourable drug susceptibilities, prolongation of the intensive treatment phase beyond 2 months may be practised. Intermittent regimens in form of administration of drugs thrice per week have also been shown to be efficacious. For treatment of relapsed smear-positive pulmonary tuberculosis, as well as retreatment after interruption, a 8-month regimen has been recommended by WHO/IUATLD, namely 2 SHRZE / 1 HRZE / 5HRE or 5H3R3E3. Bacillary susceptibilities to drugs in vitro can help to guide modification of this regimen. The use of fixed dose drug combinations (FDC) comprising 2 to 3 and even 4 drugs can enhance ease of prescription for physicians and treatment adherence by patients. When used properly, FDC tablets should decrease the risk of development of multidrug-resistant tuberculosis. The main concern in using FDC is the quality and bioavailability of its component drugs, particularly rifampicin. Directly Observed Therapy in tuberculosis has had been found to be highly efficaciously in ensuring patient adherence by experience obtained in Madras and Hong Kong many decades ago. In 1993, the WHO officially announced the new global strategy for control of tuberculosis known as Directly Observed Therapy, Short course (DOTS). The components of this strategy are discussed. DOTS is robust in achieving high success (cure + treatment completion) rate and prevention of development of acquired drug resistance. Finally, the potential role of some new rifamycins and fluoroquinolones in the management of tuberculosis are discussed.

ABC OF NATIONAL TB CONTROL PROGRAMME

I KUPPUSAMY
Institute of Respiratory Medicine, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia

The National TB Control Programme (NTP) in Malaysia was launched in 1961. At that time TB was the leading cause of mortality and morbidity. The objective was to rapidly reduce and eventually eliminate all infectious sources so that TB does not pose a health problem. The strategy was:

a. To protect at least 95% of the susceptible population less than 20 years of age with BCG vaccination.

b. To identify at least the number equivalent to the estimated annual incidence of the disease for the particular state .

c. To render at least 95 % of the infectious sources identified non-infectious by effective treatment.

Over the years BCG vaccination coverage has been uniformly good with rates approaching 100%. Case detection rate was quite stable until 1990, after which there has a progressive increase. The objective of curing at least 95% of the eases has not been reached yet. It is hoped that with increased application of the DOTS (Directly Observed treatment short course) strategy, this can realised. Initially the NTP was a vertical programme, but after 1969 it has been progressively integrated with primary health care services. Currently diagnostic and treatment services are available at district levels.

MANAGEMENT OF DIFFICULT TUBERCULOSIS

YEW WING WAI
Chief of Service, Tuberculosis & Chest Unit, Grantham Hospital, Hong Kong, P R China

The management of tuberculosis in specific settings including adverse reactions due to drugs are discussed. For management of isoniazid-monoresistant disease, only minor modification of the regimen is required. However, for multidrug-resistant tuberculosis (MDR-TB), alternative specific therapy with second-line anti-tuberculosis drugs and a fluoroquinolone should be used. For tuberculosis in pregnancy, short-course chemotherapy can be used, aside from avoidance of streptomycin. Further, the safety profiles of the second-line drugs and fluoroquinolones have not been ascertained in this setting. For treatment of tuberculosis in children, ethambutol should be avoided until the patients are at least 6 - 8 years old and capable of reporting symptomatic visual changes accurately. For HIV-infected patients, the total duration of anti-tuberculosis treatment should be 9 months, or at least 4 months after culture conversion to negative. Rifampicin should not generally be used when patient is receiving a HIV-protease inhibitor and / or a non-nucleoside reverse transcriptase inhibitor. Rifabutin can be substituted for use together with some HIV-protease inhibitors. Efavirenz can be used with rifampicin or rifabutin, though the latter requires some increase in dosage. Alternatively non-rifampicin containing regimens (such as isoniazid + pyrazinamide + streptomycin ± ethambutol), albeit less potent, can be used for extended durations to avoid clinically significant drug interactions. Drug-induced hepatitis occurs more commonly in patients with old age, malnourishment, slow acetylator phenotype, and compromised liver reserve due to chronic hepatitis B and C infection, and alcoholic liver disease. When tuberculosis is mild or has improved significantly, normalization of liver chemistry can be awaited before gradual retrial of the conventional antituberculosis drugs. Whenever possible, isoniazid and rifampicin should be included in the regimen so that treatment duration will not be unduly prolonged. In the face of extensive disease when delay in therapy is detrimental to the health of patient, ofloxacin can be used together with streptomycin and ethambutol as an interim regimen for treatment. The fluoroquinolone can also be incorporated into the definitive regimen if intolerance to isoniazid and / or rifampicin occurs. In moderate renal impairment, rifampicin, isoniazid and pyrazinamide can be given in usual dosages. Streptomycin, ethambutol, ofloxacin and cycloserine are eliminated largely through renal clearance, and dosage reduction is mandatory in the face of renal impairment. Except for rifampicin and isoniazid, the recommendations on dosage modification of other drugs during haemodialysis are still somewhat inconsistent.

ACUTE ASTHMA

LIAM CHONG KIN
Division of Respiratory Medicine, Department of Medicine, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Acute asthma is common disease presentation to the emergency department and general practice. Although a severe acute asthmatic exacerbation may occasionally develop within minutes or hours, it usually occurs against a background of long-term poorly controlled asthma that has been worsening for some days or weeks. The approach to the management of acute asthma includes (1) assessing the severity of the attack, (2) instituting the appropriate treatment, (3) assessing the response to the treatment in order to identify those patients who may require more intensive therapy or hospital admission, and (4) following-up the patient to ensure complete recovery from the attack and to reduce the risk of further exacerbation. Treatment would involve the rapid reversal of bronchospasm to relieve respiratory distress and reducing airway inflammation in order to restore the patient's lung function to the best possible level as soon as possible and to prevent early relapse.

Inhaled β-agonists are the mainstay of therapy for acute asthma. The role of adding intravenous β-agonists to frequent β-agonists is less well defined. Systemic corticosteroids promote recovery and prevent relapse after discharge from emergency room and should be given early. Oral administration of corticosteroids is equally effective as the intravenous route. However, intravenous corticosteroids may be appropriate for the severely ill patients. Ipratropium bromide is a weak bronchodilator and results in a modest improvement in airflow obstruction when added to inhaled β-agonists. Given its favourable safety profile, it can be used in combination with inhaled β-agonists in severe acute asthma. Aminophylline is an inefficient bronchodilator and has not been found by many studies to improve outcomes. Given its narrow therapeutic range and unfavourable safety profile, it should be a last-line agent or not to be used at all. Intravenous magnesium sulphate appears to improve pulmonary function in the most severely ill patients but is not useful in patients with more moderate disease. Medications used in the treatment of chronic asthma, such as inhaled corticosteroids and leukotriene-modifying agents, are making their way into the acute treatment arena.

MANAGEMENT OF MASSIVE HAEMOPTYSIS

ROSLINA ABDUL MANAP
Department of Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Massive haemoptysis is variably defined as expectoration of blood exceeding 600 mL over a 24 hour period. It is often a sign of an important underlying disease, and is potentially fatal due to life threatening asphyxiation. While only five percent of haemoptysis is massive, some studies report a mortality rate of up to 80 percent.

The acute and general management of patients with massive haemoptysis is difficult because of the multitude of potential etiologies and the unpredictable course of bleeding. There is also a lack of consensus regarding the optimal management of these patients.

Initial priorities are ensuring adequate airway protection, ventilation, and cardiovascular function Patients with poor gas exchange, rapid ongoing haemoptysis, haemodynamic instability, or severe shortness of breath should be orally intubated with a large bore endotracheal tube. Early consultation with pulmonary medicine and thoracic surgery should be obtained. by invasive Once the patient is stabilized, early bronchoscopy should be performed.

Arteriography has been a major addition to the diagnostic and therapeutic armamentarium for the management of haemoptysis. Bronchial arteriography is being used with increasing frequency because of its value in localizing the probable bleeding site and allowing therapeutic embolisation during the same procedure.

Patients with lateralised, uncontrollable bleeding should be assessed early for possible surgery.

MANAGEMENT OF ACUTE UPPER AIRWAY OBSTRUCTION IN CHILDREN

NORRASHIDAH ABDUL WAHAB
Department of Paediatrics, Hospital Selayang, Kuala Lumpur, Malaysia

BRONCHOSCOPIC PALLIATION OF LUNG TUMOURS

ALAN WK NG

Department of Respiratory Medicine, Tan Tock Seng Hospital, Singapore

Airway obstruction is not uncommon in lung cancer. Intraluminal obstruction is caused by growth of an exophytic tumour into the airway lumen. Extraluminal obstruction is caused by compression of the airway by an adjacent tumour mass or mediastinal lymph nodes.

Obstruction in the central airways is often symptomatic and potentially life-threatening. These patients are not surgical candidates because of advanced disease.

Interventional bronchoscopy techniques have, in recent years, been developed to relieve airway obstruction. Many of the procedures are high risk but they can be performed safely. Intraluminal tumours can be coagulated and vaporized with the Nd:YAG laser and subsequently resected. The ideal lesion for laser resection is a polypoidal lesion arising from a single wall and should not exceed 4 cm in length.

Extraluminal compression can be relieved with insertion of a tracheobronchial stent; which acts as a splint holding the airway open. Silicone stents are the most commonly used airway prothesis; insertion requires a specially designed introducer device and rigid bronchoscopy. Wire stents can be inserted with a flexible bronchoscope. The relief of dyspnoea following successful laser resection or insertion of a stent is immediate.

Other endobronchial modalities include brachytherapy where a high dose of radiation is given to a segment of airway marked out at bronchoscopy; electrocautery and cryotherapy and photodynamic therapy. It may also be possible to mechanically debulk an obstructing tumour, but this would be time consuming and risky when bleeding cannot be controlled.

AETIOLOGY AND ANTIBIOTIC RESISTANCE OF RESPIRATORY TRACT PATHOGENS: IMPLICATIONS ON CHOICE OF ANTIBIOTIC THERAPY

N PARASAKTHI

Department of Medicial Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Respiratory tract infections are a major communicable disease and an important cause of morbidity and mortality with pneumonia being ranked as the sixth most common cause of death. In 40-60% of cases of community-acquired pneumonia the aetiology is not identified. However, the most common etiologic agent identified in virtually all studies of CAP is *S.pneumoniae* and this agent accounts for approximately two-thirds of all cases of bacteremic pneumonia. Other pathogens implicated in RTI include *H.influenzae, M.pneumoniae, C.pneumoniae, S.aureus, S.pyogenes, M.catarrhalis, K.pneumoniae* and other Gram-negative bacilli, Legionella spp,and viruses. The frequency of other etiologies such as TB, *B.pseudomallei* and fungi is dependent on specific local etiological factors.

Resistance of *S.pneumoniae* to penicillin was first noted in Australia and Papua New Guinea in the 1960s, spread to South Africa in the 1970s and subsequently to many countries in Eurpoe, Africa, and Asia. Hot spots of penicillin-non-susceptible strains in Asia include S.Korea, Hong Kong and Japan. Reported rates of penicillin non-susceptibility in Malaysia have varied from 7% to 30%. Strains with reduced susceptibility are often resistant to other β-lactams, macrolides, trimethoprim-sulphamethoxazole. Newer respiratory quinolones have better activity versus *S.pneumoniae* when compared to the earlier flouroquinolones. Resistance of *H.influenzae* to ampicillin is about 15 - 20%, mainly secondary to β-lacatamase production and erythromycin is ineffective against the majority of strains. The increasing antimicrobial resistance in the *S.pneumoniae, H.influenzae* and *M.cattarrhalis*, the possibility of atypical pathogens and lack of microbiological confirmation impacts on the choice of empirical treatment of community-acquired RTI.

Data from animal models and clinical studies have demonstrated significant differences in the bacteriologic efficacy of antibacterials based both on potency and the ability to achieve the PK/PD parameter required for efficacy against both susceptible and non-susceptible pathogens. The PK/PD parameter for time-dependant agents such as b-lactam antibiotics and most macrolides is the unbound serum concentration that is present for 40-50% of the dosing interval. For concentration dependant agents, such as quinolones and aminoglycosides, the PK/PD parameters that correlate with bacteriologic eradication are the peak unbound serum concentration to MIC (peak:MIC) ratio. Various group have recognized the value of PK/PD relationships for predicting the clinical efficacy of antibiotics, and have developed guidelines or MIC breakpoints based on PK/PD parameters. Potent antibacterials with low *in-vitro* rates of development of resistance, rapid bactericidal activity, and optimal PK/PD parameters offer the potential to maximize clinical cure, minimize the survival of resistant mutants and limit their spread within the individual and the community.

UPPER RESPIRATORY TRACT INFECTION

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Upper respiratory tract infection (URI) is one of the most common ailments that patients bring to the primary care physician or otolaryngologist. In the management of URI, the importance of understanding the causes of these infections is evident. In this presentation, a review of pathogens of URI infections according to anatomic sites is made. The pathogenesis and current treatment strategy of chronic sinusitis is elaborated. The use of endoscopy as a diagnostic and therapeutic tool will be emphasized in the management of this condition as well as other URI. Other viral, bacterial, fungal and protozoan infections that are of special interest will also be discussed.

COMMUNITY ACQUIRED PNEUMONIA: SEVERITY ASSESSMENT AND TREATMENT

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Community acquired pneumonia (CAP) is a common and potentially fatal condition worldwide. Physicians tend to overestimate the short-term mortality and therefore unnecessarily initiate hospitalization for some CAP patients. This is highly undesirable from the health-economical and patients' points of view. It is, therefore, imperative to determine at initial diagnosis that whether or not a patient requires hospitalization.

A number of published guidelines, including those of the BTS and ATS, extensively address the treatment aspects and assessment of disease severity in CAP. Factors identified to be associated with increased mortality includes: age>65 yrs, co-existing morbid illness, tachypnoea (>30/min), diastolic BP <60mmHg, high fever (>38.3oC), altered mental alertness, WBC <4 or >20-30 x109/L, neutrophil count <1x109/L, Hct<30%, Hb<9g/dl, PaO2£60mmHg, PaCO2≥50mmHg, BUN≥7mmol/L, albumin<35g/L, bacteraemia, and unfavourable radiological appearances (multi-lobar involvement, rapid radiological progression, and pleural effusion). However, several of these factors are not readily available in the outpatient emergency setting, when decision on hospitalization has to be made rapidly. The more recently published Infectious Disease Society of America guidelines, therefore, utilize the prediction rule of the Pneumonia Patient Outcomes Research Team in risk-classifying CAP patients. For this system, age, nursing home residence status, co-existing illness, physical examination findings, and laboratory and radiographic findings are weight-scored. Patients are classified into risk classes I to V with increasing risk scores. Patients with risk classes I to III could be safely treated as outpatients, while their counterparts would require hospitalization. This strategy would reduce the proportion of inpatient care by 31%, at least in the US setting.

Initial selection of antibiotic(s) for treatment is usually, if not always, empirical as even research-orientated tertiary centers only manage to disclose 50% of the microbiological aetiology in CAP. Recommendations from the ATS, BTS, ERS, IDSA, CDC, Japanese Respiratory Society, and Canadian Thoracic Society have been published. There appears to be a universal belief that Streptococcus pneumonia is the single most important pathogen. There is also increasing emphasis on treating atypical organisms such as Mycoplasma pneumoniae and Chlamydia pneumoniae. For outpatients, most guidelines suggest the use of a macrolide or a b-lactam. In the presence of risk factors such as known antibiotic resistance, presence of modifiable factors (advanced age, COPD, or recent antibiotics or steroid therapy), a fluoroquinolone is indicated, although this might encourage development of resistance. Inpatients require treatment with a b-lactam plus a macrolide or monotherapy with a fluoroquinolone, and occasional cover for Legionella and Pseudomonas aeruginosa. While these North American and European guidelines are widely publicized and are largely evidence-based in design, their direct application for patients in the Asian Pacific region could not be assumed without caution. Our region has high prevalence of antibiotic resistance, and very significant difference in disease pattern and health care delivery systems from the West. Prospectively collected data on the microbiological aetiology of CAP are therefore needed before any empirical use of antibiotics could be scientifically justified.

PNEUMONIA IN HIV INFECTED PATIENTS

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Pulmonary infection, the most common pulmonary complication in HIV infected patients, is highly prevalent in Southeast Asia where the surveillance system is rather limited in many countries, The reported incidence of opportunistic infection is obtained mostly from samplings from late stage AIDS patients. The most common pulmonary infection is pneumocystis carinii pneumonia (PCP) of which the clinical feature is similar to that found in western countries. Diagnosis of PCP in this region is based mainly on clinical and radiographic presumptions that are less sensitive and specific. The second common pulmonary infection is pulmonary tuberculosis of which the prevalence of multi-drug resistant tuberculosis in Thailand has been shown recently in the upward trend. The delayed diagnosis of pulmonary tuberculosis is common due to poor resource utilization. The patient compliance is another major problem and the direct observe therapy cannot be applied in the vast majority of cases. The primary prophylaxis is not popular in routine clinical practice and the patient compliance is also the major limitation for its effectiveness. The two most common pulmonary mycoses are cryptococcosis and penicilliosis Pulmonary cryptococcosis is in the same situation as seen worldwide but pulmonary penicilliosis is rather unique in Southeast Asia because of its endemicity. It is the most prevalence in Thailand; however, the intracountry prevalence is much differed. For bacterial infection, the bacterial spectra and clinical feature are not different from those reported worldwide. The rare pulmonary infections reported such as toxoplasmosis and cytomegaloviral pneumonia may reflect under-diagnosis. The endemic tropical infections involving lung in this region e.g. leptospirosis, melioidosis, disseminated strongyloidiasis are surprisingly remaining silent except scrub typhus. Highly active antiretroviral therapy can be provided in only a small fraction of the patients so its influence on the incidence of pulmonary complications has not been obvious but should be monitored for the time being.

In routine clinical practice, the empirical therapy based on clinical and radiographic presumptions is widely accepted if the patient has no diagnostic sputum. The diagnostic efficacy of the sputum analysis and the presumptive diagnostic efficacy of various kinds of pulmonary infection were studied prospectively using the bronchoalveolar lavage diagnosis as a gold standard. The result of these studies can enhance the routine clinical practice of pulmonary complications in HIV infected patients in this region of the world.

PNEUMONIA IN NON-HIV IMMUNOCOMPROMISED HOST

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The increasing number of non-HIV immunocompromised patients appears to be related to the substantial progress in treatment of malignancies, connective tissue diseases and organ transplantation programmes. Pulmonary infiltrates in immunocompromised patients may be due to infectious and non-infectious processes. Infections are common and associated with high mortality rate. In acute leukemia for example, up to 75% of the patients developed pneumonia and half of the cases ended up in mortality. In renal transplant programme, 10-20% of the recipients developed pneumonia at some stage of treatment also with high mortality rate. Prompt treatment with appropriate antimicrobial agents are the key factors for successful outcome of treatment. However in most cases the confirmation of the etiologic agents usually does not happen or frequently late and empirical therapy is almost always employed. The type of immunological defects, clinical presentation, geographical and epidemiological considerations and radiological features are useful and provide clues to the probable etiology and the choice of emperic treatment. Bacteria, nocardia, fungi, viruses, mycobacteria and pneumocystis may be responsible for the pneumonia and sometimes more than one organisms may be encountered. Non invasive investigative procedures should be optimally and liberally used. Fibreoptic bronchoscopy with bronchoalveolar lavage and transbronchial biopsy although invasive had been used with low rate of complication and significant yield. Open lung biopsy or video-assisted thoracoscopic lung biopsy are rarely performed because of patients' poor condition and significant morbidity and mortality. Treatment of various types of infection and the role of prophylaxis will be discussed.

ASTHMA CONTROL : THE REAL WORLD EFFECTIVENESS

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Patients with moderate and severe persistent asthma rarely achieve the treatment goals established in the National Institutes of Health Guidelines with the regular use of a single controller medication. Therefore, when a patient requires multiple controller medications to effectively treat the disease, health care professionals should consider several factors:

* What is disease control? How does one define it?
* What are the underlying causes of insufficient response to monotherapy?
* How does one measure the relative effectiveness of various therapies? What are the endpoints to critically assess?
* What is the optimal combination of controller medication?
* What does each component of disease control offer the patient and the physician in the total picture of asthma management?

Objectives :

At the end of this presentation participants will be able to:

* Identify various endpoints, both objective and subjective, that can be used to assess asthma "control"
* Better understand overall benefits and drawbacks of components of therapy used to establish control
* Gain additional insights into implications of therapeutic selection

AIRWAY INFLAMMATION IN COPD VERSUS ASTHMA

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GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE - THE GOLD GUIDELINES

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Chronic obstructive pulmonary disease (COPD) is a major public health problem. It is a leading cause of chronic morbidity and mortality world wide and is projected to rise in rank from current twelve to fifth in the next two decades as a world-wide burden of disease according to studies conducted by the world health organization. A unified international approach is required to reverse the trends.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is conducted in collaboration between the US National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO) and the compiled guidelines provide classic evidence based documentation. Its goal is to increase awareness and decrease mortality and morbidity from this disease . This is achievable if there is a world wide effort to implement evidence based good clinical care and prevention.

Several resource publications arising from the initiative are available for dissemination and adaptation for global implementation. Publications of guidelines in themselves do not lead to improved care. Implementation is difficult, time consuming but essential for attaining these goals. Initial methods to encourage adoption of guidelines for implementation include familiarization, interactive seminars and small groups discussion.

The four components of the guidelines are:1) assessment and monitoring of disease; 2) reduction of risk factors; 3) management of stable COPD; 4) management of exacerbation. Key issues of the GOLD guidelines and differences from previous published popular guidelines will be high lighted, expanded, compared and discussed.

PULMONARY REHABILITATION vs LUNG VOLUME REDUCTION SURGERY

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Chronic Obstructive Pulmonary Disease (COPD) is considered a relentlessly disabling disease despite modern advances pharmacotherapy. In the last few decades, pulmonary rehabilitation is considered to be a an integral part of the health care delivery for these patients. Although this intervention can relieve symptoms and prevent complications, it cannot halt the progression of the disease. In the 1950's, Brantigan excised multiple wedges of emphysematous lungs. This procedure gave his patients clinical improvements in lung function, but the mortality rate was very high and was soon abandoned. In the 1990's, this surgical procedure was revived. Wakabayashi reported using laser bullectomy for patients with diffuse bullous emphysema. Cooper reported his case series of patients who underwent bilateral lung volume reduction through median sternotomy incision. This form of surgery showed improvements in dyspnea, quality of life, FEV1, room air PaO2 and 6 minute walk test. This outcome encouraged other medical institutions to perform lung volume reduction surgery (LVRS) among emphysema patients. However, data collected from Medicare showed higher acute care hospitalization and mortality rate in the post surgical period because of respiratory and non respiratory complications. Medicare discontinued its financial support for LVRS in 1995. The National Emphysema Treatment Trial (NETT), a seven year multicenter study that intends to enroll over 2,500 patients was launched in 1997. Its objective is to compare bilateral LVRS and maximal medical therapy including pulmonary rehabilitation. It poses to answer the following crucial questions:

a) How long would the benefits from surgery last?

b) What is the optimal technique for performing the procedure?

c) W hat are the clinical outcomes beyond the first few months of surgery ?

d) Can a subset of patients who would benefit from the procedure be defined?

LVRS is surrounded by many unresolved issues and cannot be recommended yet as a standard therapy.

PATHOPHYSIOLOGY OF BRONCHOPULMONARY DYSPLASIA

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PROPHYLAXIS IN CHRONIC LUNG DISEASE OF PREMATURITY

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The prevention of chronic neonatal lung disease [CNLD] remains an ongoing challenge for neonatologists. The earliest descriptions of CNLD, then called bronchopulmonary dysplasia [BPD], date back nearly 50 years. As the skills and resources of neonatologists and neonatal nurses have improved dramatically so the survival curve has shifted to the left and thus the profile of the infant with CNLD has changed. In 1967, Northway and colleagues described a small cohort of infants born at a mean age of 31 weeks weighing 1880g with BPD. Such infants today seldom develop CNLD, let alone die from this entity. Today, as with neurodevelopmental sequelae, the development of CNLD represents a major consequence of extreme prematurity [<29 weeks] and extremely low birthweight [<1000g] as it may occur in 40% of survivors. Similarly, CNLD is also more common in small for gestational age babies born less prematurely. Strategies aimed at reducing the rate of preterm delivery, reducing maternal cigarette smoking and improved tocolysis will indirectly reduce the rate of CNLD.

Immediate postnatal therapy has included early mechanical ventilation and, in the last 10-15 years, the use of systemic corticosteroids. Mechanical ventilators have become more sophisticated, ventilation strategies have improved, and surfactant therapy ahs been introduced, yet the prevalence of CNLD remains unchanged. Strategies to reduce the rate of CNLD centred upon the use of systemic corticosteroids during the first weeks of life. Regrettably, whilst there is little doubt that systemic dexamethasone therapy facilitates weaning neonates from ventilator dependency, they do not necessarily alter the length of oxygen dependency and have significant side effects. Indeed, lengthy courses of dexamethasone have been implicated as independent risk factors for poor neurodevelopmental outcome and cerebral palsy. There is a pressing need to establish whether a less potent corticosteroid given systemically for a shorter period is safe and efficacious, as studies using inhaled corticosteroids have proved ineffective in reducing the rate of CNLD.

Together with the earlier institution of CPAP therapy, researchers have turned their attention to investigating other potential contributors to the development of CNLD such as oxidative stress as reflected by markers of airway inflammation. Manipulation of the inflammatory response by means of less potent corticosteroids for shorter periods may hold promise for the future. Such promise would be tempered by proper randomised trials with long term follow-up of both neurological and respiratory outcome.

LONG TERM MANAGEMENT AND OUTCOME OF CHRONIC LUNG DISEASE

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The prognosis for preterm infants with chronic neonatal lung disease is determined by a complex interaction of neurodevelopmental outcome, respiratory function and nutritional status. These variables change with time, generally improving with the resolution of tachypnoea and oxygen dependency during infancy. From the time of discharge from the NICU, the respiratory needs of CNLD children can be considered in three stages:

1. During the first year of life

The infant may well be receiving inhaled steroids, diuretics, methyl xanthines and oxygen. The primary goals of the first year of life are to maximise growth, survive the threat of bronchiolitis [the major cause of mortality post NICU discharge in CNLD infants] and usually to wean supplemental oxygen. Airway complications, often attributed to lengthy periods of endotracheal intubation may manifest during infancy, particularly with subglottic stenosis predisposing to recurrent, severe croup.

2. During the preschool years

Approximately 30-40% of CNLD infants will present with cough, tachypnoea and wheeze of varying severities. This is managed along the lines of other children with reactive airways disease, involving the use of inhaled corticosteroids and the consideration of the use of long acting beta agonists in selected cases. Nutritional status will generally have improved with the resolved tachypnoea. Much effort focuses upon quantification of the neurological deficits and intervention for approximately 25% of very low birthweight infants. A common additional concern is the evolution of obstructive sleep apnoea, known to peak in the age group of 18 months to 3 years which is attributed to a combination of adenoid hypertrophy and the mid-face hypoplasia seen in VLBW infants.

3. During the school years

The primary goal during this time is to quantify the degree of respiratory dysfunction, which has prognostic information for the adult years. Spirometry, lung volumes and in selected cases exercise testing are indicated. In the adolescent age, one must emphasise the negative consequences of cigarette smoking upon respiratory health both acutely and potentially in terms of longevity.

The clinician should be aware of the improved respiratory outcomes associated with better neonatal management strategies in the last decade although be mindful of the implications of mild to moderate respiratory compromise upon quality of life measures both in childhood and adulthood.

MANIFESTATIONS OF OCCULT HYPOXAEMIA IN CHRONIC NEONATAL LUNG DISEASE

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Chronic neonatal lung disease [CNLD] remains a common complication of extreme prematurity despite the advent of surfactant therapy and advances in neonatal intensive care. A series of cross-sectional and prospective cohort studies in which occult hypoxemia complicating CNLD is considered in relation to known co-morbidities of prematurity: pulmonary hypertension, growth failure and sleep disturbances.

Pulmonary Hypertension

Doppler echocardiography was used as a non-invasive measure of pulmonary artery pressure [PAP] in 76 infants with CNLD and 21 sibling controls. A 24% prevalence of raised PAP during early childhood was demonstrated in infants with CNLD. There were no cases of raised PAP in the controls. There were no clinical signs of pulmonary hypertension in these children who all had normal SaO2 [> 95%] awake in room air. Raised PAP occurred independently of the severity of the clinical or radiological lung disease during the neonatal period.

Sleep, respiratory rate and growth hormone in CNLD

Overnight sleeping respiratory rates were measured in early, middle and late infancy in 23 infants [CNLD=16, controls=7] on 66 occasions. Respiratory rates [RR] for CNLD infants were stratified into AHigh RR@ and ANormal RR@ based on mean rates more than two standard deviations higher than the mean for controls. AHigh RR CNLD@ [RR > 45] infants in early infancy [1.7 ± 1.5 months] had lower birthweights [p=0.015], current weights [p=0.042], current lengths [p=0.02] and growth velocities [g gained per week: p=0.042]. Mean urinary growth hormone [U-GH] [ng U-GH/g urinary creatinine/4 hours] was higher in AHigh RR CNLD@ infants in air/usual oxygen [1932 ± 1917] than ANormal RR CNLD@ infants [394 ± 267] and controls [320 ± 186] [p=0.024]. With resolution of tachypnoea by middle infancy [6.8 ± 1.7 months], growth parameters and U-GH excretion were similar and this continued into late infancy [10.6 ± 1.9 months]. This is consistent with growth hormone resistance as a mechanism for poorer growth in tachypnoeic infants with CNLD.

Higher SaO2 in CNLD: Does it improve sleep?

The maintenance of baseline SaO2 > 95% has been advocated for infants with CNLD to overcome rapid eye movement [REM] sleep fragmentation. The effects of an increased baseline arterial oxygen saturation [SaO2 >97%] on sleep architecture were compared with those for an SaO2>95%. Decreased [median {95%CI}] REM% was observed with mean SaO2 >95% [all > 93%] which did not improve in higher inspired oxygen [SaO2>97%] [27.9%{26.8,34.5} vs 32.3% {25.2,36.0}; p= 0.560] in early infancy. REM% was unchanged in middle and later infancy [p=0.959]. Sleep quality improved with age. It was concluded that infants with CNLD who maintain an SaO2> 95% have persisting reduced REM% and that an SaO2 > 97% does not improve sleep quality in early infancy.

CLINICAL PRESENTATION OF SEVERE DIFFICULT ASTHMA: PHENOTYPES AND RISK FACTORS

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There is no agreed international consensus definition of "Severe Difficult Asthma" but there is recognition that certain asthmatics appear to be resistant to standard therapeutic regimes. These asthmatics usually have persisting or easily provokable symptoms despite being prescribed high doses of inhaled Corticosteroid together with both short acting and long acting inhaled beta agonists. This lecture explores the factors involved in preventing satisfactory settlement of the asthmatic condition, which is now widely perceived to be primarily an inflammatory disease of the airways.

Asthma and its associated bronchial inflammation can prove difficult to settle for a number of varied reasons. Firstly, there is mounting evidence that many physicians and their patients may not appreciate the degree of asthma treatment required, leading to a susceptibility to acute exacerbation, but without necessarily many intercurrent symptoms. This may lead to a false perception of Difficult Asthma. The way many of the published asthma treatment guidelines approach treatment and asthma assessment may in fact contribute to this difficulty, as the dose response curves to inhaled steroid are different for exacerbation control and lung function measurement.

Secondly, non-compliance is a major cause of poor asthma control. Whilst secondary non-compliance is well recognised and frequently addressed, the primary and hidden varieties have been given little attention in the literature but do prove in practice to be significant factors in preventing adequate control.

Thirdly, co-existing pathologies such as allergic rhinitis and gastro-oesophageal reflux with associated oesophagitis may also adversely influence the asthmatic inflammation by both hormonal and neural mechanisms, preventing satisfactory asthma settlement until the co-morbidity is treated.

Fourthly, a significant minority of asthmatics suffer continuing symptoms due to dysfunctional breathing. This condition can produce symptoms virtually indistinguishable from active asthma, often resulting in huge increases in asthma medication to the patient without any appreciable benefit.

Finally, there is a small minority of asthmatics whose bronchial inflammation is truly steroid resistant, necessitating therapy with immuno-suppressants. Exhaled Nitric Oxide estimation may prove to be a useful measure in identifying these patients.

MANAGEMENT OF ASTHMA IN 2001

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Objectives :

1. Describe the histopathological findings associated with inflammation and airway remodeling.
2. Understand the implications of inflammation and airway remodeling in management of patients with asthma.
3. Review the role of anti-inflammatory therapies in the management of asthma.

Summary : Asthma is a heterogeneous syndrome. However, airway inflammation is present in all types of asthma and is a driving force for the array of symptoms associated with this common and expensive chronic illness.

Eosinophils are one of the most important cells involved in the inflammatory response as shown by their abundance in blood, sputum, bronchoalveolar lavage fluid, and lung tissue from patients with asthma. Through the release of many factors, including leukotrienes, eosinophils promote changes in lung parenchyma and contribute to airway hyperresponsivenesss and airway remodeling.

Structural cells in the airway also contribute to airway remodeling. Airway smooth muscle, traditionally considered only for its contractile properties, can undergo hyperplasia and/or hypertrophy leading to airway wall thickening. Myofibroblasts emerge may be the principal proliferating cell type that contributes to the progression of airway fibrosis. In vitro studies have demonstrated that various pro-inflammatory mediators, growth factors and components of the extracellular matrix influence airway smooth muscle and myofibroblast growth. Airway smooth muscle also can secrete components of the extracellular matrix, adhesion molecules, as well as various cytokines.

Proliferating airway smooth muscle cells can now be regarded as cells that undergo phenotypic modulation from a contractile to synthetic-proliferative state and perpetuate airway inflammation.

Persistent airway inflammation is believed to be a key stimulus that promotes irreversible structural remodeling of the asthmatic airway. Current evidence suggests that inhaled corticosteroids and long-acting _2-agonists do not completely reverse airway hyperresponsiveness and may not effect airway remodeling. Newer studies suggest that leukotriene modifiers and other anti-inflammatory agents in development, may modify airway remodeling.

The goals of asthma management are to maximize pulmonary function and improve quality of life for the patient. The art of asthma care is to prevent or decrease the need for hospitalizations through effective outpatient management of asthma. In this lecture, we will discuss the concept of airway remodeling and evaluate current pharmacotherapeutic approaches and their effects on airway inflammation and the architecture of the asthmatic airway.

DIFFICULT ASTHMA IN CHILDREN

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Difficult asthma may be defined as the persistence of troublesome symptoms - frequent daytime (including exercise-induced) or nocturnal symptoms, frequent need for (2-agonists and/or oral corticosteroids and deterioration in pulmonary function - in spite of receiving high doses of inhaled (i.e. >800 mcg beclomethasone or budesonide or >400mcg fluticasone in children) or oral corticosteroids. Brittle asthma with relatively mild interval symptoms but acute severe attacks is another difficult category.

Alternative diagnoses like immunodeficiency, gastro-oesophageal reflux, laryngomalacia and other congenital anomalies, vocal cord dysfunction, heart failure, ciliary dyskinesia, cystic fibrosis, bronchopulmonary dysplasia need to be excluded by careful history-taking, examination and investigations. A simple chest x-ray and full blood count and differential are first steps in the investigatory pathway. Useful pointers in the history such as age of onset, recurrent fevers and infections, failure to thrive, feeding difficulties like vomiting and breathlessness, abnormal stools, inspiratory vs. expiratory noises will suggest other diagnoses and point towards specific investigations like measurement of immunoglobulins, sweat test, CT scan, flexible bronchoscopy, investigations for reflux, search for tuberculosis, etc.

The psychosocial aspect needs investigation.

Therapeutic measures include: -

i) optimizing asthma medication

High-dose inhaled steroids as above are complemented by long-acting (2-agonists. Leukotriene antagonists, theophylline and ipratroium bromide may also be useful. The importance of compliance and the correct use of inhaler devices and drugs cannot be over- emphasized. Education is essential and a simple regime aids compliance. The use of a spacer helps in delivery.

ii) environmental control

As the majority of asthmatics are allergic to house dust mites, general control measures should be instituted. The need for control of other specific triggers may be indicated by the history and investigations.

iii) trial of oral steroids

Early use of oral steroids in an attack is indicated. Some children will be steroid-dependent and require regular oral steroid therapy with its attendant side-effects. Very few children are steroid resistant with persistent symptoms on high doses.

iv) other treatments

There are few reports of alternative treatments in children although methotrexate and intravenous immunoglobulins have been tried.

The aim in the care of the child with difficult asthma is for accurate diagnosis, optimal therapy and minimal side-effects in the growing or developing child. This requires a structured, systematic approach with an individual touch.

DIAGNOSTIC APPROACH TO PLEURAL EFFUSION

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Pleural effusion is a common condition encountered in the clinical practice. Understanding of mechanisms of the pleural effusion development is essential to identify possible causes and arrange appropriate investigations. Pleural effusion is classified into either transudates or exudates based on the pleural fluid total protein level. Common causes of pleural transudates include congestive cardiac failure, nephrotic syndrome and chronic liver disease. Associated clinical features are usually present which makes the diagnosis is usually obvious and warrants no further investigation. In contrast, the diagnosis of exudative pleural effusion can be sometimes challenging. The possible causes range from infection, malignancy, connective tissue diseases and granulomatous diseases. A pleural effusion is normally diagnosed by chest radiography. Diagnostic thoracocentesis is essential to determine the macroscopic appearances of the pleural fluid and its biochemical contents including pH, protein, albumin, glucose, and lactate dehydrogenase levels. The fluid specimen should be examined for differential count and for malignant cells. The specimens are routinely sent for microbiology examination to rule out infective causes. Additional specific investigations such rheumatoid factor, antinuclear antibodies and amylase are required according to clinical suspicions. Pleural biopsy should normally be performed at the same sitting, which will definitely increase the diagnostic ability. Further diagnostic tests may be necessary to assist in either the diagnosis or treatment. These investigations include bronchoscopy, ultrasound and CT scan of the thorax. If pleural aspiration and biopsy fail to give the diagnosis, thoracoscopy can be carried out using rigid thorascope or video-assisted techniques with biopsy of any pleural lesions seen.

MANAGEMENT OF PARAPNEUMONIC PLEURAL EFFUSION (PPE)

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Parapneumonic pleural effusions (PPE) are common and potentially serious complications of pneumonia. The management of PPE involves early diagnosis, adequate empiric antibiotic cover and appropriate categorizing for risk of poor outcome. High risk patients need safe and expedient drainage of the infected pleural space. The management options include thoracentesis, tube thoracostomy, adjunctive intra-pleural fibrinolytic therapy and surgical drainage. The methods of surgical drainage include thoracoscopy, thoracotomy and decortication. The relative clinical efficacies of some of these treatment options have been studied in a small number of controlled clinical trials. Furthermore, results of these controlled studies have been systematically reviewed by expert panels. However, based upon the limited clinical evidence, expert reviewers were unable to recommend a best method of pleural drainage. There is consensus however that an aggressive approach with a view to early surgical drainage results in shorter hospital stays and may be more cost effective than conservative management. This review discusses the clinical evidence and describes an aggressive sequential management strategy which combines intra-pleural fibrinolysis with early surgical drainage.

MANAGEMENT OF PNEUMOTHORAX

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Spontaneous pneumothoraces, which occur in the absence of thoracic trauma, are classified as primary or secondary. Primary pneumothoraces affect patients who do not have clinically apparent lung disorders. Secondary pneumothoraces occur in the setting of underlying pulmonary disease, which most often is COPD. Though spontaneous pneumothoraces are one of the commonest respiratory causes of hospital admission, generally accepted guidelines on management of these patients do not exist till recently.

Clinically stable small spontaneous pneumothorax should be observed in the emergency department for 3-6 hours and discharged home if a repeat CXR does not show progression, with a follow up appointment for another CXR in 1-2 days, depending on circumstances. Clinically stable patients with large pneumothoraces should undergo a procedure to reexpand the lung and should be hospitalized. Using a small-bore catheter or placement of a chest tube should reexpand the lung.

Clinically unstable patients with large pneumothoraces should undergo hospitalization with insertion of a chest catheter to reexpand the lung. A large tube may be used if the patient is anticipated to have a bronchopleural fistula. Chest tubes should be removed in a staged manner so as to ensure that the air leak into the pleural space has resolved.

For patients with persistent air leaks, continued observation for 4-5 days for spontaneous closure of the bronchopleural fistula. Beyond 5 days these patients should be evaluated for surgery to close the leak and to perform pleurodesis procedure to prevent recurrence. Most patients should not be managed with chemical pleurodesis by instilling sclerosing agents through the chest tube except in special circumstances in which surgery is contraindicated or patients refuse an operative procedure. If chemical pleurodesis is performed, deoxycycline or talc slurry is the preferred agent.

Procedures to prevent the recurrence of a primary spontaneous pneumothorax should be reserved for the second pneumothorax. Thoracoscopy is the preferred intervention, with or without video assistance. Patients with apical bullae visualized at surgery should undergo intraoperative bullectomy.

Clinically stable patients with secondary pneumothoraces should be hospitalized and should not be managed in the emergency department. The size of chest tubes used for patients with secondary pneumothoraces depends on clinical circumstances. Patients should not be referred for thoracoscopy without prior stabilization with the chest tube. Intervention to prevent recurrence after the first occurrence is recommended to be done after the first episode because of the potential lethality of secondary pneumothoraces.

ROLE OF VIDEO-ASSISTED THORACOSCOPY

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NON-CYSTIC FIBROSIS BRONCHIECTASIS IN CHILDREN

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The epidemiology of bronchiectasis (BR) in Malaysia is not known but clinical experience indicates that it is now an uncommon condition in paediatric practice. Better management of acute respiratory infections and an excellent immunisation programme may have contributed to the reduced incidence. BR is defined as dilated bronchi associated with varying degrees of acute and chronic inflammation as well as fibrosis. BR begins after an acute airway injury such as infection and or aspiration of gastric content.

A vicious cycle of inflammation, tissue destruction and impairment of mucociliary transport contribute to chronic inability to sterilise the airways.

BR should be suspected in a child with chronic productive cough. A plain chest radiograph is useful but a high-resolution computerised tomography (HRCT) is the diagnostic tool of choice. Once diagnosis is made investigations should be directed towards finding the aetiology of BR. Important causes in the local setting include post infectious (tuberculosis, measles, viruses, necrotising bacterial pneumonia), chronic aspiration (gastro-oesophageal reflux, swallowing incoordination), retained foreign body, immunodeficiency and idiopathic.

Therapy is directed at breaking the cycle that leads to progressive airways damage. Antibiotics and chest physiotherapy are often employed. The role of bronchodilators, anti-inflammatory and viscosity reducing agents are controversial. Surgery is not recommended in generalised disease but may be useful in troublesome localised lesions.

MANAGEMENT OF PARAPNEUMONIC EFFUSION AND EMPYEMA IN CHILDREN

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Pleural infection complicating childhood pneumonia results in the transformation of a free-flowing parapneumonic effusion into an empyema, a multi-loculated fibrotic and purulent fluid collection. The appropriate treatment of childhood parapenumonic effusion and empyema remains controversial, as it is largely dependent on individual experience.

The main principles of treatment include early diagnosis, antibiotics and prompt chest tube drainage. Parapneumonic effusion alone in the absence of pleural infection will respond to antibiotics and does not indicate the need for continuos chest tube drainage. Purulent pleural fluid although the most obvious feature of empyema may not be the best indicator for the timing of chest tube insertion. Pleural fluid acidosis, rising LDH and falling glucose are a few reliable indicators that an empyema is developing, warranting prompt drainage.

A large bore chest tube catheter is highly recommended and inserted as early as possible upon diagnosis of empyema. Inadequate tube size and delayed insertion of the chest tube is associated with failure of pleural fluid drainage. The development of loculations, organizing fibrosis and development of pleural peels heralds the need for surgical intervention namely a thoracotomy and decortication. Appropriate antimicrobial therapy must be prolonged for up to 6 weeks duration.

There is growing enthusiasm in the use of intrapleural fibrinolytic agents in improving chest tube drainage and avoiding the need for surgical intervention. Experience of its use in childhood empyema although limited has been promising.

Prospects for childhood empyema and parapneumonic effusion treatment are also improving; with the development of more tolerable chest tube drainage techniques and less invasive surgical procedures ie thoracoscopy decortication.

ROLE OF BRONCHOSCOPY IN AIRWAY DISEASE

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Flexible bronchosope is an important diagnostic tool in the paediatric airway. The diagnostic flexible bronchoscope is indicated when the information desired can be obtained by this technique. The indications of this procedure is stringent. The benefits of performing must outweigh the risks.

One of the most important aspect is learning the indications. The bronchoscopist must be able to determine when the patient will benefit from this procedure and to assess the risks benefit ratio.

Indications for dioagnostic flexible endoscopy in infants include congenital or acquired stridor, abnormal cry or hoarseness of voice, endotracheal tube extubation, suspected airway obstruction, unilateral lung hyperinflation and suspected artificial airway complications. In most series in infants stridor is the commonest indication. The most common findings are laryngomalacia, subglottic stenosis and vocal chord paralysis. In children the indications include stridor, abnormal voice, persistent atelactasis, recurrent or persistent pulmonary infiltrates, equivocal airway foreign body, lung lesions of unknown aetiology, haemoptysis, failed extubation and suspected artificial airway complications and to obtain lower airway secretions and/cells by bronchoalveolar lavage.

Flexible bronchoscope is not advocated for foreign body removal in children with high risks for foreign body aspiration

Other therapeutic indications include difficult intubation, therapeutic bronchoalveolar lavage removal of airway secretions and mucus plugs.

TUBERCULIN SKIN TESTING AMONG HEALTH CARE WORKERS IN UNIVERSITY MALAYA MEDICAL CENTRE

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Objectives: To determine the occupational risk for Mycobacterium tuberculosis infection among health care workers (HCWs) and to examine the utility of tuberculin skin test (TST) in a developing country setting with high prevalence of BCG vaccination.

Setting: University Malaya Medical Centre (UMMC), a tertiary referral centre and a teaching hospital in Kuala Lumpur.

Methods: A cross-sectional TST survey, including a risk assessment questionnaire of HCWs in UMMC was conducted between 8.1.2001 and 28.2.2001.

Study populations: HCWs working in medical wards (area with higher level of exposure to TB) and in surgical and orthopaedic wards (area with lower level of exposure to TB) were recruited.

Results: Of 263 HCWs tested, 137 (52.1%) had indurations of (10mm and 69 (26.2%) had indurations of (15mm. Medical wards HCWs were at significantly higher risk of positive TST than surgical/orthopedic wards HCWs [60.8% versus 41.7% TST positivity at (10mm cut-off point; odds ratio: 2.18 (95% CI: 3.57, 1.33, p=0.002) and 34.2% versus 16.7% TST positivity at (15mm cut-off point; odds ratio: 2.61 (95% CI: 4.71,1.44, p=0.002), respectively]. HCWs who had had TST before were also found to be at significantly higher risk of positive TST at either (10mm or (15mm cut-off point. Duration of employment of >1 year and nurses were the other 2 factors significantly associated with a positive TST at (15mm cut-off point but not at (10mm cut-off point. Age, gender, ethnic group, family history of TB and previous BCG vaccination were not significant predictive factors for a positive TST at either cut-off point.

Conclusions: UMMC HCWs had an increased risk for Mycobacterium tuberculosis infection. This risk was significantly associated with the level of exposure to tuberculosis, in particular occupational exposure. TST is a useful tool in assessing this occupational risk. A TST induration cut-off point of (15mm may correlate better with Mycobacterium tuberculosis infection than does a cut-off point of (10mm in a setting with high prevalence of BCG vaccination. Effective and affordable infection control measures are needed to reduce this occupational risk.

SKIN PRICK TEST REACTIVITY TO COMMON AEROALLERGENS IN ASTHMATIC PATIENTS WITH AND WITHOUT RHINITIS

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Study objective: To study the prevalence of skin prick test (SPT) reactivity to common aeroallergens among asthmatic patients with and without rhinitis.

Methods: Asthmatic patients attending the Asthma Clinic, University Malaya Medical Centre, Kuala Lumpur underwent SPT with 8 aeroallergens (Dermatophagoides pteronyssinus, Dermatophagoides farinae, cat fur, cockroach, Acacia sp., Bermuda grass, Aspergillus fumigatus and Aspergillus niger). Any history of rhinitis and the age of onset of asthma were recorded. The severity of the patient's asthma was classified according to clinical features and treatment intensity during the 3-month period prior to the skin prick test.

Results: Of 206 asthmatic patients [150 females; mean age, 48.0 (+ 15.5) years; range, 12 to 76 years] who underwent the SPT, 140 (68.%) were reactive to at least one of the aeroallergens. Among the SPT-positive patients, prick test reaction was most commonly to the house dust mites, D. pteronyssinus (93.6%), and D. farinae (81.4%), followed by cat fur (20.0%), cockroach (7.9%), Acacia sp. (7.9%), Bermuda grass (7.9%), A. fumigatus (0.7%) and A. niger (0.7%). The majority of the SPT-positive patients were younger than 40 years at the time of onset of their asthma. 111 (53.9%) patients gave a history of rhinitis and 95 (85.3%) of these patients were SPT-positive compared to only 45 (47.4%) of 95 patients with asthma symptoms alone ($p<0.001$). There was no significant difference in asthma severity between the SPT-positive and SPT-negative patients.

Conclusions: The prevalence of SPT reactivity to common aeroallergens is high among Malaysian asthmatics, particularly in those with an early age of onset and in those with coexisting rhinitis. The house dust mites (D. pteronyssinus and D. farinae) are the commonest aeroallergens causing sensitisation in asthmatics. The clinical severity of asthma is similar in SPT-positive and SPT-negative patients.

SURGERY IN THE MANAGEMENT OF THORACIC INFECTIONS AT SULTANAH AMINAH HOSPITAL

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Surgery prevents life threatening complications, improves the quality of life and improves lung function of patients with thoracic infections not amenable to medical therapy alone. A retrospective review of the spectrum of surgery in this group of patients at Sultanah Aminah Hospital was performed.

Between November 1996 and April 2001 our department performed thoracic surgery on 329 patients. Seventy-eight patients (24%) underwent surgery for thoracic infection, of whom 47 (60%) were male and 31 (40%) were female. The mean age is 33.2 +/- 20 (40 days- 69 years). Fifteen patients were less than 12 years old and 3 patients in this group were less than 1 year old. Thirty patients underwent decortication for empyema thoracis that were bacterial in origin. All these patients had the operated lung fully expanded prior to discharge from hospital. Thirty-four patients underwent lung resection for bronchiectasis, aspergilloma, cryptococcus neoformans, abscesses and various solitary nodules of infective origin. Four patients had video-assisted thoracoscopic surgery for pleural biopsy. Five patients with mediastinal lymphadenopathy had cervical mediastinoscopy and biopsy of lymph nodes. Two patients had rib resection, 1 patient underwent thoracoplasty and 1 patient had thoracotomy to close a bronchopleural fistula that was infective in origin. There were three perioperative deaths, 2 of which were unrelated to the primary procedure.

Although the spectrum of thoracic disease in our hospital has a varied aietiology, thoracic infections form a significant part of the thoracic workload unlike in the West.

NEUTROPHIL FUNCTION AND SERUM INTERLEUKIN-8 IN PATIENTS WITH CHRONIC BRONCHIECTASIS

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Objectives: There are increased levels of neutrophils, neutrophil proteases and IL-8 in sputum and bronchoalveolar lavage in patients with chronic bronchiectasis. The aims of this study are to investigate whether (a) the peripheral blood neutrophils are activated or 'primed' and (b) the serum interleukin-8 level, a potent neutrophil chemotactic factor, is increased in patients with chronic bronchiectasis.

Methodology: Blood samples were taken from 26 patients with stable chronic bronchiectasis and 20 controls comprising of normal healthy subjects. The neutrophils were isolated and the neutrophil function test was then performed by using the chemiluminescence method. Serum interleukin-8 levels were measured by using the ELISA method. The neutrophil function test was done on the same day the blood samples were taken to optimize the accuracy of the results.

Results: There was increased neutrophil function in patients with bronchiectasis compared to the control group ($p<0.05$). However there was no significant difference in the serum interleukin-8 levels between the two study groups.

Conclusion: The significant increase in peripheral blood neutrophil function may contribute to the ongoing inflammation in chronic stable bronchiectasis. However there was no significant rise in serum interleukin-8 levels. Other factors are probably involved in the activation of the peripheral blood neutrophils.

A RANDOMISED OPEN COMPARATIVE STUDY OF ORAL LEVOFLOXACIN VERSUS ORAL AMOXYCILLIN/CLAVULANATE POTASSIUM FOR THE TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA

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Objectives: This study aimed to compare the efficacy and safety of oral levofloxacin 300 mg once daily with amoxicillin/clavulanate potassium 375 mg thrice daily in the treatment of community-acquired pneumonia in adult.

Methods: Sixty patients with confirmed diagnosis of mild to moderate community-acquired pneumonia were enrolled in this randomised, open comparative trial. Patients were evaluated before, during (day 3, 7, 10 and 14 of antibiotic), and 4 to 5 weeks post-therapy.

Results: The patients were randomised into levofloxacin treatment arm (n = 31) and amoxicillin/clavulanate potassium treatment arm (n = 29). Both treatment arms were similar in the demographic characteristic, clinical presentations at baseline and duration of antibiotics given. Clinical efficacy, severity score, safety of the drugs and aetiological organisms were the study end points. Clinical response was rated as a success (patient cured or improved) for 90.3% (28/31) of clinically evaluable levofloxacin-treated patients and 93.1% (27/29) of clinically evaluable amoxicillin/clavulanate potassium-treated patients. No relapse was seen within 4 weeks of study population. The evaluation of severity score for cough and sputum demonstrated a difference in clinical response on day 3 of antibiotic with levofloxacin-treated group achieved better and faster improvement compared to amoxicillin/clavulanate potassium-treated group. Drug related adverse events were described in 16.1% of levofloxacin and 27.6% of amoxicillin/clavulanate potassium-treated group. The adverse effects were mild in both treated groups and there was no need to stop treatment in any patients. No laboratory changes occurred in any patients while on treatment. Both treatments were generally well tolerated with most common adverse events in both groups affecting the gastrointestinal tract. The common isolates were Klebsiella species (8.4%), beta-haemolytic Streptococcus (3.4%), Enterobacter species (3.3%), Acinetobacter species (1.7%), Branhamella species (1.7%) and Stenotrophomas maltophilia (1.7%). No resistance was found with levofloxacin group. However, Stenotrophomonas maltophilia was found to be resistant to amoxicillin/clavulanate potassium in-vitro. The limitations of this study were the small sample size and the subjectiveness in some of the study parameters, including the measurement of cough, dyspnoea and chest pain.

Conclusions: When given orally, a once daily 300 mg dose of levofloxacin was as effective and well tolerated as amoxicillin/clavulanate potassium 375 mg thrice daily for mild to moderate community-acquired pneumonia but with levofloxacin a better and faster improvement seen by day 3 of antibiotic.

LACK OF CORRELATION BETWEEN ASTHMA SYMPTOMS AND OBJECTIVE MEASURES OF AIRFLOW OBSTRUCTION IN ADULT ASTHMATICS

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Study objective: To determine the relationship between asthma symptoms and the degree of airflow obstruction as measured by the forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR) in a group of adult asthmatics.

Methods: During a 2-week period, study patients recorded in diary cards daytime and nocturnal asthma symptoms. The frequency of daytime asthma symptoms and their effects on the patients' daily activities were rated from 0 (no symptom/effect) to 6 (maximum symptom/effect). Their use of inhaled salbutamol for symptom relief and their prebronchodilator PEFRs prior to bedtime and on waking in the morning were also recorded. Pre- and postbronchodilator (200 (g of salbutamol) FEV1 and PEFR were measured at the initial (visit 1) and follow-up clinic visit at the end of 2 weeks (visit 2).

Patients: 46 adults [mean age, 44.3 (+ 11.9) years] with clinically stable chronic asthma [mean duration, 19.5 (+ 12.7) years] attending the asthma clinic who volunteered for a placebo-controlled study of an investigational asthma therapy.

Results: Asthma symptoms did not correlate with the degree of airflow obstruction as determined by home morning and bedtime PEFRs, highest and lowest home PEFRs, clinic PEFRs, and clinic FEV1, except for FEV1 measured at clinic visit 2 (mean daily asthma symptom score over 2 weeks vs percent predicted prebronchodilator FEV1: $r = -0.358$, $p = 0.024$). There was a modest correlation between asthma symptoms and use of inhaled relieve salbutamol (mean daily asthma symptom score over 2 weeks vs average daily dose of salbutamol use: $r = 0.481$, $p = 0.001$).

Conclusions: Asthma symptoms generally do not correlate with the level of airflow obstruction in adult asthmatic patients as assessed by home PEFR monitoring and clinic measurement of FEV1 and PEFR.

LUNG CANCER CELL TYPE AND DIAGNOSTIC YIELD OF BRONCHIAL WASHING, BRONCHOALVEOLAR LAVAGE, ENDOBRONCHIAL BIOPSY, TRANSBRONCHIAL BIOPSY AND BRONCHIAL BRUSHING SPECIMENS OBTAINED DURING FIBREOPTIC BRONCHOSCOPY

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Background: The use of fibreoptic bronchoscopy in the investigation of patients suspected to have lung cancer is well established. Very limited data are available regarding the effect of lung cancer cell type on the relative diagnostic yield of the various bronchoscopic sampling procedures.

Objective: The aim of this study was to determine whether the diagnostic yield of bronchial washing, bronchoalveolar lavage, forceps endobronchial biopsy, transbronchial biopsy and bronchial brushing specimens obtained at fibreoptic bronchoscopy examination for lung cancer was dependent on the cell type.

Patients and methods: A retrospective analysis of patients who underwent fibreoptic bronchoscopy examination for lung cancer in our department from September 1991 to August 1999.

Results: Of 508 patients who underwent fibreoptic bronchoscopy examination for lung cancer, bronchoscopically visible tumours were found in 342 (67.3%) patients. Of these, 130 (38%) were squamous cell carcinoma (SCC), 106 (31%) adenocarcinoma, 56 (16.4%) small cell lung cancer (SCLC), 40 (11.7%) undifferentiated carcinoma and 10 (2.9%) other cell types. The proportions of the main cancer cell types with bronchoscopically visible tumours were: small cell lung cancer (SCLC) (86.2%), squamous cell carcinoma (SCC) (84.4%), undifferentiated carcinoma (61.5%), and adenocarcinoma (52.2%). Compared to the other cell types, adenocarcinoma was less commonly associated with bronchoscopically visible tumours ($p<0.0001$). Bronchial washing, bronchoalveolar lavage, endobronchial biopsy, transbronchial biopsy and bronchial brushing were performed on 256, 158, 326, 54 and 140 patients, respectively and these sampling procedures were diagnostic for lung cancer in 28.5%, 22.2%, 78.5, 31.5 and 41.4% of patients, respectively. Bronchial washing was less likely to be diagnostic in patients with undifferentiated carcinoma than in those with the other cell types ($p=0.001$). The cell type had no effect on the diagnostic yield of bronchoalveolar lavage. Endobronchial biopsy was less likely to be positive in patients with undifferentiated carcinoma ($p<0.0001$). Transbronchial biopsy was more likely to be positive in patients with adenocarcinoma ($p=0.014$). Bronchial brushing was more likely to be positive in patients with bronchoscopically visible tumours ($p=0.008$). For patients with bronchoscopically visible tumours, bronchial brushing was least likely to be diagnostic in those with undifferentiated carcinoma ($p=0.009$).

Conclusion: The diagnostic yield of the different bronchoscopic sampling procedures in patients with lung cancer is dependent on the cell type and also on whether the tumour is visible bronchoscopically in the case of bronchial brushing.

NON-SMALL CELL LUNG CANCER IN YOUNG AND ELDERLY PATIENTS

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Background: There is little data on non-small cell lung cancer (NSCLC) in very young and very old patients.

Objective: To compare the clinicopathological features of NSCLC in young and elderly patients.

Methods: We reviewed the clinicopathological data of patients with histologically and/or cytologically confirmed primary lung cancer diagnosed at our medical centre from October 1991 to September 1999.

Of 510 patients with NSCLC diagnosed during this period, 32 (6.3%) were aged below 40 years (the young group) and 19 (3.7%) were aged 80 years and above (the elderly group) (Table 1). There was no difference in the male-to-female ratio between the young, middle-aged (from 40 to 79 years) and elderly groups.

Table 1 Clinicopathological features of non-small cell lung cancer (NSCLC) in different age groups

	Age at diagnosis (yr)			
	< 40	40 - 79	> 80	P value (χ^2 test)
No. of patients	32	459	19	
Mean age (+ SD) (yr)	33.4 (+ 4.2)	60.8 (+ 9.4)	82.6 (+ 2.8)	
Gender				
Male	20 (62.5)	336 (73.2)	15 (78.9)	0.348
Female	12 (37.5)	123 (26.8)	4 (21.1)	
Smoking status				
Smoker	12 (37.5)	361 (78.6)	14 (73.7)	<0.001
Never smoker	20 (62.5)	98 (21.4)	5 (26.3)	
Cell type				
Adenocarcinoma	24 (75)	219 (47.7)	9 (47.4)	0.012
Other NSCLC	8 (25)	240 (52.3)	10 (52.6)	
Clinical stage at diagnosis				
I - III	11 (34.4)	273 (59.5)	15 (78.9)	0.004
IV	21 (65.6)	186 (40.5)	4 (21.1)	
WHO performance status at diagnosis				
0 - 2	17 (53.1)	339 (73.9)	13 (68.4)	0.038
3 - 4	15 (46.9)	120 (26.1)	6 (31.6)	

Conclusions: Compared to elderly patients, significantly higher proportions of young patients were never smokers and had metastatic disease at the time of diagnosis. Although the proportions of young patients who had adenocarcinoma and poor performance status were high, these were not significantly different from those of elderly patients.

VINORELBINE AND CISPLATIN IN THE TREATMENT OF LOCALLY ADVANCED AND METASTATIC NON-SMALL CELL LUNG CANCER

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Objective: To better define the activity and toxicity of vinorelbine/cisplatin as first line chemotherapy in patients with locally advanced and metastatic non-small cell lung cancer (NSCLC) in Malaysian patients.

Patients and Methods: Between August 1999 and Jan 2001, chemotherapy naïve patients with stage IIIa to stage IV NSCLC, who consented to chemotherapy received vinorelbine 25 mg/m2 on days 1and 8 and cisplatin 80 mg/m2 on day 1 every 3 weeks. Patients were evaluated for performance status, symptom improvement, toxicity profile and tumour response.

Results: Twelve patients with the median age of 53.5 (range 24-68 years) received chemotherapy as scheduled, totaling 46 cycles. Seven patients had adenocarcinoma, 4 squamous carcinoma and one poorly differentiated carcinoma. Ten patients had stage IV disease while one patient each had stage IIIa and stage IIIb disease respectively. One patient received radiotherapy to the brain for symptomatic brain metastasis. Patients' performance status (PS) (WHO criteria) were as follows: 4 had PS 1, 6 PS 2, and one each PS 3 and 4.

The regime was well tolerated without any chemotherapy related deaths. The major toxicities (WHO grading) were haematological; one patient each with Grade 3 anaemia, Grade 3 and Grade 4 leucopenia, two had Grade 3 neutropenia and 5 had Grade 4 neutropenia but not associated with fever. Non haematological toxicities were only significant (Grade 3 or 4) in the following; 3 had Grade 3 alopecia and one had Grade 3 phlebitis.

After 3 cycles (total 34 cycles), 3 patients demonstrated partial response, 2 stable disease and the rest progressed. Chemotherapy was stopped after one cycle in one patient due to progression. One patient who had partial response opted to continue treatment elsewhere. For the 4 patients who completed 6 cycles, 2 demonstrated stable disease and 2 partial response. Time to disease progression and survival data were not available.

At the time of chemotherapy completion, symptom improvement was reported in all but one patient. Similarly, PS was better in 4, stable in 6 but declined in 2 patients whose disease progressed.

Conclusions: In patients with locally advanced and metastatic NSCLC, vinorelbine/cisplatin is a well tolerated and active regimen which offers symptom palliation and improved performance status in a significant proportion of patients.

EXTRAPULMONARY COMPLICATIONS IN CHILDREN HOSPITALISED WITH MYCOPLASMA PNEUMONIA

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Background: Mycoplasma pneumoniae is an important cause of pneumonia in older children. Extra-pulmonary complications although uncommon is well described in association with Mycoplasma pneumoniae infection in children. We determined the occurrence of extra-pulmonary complications and outcome in Malaysian children hospitalized with Mycoplasma pneumonia.

Methods: Serum particle agglutination (SERODIA-MYCO II) for Mycoplasma pneumoniae was done for 170 children aged 1 month to 15 years who were admitted with pneumonia over a consecutive 6-month period. A positive serological diagnosis was made if the acute phase serum titer was more than 1:160 or paired samples taken 2 - 4 weeks apart showed a four-fold rise in the serum titer.

Results: Mycoplasma pneumoniae was the cause of pneumonia in 40 (23.5%) children. Extrapulmonary complications were evident in 7 (17.5%) children. The extra-pulmonary complications encountered included hepatitis (3 children), arthritis (3 children), maculopapular rash (2 children), myocarditis (1 child), encephalopathy (1 child) and autoimmune haemolytic anaemia (1 child). All but one child survived with the appropriate antimicrobial therapy.

Conclusion: The outcome of Mycoplasma pneumoniae infection in children is generally favorable. Extra-pulmonary complications are commonly encountered.

THE COST OF TREATING CHILDREN HOSPITALIZED WITH RESPIRATORY SYNCYTIAL VIRUS INFECTION AND ITS IMPLICATIONS ON PASSIVE IMMUNISATION STRATEGIES

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Background: Respiratory syncytial virus (RSV) infection bronchiolitis is a common cause of hospitalization in the very young child. We determined the direct cost of hospital resource utilization in the treatment of children admitted with RSV bronchiolitis and the potential cost-savings with the use of passive immunization for high-risk infants.

Methods: We reviewed 216 children aged <24 months who were admitted with RSV infection between 1995-1997. A detailed audit of the hospital resource consumption was performed for each subject. The cost-saving of passive immunization using monoclonal RSV antibodies (Palivizumab) was determined by assuming an efficacy of 0.5 in hospital admission reduction with its administration during the 5 month peak infection period to high-risk infants. Criteria includes infants <28 weeks and 28-32 weeks gestation up to 12 months and 6 months of age respectively or infants with BPD aged <2 years at the onset of the anticipated RSV season.

Results: The hospital treatment cost of 1064 bed-days amounted to RM244255.26. Each child occupied a median of 4.0 bed-days with a median cost of RM645.95 (IQ 486.72-944.20) for the hospitalization. Children who were premature and with an underlying illness were more likely to have a longer hospital stay, higher treatment cost and greater need for intensive care. Ten (42%) of 24 ex-premature infants fulfilled the recommended criteria for passive immunization. Its use would result in an incremental cost of RM119.27 to a cost saving of up to RM3.45 per infant for each hospital day saved.

Conclusion: Ex-prematurity and the presence of an underlying illness significantly escalated the direct treatment cost of RSV infection. Current guidelines developed for the use of passive RSV immunization do not appear to be cost-effective if adopted for Malaysian children.

THE LATE PRESENTATION OF LUNG CANCER

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Background: Lung cancer is the leading cause of cancer deaths in Malaysia. Early stage disease is often curable with surgical resection. However, most patients present with unresectable or metastatic disease.

Objective: This study was undertaken to assess the delays in the diagnosis of lung cancer and factors that may have contributed to these delays.

Methods: This was a prospective study on lung cancer patients presenting to the Respiratory Unit between September 1988 and June 2000.

Results: A total of 89 newly diagnosed and histologically or cytologically confirmed lung cancer patients were investigated. Sixty-six (74.2%) of them were males. Present or past smokers constituted 82% of the patients. These patients were 29 to 85 years old (mean age (S.D.), 61.1 (12.1) years(at diagnosis. The ethnic distribution of patients were 64% Chinese, 25% Malay, 9% Indian and 2% others. A high proportion (77%) of these patients had either no formal education (21%) or only primary level education (56%). As many as 89% of patients with non-small cell lung cancer had stage 3b or 4 disease at presentation. Of the patients with small cell lung cancer, 77% of them had extensive disease at diagnosis. Cough was reported as the first symptom in 64% of the patients, weight loss in 7.9% and chest pain in 6.7%. Only 6.7% of the patients thought that lung cancer was the cause of their symptoms. While 12.4% of the patients attributed smoking as the cause of their symptoms, 38.2% of them had no idea what had caused their illness. The median interval between the onset of first symptom and first medical consultation (patient's delay) was 30 days (range: 0-510 days). The median interval between the first medical consultation and presentation to the respiratory unit (doctor's delay) was 60 days (range: 0-545 days). The median interval between the onset of first symptom and presentation to the respiratory unit (total delay) was 107 days (range: 0-570 days). The mean (S.D.) number of doctors consulted by these patients was 2.6 (1.7). There was no significant difference in the length of delays among the patients according to different ethnic groups and different educational levels (p-values > 0.05). Patients' perception of their symptoms also had no bearing on the length of delays. For both non-small cell and small cell lung cancer, the length of delays did not differ significantly between patients with early and advanced disease (p-values > 0.05).

Conclusion: There are considerable delays in the presentation of patients with lung cancer in our local population.

EARLY EXPERIENCE WITH AIRWAY RESECTION AND STENTING

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We would like to report our early experience with airway procedures (resection and stenting) on the following 3 patients. The first is the case of a 14-year old girl who underwent distal tracheal resection with end-to-end anastomoses for mucoepidermoid carcinoma. The second patient is a 22-year old lady with tuberculous stricture of the left main bronchus and collapse of left lower lobe. She underwent dilatation and Polyflex stent insertion of the left main bronchus. The third patient is a 38-year old man with haemoptysis and stridor secondary to adenoidcystic carcinoma occluding the right main bronchus and carina. He underwent diathermy resection and subsequent Polyflex stent insertion of the distal trachea, carina and proximal left main bronchus.

SURGICAL MANAGEMENT OF PULMONARY ASPERGILLOMA

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Pulmonary aspergilloma is a potentially life-threatening disease resulting from colonization of lung cavities by the ubiquitous fungus Aspergillus fumigatus. Surgical resection remains the definitive treatment of choice but is reported to be associated with high morbidity and mortality.

A retrospective review of patients with pulmonary aspergilloma who underwent surgery at our hospital was conducted.

Between November 1996 and April 2001, 8 patients underwent lung resection for the treatment of pulmonary aspergilloma. There were 5 female and 3 male patients with a median age of 39.4 years (range 24 to 67 years). All patients had previous tuberculosis. Haemoptysis was the predominant symptoms in all cases and 50% of them were admitted at least thrice for life-threatening haemoptysis. Surgical procedures performed were 2 single lobectomy, 4 bi-lobectomy, 1 wedge resection and 1 completion pneumonectomy. There was no operative mortality. Mean post-operative stay was 14 days (range 7 to 30 days). Six of the 8 patients had an uneventful recovery. Two patients required re-thoracotomy for bleeding (both were thrombocytopenic pre-operatively), one of whom subsequently developed lung collapse secondary to sputum retention requiring bronchoscopy. Four patients (50%) did not require any blood transfusion. Seven patients had their residual lung fully expanded prior to discharge from hospital. Follow-up is 100% complete with median follow-up of 24 months (mean 23 months; range 4 to 46 months). All the patients are doing well with no recurrent haemoptysis.

With appropriate pre-operative preparation and meticulous surgical technique, patients with aspergilloma can be operated on with acceptable morbidity and can remain free from recurrent haemoptysis.

CLINICO-EPIDEMIOLOGIC STUDY OF ACUTE RESPIRATORY TRACT INFECTIONS (ARI) AMONG THE STUDENT COMMUNITY OF UNIVERSITY PUTRA MALAYSIA (UPM)

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Acute respiratory tract infections (ARI) are commonly encountered and their prevalence appears to be increasing. The economic burden of these infections on the society is enormous due to the increasing health care cost, absenteeism and loss productivity when working adults are involved. Recurrent respiratory infections can lead to chronic airway diseases and chronic ill health. The management care of these conditions is often complicated by the emergence of antibiotic resistance among some of the commonly implicated pathogens. Little published data are available from tropical countries on epidemiology of ARI among adults in a general practice setting.

Objective of study. To determine the clinico-epidemiology patterns of acute respiratory tract infections among the student community visiting the Student Health Centre (SHC) in Universiti Putra Malaysia.

A descriptive study of prospective ARI subjects among the students (17-40 years of age) visiting the SHC of Universiti Putra Malaysia in the year 1998 was carried out. An illness was considered to be an ARI if at least three of the following complaints were present : running or blocked nose, phlegm (post nasal drip), sore throat or difficulty in swallowing, fever or body pain, ear pain or discharge, hoarseness of voice, headache and cough of less than one week's duration with or without sputum and with or without difficulty in breathing. Data from general physical and clinical examination, and information on management and follow-up care were recorded in accordance to a pre-designed protocol. A random sample of 150 ARI subjects was evaluated for details information.

The total number of ARI cases seen at the SHC, UPM was 22444 in 1997, 22317 in 1998, and 24893 in 1999. The 22317 episodes of ARI observed in 1998 were among 2250 students with an average of 6 episodes per student. The ARI cases were 50.91% of the total cases attended to at the SHC. There was no gender effect observed, 51% were males and 49% females. The mean age was 22 year, and the most common group was the second year students. Antibiotic used 89.3%, self-medication was practiced by 45.3%, 12.3% of the cases had cough with sore throat along mucosa itching. Stick leave for 3 days was given to 54% of the students.

This study on students of UPM with ARI serves as a microcosm for sufferers from ARI and may be used to develop ways to manage the problem effectively. This in turn would help improve the life and work of students in particular, and individuals of other sectors.

RECURRENT RESPIRATORY INFECTION DUE TO SILENT G.O.R. AND ROLE OF 24 hrs pH METRY IN ITS EVALUATION

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Gastrooesophageal reflux is common in both term and preterm infants. Reflux may manifest as vomiting or atypically as recurrent respiratory tract infection in infants or as recurrent bronchopneumonia, apnoea, bradycardia, night cry, irritability, feeding resistance, recurrent sinusitis, otitis media, or as recurrent abdominal pain in verbal children. In order to diagnose the silent cases of GOR 24 hr pH monitoring is widely used. Standardised protocols for oesophageal pH monitoring are well established, quantitative measure of reflux duration, Information of reflux frequency, information on when reflux occurs, symptoms - reflux correlation and information on the oesophageal clearence of refluxed acid could be obtained and quantified. Once the diagnosis is confirmed as GOR these infants of silent variety are managed in the same way as the other group and given prokinetic therapy as well apart from small and frequent feeding, feeding thickeners, postion after feeding and avoidance of jiggling in the cradle. Eventually as months go the maturation factor sets in and reflux caeses, judged clinically by the absence of recurrent respiratory tract infection, thriving normally. Paper being presented to highlight the silent GOR group and pH metry role in its Evaluation.