The 3rd Ministry of Health-Academy of Medicine Malaysia Scientific Meeting & International Congress of Medicine in the Tropics was held at the Shangri-La Hotel, Kuala Lumpur from 1st to 4th November 2000. Abstracts of papers presented follow:

PRE-CONFERENCE WORKSHOP ON GOOD CLINICAL PRACTICE

Health research in Malaysia

Ismail MERICAN

Deputy Director General of Health (Research & Technical Support), Malaysia

Research is a process of enquiry that produces knowledge to improve the diagnosis, treatment, control and prevention of disease. There are two interlinked categories of research: that which increases the understanding of health, ill health and the process of healthcare and that which enables assessment of interventions to promote health, prevent ill health or improve the process of healthcare. The setting up of the National Institutes of Health (NIH) in the Ministry of Health (MOH) will strengthen its research component and bring together under one umbrella five institutes, in order to create a seamless continuum from the identification of research priorities and research questions through carrying out the research to the utilization of the research results in health policy formulation, health management, health promotion and development of better tools for the diagnosis and treatment of nationally important diseases. The Institute for Medical Research (IMR) will focus on biomedical research and the Institute of Public Health (IPH) will be the national focal point for health systems research while the Institute of Health Management (IHM), the Institute of Health Promotion (IHP) and the Network of Clinical Research Centres (CRC) will focus on management research and training for professional staff, socio-behavioural research and clinical research, respectively. Other new institutes may be added in the future, depending on our needs and the progress made in particular areas of research e.g. environmental health research and traditional medicine research. The NIH will help prioritize research activities in health and allocate resources, promote institutional and research capacity strengthening, integration of different skills and greater interaction between researchers, fund managers and policy makers. It will also provide for linkages and networking with other centres of excellence, locally and abroad and help create and enhance the career development of our researchers and scientists. Funding is always a challenge and very competitive and new ways of procuring funds, other than using the Intensification of Research in Priority Areas (IRPA) mechanism, are being explored. Research priority areas for the 8MP (2001-2005) have been identified, with input from all stakeholders in health. Drug-related clinical research is on the increase and in 1999, there were 2 phase I, 5 phase II, 21 phase III and 8 phase IV clinical trials. Several initiatives have been taken over the last 2 years to facilitate quality research. These include the publication of various useful procedural manuals and the Malaysian guidelines for Good Clinical Practice (GCP). The Government has introduced several initiatives to encourage research and development in the private sector which can invest and capitalize on the "best buys" concept where indigenous technology is used to exploit the local market to offset the stiff competition from developed countries e.g. investing in product research and development in tropical diseases like malaria. Traditional medicine research is yet another area that has yet to be fully exploited and viable partnerships between MOH, other ministries, research institutions, the academia, the industry and others are necessary to co-ordinate and harness the expertise available in the country. The future of health research in this country is promising but a lot needs to be done to strengthen our research capacity and capability and establish linkages and forge strategic partnerships with other renowned research institutions worldwide, before Malaysia can be regarded as a major research player in the international arena.

Principles of good clinical practice (GCP)

NOR SHAHIDAH Khairullah

Malaysian Liver Foundation, Malaysia

Clinical trials are defined as a systemic administration of drugs which includes common drugs, radioactive drugs, natural and related remedies and some preparations for external application, or the use of a medical device for the purpose of discovering or confirming efficacy, patterns of adverse effects, pharmacokinetics, etc. These studies are required prior to registration of a new drug or a medical device to ensure the efficacy and safety of these drugs and treatment methods that may be administered to thousands of patients. A clinical investigator has the responsibility for both the patients' well being and that the treatment being offered is the most appropriate in any given case. In order to ensure this, the investigator is obligated to conduct clinical trials within the guidelines of Good Clinical Research (or "Trial"). The term "Good Clinical Practice" (GCP) is accepted internationally and is a term coined for labeling a collection of recommendations, rules and guidelines about how good clinical research ought to be performed. The Food And Drug Agency (FDA) in the United States was the first to issue these kinds of rules and guidelines in the 1960s. The European Union (EU) established guidelines applicable to the entire EU in May 1990. Japan has produced similar guidelines and the WHO has also released guidelines intended for use outside the USA, Europe and Japan. Work which began years ago to further harmonise the US, European and Japanese guidelines within the framework of a large international cooperative forum collectively called The International Conference of Harmonisation (ICH) has resulted in the formalisation in May 1996 of the ICH-6 GCP guidelines. These guidelines are applicable to all clinical trials carried out after January 1997 within the ICH's jurisdiction i.e. USA, EU and Japan. GCP has several purposes. The two principal ones are the protection of the patient's own self interest based on ethical principles originated in the Declaration of Helsinki, and to establish that clinical research be correctly carried out using high standards of quality and in such a manner that it may be verified later. The patient's own interest is primary, and their safety and integrity are protected, prevailing over interests of science and society. This is made possible by emphasizing the role of the ethics committee and making them strictly obligatory. The content and quality of information given to patients is of central significance. The principles also detail instructions about how adverse events are to be collected and reported. Both the quality and verification functions are ensured via instructions on how the study is to be set up, how data is gathered, verified regularly and then stored away for any later inspection. Systems with procedures that assure the quality of every aspect of the trial should be implemented and are emphasized within the principles of GCP.

Investigator's responsibilities

CC LANG

University of Malaya Medical Centre, Kuala Lumpur, Malaysia

The Malaysian Guidelines for Good Clinical Practice was launched last year in order to establish globally applicable standards in the conduct of biomedical research on human subjects in this country. This paper will discuss the functions, obligations and responsibilities of the investigator as defined in these guidelines.

Informed consent

LOKMAN HAKIM S

Institute for Medical Research, Kuala Lurnpur, Malaysia

Informed consent (IC) is a prerequisite for participating in a trial, especially in protocols planned for regulatory submission. The principle of respect for the person (to treat a subject as an autonomous individual) requires that the subject give informed consent to participate in the research project. The

introduction of something new-unknown modifies the implicit contract between the patient and the care provider. Decisions related to care are made on the basis of a protocol that addresses the patients not only as an individual but also as part of a randomised (not personalised) decision process. Random allocation assigns unpredictably, the exposure to an experimental therapy and thus the chance to experience specific benefits and specific risks. Therefore, IC expresses the respect due to the patients who are in the position of choosing whether or not to enroll, and it protects those who propose the new-unknown. It is a process by which a subject voluntarily confirms his/her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. The essential elements (content) in the IC outline the required facts for the patient to make a reasonably informed decision. In legitimate clinical trials, consent procedures should focus on information and on communication and participation of the care provider/investigator and the patient. If the goal of the trial is not directly towards improving patient care, formal IC become more critical and emphasis should be focussed on the conditions of expression of consent.

Sponsor responsibilities

Erike DE VERGA

Sponsor responsibilities, as defied by ICIH GCP cannot be seen isolated from the responsibilities of the investigator and the IRB/IEC. Main categories of sponsor responsibilities are Quality Assurance and Quality Control; Medical Expertise; Trial Design, Trial Management, Data Handling, Record Keeping and Independent Data Monitoring Committee; Investigator Selection; Allocation of Duties and Functions; Compensation to Subjects and Investigators; Financing; Notification/Submission to Regulatory Authorities; Confirmation of review by ERB/IEC; Information of Investigational Products; Manufacturing, Labeling and Coding Investigational Products; Supplying and Handling Investigational Products; Record Access; Safety Information; Adverse Drug Reaction Reporting; Monitoring; Audit; Noncompliance; Premature Termination or Suspension of a Trial; Clinical Study reports and Multicenter Trials. A sponsor may transfer any or all responsibilities to a CRO, however the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. The sponsor is responsible for selecting investigators/institutions. Each investigator should be qualified by training and experience and should have adequate resources to properly conduct the trial for which the investigator is selected. The monitor is the main communication link between the sponsor and the investigator. Monitors are appointed by the sponsor and should be qualified by training, and should have the scientific and/or clinical knowledge to monitor the trial adequately. Monitor's detailed responsibilities are defined by ICH GCP. The monitor visits the site regularly and provides a written monitoring report to the sponsor. The sponsor is responsible for implementing quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data are generated, documented, and reported in compliance with the protocol, GCP, and the applicable regulatory requirements.

Adverse event reporting

ABIDA Syed Haq

National Pharmaceutical Control Bureau, Ministry of Health Malaysia

With the use of any medication comes the possibility of unintended consequences. If the safety of a product is to be assessed and monitored properly, then clearly the registration holder, regulatory authorities, practitioners and consumers must have confidence in the quality and accuracy of the data used to analyze the risk-benefit assessment of a product both before and after it is marketed. During clinical trials, all adverse events (AE), which are defined as any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment, must be reported by the investigator to the sponsor and ultimately to the regulators. By definition, a serious adverse event or reaction is any untoward

medical occurrence that at any dose may result in death, is life-threatening, requires/prolongs hospitalisation causes significant disability/incapacity or congenital abnormalities. Investigators must notify sponsors of serious, unexpected events or death while on the study or within 30 days of treatment, within 2 days of the event and followed-up by a detailed written report within 7 calendar days. Within 7 days, the sponsor should notify all concerned investigators and regulators of findings that could affect adversely the safety of subjects, impact the conduct of the trial or alter the ethics committee's approval/opinion to continue the trial. For marketed products, all adverse reactions, which can be simply defined as an AE where a causal relationship with the drug is suspected, must be reported based on the timelines defined in the protocol s/regulations. It cannot be too strongly emphasized that a reporter is not required to judge whether an event was drug induced though he may usefully express an opinion. For serious AE encountered during preregistration clinical trials, an assessment of causality should be made based on follow-up information which has been evaluated by the investigator. Drug research does not stop when a drug is marketed. Industry and practitioners need to understand that drug safety is a continuum throughout the life of a product and they have a moral obligation to inform regulators on any reactions encountered.

Malaysian GCP guidelines

NOR SHAHIDAH Khairullah

Malaysian Liver Foundation, Malaysia

Throughout the world, thousands of drug trials are performed each year for efficacy and sfety confirmation of new strengths or indications for either existing drugs, generic preparations or completely new substances. In Malaysia, there has been an increasing demand for such drug related research by pharmaceutical companies in recent years as they begin to appreciate the value of collaboration with our local clinicians. The evolution of the Malaysian GCP guidelines started off sometime in 1997 when some researchers in the Malaysian Liver Foundation realising the generall lack of awareness and adherence to GCP of many of our clinical trialists decided to organize the first GCP workshop in collaboration with the Ministry of Health as a precongress activity of a regional Hepatobiliary Meeting "The Liver Update". A spinoff from this precongress workshop were a series of other GCP workshops conducted in the country. In 1999, during the 3rd Liver Update, another precongress workshop was organised to deliberate over a consensus guidelines to cater for our local requirements. This special meeting was chaired by the subcommittee charged to develop the document by the Ministry of Health's Steering Committee for Clinical Research which was later deliberated, discussed, voted on and passed by representatives from the local universities, pharmaceutical industries, drug control authority, pharmaceutical associations as well as consumer associations during the 33rd Malaysia-Singapore Congress of Academy of Medicine in August 1999. The Malaysian GCP guidelines was officially launched in November 1999 by the Director General of Health and has since been used for the conduct of GCP workshops and training throughout Malaysia. The Malaysian guidelines for GCP is adapted from the ICH Harmonised Tripartite Guideline E6 GCP guidelines with local requirements added in to reflect local legislations and practices.

Clinical trial protocol, essential documents for the conduct of a clinical trial

Erike DE VERGA

The protocoldescribes the objective(s), design, methodology, statistical considerations and organization of the trial. The contents of the protocol should generally include all topics described in the ICH GCP guidelines. Since the protocol and the clinical trial/study report are closely related, the ICH guidelines for Structure and Content of Clinical Study Reports may need to be considered when writing a protocol. Essential Documents individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. These documents serve to demonstrate the

compliance of the investigator, sponsor and monitor with the standards of GCP and with the applicable regulatory requirements. Essential documents also serve a number of other important purposes. Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor. These documents are also the ones that are usually audited by the sponsor's independent audit function, and inspected by the regulatory authorities as part of the process to confirm the validity of the trial conduct and the integrity of the data collected. ICH GCP specifies which documents should be filed either at the investigator/institution or sponsor files, or both. The essential documents are grouped in 3 sections: before, during and after the trial, according to the stage of the trial in which they are typically generated.

PLENARY LECTURES

100 years of medical research in Malaysia.

M JEGATHESAN, * Sew Keoh TEN and * Munn Sann LYE

Sistem Hospital Awasan Taraf, Kuala Lumpur and *Institute for Medical Research, Kuala Lumpur, Malaysia

The hundred years story of health research in Malaysia parallels that of the history of the Institute for Medical Research (founded 1900) for the first seven decades. After that the medical faculties of our universities incrementally make their presence felt as key players on the national scene. The story is perhaps best told in terms of three eras: 1900-1963, the IMR era (both pre- and post independence); 1963-1986, the era of the advent of the universities and from 1986 onwards, the era of IRPA (the Intensification of Research in Priority Areas). It is a story earmarked by pioneers, personalities, partnerships and breakthroughs. Personalities like Hamilton Wright, Ungku Omar, Danaraj, Khalid Sahan, Omar Abdul Rahman and Abu Bakar Suleiman. Partners like the United States Army Medical research Unit, the Hooper Foundation, the WHO, SEAMEO-TROPMED, IDRC and JICA, universities in Europe, North America and Japan. Breakthroughs like the discovery of the cause of beriberi, the field stain, in vitro culture of filarial larvae, commercialiable diagnostic kits, and various findings that led to significant policy change and/or program implementation in areas such as applied nutrition, diarrheal disease, acute respiratory infection, antibiotic and disinfectant usage and vector borne diseases. It is a story of gradual build up of research capacity and institutional strengthening and funding sources albeit with occasional land marking spurts. Timely stocktaking at the turn of the century will reveal how health research has fared in this country, not only in comparison with the community of nations at large but also with other sectors within the country and with its overall socioeconomic development. We leave the century with a good national research infrastructure and mechanism in place but with clear gaps and shortfalls, particularly in the area of human resources and appropriate research mix. The lessons learnt will serve as a backdrop and help forge new visions and action plans for the coming decades. Proposed strategies should include profile enhancement of research and researchers, debureaucratisation of procedures and mechanisms, internalization and internationalization of research as well as the emplacement of a seamless research continuum.

Prion disease

Janice R ANDERSON

Department of Histopathology Addenbrooke's Hospital Cambridge United Kingdom

Bovine spongiform encephalopathy (BSE), a previously unknown disease of cattle, became a focus of world attention as it reached almost epidemic proportions in the UK in the 1980's. Predictions that it would be transmissable to man appeared to have been confirmed when a new variant of Creutzfeldt-Jakob Disease (CJD), a hitherto obscure dementing disorder, was detected in 1996. Histological similarities between the brains of sheep suffering from scrapie and of humans dying of kuru and Creutzfeldt-Jakob Disease led to discovery of transmissable human neurodegenerative

diseases with an apparently unique pathogenesis. The only identifiable source of infectivity in scrapie-infected animal brain was a protein designated PRION protein (PrP) by Prusiner, (from PROteinaceous INfectious particle). It was shown to be homologous with a larger, normal, membranebound protein encoded by a highly conserved host cell gene but a different tertiary structure of PrP conveyed resistance to proteolysis and ability to polymerise into amyloid fibrils. The relevance of PrP was strengthened by discovery of rare familial human neurodegenerative diseases, including familial CJD, linked to mutations in the PRP genome. The majority of cases of CJD are sporadic and lack PrP gene mutation but both forms have been transmitted to laboratory animals. Iatrogenic human disease has also been transferred via corneal and dural grafts and pituitary-derived growth hormone. The enigma of PRION infectivity is explained by catalytic conversion of the normal to the abnormal protein via dimerisation. Separation of heterodimers initiates a chain reaction and progressive accumulation of prions ultimately leads to spongiform encephalopathy and widespread neuronal death. Certain human PrP isoforms may have a greater susceptibility to dimerisation and conformational transformation. If PrP is the seed, theoretically CJD may arise through germ-line mutation, accidental inoculation, or somatic mutation. Conformation and glycosylation distinguish different PrP strains. Whereas there are multiple PrP strains of scrapie only three are identified in sporadic CJD. In 1986 another prion disease BSE emerged in cattle in the UK. BSE is widely believed to have been transmitted through the food chain and in 1996 a new variant of human CJD with the same strain characteristics appeared in young persons. Whilst it is postulated that new variant CJD was transmitted to man through consumption of contaminated beef there are many uncertainties. The real human risk is unknown and even the 'prion only'hypothesis is still challenged.

Vector-borne diseases and human development

Harold TOWNSON

Liverpool School of Tropical Medicine, United Kingdom

This plenary paper discusses the influence of vector-borne disease on human development. Estimates are provided of the economic impact of the most important vector-borne diseases, as well as their contributions to disability and overall mortality. The risk from emergent vector-borne diseases and their possible globalisation will be evaluated. Attention will also be given to ways in which development may lead to new problems with vector-borne disease. The paper will conclude with a consideration of the needs for both surveillance and responsive public health units. The costs of emergency interventions where new outbreaks occur can be high. Furthermore, on a global basis, declining human capacity within the field of vector-borne disease epidemiology and control is reducing our capacity to deal with the threats these diseases pose to human health and development.

HIV management and treatment strategies

Praphan PHANUPHAK

Faculty of Medicine, Chulalongkorn University and the Thai Red Cross AIDS Research Centre, Bangkok, Thailand

HIV-infected individuals require both psychosocial and medical care, starting from the first day of known seroconversion. Regular medical and immunologic (CD4+ cells) follow-up is essential to prevent rapid progression of disease. Prophylaxis of certain opportunistic infections (OI) and antiretrovirals (ARV) can be initiated, whenever possible, according to set clinical and immunologic criteria before the individuals become sick. For countries with high incidence of tuberculosis and cryptococcal meningitis, primary prophylaxis of these 2 conditions is considered cost-effective, even with limited resources. However, it is not routinely practiced in Thailand. Diagnosis and treatment of certain OI's such as MAC and CMV in developing countries are limited by the cost of investigations and treatment as well as by physician's attitude to the performance of invasive investigations. Antiretrovirals are expensive, therefore, often regarded as impossible therapeutic approach for developing countries. However, efforts should be made both at the governmental,

physician, patient, private and community levels to seek strategies that will enhance access to ARV to as many patients as possible. Concerted efforts and commitment from all key players in Thailand, including the pharmaceutical industry, are good examples for countries with similar economic levels to learn. Although drug price eventually has to come down, highly active antiretroviral therapy (HAART) is still far from real most developing countries. Less than ideal but readily affordable regimens such as double or triple nucleosides, hydroxyurea and structured treatment interruption (STI) must be seriously evaluated in each local setting. Although the benefit may not last long, these regimens may prove cost-effective if they are given at the critical timing which may be much later than that recommended in the West.

SPONSORED SYMPOSIA

Extended-spectrum beta-lactamases (ESBLs) - Are we the culprits?

David L PATERSON

University of Pittsburgh Medical Center, Pittsburgh, USA

Extended-spectrum beta-lactamase (ESBL) producing organisms are predominantly found in hospitalised patients, especially those residing in Intensive Care Units. Prolonged hospitalisation and greater severity of illness are clearly risk factors for acquisition of ESBL producers. Patients undergoing haemodialysis and those with severe burns are also at increased risk. Although published reports of outbreaks of ESBL producers in nursing home mainly emanate from North America, unpublished experience suggests that nursing home outbreaks occur worldwide. True communityacquired cases of infection have been infrequently reported, although increasing use of orally administered third generation cephalosporin may lead to more cases in the future. It is clear that in both hospitals and nursing homes, asymptomatic carriers of ESBL producers substantially outnumber those with clinical disease. Outbreaks of infection frequently occur with organisms of the same clone, indicating failure of adequate infection control measures. Additionally, prior use of third generation cephalosporins such as ceftriaxone (usually as empiric therapy) is a major risk factor for development of ESBL producers. Control of outbreaks of ESBL producing organisms has been achieved with restriction of use of cephalosporins and enhanced infection control procedures. Patients with serious infectious due to ESBL producers most commonly present with hospital-acquired pneumonia, intraabdominal abscesses related to previous abdominal surgery, bacteremia related to use of intravascular or urinary catheters and bum wound infections. A number of cases of nosocomial meningitis complicating neurosurgical procedures have been described. Successful clinical outcome has most frequently been associated with use of imipenem. Quinolones should be regarded as second-line therapy. Increasing chromosomally mediated quinolone resistance and now the advent of plasmidmediated quinolone resistance limit the usefulness of this class against organisms like cephalosporinresistant Klebsiella. Cefepime, ticarcillin/clavulanate and piperacillin/tazobactam have not been extensively tested in treatment of serious infections with ESBL producers; clinical failure may be related to rising MICs for these antibiotics as inoculum of organisms rises. These antibodies should not be used for serious infectious with ESBL producers if imipenem is available. Challenges to the control and treatment of ESBL producers in the future will include the advent of strains with multiple resistance mechanisms (that is, emergence of "panresistant" ESBL producers) and detection of ESBLs in increased frequency in bacteria other than K. pneumoniae.

NSAIDs and the GI tract: past perspectives and future promises Richard H HUNT

Division of Gastroenterology, McMaster University Medical Center, Canada

The gastroscopic demonstration of gastrotoxicity of aspirin was first demonstrated century ago and the gastrointestinal adverse events of non-steroidal anti-inflammatory drugs (NSAIDs) have been increasingly reported in the literature ever since. Despite their undoubted efficacy for the treatment

of joint inflammation and musculoskeletal injury, a significant proportion of patients taking NSAIDs may experience gastrointestinal symptoms usually dyspepsia, and endoscopic abnormalities, which range from petechial hemorrhages to fatal' complications of peptic ulcer. The risk of developing a severe GI adverse event varies from patient to patients and from NSAID to NSAID. Numerous epidemiological studies have shown that the use of NSAIDs increases the overall risk of peptic ulcer bleeding (OR 3.09-4.5) adverse events-related hospitalisations (OR 3.9-5.5), GI surgery (OR 7.75), and GI adverse events-related death (OR 4.79-7.62). Certain factors may predispose NSAID users to a greater risk of developing a severe GI event including: patients older than 60 years (OR 2.86), previous ulcer history or ulcer bleeding (OR 4.76-9.5), high dose or multiple NSAIDs (OR 4.0-23.3), concomitant corticosteroid therapy (1.83-4.4), and concomitant anticoagulant therapy (OR 2.1-16). Many agents have been developed to minimize these side effects with varying degree of success and acceptance. Currently, seven classes of FDA approved NSAIDs are available in the USA. These are proprionic acids, anthranilic acids, salicylic acids, acetic acids, oxicams, naphthylalkanones and cyclo-oxygenase-2 (COX-2) specific inhibitors. Results from the ARAMIS database of adverse events and meta-analysis have shown that, among the conventional NSAIDs, ibuprofen and salsalate are the least toxic NSAID, whereas tolmetin, fenoprofen, indomethacin, piroxicam, ketoprofen and azapropazone are among the most toxic to the GI tract. More recent analyses have suggested that some newer NSAIDs including nabumetone, meloxicam and etodolac have a significantly lower incidence of severe GI side effects, expressed as PUBs than comparator NSAIDs. This is believed, at least in part, to be due to a preferential inhibition of COX-2 by these NSAIDs. Subsequently, it was suggested that there is a correlation between the risk of GI complications and the potency of selective inhibition of COX-2/COX-1. The more selective inhibition of COX-2 over COX-1, the less the risk of GI complications. However, the assay methods used with the conventional NSAIDs have been widely variable and these ratios are controversial. Nevertheless, with the-recent development of highly specific COX-2 inhibitors such as celecoxib (Celebrex) and rofecoxib (Vioxx), GI toxicity appears to be minimised. Data on GI safety with these two agents have shown significantly lower gastric mucosal damage as assessed in short term endoscopic studies compared to naproxen or ibuprofen, and virtually no difference compared to placebo. Even at doses 2-4 times higher than those known to be effective for treating osteoarthritis, rofecoxib has been shown to be as safe as placebo and does not increase fecal blood (51Cr labelled red blood cells) loss. Furthermore, macromolecular permeability of the small intestine is not increased by rofecoxib, in contrast to that seen with indomethacin. Endoscopic studies in OA patients, including those considered at high risk (prior ulcer history, age etc.) taking rofecoxib over six months have shown no significant increase in ulcers over placebo and significantly less than ibuprofen. Moreover, patients taking the COX-2 specific inhibitor had fewer dyspeptic symptoms, required less GI medications and underwent fewer clinically driven GI investigations than those taking non-specific NSAIDs. Analysis of the adverse events in clinical trials of celecoxib and rofecoxib indicates an approximately 50% risk reduction for perforations, ulcers and bleeds and the recent VIGOR study confirms reductions of > 50% in clinical upper GI events (54%), complicated upper GI events (57%) and any GI bleeding (62%) in a prospective outcome study of more than 8000 RA patients taking rofecoxib as compared to naproxen. There was a slight but significantly lower rate of myocardial infarction in those taking naproxen (0.1%) compared with those taking rofecoxib (0.4%), which is considered due to a protective effect of naproxen which effects an -95% inhibition of thromboxane across the whole dosing interval, and this is likely to provide a protective effect similar to that of aspirin. The introduction of COX-2 specific agents offers the opportunity for safe and effective treatment for patients who are at high risk for developing GI complications. Large, long-term, randomised and controlled studies are needed in the future to access the overall safety of COX-2 specific inhibitors, especially in organs outside the GI tract.

MIXED SYMPOSIUM 1: MALARIA UPDATE

Malaria vaccines

FEG COX

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, UK

Despite vast expenditure of time and money, progress towards a vaccine against malaria has been slow and disappointing but the future is more promising. There are currently five approaches to the development of a vaccine: (1) pre-erythrocytic vaccines directed against the sporozoite and the early liver stages, (2) erythrocytic vaccines directed against the asexual blood stages and, in particular, the merozoite as it invades the red cell, (3) combination (cocktail) multi-stage vaccines incorporating the genes for antigens representing different stages in the life-cycle, (4) transmission-blocking vaccines directed against the sexual stages in the blood and in the mosquito and (5] anti-disease vaccines directed towards neutralising parasite products or by-products involved in pathology. Vaccines based on the repeat region of the circumsporozoite protein (CSP) have not been successful but newer recombinant vaccines based on molecules from the non-repeat CSP regions are currently being assessed. The emphasis is also switching from antibody inhibition of sporozoite activity to possible cytotoxic responses directed against the early liver stages. Experimental vaccines based on the erythrocytic stages have used a large number of different antigens associated with merozoites and schizonts but attention is gradually being focused on a few relevant ones such as the merozoite surface protein (MSP-1). So far, the only widely tested erythrocytic vaccine is a synthetic one, SPf66 based on three asexual stages proteins. Preliminary studies in South America indicated that SPf66 reduced the number of episodes of malaria but it was less successful when used to immunise children in sub-Saharan Africa. Experimental studies suggest that it should be possible to develop a vaccine against malaria and, drawing on the potential of molecular biology, attention is now centering on the construction of multi-stage vaccines incorporating the genes for up to 21 antigens and trials of these are currently being planned. There have been no trials using transmission-blocking or anti-disease vaccines but the genes for the molecules involved may be incorporated into combination vaccines in future. However, there are major hurdles to be overcome and a widely available commercial vaccine will be many years away.

Research on antimalarial drugs at the Bangkok Hospital for Tropical Diseases, Thailand

Sornchai LOOAREESUWAN

Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

With the emergence of multidrug resistant falciparum malaria in Thailand, new drugs and drugs in combination are urgently needed. New antimalarial drugs have been investigated at the Hospital for Tropical Diseases in the recent years. Atovaquone, a hydroxynaphthoquinone, was evaluated and found that Atovaquone alone proved safe and effective. All patients treated had clinical cure, however, one third of patients had late recrudescence (RI). When it was combined with proguanil, the cure rate increased to 100%. This combination is now developed as a fixed drug named Malarone®. Artemisinine derivatives such as artesunate, arteniether, arteether, dihydroartemisinin are also tested at the Bangkok Hospital for Tropical Diseases. Artesunate and artemether alone with a total dose of 600 to 750 mg. given over 5-7 days produced cure rates of 80 to 95%. Artesunate or dihydroartemisinin suppositories with the dose of 10 mg/kg/day have been proved successful for the treatment of severe malaria. The artemisinin derivatives when used in combination with mefloquine given over 3 days improved cure rates to 95-100%. Dihydroartemisinin alone with a total dose of 480 mg given over 5 days gave a cure rate of 90%. Arteether, a WHO/TDR supported drug, has been evaluated in the hospital and now has been registered for use in severe malaria under the name artemotil. Other combinations (artemisinin derivatives combined with lumefantrine or doxycycline and mefloquine combined with tetracycline or doxycycline) have also been evaluated with improvement in cure rates. Recently, a fixed drug (artemether plus lumefantrine) named Coartem® (six doses

given over 72 hours) proved safe and effective for treatment of falciparum malaria and has been registered for used in many western countries. At present, studies with the combination of artemisinin derivatives plus mefloquine (in various doses and duration of treatment) are being investigated. In general, artemisinin derivatives (12 mg/kg given over 2-3 days) combined with mefloquine (25 mg/ kg total dose) has been a standard regimen for treatment of multidrug resistant falciparum malaria in Thailand. Until proven otherwise, the drug combinations are still recommended for all adult patients suffering from acute uncomplicated falciparum malaria contracted in multidrug resistant areas. In severe malaria, the choice of antimalarial chemotherapy depends on the clinical severity, the drug sensitivity of the parasites and the availability and preparation of the drug. Chloroquine is still the drug of choice for chloroquine-sensitive parasites occurring in some areas in Africa. Quinine and quinidine are the only widely available drugs which are effective against chloroquine-resistant strains. Two new synthetic antimalarial drugs, mefloquine and halofantrine are also effective against chloroquine resistant strains, but they have no parenteral formulation and cases of resistance to these drugs have already been reported. Qinghaosu (artemisinin and ancient Chinese herbal medicine) and its derivatives have been used successfully in treating both uncomplicated and severe falciparum malaria. Their effectiveness in eliminating the parasites have been extensively documented, however, the recrudescent rate is rather high (10-30%). The recrudescent rate depends upon the dose, duration of artemisinin derivatives used and severity of disease: the more severe the higher the recrudescent rate. Intravenous artesunate (2 mg/kg/day, with a loading dose, total dose of 480 mg) is effective but not available in some countries. Recently, intramuscular arteether (Artemotil®) developed by a Dutch company under support by WHO/TDR has proved safe and effective for the treatment of severe malaria. It is useful in remote areas where intravenous facilities are not available. In remote areas, artesunate suppositories is preferable as it can be applied by unskilled personnel (e.g. mothers, health staff). The early treatment before reaching hospital might reduce mortality and morbidity of malaria. In summary, in Thailand drugs for treatment of uncomplicated malaria is the combination of artesunate (10 mg/kg/day) plus mefloquine (8 mg/kg/day) given for 3 days or Coartem® (six doses in 2 days) or quinine 10 mg/kg 8 hourly plus tetracycline 250 mg 6 hourly for 7 days, in patients aged 8 years and over. In treating severe malaria, early diagnosis and early treatment are vital and the aim is to save the patient's life. Prompt administration of an adequate and effective antimalarial drug is needed once the diagnosis is made. The antimalarial drugs of choice are intravenous quinine, or artemisinin derivatives. Other symptomatic and supportive treatment include careful monitoring of fluid input and urine output, frequent observations for complications with appropriate treatnient and good nursing care. In spite of these efforts, the mortality of severe malaria is still high.

Roll back Malaria

Ah Suan TEE

Malaysia

There are at least 300 million cases of acute malaria in the world each year with many of them causing severe illness associated with time away from work or studies. Each year, at least a million people die of malaria in tropical and subtropical regions of all continents, particularly in Africa. Among the most vulnerable populations are children under five and pregnant women. The disease is a particular burden for the poorest countries. In several regions - particularly Asia and Latin America - mortality levels have declined. However, progress is now threatened as a result of the emergence of drug resistant forms of the parasite and new epidemics, which reflect climate change, population movements or breakdown in control measures. A range of interventions has been shown to be effective in reducing the malaria burden but many of these have been used inefficiently or underexploited. To counter the malaria scourge, the Roll Back Malaria (RBM) initiative was announced in July 1998 by Dr. G.H. Brundtland, the Director General of WHO, and officially launched with the World Bank, UNDP and UNICEF in October 1998 with the aim of halving deaths due to malaria by 2010. The six elements of the RBM strategy build on the WHO global malaria control strategy which was endorsed in Amsterdam in 1992. RBM is also supporting malaria eradication where feasible (e.g. the European and Eastern Mediterranean Regions). Monitoring and evaluation of programme impact is a cross-cutting feature of all interventions.

MIXED SYMPOSIUM 2: SEPSIS SYNDROME

Resistance patterns of nosocomial pathogens in intensive care units in Malaysia N PARASAKTHI

Department of Medical Microbiology, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

Management of critically ill patients with infections in intensive care units poses many challenges. The use of broad-spectrum antibiotics in such settings is high and may predispose to the development of resistant organisms that may then become disseminated by nosocomial transmission. Infections with methicillin-resistant staphylococci and Gram-negative bacilli are common in intensive care units. Extended-spectrum b-lactamase (ESBL) producing Klebsiel/a, inducible-Enterobacteriaceae and carbapenem-resistant P. aeruginosa and Acinetobacters are of particular concern as nosocomial pathogens in Malaysia. Between 1997 and 1998, a multi-centre study was carried out to determine the species prevalence and antimicrobial susceptibility pattern among Gram negative bacilli in four adult ICUs in Malaysia. Four hundred and ninety-nine isolates of which 411 were nonduplicates and 86 were repeats, were obtained from 288 patients. The most common isolates in order of frequency were Acinetobacters (34%), P. aeruginosa (24%), Klebsiella (22%), inducible Enterobacteriaceae (7%) and E. coli (6%) Seventy of the isolates were from blood; Acinetobacters were the predominant isolate from bacteremic infections followed by Klebsiella species and P. aeruginosa. Inducibles accounted for a small proportion (7%) of bacteremic infections. The species prevalence of isolates from CVL and respiratory tract was also reflective of the overall distribution of the isolates from all body sites.

Sepsis - pathogenesis and pathophysiology

David L PATERSON

University of Pittsburgh Medical Center, Pittsburgh, USA

Sepsis and its sequelae represent a continuum of clinical and pathophysiological severity. The following clinically recognizable stages can be seen: (I) sepsis - the systemic response to infection manifested by two or more of (a) temperature of>38°C or <36°C, (b) tachycardia (>90 beats/minute), (c) tachypnoea (>20 breaths/minute) or PaCO₂<32 mm Hg, (d) white blood cell count >12 x 10⁹/L, or $<4 \times 10^9/L$, or >10% immature (band) forms; (2) severe sepsis - this is sepsis associated with organ dysfunction or hypoperfusion, as manifest by alteration in mental state, hypoxaemia, elevated plasma lactate level or oliguria (urine output <30 mL for at least one hour); (3) septic shock - this is sepsis induced hypotension (i.e. a systolic blood pressure <90 mmHg or a reduction of >40 mm Hg from baseline) despite adequate tluid resuscitation; and finally (4) multiple organ dysfunction syndrome (MODS) which can be broadly defined as the presence of altered organ function in an acutely ill patient such that homeostasis can not be maintained without intervention. Both Gram positive and Gram negative bacteria induce a variety of pro-inflammatory mediators, particularly cytokines (interleukins and tumor necrosis factor). Such cytokines play a pivotal role in initiating sepsis and shock. Of particular relevance for the induction of cytokines are three types of bacterial cell wall components - endotoxin (lipopolysaccharide - present only in Gram negative bacteria), peptidoglycan (present in Gram positive and Gram negative bacteria) and lipoteichoic acid (present only in Gram positive bacteria). Some bacteria also secrete powerful exotoxins that are not a part of the cell wall. A complex, cascading interaction occurs between tumor necrosis factor, interleukins 1, 6 and χ complement, the intrinsic coagulation pathway, nitric oxide, neutrophils and lipid mediators. These mediators have effects on every organ system in the body and result in the clinical manifestations of sepsis described above.

Sepsis - treatment strategies

David L PATERSON

University of Pittsburgh Medical Center, Pittsburgh, USA

Treatment of sepsis entails a rapid, but thorough, early evaluation and urgent resuscitative efforts carried on in parallel with efforts to determine the source of sepsis and properly directed empirical antimicrobial therapy. When initial resuscitation has been accomplished and diagnosis established, definitive medical and surgical management of the infectious problem follows with continued careful attention to organ system dysfunctions. Numerous authors have found that the most important predictive factor of outcome in sepsis was the adequacy of early antimicrobial therapy. The majority of episodes of sepsis are due to Gram negative bacterial infection. Unfortunately, empiric antibiotic choice is made difficult by multiple antibiotic resistance mechanisms exhibited by these organisms. Foremost of these is beta-lactamase production. Klebsiella pneumoniae and Escherichia coli may produce extended-spectrum beta-lactamases (ESBLs) which can inactivate third generation cephalosporins, aztreonam and penicillins such as piperacillin or ticarcillin. An association exists between ESBL production and ciprofloxacin resistance further limiting antibiotic options for this type of infection. Imipenem remains active against ESBL producing organisms and in clinical trials has been associated with the lowest mortality rate for this type of infection. Gram negative organisms such as Enterobacter, Serratia and Citrobacter may produce a different type of beta-lactamase (termed ampC) which also inactivates third generation cephalosporins, aztreonam and penicillins such as piperacillin or ticarcillin. Imipenem, quinolones and aminoglycosides remain active against such organisms. *Pseudomonas aeruginosa* is probably the most difficult organism to treat in sepsis. Antibiotic options are limited by an impermeable outer membrane plus a wide variety of betalactamase enzymes. Combinations of active drugs are often used to treat sepsis due to P. aeruginosa.

MIXED SYMPOSIUM 3: HEMOSTASIS AND THROMBOSIS

The missing growth factor - thrombopoietin

Beng Hock CHONG

The Centre for Thrombosis and Vascular-Research, University of New South Wales and Haematology Department, Prince of Wales Hospital, Sydney, NSW, Australia

It is known for many years that there are megakaryocyte (MK) -specific growth factors but these factors were not isolated nor characterized. Studies in 1980s and early 1990s suggested the existence of two factors: Megakaryocyte-ColonyStimulatingFactor (MK-CSF) which stimulates megakaryocyte proliferation and Thrombopoietin (TPO) which induces megakaryocyte differentiation. It was not until 1994, when four groups independently cloned and characterized this elusive growth factor. This factor in fact has the activity of both MK-CSF and TPO, and for simplicity, it is now called TPO. The main sources of TPO are liver, kidney and bone marrow but it is also expressed at very low levels in many tissues. Gene knock-out studies showed that it is the major regulator of platelet production. The liver and kidney TPO production is constant but bone marrow stromal cell TPO production varies inversely with the circulating platelet level. This indicates that there is a local feed back control in the marrow where platelets are produced. We found that the local regulation is mediated by MK and platelet a-granular proteins such as platelet factor 4 (PF4) and thrombospondin. TPO regulates megakaryocyte proliferation and differentiation by binding to its receptor, c-mpl on MK cells, and activates specific intracellular signal transduction pathways (e.g. Jak2/Stat3 and 5) and transcription factors (e.g. GATA 1 & 2 and FOG). These processes lead to activation or repression of genes that control megakaryocyte development and consequently platelet production.

Management of ITP in pregnancy

Muhammad Abdul JAMIL

Department of Obstetrics and Gynecology, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Idiopathic thrombocytopenic purpura (ITP) occurs more commonly in young women and is one of the commonest immune mediated disorders in pregnancy. Four clinical situations are recognized. 1. Gestational thrombocytopaenia. A condition in pregnancy invariably associated with a platelet count of greater than 100 x 10⁹/L and is associated with a very low incidence of fetal thrombocytopenia. 2. Thrombocytopaenia due to maternal disease.e.g. SLE, antiphospholipid syndromes, HIV infection and drugs such as heparin. Serious obstetrical disorders like abruptio and IUD is also associated with thrombocytopenia. 3. Autoimmune thrombocytopenia. Commonly associated with low platelet counts in the fetus at an estimated incidence of 20-40% (recent papers indicate a lower estimate). The management of ITP in pregnancy is complicated by the fact that fetal thrombocytopenia is difficult to diagnose and carries substantial risks during the delivery process with rare cases of fetal hemorrhage. 4. Alloimmune thrombocytopenia. A serious fetal disorder with no maternal significance occurring in 1 in 2000 pregnancies. It is caused by the passage of maternal IgG antibodies against fetal alloantigens on the fetal platelets. Unfortunately there are no laboratory studies that can be precisely performed in the mother that may predict the occurrence of fetal thrombocytopenia. Maternal management is usually directed towards treatment of maternal symptoms. Maternal treatment is inconsistently associated with changes in the fetal platelet count. Obstetric management is aimed at reducing the risks of life threatening fetal hemorrhage occurring at the time of delivery and is directed towards the obtaining of fetal platelet samples in order to plan an appropriate strategy for delivery. Fetal blood samples are obtained either by a scalp vein puncture at the time of delivery or earlier in gestation by the use of percutaneous umbilical blood sampling (PUBS). Fetuses with platelet counts of less then 50 x 109/L are generally delivered by cesarean section whereas those with counts greater than 50 x 109/L are allowed to proceed with vaginal delivery. The use of IV IgG therapy during pregnancy has theoretical implications on improving platelet counts in the mother at risk of severe hemorrhage. It however cannot be considered to be appropriate treatment for the prevention of fetal thrombocytopenia, since the exogenous transport of IV IgG across the placenta appears to be inconsistent and unpredictable. Conclusion: ITP in pregnant women carries a small morbidity risk to the fetus. In contrast alloimmune ITP results in platelet destruction in the fetus with risk of bleeding in the fetus and effort should be made to identify high risk fetus and to consider intrauterine intervention to prevent intracranial bleeding.

Heparin-induced thrornbocytopenia

Rudy Seok Ching YEOH

Faculty of Medicine & Health Sciences, University Putra Malaysia, Selangor, Malaysia

Heparin is widely used in medicine for the prevention and treatment of thromboembolic disease. One potentially fatal side effect of heparin that is increasing being recognized is heparin-induced thrombocytopenia (HIT). This condition is associated with potentially fatal thromboembolism involving both the venous and arterial systems. In addition to this, a new syndrome of warfarin-induced acral tissue necrosis in patients with HIT and deep venous thrombosis was recently described. Two clinically distinct types of HIT have been described: type I and type II HIT. Type I HIT is characterized by an early onset (usually within 48 hrs of commencing heparin), mild thrombocytopenia (platelet count rarely dropping below $100 \times 10^9/L$) and occasionally platelet count returning to normal even with continuation of heparin therapy. The underlying cause is non-immune in nature and this type is of no known clinical significance. HIT type II is an immune-mediated reaction caused by an immunoglobulin (usually IgG) that occurs 5-14 days after commencement of heparin. It has been clearly demonstrated that the target antigen recognized by the HIT-IgG is a heparin/platelet factor 4 complex. The 2 most commonly used laboratory methods are the serotonin

release assay (SRA) and the platelet aggregation test (PAT). Both are functional assays. Recently antigenic tests have come into use, using enzyme-linked immunosorbent assay (ELISA), whereby the patient immunoglobulin (antibody) recognizes the heparin/platelet factor 4 complex (antigen). Treatment includes stopping heparin. The 2 currently favoured drug treatment options are danaparoid and hirudin. Argatroban is another promising agent.

MIXED SYMPOSIUM 4: CHRONIC BACK PAIN

Multidisciplinary approach to the management of chronic back pain

MS CARDOSA

Anaesthesia Unit, Hospital Selayang, Selangor, Malaysia

Approaches to the management of chronic back pain range from administration of various types of analgesics to surgery and nerve blocks to physiotherapy and manipulation, either singly or in combination. Multidisciplinary management of chronic pain is based on the biopsychosocial model of chronic pain, which recognizes that nociception and pain are interlinked with suffering and pain behaviour which in turn is linked with the environment of the patient. Multidisciplinary management of chronic back pain addresses three aspects of the problem: medical, physical and psychological, beginning with the multidisciplinary assessment of the patient. The members of the team include a pain specialist (an anaesthetist, physician or surgeon), who assesses the patient from the medical viewpoint, a physical therapist who assesses the patient's musculoskeletal system and physical function and a clinical psychologist or psychiatrist who assesses psychological factors. Pain Management Programs employ a combination of education, rationalisation of medication, a graded physical therapy program and cognitive behaviour therapy, with the overall aim of helping patients learn to manage their pain, to lessen distress and suffering, to improve mood, to increase function and accelerate return to a normal life. Meta-analyses of studies that evaluated the efficacy of multidisciplinary treatments for chronic back pain revealed that multidisciplinary treatments are superior to no treatment, waiting list, and single-discipline treatments like medical treatment or physical therapy. There were also additional benefits of earlier return to work and decreased use of the health care system. In Malaysia, although there are pain clinics where multidisciplinary assessment of patients with chronic pain are carried out, to date there are no multidisciplinary Pain Management Programs available. The challenge facing Pain Management practitioners in Malaysia is how to carry out a Pain Management Program in a multiethnic, multicultural society.

Surgery for a 'failed back'

ABDUL MALIK Hussein

Malaysia

It is estimated that good outcome from spinal surgery ranges from 50% - 80% depending on the skill of the surgeon and complexity of the case. We discuss the causes, investigation and treatment of a 'failed back'.

Review of non-surgical treatment modalities

TL LEE

Department of Anaesthesia, National University of Singapore, Singapore

Low back pain (LBP) is a major health problem and a major cause of medical expenses, work absenteeism and disablement. Although LBP usually is a self-limiting and benign disease that tends to improve spontaneously over time, a large variety of therapeutic interventions are available for its management. However, the effectiveness claimed for most of these interventions have not been

convincingly demonstrated and consequently, the therapeutic management of LBP varies widely. Ongoing literature searches and analyses have identified four alternative treatment categories as having at least some evidence to support clinical efficacy for the treatment for back pain: acupuncture; homeopathic therapies; manual/manipulative therapies; and mind-body therapies. Modern acupuncturists use not only traditional acupuncture points (APs) but also non-meridian APs and trigger points. Acupuncture commonly includes manual stimulation of the needles, but various adjuncts often are used in modem forms of the therapy including electrical acupuncture, injection acupuncture and acupuncture with moxibustion. It has been suggested that acupuncture might act according to principles enunciated by the gate control theory of pain. There also is some evidence that acupuncture may stimulate the production of endorphins, serotonin and acetylcholine in the central nervous system, enhancing analgesia.

MIXED SYMPOSIUM 5: PAEDIATRIC INTENSIVE CARE

The use of albumin in the ICU

Lucy Chai See LUM

Division of Paediatric Critical Care, Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

In this era of cost-conscious health care, the rational use of albumin should be reviewed carefully. Albumin is the main product of protein synthesis in the liver. It has a molecular weight of 69,000 Daltons. Albumin is an active molecule that not only facilitates fluid retention in the intravascular space by its oncotic pressure but also binds to calcium, bilirubin and most drugs to alter their 'free' and active concentrations. Albumin binds exogenous toxins and is a scavenger of oxygen derived free radicals. Hypoalbuminaemia is a widely accepted biologic marker of metabolic stress. Its presence has been suggested as an indicator of risk of mortality and morbidity in acutely ill patients. A rather simplistic response from this association is the use of exogenous albumin transfusion in increase serum albumin concentration in hypoalbuminaemia. Human albumin solutions are also used in the management of shock and other conditions in which restoration of blood volume is urgent. The Cochrane injuries Group's meta-analysis of 32 randomized controlled trials in critically ill patients with hypovolaemia from trauma, surgery or bums showed that the risk for death in the albumin treated group was higher than in the comparison group. This could be explained that in disease states where increased permeability of vessels is a main feature, administration of albumin is less effective in maintaining the plasma volume than in healthy individuals who have normal vessel permeability. Low serum albumin should not be an indication for albumin supplementation. When seen in the complexity of the patient's problems, the serum albumin is an insignificant parameter for determining therapy aimed at improving the survival chances of severely ill patients.

Role of nitric oxide in ARDS

Swee Fong TANG

Department of Paediatrics, Faculty of Medicine, National University of Malaysia, Malaysia

Despite advances in intensive care and ventilator management, the diffuse lung injury process, known as acute respiratory distress syndrome, or ARDS, continues to be associated with significant morbidity and mortality in children. The main pathophysiological processes in ARDS are pulmonary arterial hypertension and intrapulmonary shunting leading to severe hypoxaemia. Conventional management has included the use of high fractional inspired oxygen, inotropic support and intravenous vasodilators. However, the use of intravenous vasodilators is limited by systemic hypotension and worsening of ventilation-perfusion matching. The role of inhaled nitric oxide in ARDS include lowering of pulmonary arterial pressures and pulmonary vascular resistance, improving the distribution of pulmonary blood flow to improve ventilation-perfusion matching and reducing lung oxidant stress and inflammation. Various studies have demonstrated the acute physiologic

effects of inhaled nitric oxide in improving oxygenation and lowering pulmonary vascular resistance. The optimal doses of inhaled nitric oxide required to improve oxygenation is not well defined hut doses as low as 1 ppm has been shown to be efficacious. Overall inhaled nitric oxide therapy have not been associated with significant toxicities. It, however, remains uncertain whether these improvements in oxygenation and pulmonary haemodynamics actually translate to significant benefits in long-term outcomes, as recent studies have not shown a reduction in mortality or morbidity. This may be related to the heterogeneous patient populations with ARDS with multiple complicating factors. Further studies are required toward developing a greater understanding of the determinants of nitric oxide responsiveness and its relative role in the complex management of acute respiratory failure.

The critically ill child: how much analgesia, how much sedation? FADHILAH Taib

Department of Anaesthesia and Intensive care, Hospital Kuala Lumpur, Malaysia

Sedation and analgesia in the paediatric intensive care unit are essential parts of the management of the critically ill child. It facilitates both therapeutic and diagnostic procedures, ensures patient comfort especially those receiving assisted ventilation, reduces distress in the child and as a result reduces parental anxiety. Analgesia means relief from pain. Pain has very undesirable consequences in the critically ill and can lead to significant physiologic responses e.g. tachycardia, hypertension, increased generalised and myocardial oxygen consumption, immunosuppression, catabolism and hypercoagulability. Children in ICU experience pain for various reasons: a) Pathology e.g. trauma, fractures, operations; b) Diagnostic procedures e.g. insertion of monitoring lines; c) Therapeutic procedures e.g. presence of endotracheal tubes, physiotherapy; d) Prolonged stay in one position (usually supine) can itself give rise to pain and discomfort. Most ICU patients need to be sedated in order to tolerate the endotracheal tube as well as comply with the ventilator. Asynchrony with the ventilator may cause hypoxaemia, hypercarbia and trauma to the respiratory system. Respiratory depression as well as the antitussive effect of certain drugs is helpful in achieving patients' compliance. Most ICUs are noisy places, brightly lit with ongoing activity often round the clock. This not only precludes any sleep and/or rest for the patients but also gives rise to anxiety and agitation. Older children may be anxious because of anticipation of real or imagined catastrophic events or may consider themselves in danger of death. Agitation can cause harm to the child e.g. child falling out of bed. displacement of drips, invasive monitoring lines, endotracheal tube and increase oxygen consumption. Sedation helps to relief discomfort and agitation, blunting of autonomic responses to pain and facilitation of nursing care. Sedation may also be required to reduce raised intracranial pressure, to sedate patients in whom neuromuscular paralysis is indicated and to facilitate long term ventilation and other organ support in patients with multiple organ dysfunction syndrome. Agitation may be caused by hypoxia, hypercarbia or carinal irritation, thirst, itching, stiff joints, plaster casts, sticking plaster or tight dressing, full bladder and rectum, too much suctioning of the airway and aggressive physiotherapy. The problems are less obvious and do not necessarily need to resort to pharmacological means for their resolution. Adequate nurse staffing of the ICU is important which allows for proper nurse/patient ratio. This allows the nursing staff to be able to respond to various situations that cause discomfort to the critically ill. Passive joint movements, regular turns and positioning may be useful adjuncts for patient comfort. It is important to remember, however, that even in the high-technology PTCU environment, verbal and physical reassurance remains a powerful tool for providing comfort and anxiolysis to the critically ill child. There is no pharmacologic equivalent of human compassion. 1. Appropriate analgesia and sedation in the critically ill child can be a complex process. The patients have specific requirements and altered physiology and pharmacology. Listed below are Some of the problems faced in achieving ideal conditions of sedation and analgesia in the critically ill child and their practical issues will be discussed: Pharmacology in the critically ill. 2. Ideal agents for analgesia and sedation - Benzodiazepines (Midazolam, Diazepam). Opiates (Morphine), Propofol, Keamine, Chloral hydrate, Promethazine, regional analgesia and local anaesthetics. 3. Scoring sedation and analgesia in the critically ill child. As a conclusion it is futile to believe that one drug will achieve optimal goals of sedation and analgesia in all our patients. A "cookbook" approach is impossible because of the diversity of patients and clinical scenarios. The best practical approach should be based on multiple target setting, teamwork and communication.

MIXED SYMPOSIUM 6: EMERGING AND RE-EMERGING DISEASES

New diagnostic tools

Jane CARDOSA

Malaysia

Abstract not available

Re-emerging diseases: tuberculosis

I KUPPUSAMY

Institute of Respiratory Medicine, Hospital Kuala Lumpur

Tuberculosis is as old as humankind. It never really disappeared from the surface of this earth. Following the epidemics that occurred in Europe during the 18th century there was a steady decline in tuberculosis cases and mortality. This was even before effective chemotherapy became available in the middle of the last century. However, this decline was accelerated with the widespread implementation of effective chemotherapy. Further innovative approaches to chemotherapy such as ambulatory treatment approaches and short course directly observed treatment gave rise to optimism with regards to possibility of elimination if not eradication of the disease. However this optimism was short-lived. From the mid 80's of the last century case notifications, the world over, began to rise. Although this increase was first perceived in the developed and industrialized countries, it quickly also involved most developing third world countries. Although the major factor identified for causing this resurgence is the HIV/AIDS pandemic, other factors such as complacency and neglect of the disease by the medical fraternity, lack of political will and commitment, war, famine and poverty were also contributory. The WHO has taken the unprecedented step in 1993 of declaring tuberculosis as a global emergency and has increased its assistance and funding to poorer nations to strengthen tuberculosis control activities. It has also adopted the DOTS strategy, which has been shown to achieve high completion and cure rates and is aggressively promoting it worldwide. We are now faced with another emerging spectre; that of multi-drug resistant tuberculosis (MDR-TB). The WHO has also acknowledged the need for a special programme of care for these cases with the 'DOTSplus' concept in areas with substantial levels of resistance. Strategies and targets have been revised with the aim of elimination of the disease in the next two to three decades.

Outbreak of Nipah virus encephalitis among humans, Malaysia, 1998-1999.

MS LYE¹, UD PARASHAR², GL ONG⁵, AW MOUNTS², P KITSUTANI³, M TAHA⁴, AS TEE⁴, AB SULEIMAN⁴, TG KSIAZEK³, BL ONG⁶ and Aziz JAMALUDDIN⁷

Institute of Medical Research, Kuala Lumpur, Malaysia, Centres for Disease Control and Prevention (CDC), Atlanta, GA, USA, CDC, Ministry of Health, Kuala Lumpur, Malaysia, Sarawak Health Department: Department of Veterinary Services, and Veterinary Research Institute.

From September 1998 through April 1999, 265 human cases of febrile encephalitis (105 [39.6%] fatal) were reported to the Malaysian Ministry of Health. Four clusters of cases were identified. The first cluster was in Perak state; the second cluster occurred in Sikamat in Negeri Sembilan; the third and largest cluster was in Bukit Pelandok in Negeri Sembilan State and the fourth cluster occurred in a region of Selangor state adjacent to the affected area near Bukit Pelandok. Among the Nipah

cases, the mean age was 38 years (range, 2 to 75 years); 80.6% were male. 69.4% were Chinese; 16.4% were Indian, 4 (2%) and the rest belonged to other ethnic groups. The apparent source of infection among most cases appeared to be exposure to sick pigs. A case-control study showed that most patients were pig farmers. Clinically undetected Nipah infection was noted in 10(6%) of 166 community-farm controls (persons from farms without reported encephalitis patients) and 20(11%) of 178 case-farm controls (persons from farms with encephalitis patients). Case patients (persons with Nipah infection) were more likely than community-farm controls to report increased sick/dying pigs on the farm (59% versus 24%, p=0.001) and were more likely than case-farm controls to perform activities requiring direct contact with pigs (86% versus 50%, p=0.005). Only (8%) cases reported no contact with pigs. The outbreak stopped after pigs in the affected areas were culled. Direct, close contact with pigs was the primary source of human Nipah infection but other sources (e.g., infected dogs and cats) cannot be excluded.

MIXED SYMPOSIUM 7: SYSTEMIC FUNGAL INFECTION

Systemic fungal infections

Kee Peng NG

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

Candida is recognized as one of the most important pathogen of systemic fungal infections. There are 196 species in the genus Candida, however, only a few Candida species are important human pathogens. The Candida species commonly isolated from blood stream are C. albicans, C. parapsilosis, C. tropicalis, C. guilliermondii, C. glabrata, C. krusei and C. lusitaniae. C. albicans was the most frequently isolated species from blood of patient with systemic Candida infection. However, during the past 2 decades, a substantial shift in the epidemiology of systemic candidiasis occurred due to different Candida species. Globally there was an increase in the isolation of non-albicans Candida like C. parapsilosis, C. krusei, C. tropicalis and C. glabrata from blood of patients with systemic candidemia. C. dubliniensis, a recently identified species closely related to C. albicans, has been implicated as a pathogen in systemic fungal infection among immunocompromised patients. Nine Candida species were isolated in blood cultures in University Hospital, these included C. albicans, C.tropicalis, C.parapsilosis, C.famata, C. glabrata, C.guilliermondii, C.krusei, C.rugosa and C.zeylanoides. The frequency of isolation of C.albicans was 14.2% in 1997, the rate dropped to 13.9% in 1998 and to 6.5% in 1999. C.parapsilosis was the most common isolate, in 1997, 57.2% in 1977, 58.3% in 1998 and 35.5% in 1999. In 1997, C. tropicalis constituted 17.2% of the Candida species isolated; the figure in 1998 was 16.6% but in 1999, the rate increased to 45.2%. No C.dubliniensis was identified among the Candida isolates. Recurrent systemic candidiasis was noted among the patients. These recurrent infections may be due to breakthrough infection; the Candida species isolated were predominately non-C. albicans. Systemic candidiasis caused by more than one species of Candida was also noted in critically ill patients. In such instance, two Candida species e.g.: C.rugosa and C. glabrata, C.albicans and C. tropicalis were isolated from a single blood culture. Molds were the second most common fungal pathogens isolated from blood of patients with systemic fungal infections. These included Apergillus species especially Asp.niger, Asp.fumigatus, Asp. oryzae. and Asp. utus, Penicillium marneffei, Paecilomyces species. Chrysopsorium species and Fusarium species. Norcardia asteroides, an Actinimycetes, was also a fungal pathogen identified among the isolates. *Conclusions:* It is important to continue monitoring the shift in fungal pathogens. The emergence of non-albicans Candida as the most important causative agent of systemic fungal infection is an important finding. With the availability of new antifungal agents with enhanced activity and less toxicity, more frequent use of antifungal prophylaxis is likely to occur, the risk for the emergence of drug resistant Candida species are eminent.

Epidemiology, diagnosis and treatment of systemic candidiasis

Deborah MARRIOTT

St. Vincent's Hospital. Sydney, Australia

There are three important questions to be answered in relation to serious Candida infection in the immunocompromised host. First, are *Candida* species significant pathogens in this patient group; second, what is the epidemiologic pattern of the various Candida species; and third, how is systemic Candida infection best managed in the year 2000. There is now considerable evidence that Candida spp. are important nosocomial pathogens with a number of studies confirming that they are in the top five species of microorganisms isolated from blood regardless of the patient type or hospital location within the hospital. The attributable mortality of approximately 40%, the highest of any nosocomial pathogen, highlights the significance of candidaemia and the importance of early recognition and institution of therapy. This represents a major shift of paradigm in the management of patients from whom Candida species have been isolated from blood cultures. Previously these organisms were thought to be inconsequential isolates and were ignored. However the recognition of secondary complications such as endophthalmitis or osteomyelitis and the high attributable mortality has led to earlier, more aggressive therapeutic intervention. Laboratory speciation of Candida isolates from sterile sites is essential as the species is an important predictor of antifungal susceptibility. Currently the choice of treatment for systemic candidiasis is amphotericin B or fluconazole. These agents which have been shown to be equivalent in both neutropenic and nonneutropenic patients in several randomised, controlled studies. A number of new antifungal agents, including the extended spectrum azole drugs voriconazole, posiconazole and ravuconazole and the echinocandin caspofungin are undergoing phase II/III clinical trials and will enhance the repertoire available to treat serious Candida infection, particularly with species resistant to the current azole agents.

MIXED SYMPOSIUM 8: GLUCOSE-6 PHOSPHATE DEHYDROGENASE DEFICIENCY

Spectrum of G6PD mutations

AINOON Othman

Department of Pathology, Faculty of Medicine. Universiti Kebangsaan Malaysia

G6PD deficiency is the commonest enzymopathy in human estimated to affect 400 million individuals. The haemolysis in G6PD deficiency is thought to be produced by oxidative damage to red cell proteins. Since G6PD is the only source of NADPH in red cells the deficient cells are more susceptible than the normal red cells to oxidative damage. Haemolytic anaemia induced by certain drugs, chemical substances, fava beans and infections and the association with severe neonatal jaundice and risk of kemicterus has made G6PD deficiency a public health problem in many countries. Some G6PD-deficient individuals suffer from chronic haemolytic anaemia. Indeed it has now been established that G6PD deficiency is a heterogeneous disorder. Biochemical characterization has led to the description of no less than 442 G6PD-deficient variants with at least 229 variants characterised by methods agreed upon by WHO expert group. The cloning of the X-linked cDNA by Persico et al (1986) and the gene encoding for G6PD by Martini et al (1986) allowed the primary sequence of G6PD gene to be deduced. With the 'advent of the PCR technique, sequencing the mutant genes became easier and more rapid. To date, at least 100 different G6PD mutations have been discovered. The majority of the variants are polymorphic, occurring in area endemic for malaria with variant alleles (WHO class I & II variants) reaching high frequencies of 1 - 50 percent in various parts of the world and deficient individuals, though essentially asymptomatic in the steady state, have a risk of acute haemolytic attacks. The sporadic G6PD-deficient variants (WHO Class I) occur at low frequencies anywhere in the world and they usually present with severe phenotype, namely chronic nonspherocytic haemolytic anaemia (CNSHA). In both polymorphic and sporadic variants there is always some residual enzyme activity and this is invariably lower in RBCs than in other cells suggesting that instability of mutant G6PD molecules is probably the commonest cause of G6PD deficiency. Molecular analysis has proved to be valuable for diagnosis and to define which mutations

account for G6PD deficiency in various populations. However, with the construction of a 3-d model of the tertiary structure of human G6PD based on the structure of a bacterial G6PD by Naylor et al (1996) attempts have been made to use these mutations to identify the role of the different domains of the G6PD enzyme and individual amino acid residues in the stability of the protein and explain the clinical heterogeneity. This paper will discuss the frequency of mutations in various populations including some data on Malaysian G6PD deficiency, the distribution and nature of the mutations in a model of a 3-d structure of human G6PD that has enabled researchers to speculate some of the possible mechanisms underlying G6PD deficiency.

G6PD Deficiency and Public Health Practice

NARIMAH Awin

Family Health Development Programme, Ministry of Health Malaysia

Public health is a specialty in medicine and is based upon a defined scientific body of knowledge. Public health specialists use the natural, biological (including medical) and behavioral sciences. The extent of each of these varies, but much use is made of the discipline of epidemiology. Public health practice aims to reduce ill health in populations and for this, it uses a variety of methods, and these can be summarised as:- (i) ensuring a safe environment, (ii) enhancing immunity, (iii) behaving sensibly including good nutrition and diet, (iv) having well-born children and (v) providing appropriate and prudent health care. In preventing disease, public health practice uses different levels of prevention. Health promotion refers to the overall activities that maintain a state of good health, and depend to a large extent on the non-health sector. Primary prevention is the avoidance or elimination of the causes or determinants of disease, if they are known and something can be done about them. Secondary prevention is early detection of departures from health, so that they can be corrected, and often this takes the form of screening. Tertiary prevention is the diminution of ill effects of disease that has occurred including rehabilitation and avoiding recurrence. In deciding to screen for any disorder certain criteria must be followed, and these relate to (a) the disorder to be screened, (b) the screening test available and (c) the health delivery system. G6PD deficiency as a genetic disorder manifests generally in mild forms, mostly as haemolytic anaemia when the deficient person is challenged with certain drugs (the most well known is primaquine) and the fava bean. The anemia is often self-limiting. However, the disorder is a common cause of neonatal jaundice (NNJ) in many countries. NNJ which affects about half of new-born infants and up to a third of these are of sufficient severity to make it a public health problem of importance; indeed a few infants progress to kemicterus, a very severe complication. Therefore as far as the disease is concerned, there is adequate justification to have a nation-wide screening for any known cause of NNJ, such as G6PD Deficiency. There is a simple. easy, reliable and cheap screening test to detect this genetic disorder in newborns and parents of those affected are then appropriately counseled about the drugs and foods to be avoided to prevent haemolytic anaemia. The availability of the test further justifies nation-wide screening for this disorder. The Ministry of Health through the Family Health Development Programme has implemented this screening strategy for several years and there is evidence to show its effectiveness, efficiency and impact.

Glucose-6-phosphate dehydrogenase deficiency and kernicterus

Nem-Yun B00

Neonatal Intensive Care Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia

Severe neonatal hyperbilimbinemia associated with glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common problem in many parts of the world. Common factors identified to be associated with increased risk of hyperbilimbinemia are infection, and exposure to chemicals and fava beans. When treated late, severe hyperbilirubinemia causes kemicterus with resultant brain damage. Exposure to oxidant agents with acute onset hemolysis has been identified as an important cause of severe neonatal hyperbilimbinemia, even in the absence of haematological evidence.

Measurement of endogenous production of carbon monoxide by determining the serum level of carboxyhaemoglobin has helped identified cases due to hemolysis in the absence of haematological indices. However, numerous studies have shown that not all cases of severe hyperbilirubinemia are due to hemolysis. With the development of a simple method of measuring total serum conjugated bilirubin, bilirubin monglucuronide and diglucuronide, deficient conjugation of bilirubin is now identified as a second important cause of severe neonatal hyperbilirubinemia. No consistent correlation has been found between the level of G6PD enzyme activities and the degree of hemolysis and bilirubin production. It is not sure at this juncture whether the different genetic variants of G6PD deficiency plays any role in the degree of hemolysis, bilirubin excretion, and severity of neonatal hyperbilirubinemia. The most effective treatment of hyperbilirubinemia is still phototherapy and, when severe, exchange transfusion.

MIXED SYMPOSIUM 9: OLD DRUGS NEW USES

Arsenic trioxide in acute promyelocytic ieukemia

Min Hong SAW

Lam Wah Ee Hospital, Penang, Malaysia

90% of Acute Promyelocytic Leukemia (APML) is characterized by translocation between chromosome 15 and 17. The breakpoint on chromosome 15 involves an oncogene known as PML (Promyelocytic Leukemia gene) and the breakpoint on chromosome 17 involves a gene encoding for retinoid acid alpha- receptor (RAR- alpha). The hybrid produced a fusion protein of PML- RAR-alpha. It would appear that retinoid acid receptor is important for the maturation and differentiation process of myeloid cells. Disruption of the RAR gene causes the myeloid cells to be arrested at the promyelocytic stage. Recent studies indicate that the molecular process involved the acetylated status of the histone protein. The diagnosis of APML is achieved microscopically by the presence of abnormal promyelocytes. These cells normally have heavy granulation in the cytoplasm except in the variant form. The cytochemistry stains very heavily for myeloperoxidase. Immunophenotyping showed the leukemic cells to be CD34, HLA-DR and CD56 negative, CD13 and CD33 positive. Clinically, dangerous coagulopathy and susceptibility to sepsis characterize the illness. The risk of bleeding is particularly high at the onset of induction chemotherapy. This complication has been substantially reduced when All trans- retinoic acid (ATRA) was introduced. The use of ATRA to treat APML epitomized the ideal form of cancer treatment. The drug induces differentiation instead of cell lysis in the immature leukemic cells. The coagulopathy is avoided when there is no sudden release of abnormal amount of the enzymes from the cells. However, ATRA does not cure the APML, and combination with chemotherapy is necessary. Despite this encouraging development 35-45% of the patients will still relapse. Treatment of these relapsed cases is difficult and often results only in a short period of remission. New therapeutic agents have been tried, the most promising of them all is Arsenic Trioxide (As_2O_3). Arsenic Trioxide appears to have biphasic action against the APML cells. At low dose it seems to induce differentiation and at higher dose it causes apoptosis in the leukemic cells. More importantly this compound appears to be effective both in the ATRA sensitive and resistant APML cells. Therefore the drug can be used up front to treat both the newly diagnosed as well as the relapsed cases. The availability of this drug further improved the outlook of APML and made this an eminently curable disease.

Newer uses of aspirin

A AZIZ BABA

Department of Medicine, Universiti Sains Malaysia, Kubang Kerian, Kelantan

Aspirin was first used as an analgesic, antipyretic and an anti-inflammatory agent. Subsequently, many clinical studies including prospective randomised trials, have definitively established the beneficial role of aspirin in secondary and to a lesser extent primary prevention of thromboembolic

problems. In recent years, efforts have focused on defining possible new uses of aspirin including chemo prevention of cancers and neurodegenerative diseases. There have been several observational studies of the effects of exposure to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDS) and the subsequent development of colorectal cancer. Collectively, these studies demonstrate that continuous use of aspirin and other NSAIDS results in a 40-50 % reduction in the relative risk of colorectal cancer. NSAIDS inhibit both isoforms of COX, COX-1 and COX-2. Because COX-2 levels are increased in a number of solid tumors, it may serve as a molecular target for cancer prevention. COX-2 expression may also be upregulated in patients with Alzheimer's disease; observational studies have also shown a reduced incidence of Alzheimer's disease in regular users of aspirin. Current research efforts have been focused on understanding the molecular basis for the chemoprotective effects of aspirin and other NSAIDS. It is likely, however, that emphasis will shift from aspirin and other non selective COX inhibitors to the selective COX-2 inhibitors to avoid side-effects associated with COX-1 inhibition.

Biochemical modulation of drug resistance in chemotherapy

Gerard Chin Chye LIM

Department of Radiotherapy and Oncology, Hospital Kuala Lumpur, Malaysia

Resistance to chemotherapy arises through several mechanisms, such as suboptimal delivery of the drug to tumour cells, inherent resistance of the tumour cell to the drug, as well as acquired resistance. Biochemical modulation represents one of the mechanisms by which synergism occurs between two or more drags in combination, whereby bioavailability and/or intracellular exposure of the drug on the target molecules are enhanced. Ensuring an optimal tumour cell kill from the beginning of chemotherapy will help to reduce the likelihood of development of drug resistance. *Improving drug* delivery to tumour cells: Taking the example of 5-fluorouracil (5-FU), strategies at maximising the clinical efficacy of the drug have included administration by prolonged dosing via the oral route. The absorption of oral 5-FU may be more consistent if its metabolism by dihydropyrimidine dehydrogenase (DPD) in the gastrointestinal tract is avoided. This is attempted either through the administration of oral 5-FU precursors (eg capecitabine, tegafur), or by inactivating DPD with drugs combined with oral 5-FU, eg uracil. Other agents used with 5-FU precursors which decrease the associated gastrointestinal toxicity, eg through selective inhibition of 5FU phosphorylation in the gastrointestinal tract by potassium oxonate, will improve the therapeutic ratio of 5-FU. Modifying metabolic pathway of cytotoxic drugs inside target cells: The cytotoxic effect of 5-FU is enhanced by folinic acid (calcium leucovorin) which leads to stabilisation of the ternary complex between fluorodeoxyuridylate (FdUMP), thymidylate synthase, and 5, 10-methylenetetrahydrofolate within the target cells. 5-FU may also be biochemically modulated by other cytotoxic drugs, eg methotrexate, which is an inhibitor of dihydrofolate reductase. Other agents which have been used to augment the cytotoxic activity of 5-fluorouracil through biochemical modulation include cisplatinum, Nphosphonacetyl-L.-aspartic acid (PALA), recombinant interferon alfa-2a (IFNalpha-2a) and levamisole. Biochemical modulation of cytosine arabinoside (AraC) with inhibitors of ribonucleotide reductase aims to improve the cytotoxicity against leukaemia by raising intracellular levels of AraC triphosphate. Summary: Biochemical modulation is a clinically useful strategy through which the development of chemotherapy regimes with better therapeutic ratios is possible.

MIXED SYMPOSIUM 10: MANAGING SEVERE PRE-ECLAMPSIA

Managing severe pre-eclampsia - physiological and pharmacological considerations YK CHAN

Department of Anaesthesiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Pre-eclampsia describes the development of hypertension with proteinuria and or oedema in parturients after the twentieth week of gestation. This is a multiple organ system disease, the

aetiology of which has not been thoroughly elucidated. There is a suggestion of it being due to failure of the second wave of trophoblastic migration resulting in the retention of the muscular structure of the maternal spiral arteries which fails to adapt to become low-resistance vessels. This failed trophoblastic migration also encourages the production of increased free radicals and lipid peroxides. These enhance the production of potent vasoconstrictors which is reflected in the impaired blood supply to various organs including the maternal supply to the fetus. The severity is measured by the degree of impairment in the performance of these organs. There is increased blood pressure with elevated systemic vascular resistance, with a suggestion of reduced blood volume that is not totally substantiated in other studies. The oncotic pressure is reduced and with increased vascular permeability may predispose these parturients to pulmonary oedema. They have increased hypercoagulability with activation of the fibrinolytic system and platelet activation. Renal ischaemia impairs glomerular function with associated proteinuria. Distension of the liver capsule by oedema or subcapsular or parenchymal bleeding underlies the epigastric or subcostal pain complained of by those with severe pre-eclampsia. Cerebral manifestations of impaired blood supply include severe headache, visual disturbances and hyperreflexia which could be due to vasospasm, microinfarctions, thrombosis, punctate hemorrhages or cerebral oedema. Studies show aspirin prophylaxis may have some role in reducing the incidence. Magnesium sulphate has been used for seizure prophylaxis and this has been shown to be more effective than phenytoin. Various antihypertensives have been used with hydralazine, labetolol and sodium nitroprusside being the commonest agents used.

The management of pre-eclampsia

Alex MATHEWS

Hospital Kuala Lumpur, Malaysia

Pre-eclampsia affects 2-8% of all pregnancies. Eclampsia is not uncommon and mortality associated with eclampsia is a matter of concern. In the 1995-1996 report of the Confidential Enquiries into Maternal Deaths in Malaysia several deaths were attributable to hypertensive disorders especially eclampsia. Management of this condition revolves around: (i) control of hypertension to reduce the risk of maternal cerebral hemorrhage and also to allow prolongation of pregnancy. (ii) Control of fits and prevention of recurrence of fits. (iii) Delivery of the fetus. All other measures are supportive of systems that can fail, namely, renal, coagulation, hepatic and cardiopulmonary or management of complications like intracerebral hemorrhage. Early intervention to treat or deliver reduces morbidity and mortality of both mother and baby. Recent improvements in understanding of the management of the condition include the use of magnesium sulphate in prevention of recurrent fits, the role of calcium supplementation, antioxidants and aspirin in prevention. The choice of anti-hypertensives has been studied (mainly between hydrallazine, labetolol, nifedipine and methyldopa) and there appear to be inadequate data for reliable conclusions.

Severe pre-eclampsia: managing the neonate

Nyok Ling LIM

Department of Paediatrics Hospital Selayang, Malaysia

The major concern for hypertensive diseases of pregnancy rests with the patient who has severe preeclampsia/eclampsia. Surveillance for foetal compromise is necessary besides controlling blood pressure and preventing seizures in the mother with preeclampsia. It's being found that pharmacologic treatment of women with hypertension reduces perinatal deaths but does not affect intrauterine growth retardation. Severe reductions in blood pressure however, and seizures are especially hazardous to the foetus. Risk of foetal death is 10-37% in eclampsia. Optimum time and route for delivery must be planned if mother's condition does not improve and or foetal compromise is significant. It is to be remembered that well-being of the mother does not always equate to well-being of the foetus. In the likely presence of foetal pulmonary immaturity (<34 weeks or as documented in the amniotic fluid) antenatal corticosteroid must be considered. A paediatric doctor must be

available at delivery of the baby who may have immediate complications of prematurity and asphyxia. Specifically risks of abruption and effects of antihypertensive drugs must be anticipated. Ventilatory and cardiovascular support are often necessary especially in the presence of maternal magnesium sulphate infusion or other drug therapy. Other essential aspects of neonatal intensive care for the small and ill infant include surfactant therapy, cardiorespiratory monitoring, prevention of infection, and 'aggressive' nutrition which is particularly important in the light of nutritional programming in foetal and early postnatal life for subsequent long term adult-onset diseases. Immediate neonatal outcome however is largely dependent on the weight and gestation and 'asphyxia status' of each child.

MIXED SYMPOSIUM 11: ORANG ASLI HEALTH

Health development for Orang Asli: future perspectives

Mohd SUHAIMI B A Majid

Department of Aborigines Affairs, Malaysia

The community of indigenious ethnics in Peninsular Malaysia are estimated at 120,000 as in year 2000 with 18 different subethnics with distinct cultural-linguistic and anthropological origins. Prior to the 1950s, there was no access to modern medicine and the aborigines were depending solely on their own traditional health practices. The concept of illness was also a misfit. They believed that they were not sick as long as they can go out working and taking their food well. To date, considerable improvement of their health status have been observed, in particular their life expectancy rate, perinatal and maternal mortality rates but certain ailments such as malaria, tuberculosis, leprosy, intestinal infestations, fungal skin infestations and chronic forms of protein-energy malnutrition are beyond acceptable norms.

Understand Orang Asli reproductive health from an anthropological and gender sensitive perspective

Shanthi THAMBIAH

Gender Studies Programme, Faculty of Arts and Social Sciences, University of Malaya, Malaysia

An analysis of Orang Asli reproductive health must be contextualised within their belief systems, gender ideologies and the indigenous medical systems which are all interrelated and connected. The process of understanding Orang Asli reproductive health and childbirth practices must include an investigation into sex roles and the status of local childbirth attendants within the context of present-day realities. An investigation of gender ideology and behaviour provides insights into symbolic systems and their relation to empirical reality. This kind of analysis shows a decline in their reproductive health as their egalitarian gender ideologies are being subverted by hierarchical gender ideologies. Their belief system relating to a notion of shared pregnancy between men and women is being eroded by greater interaction with their sexually segregated neighbours and with the introduction of the modem sexually segregated notion of pregnancy as an all female experience. This decline in the notion of shared pregnancy between the sexes has contributed to a rise in childbirth complications and a decline in the overall reproductive health of Orang Asli women.

Medical anthropology

AYOB B Bah Los

Malaysia

Abstract not available

Current nutritional status of Orang Asli

Geok Lin KHOR

Universiti Putra Malaysia

A comprehensive insight into the various medical and health issues, including nutrition, that affect the Orang Asli is provided in a recent biomedical bibliography by Baer (1999). Besides this, nutrition studies undertaken in the 1990s will be included in this presentation, which will focus on children and women. Childhood malnutrition in Orang Asli has persisted since the colonial era often at levels of severity that are higher than that in other poor rural communities in Malaysia. Prevalence of underweight and stunting are reported in one-third to three-quarters of the children studied. Such serious levels of malnutrition are found in a wide spectrum of habitats from interior to periurban villages. The low nutritional status of Orang Asli children can be attributed directly to **poor** diet and high helminthic infestation. The latter is widespread in young children ranging from one-third with **hookworm** to over three-quarters with **ascaris** and **trichuris**. Anaemia is a common finding in children and also among the females especially in the reproductive age. Dietary intake of calories and most nutrients particularly iron is inadequate in all age groups. Nonetheless, overweight problem has emerged as documented in some periurban villages particularly among the women. While this overweight problem needs to be addressed, greater efforts are needed to alleviate the severity of under-nutrition problems as they continue to beset the Orang Asli.

MIXED SYMPOSIUM 12: MANAGING AN OUTBREAK

Principles of managing an outbreak

Hitoshi OSHITANI

World Health Organization, Regional Office for the Western Pacific

Outbreaks of communicable diseases continue to occur throughout the world. Early detection and rapid response are essential to minimize the impact of an outbreak. Public health officials recognize outbreaks through various sources, including notification from clinicians, routine surveillance, and mass media. However public health response to such information is often delayed due to late reporting. Therefore it is necessary to strengthen the mechanism to detect and report outbreaks effectively and rapidly. Once outbreak is recognized, outbreak investigation is carried out. Outbreak investigation provides useful information such as transmission route and source of infection to control the outbreak. Proper epidemiological skills are essential to conduct epidemiological outbreak investigations. The field epidemiology training programme (FETP) have been established in many countries to train public health officials on such skills. To respond to outbreaks effectively, complete preparedness plan should be developed. It is also important to improve outbreak response capacities at district, state and national level. Coordination is another important component to respond to outbreak, coordination include those among different programmes in the Ministry of Health and also with other ministries. International collaboration is sometimes required to respond to major or unknown disease outbreaks. World Health Organization (WHO) is establishing a Global Outbreak Alert and Response Network to coordinate such international collaboration.

Responses to a newly emerging disease outbreak

MOHAMAD TAHA Arif

Ministry of Health, Malaysia

The purpose of the presentation is to describe the responses to a newly infectious disease outbreak as exemplified by the response to the **Nipah** Virus Outbreak of 1999. The law requires that the occurrence of 27 specific diseases and conditions be notified to the Medical Officer of Health. In the response, one has to look at various issues at clinical, epidemiological and public health levels. These

should include outbreak verification, case definition, laboratory, support, clinical diagnosis and management. The outbreak investigation would require the identification of the causative agent, the predisposing factors, source of infection, mode of transmission, the incubation period, risk factors and others. These knowledge would be useful in strengthening surveillance and the institution of specific control measures. The latter would include the elimination of the source of infection, cutting the transmission, self-protection, immunization, quarantine, environmental control, law enforcement and others. In this process one has to look at human resources from within the country and outside, rapid response team, intelligence team, food organization, financial needs and appropriate risk communication. Information gathered from the clinical, laboratory and epidemiological investigations need to be made known to all parties involved in the outbreak response. This will strengthen further the surveillance, control and inventive actions. Post-outbreak management and documentation are equally important.

Management of Enterovirus Outbreak in Sarawak 1997

Andrew KIYU, Flora ONG, KAMALIAH Moh Noh, MOHD TAHA Arif, Lye Munn SANN, JAMILAH Hashim, Sik King YAO, JAMAIL Muhi, Choo Huck 001, ZULKIFLI Jantan, Fauziah Z EHSAN and KUMARAJOTHY Supramaniam

Sarawak Health Department, Malaysia

Between 15 April and 30 June 1997, 29 previously healthy infants and young children died in Sarawak as a result of cardiovascular collapse after a short febrile illness. Those 29 fatalities occurred during an outbreak of hand, foot and mouth disease in the community. The cause of the outbreak of sudden deaths was initially unknown. So the management and control measures were based on a working hypothesis of it being due mainly to enteroviruses. The measures taken were focused on: (1) setting up of surveillance mechanisms for hand, foot and mouth disease (HFMD) and related diseases, namely (a) HFMD, (b) acute flaccid paralysis, (c) aseptic meningitis and encephalitis, (c) other very ill children; (2) field investigations, namely (a) investigation of fatal cases, (b) investigation of contacts of fatal cases, (c) case-control study, (d) toxicologic investigation, (e) serologic case control study, and (f) micronutrient surveys; (3) institution of specific control measures which were aimed at reduction of disease transmission and prevention of infection, namely (a) closure of preschools and kindergartens, and swimming pools, (b) setting up isolation and observations wards, (c) mandatory notifications, (d) mandatory post-mortems, (e) health education, (f) staff protection, and (g) vector control measures.

Public Health and infection control of the Bird Flu outbreak - the Hong Kong experience. WH SETO

Queen Mary Hospital, The Hospital Authority, Hong Kong and University of Hong Kong.

A brief historic account of the outbreak leading to the slaughter of the chickens will be described. The theoretical basis for this endeavor will be presented with results of the post-slaughter monitoring programme. At that time, 44 public hospitals in Hong Kong are administered by a single organization, the Hospital Authority and clinical cases were managed in these hospitals. Over 2960 patients were admitted for investigations of H5N1. A multidisciplinary task force of hospital specialists prepared a guideline for hospital procedures, which was implemented under its supervision. Key measures taken will be described. These include measures taken in informing the public, the provision of rapid viral diagnosis, and the guidelines for infection control and treatment. Data will be presented to show success in managing public fear and how the presence of an infection control infrastructure was critical in the handling of the outbreak throughout the temtory.

MIXED SYMPOSIUM 13: CRITICAL CARE MEDICINE

Acute respiratory distress syndrome

Patrick SK TAN

University Malaya Medical Centre, Kuala Lumpur, Malaysia

Acute lung injury results from different types of cellular injury to the lungs and different systemic conditions are also associated with acute lung injury (ALI). Acute lung injury has been graded in its severity of manifestations by a lung injury score, the most extreme form being synonymous with acute respiratory distress syndrome (ARDS). This concept was adopted by the 1994 Consensus Conference of American and European Investigators who agreed that the diagnostic criteria for ALI should include acute onset, bilateral chest radiographic infiltrates, a pulmonary artery occlusion pressure below 18 mm Hg or absence of evidence of left artrial hypertension, impaired oxygenation regardless of the positive end-expiratory pressure (PEEP) with a Pa02/FI02 ratio < 300 torr (<40 kPa) for ALI and < 200 torr (<40 kPa) for ARDS. Severe hypoxemia occurs as a result of intrapulmunary shunt, aggravated by edema and atelectasis. In the early stages of ALI, neutrophils and mesenchymal cells aggregate in the interstitium. The squamous epithelium is severely damaged and alveolar Type I cells are replaced with proliferating Type II cells. Pulmonary capillary endothelium is well preserved initially but endothelial damage results in increased permeability to water and protein, causing oedema to accumulate in the interstitium and alveoli. At a later stage, obliteration of capillaries by endothelial damage, cellular aggregation and microthombi may account for pulmonary hypertension in ARDS patients. The aetiologic role of bacterial or other infection occumng after the onset of ALI and ARDS is uncertain. The histological changes of ARDS are believed to be uniformly diffuse; however, Gattinoni, et al. have demonstrated that the progressive bullous changes of late ARDS are preferentially distributed in dependent lung regions. ALI and ARDS may represent the pulmonary manifestation of an inflammatory response to tissue injury occumng in different organs, accounting for their respective dysfunction or failure. Neutrophils have been shown to be present in large quantities in bronchoalveolar lavage fluid of ARDS patients, together with proinflammatory cytokines such as TNF, IL-1. Evidence from clinical and experimental investigations has led to the hypothesis that the lung and other organs are damaged as part of a neutrophil-dependent response, involving the release of antioxidants, catalase, and markers of endothelial injury such as endothelin-1 and von Willebrand factor. Other possible mediators of inflammation in ARDS, such as platelet activating factor, prostaglandins and products of disseminated intravascular coagulation are being studied. Procollagen peptides present in bonchoalveolar lavage fluid represent another group of factors which possibly influence pulmonary fibrosis in late ARDS. In numerous experimental studies, mechanical ventilation using large tidal volumes and high peak inspiratory pressures with low or no PEEP has been shown to induce hyaline membrane disease histologically similar to that seen in ARDS. Mechanical ventilation with PEEP has been shown in numerous studies to improve oxygenation in patients with acute hypoxemic respiratory failure due to ALI and ARDS. PEEP increases alveolar plateau pressures, aids alveolar recruitment, and improves functional residual capacity and arterial oxygenation. Recruitment of alveolar lung units is maximal when PEEP is around 15 to 20 cm H₂O. PEEP may also reverse hydrostatic mechanisms which allow accumulation of extravascular lung water. An 'open lung approach', based on ventilating using small tidal volume (6 to 8 ml/kg body weight), PEEP at a level above the measured lower inflection point on the pressure-volume curve for that patient (commonly 15-18 cm H₂O in adults), pressure-limited ventilation (< 30 cm H,O) and permissive hypercapnia was shown by Amato, et al, to improve oxygenation in ARDS although there was no impact on mortality because of the study's small sample size. The disparity of subsequent ARDS randomized trials of pressure limited ventilation resulted in confusion until subsequent analysis showed that negative results in three of these trials could have arisen because of insufficient differences in plateau pressure, a surrogate for end-inspiratory alveolar pressure, between the two treatment groups. Results from the Acute Respiratory Distress Syndrome Network showed that small tidal volumes (6 ml/kg) reduced mortality by 22 percent, are in keeping with the findings of Amato, et al, and have closed an era in research on the Acute Respiratory Distress Syndrome. References: (1) Gattinoni L, Bombino M, Pelosi P et al. Lung structure and function in different stages of severe adult respiratory distress syndrome. JAMA 1994; 271:1772-9. (2) Amato

MBP, **Barbas** CSV, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998; 338: 347-54. (3) Steward TE, Meade MO, Cook DJ, et al. Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. N Engl J **Med** 1998; 338: 355-61. (4) Brochard L, **Roudot**-Thoraval F, Roupie E, et al. Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. Am J Respir Crit Care Med 1998; 158:1831-8. (5) **Brower** RG, **Shanholtz** CB, Fessler HE, et al. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. Crit Care Med 1999; 27: 1492-8. (6) The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med **2000**; 342: 1301-8.

Disseminated intravascular coagulation (DIC)

BH CHONG

Centre for Thrombosis and Vascular Research, University of New South Wales and Haematology Department, Prince of Wales Hospital, Sydney, NSW, Australia.

DIC is an acquired clinical syndrome characterized by the widespread intravascular activation of blood coagulation, generation of thrombin and fibrin thrombi, consumption of blood clotting factors and platelets. It can be caused by a variety of conditions including severe infection, trauma, malignancy, obstetrical calamities (e.g. amniotic fluid embolism), severe hepatic failure, snake bites and transfusion reactions. These causes may induce a massive inflammatory response with release of proteases, cytokines and hormones from inflammatory and vascular cells leading to extensive microvascular endothelium damage. Depending on the severity of the condition, it may result in bleeding and/or end organ damage. Diagnosis of DIC is based on clinical features (the presence of one of the causes listed above, evidence of bleeding and/or end organ failure) and coagulation abnormalities (prolonged clotting times, reduced plasma fibrinogen, increased fibrin monomers, fibrin degradation products or d-dimers and thrombocytopenia). The Subcommmittee on DIC of the International Society on Thrombosis and Haemostasis has recently put forward the concept of "overt DIC" and "nonovert DIC" and has devised a scoring system for their diagnosis. It is believed that the detection of nonovert DIC will result in earlier diagnosis and treatment of the condition. Hopefully this could lead to a better outcome. The most important step in the management of DIC is treatment of the cause. Infusion of plasma, cryoprecipitate, clotting factors and platelets may help to correct the coagulopathy and hence may prevent or stop the bleeding in DIC. The use of heparin is controversial as it may cause bleeding. It may be helpful in the treatment of patients with extensive thrombosis and multiple end organ damage. New treatments e.g. antithrombin III infusion have yielded only variable results.

Acute renal failure in the critically ill

ZAKI MORAD Mohd Zaher

Hospital Kuala Lumpur, Malaysia

In the critically ill, acute renal failure (ARF) which usually takes the form of acute tubular necrosis (ATN) is a common complication, which is associated with a high mortality. While the prognosis of ARF due to medical and obstetric causes has improved tremendously, that associated with ATN has remained relatively unchanged. Since the early 1980's mortality in patients with ATN in the intensive therapy units has been around 40-60%. In part this is due to changing patient demographics. More elderly patients undergo complex surgery such as cardiac surgery. Patients in intensive therapy units often have severe sepsis, are hemodynamically unstable, on multiple drugs including vasopressors and are sometimes subjected to imaging studies involving radiocontrasts. These factors promote continuing renal ischemia thus delaying recovery of ATN. Multiorgan failure (MOF) states are frequent in these patients and mortality rates increase in proportion to the number of organs that fail.

The management of severely ill patients with ATN has seen a number of changes in recent years particularly in renal replacement therapy. Nonetheless the major thrusts in the management continues to be prevention and treatment of sepsis and maintenance of adequate effective blood volume. Infection continues to be the major cause of death. Nutritional support in the form of enteral and parenteral is important. Critically ill patients with ATN are hypercatabolic and thus choice of renal replacement therapy is important. While peritoneal dialysis can be performed in some patients most would require a more efficient dialysis technic to remove excess wastes and fluids. Thus daily hemodialysis has been advocated by some and there is some evidence that this improves patient survival. The choice of the dialysis membranes is of interest. It has been shown, though not conclusively, that the use of biocompatible synthetic dialysis membranes improves patient survival and reduces the need for frequent dialysis and length of stay in ICU. Lastly, there has been a major shift towards using a form of continuous renal replacement therapy (CRRT) in the treatment of ATN in the critically ill patients. A major advantage of a continuous treatment apart from constant removal of wastes and immunomodulatory vasoactive substances found in sepsis is that there are fewer tendencies to hypotension compared to daily or intermittent hemodialysis.

MIXED SYMPOSIUM 14: ONCOLOGY

Tumour markers

Leslie C LAI

Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, Malaysia.

The term 'tumour markers' embraces a broad spectrum of molecules of widely divergent characteristics. These molecules share an association with malignancy that allows their application in one or more of the following: diagnosis, screening, monitoring and prognosis in cancer patients. Due to the lack of sensitivity and specificity most tumour markers are not helpful in screening or diagnosis of a specific cancer. With few exceptions, tumour markers are also not of much use in determining prognosis of cancer patients. The main use of tumour markers is in monitoring of response to treatment and early detection of relapse. In the USA the National Academy of Clinical Biochemistry (NACB) has introduced a process known as Standard of Laboratory Practice (SOLP), designed to recommend guidelines in focused areas of clinical laboratory medicine. One such SOLP considered the utilisation of tumour markers in the management of patients with cancer. Moreover, in the USA the Food and Drug Administration (FDA) tightly regulates the measurement of tumour markers. The European Group on Tumour Markers published their guidelines on utilisation of tumour markers in 1999 and these closely reflect the recommendations of the NACB. The SOLP on tumour marker utilisation made specific recommendations which include the use of prostate specific antigen (PSA) in screening and monitoring prostate cancer, CA15-3 in monitoring advanced breast cancer, CA125 in monitoring ovarian cancer under specific clinical conditions, calcitonin as a diagnostic indicator of medullary thyroid carcinoma, alphafoetoprotein (AFP), human chorionic gonadotrophin (hCG) and lactate dehydrogenase (LDH) in evaluating and staging germ cell tumours and immunofixation and quantification of immunoglobulins and light chains in evaluating monoclonal gammopathies. These tumour marker guidelines should be adopted on an international basis.

Viruses and cancer

R PATHMANATHAN

Subang Jaya Medical Centre, Kuala Lumpur, Malaysia

Viruses are now accepted as *bone fide* aetiological agents of human cancer; these include the **Epstein**-Barr virus, the hepatitis B and C viruses, human papillomaviruses, and the human T-cell leukemia virus type 1, plus several candidate human cancer viruses. It is estimated that 15% of all human cancers worldwide are caused by viruses. Typically, such viruses exist in latent form or as persistent infections in the human host. One possible scenario correlates oncogenesis with enhanced viral

activation against a background of compromised immune control or viral overload. Generally, **virus**-associated cancers tend to occur early to mid-life and are an important cause of morbidity and mortality. It is becoming increasingly recognized that these malignancies may also occur as "opportunistic malignancies", especially in HIV-infected persons. In all these cases, infection alone is unlikely to be the sole causative factor, and the importance of multiple factors modulating oncogenesis cannot be overemphasized. Future directions for tumour virus studies are discussed.

New treatment modalities

KC SOO

Singapore

Cancer is an increasing important cause of death. In Singapore, one in four deaths is due to the disease. Survival to a large extent is determined by the stage of the disease, though in some instances the quality of therapy may also have a significant impact. Multi-disciplinary care has been the cornerstone of cancer management, and has involved local control with surgery or radiation and chemotherapy in an adjuvant and more recently in a neo-adjuvant setting. New modalities in treatment have developed with better understanding of fundamental biological processes and emerging technologies. These would involve immune modulation strategies, gene and viral therapies, alteration of expression of major histocompatibility molecules, etc. Other novel therapies would involve refinements of current standard therapies e.g. 3D conformal radiotherapy, photodynamic therapy and viral enhancement of chemotherapy to be discussed will be some of these new therapies undergoing trials at the National Cancer Centre, Singapore.

MIXED SYMPOSIUM 15: STEM CELL TRANSPLANTATION

Stem cell transplantation: detection of engraftment by molecular methods Rahman JAMAL

Paediatric Haematology and Oncology Unit, Department of Paediatrics, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Allogeneic bone marrow and allogeneic stem cell transplantation have become standard therapies for patients with haemopoietic disorders, including leukaemias, lymphomas and aplastic anaemias. It is the aim of the haematologist to achieve total engraftment of the donor marrow in a state of stable immune tolerance and a stable haemopoietic chimerism. Crude tests of engraftment include the recovery of counts and the testing of the blood groups in the post-transplant period, but these approaches have their own limitations. The advent of molecular methods have superseded these crude approaches and have offered a more rapid and more accurate assessment of engraftment and the chimeric state and at a much earlier post-transplant stage. Within this molecular approach, several methods have been devised. Amongst them is the use of restriction fragment length polymorphisms (RFLPs), use of microsatelites and variable number tandem repeats (VNTR) (Sreenan et al., 1997). The use of an even more elegant method has also been tried i.e. the use of short tandem repeats (STR) (Frankel et al., 1996). The rationale is simple. In the genetic sequence of an individual there are short repeats of DNA sequences and this phenomenon varies from one person to another in terms of the number of repeats for each particular sequence. Hence, this polymorphism for the STR and VNTR in each individual offers a molecular pattern, which is unique for every individual. Using the polymerase chain reaction method to amplify the VNTR or STR, one can then identify the presence of small numbers of donor cells in the peripheral blood of the recipient in a very sensitive manner. The theoretical advantages of VNTR and STR analysis include increased sensitivity, the use of smaller quantities of DNA, easier preparation of the DNA, faster turnaround time, the elimination of restriction enzymes and radioisotopes. This state-of-the-artapproach for the analysis of engraftment and chimerism in post bone marrow transplant patients allows for the earlier detection of engraftment, prediction of disease relapse and graft rejection.

Stem cell transplant -

Min Hong SAW

Hospital Lam Wah Ee, Penang, Malaysia

Haematopoietic stem cells (SC) belong to a heterogeneous group of cells that are pluripotent, capable of self-renewal, and able to reconstitute an ablated marrow. Small numbers of the stem cells may contribute to fairly large part of the mature haematopoietic cells, or different clones may take turns to produce blood cells at different time frames. There are also differences between the clones in terms of the "primitiveness", and some are more totipotent than others. SC transplantation involves a process where the preserved and frozen stem cells which have been spared "conditioning", are returned to the recipient for re-engraftment of the marrow. The conditioning treatment is aimed at eradicating malignant cells and at making the host immune system more receptive to allogeneic cells. This is achieved by high dose chemotherapy +/- radiotherapy. The same concept has also been applied to autologous transplant except in this case no immune reaction happened. This concept of using overwhelming cytotoxin to overcome the resistant residual tumour cells has been modified recently. It is now widely accepted that transplantation is a form of immunotherapy. The high dose treatment will only cure a small proportion of patients, the great majority depends on the immune system to eradicate the residual tumour cells. The immune cells can be potent in killing the cancer cells. This is done either through the release of granzymes from the reactive immune cells, or by the activation of FAS receptor which induces apoptosis in the target cells. Currently there are three different sources of SC in allogeneic transplantation whether related or unrelated. These are the bone marrow, the peripheral blood (PBSC) and the cord blood. It is possible that bone marrow may become less important as a source of SC for transplantation. The rapid engrafting ability of the PBSC has been demonstrated over eight years ago. This rapid recovery of blood counts has been translated into lesser procedure-related morbidity and mortality in SC transplantation. As such it has been shown to give better overall results in the setting of transplantation for CML. SC from cord blood have several advantages. Cord blood SC have certain proliferative advantage, moreover the immune system is much more tolerant and less reactive leading to a less stringent criterion for HLA matching between the donor and recipient. However, the low numbers of nucleated cells during repletion lead to a very delayed engraftment in some cases. Slow recovery of cell counts increases the complication rate of the transplant. Future use of ex-vivo expansion of the cord blood SC may overcome this problem, and cord blood could become a valuable and important source of SC for transplantation.

Allogeneic minitransplant: who would benefit?

SK CHEONG

Department of Haematology & Transplantation, MAKNA-HUKM Cancer Institute, Hospital Universiti Kebangsaan, Kuala Lumpur, Malaysia

Allogeneic bone marrow or peripheral blood stem cell transplantation traditionally uses myeloablative regimen for conditioning to enable grafting of donor's stem cells. Animal experiments have shown that a milder non-myeloablative conditioning regimen does allow engraftment to occur. This procedure is known as minitransplant. Non-myeloablative conditioning regimens are low-intensity immunosuppressive treatment given to the recipient before infusion of donor's stem cells. It was reported to have decreased immediate procedural mortality, in particular secondary to acute graft versus host reaction. However, it did give rise to higher risks of graft rejection, tumour tolerance and disease progression. Fortunately, appropriately administered donor lymphocyte infusion has been shown to establish full donor chimerism (complete donor stem cell grafting in the recipient's bone marrow) and potentiate anti-tumour effect (graft versus tumour reaction). The reduction of immediate transplant mortality allows the procedure to be carried out in older age groups, patients with concomitant disease such as invasive mycosis that otherwise would have made the patients unfit for the procedure, patients with non-malignant disorders such as congenital immune deficiencies, autoimmune disorders or thalassaemia majors. The regimen also allows transplantation of genetically manipulated haemopoietic stem cells (gene therapy) to be carried out more readily in the immediate future.

MIXED SYMPOSIUM 16: DRUG DEVELOPMENT IN TROPICAL DISEASES

Natural drug products - HIV/AIDS drug development

Tuah JENTA

Sarawak MediChem Pharmaceuticals. Inc.

The calanolides are naturally occurring pyranocoumarins that exhibit a range of anti-viral and antimicrobial activities. Calophyllum lanigerum and Calophyllum teysmannii (rainforest trees more commonly known as bintangor trees) are natural sources of calanolide A and calanolide B respectively. Both compounds exhibit anti-HIV and anti-tuberculosis activities. Dihydrocostatolide and oxocalanolide are semi-synthetic derivatives of the naturally occurring calanolides, and also exhibit anti-HIV activity. Oxocalanolide is also active towards human cytomegalovirus (HCMV). Sarawak MediChem Pharmaceuticals, Inc is coordinating pre-clinical and clinical drug development programmes with the naturally occurring and semi-synthetic calanolides. Our company is based in Chicago and represents a Joint Venture between the Sarawak Government and Advanced Life Sciences, Inc. Calanolide A is currently in Phase I/II clinical development and has already demonstrated anti-HIV activity in HIV-infected patients. A separate pre-clinical programme, supported by the U.S. National Institute of Allergy & Infectious Diseases (NIAID), is investigating the anti-tuberculosis properties of calanolide A. Unlike calanolide B, calanolide A exists in **only** very small quantities in its natural form. Therefore, for the purposes of clinical study, quantities of calanolide A are manufactured using proprietary chemical processes that are owned and patented by Sarawak MediChem. Pre-clinical programmes for calanolide B and dihydrocostatolide (to develop their anti-HIV activities) are supported through the Developmental Therapeutics Program of the U.S. National Cancer Institute (NCI). A pre-clinical programme to evaluate the anti-HCMV activity of oxocalanolide is supported by the U.S. NIAID.

Clinical trial development

P OLLIARO

Switzerland

Abstract not available

IMR SYMPOSIUM 1: NUTRITION UPDATE

Nutrition for diabetes

Paulo POZZILLI

University Campus Biomedico, Rome, Italy and Department of Diabetes and Metabolism, St Bartholomew's Hospital, London, UK.

Optimum dietary approaches in Type I and Type II are similar in both disease conditions. The goal of dietary therapy for management of diabetes, as outlined by the American Diabetes Association, include normalization of blood glucose levels, optimization of blood lipoprotein levels, provision of adequate energy for attaining a desirable body-weight and prevention of acute and chronic complications, in addition to improvement of overall health. Specifically, for patients with Type II diabetes mellitus, there are two major considerations for achieving these goals: (a) diet composition and (b) reduction in total energy intake to achieve desirable body-weight. Reduction of body fat is the cornerstone for management of Type II diabetes; however, long-term weight management remains a challenge for patients and health-care professionals. Implementation of an optimal diet is a complex process encompassing the elements of diet composition but extending into lifestyle changes necessary to overcome barriers to dietary compliance. Owing to its complicated nature, this

challenge requires many different tools and techniques to meet the individual patient's needs. Barrier to successful weight loss in patients with Type II diabetes include:-Physical inactivity: Physical limitations secondary to illness or injury, Sedentary occupation and leisure-time activities; -Medications: Stimulate appetite and/or lead to increased food intake, Decrease metabolic rate; -Education: Poor understanding of diet/disease relationship, Misinformation, Lack of referral for dietary counseling/follow-up; -Psychological factors: Sense of isolation, Feelings of deprivation, Negative emotions, Denial of condition; -Lifestyle/environment: Time pressures/competing priorities, Lack of support from family/friends, Social events. Follow-up educational sessions with the dietician is important and focus on various topics such as food composition, food labeling, shopping, recipe adaptations, and eating in restaurants. Dietitians teach patients to use food records in conjunction with blood glucose records to observe patterns in blood glucose control. A problemsolving approach is used to analyze individual blood glucose response to food, activity and drugs. Patients are then able to make adjustments in food intake and/or insulin dosage to maintain target blood glucose levels. Algorithms for food, medication and activity can be developed to help manage diabetes on a daily basis. Small careful steps over weeks or months help move the patients toward nutrition goals. Follow-up sessions by the dietician can be accomplished via clinic visits and telephone conversations to facilitate problem solving. Family members should be involved in the nutrition education process and are encouraged to follow the same life-style recommendations as the person with diabetes.

Changes in dietary patterns and chronic diseases: where are we heading?

E-Siong TEE

Division of Human Nutrition, Institute for Medical Research, Kuala Lumpur, Malaysia

Rapid and marked socioeconomic advancements in Malaysia for the past two decades have brought about significant changes in the lifestyles of communities. These include significant changes in the dietary patterns of Malaysians e.g the increase in consumption of fats and oils and refined carbohydrates and a decreased intake of complex carbohydrates. This resulted in a decline in the proportion of energy from carbohydrates, while an increase in the percentage contribution of fat has been observed. Changes in meal patterns are also evident: more families eat out, busy executives skip meals, the younger generation miss breakfasts and rely too much on fast foods. Many Malaysians have the mistaken belief that the taking of vitamin and mineral supplements can make up for the lack of these nutrients in their daily diets. In addition, communities have become generally more sedentary. All these changes have brought about undesirable effects with significant proportions of the affluent segments of the population'being afflicted with various non-communicable diseases associated with overnutrition, namely obesity, hypertension, coronary heart disease and cancers. Nutrition activities and programmes are now being directed to tackle this increasing trend, whilst still attempting to eliminate the undernutrition problems. The ultimate strategy towards achieving a healthy nation is the promotion of a healthy lifestyle, including inculcating a culture of healthy eating. Comprehensive long tenn programmes, including a series of Healthy Lifestyle (HLS) **Programmes** have been carried out by the government. The implementation of these programmes is, however, a challenge to health and nutrition workers. There is a need to examine the strategies for nutrition education to ensure more effective dissemination of information. The challenge is to determine how best to promote healthy eating within the present scenario of rapid urbanisation. "western" dietary pattern influence, a whole barrage of convenience and "health" foods and nutrition misinformation.. Malaysia continues to march ahead with its development plans to elevate the nation and its people to an even higher level of socio-economic status. The crucial question is: are we able to arrest the increase in these diet-related chronic diseases? Or are we heading towards further deterioration in dietary pattern and increase in these diseases? It will be a difficult and challenging journey ahead, requiring the concerted effort of all in the country.

Current trends and controversies in parenteral nutrition TM RAMANUJAM

Department of Surgery, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

Parenteral nutrition was successfully applied as a basic and clinical technique 30 years ago. Despite many unanswered questions, parenteral nutrition represents a major breakthrough in the long periods of survival of patients who cannot take adequate enteral intake. Although its efficacy is well proven in certain areas, such as short bowel syndrome and tropical inflammatory bowel disease, its use in other areas remains controversial. Critical evaluation of the patients receiving parenteral nutrition has lead to better understanding of the need for nutritional support and its timing of administration especially in critically ill patients. Indirect calorimetric studies in these patients have confirmed that the previous estimated requirement (3000-4000 caloriesIday) is very high and the actual measured resting expenditure is around 1400 calories lday in adults. A similar downward trend has been proven in paediatric patients as well. The role of early. "aggressive" nutritional support has been questioned. The major danger of aggressive nutritional support in malnourished patients - the "Re-feeding" syndrome has been identified. Newer techniques of administration, newer and refined nutrition formulations for infants and adults, and those with specific organ dysfunction are being developed and used. Newer indications for TPN are being evaluated. Cholestasis remains as the major unresolved problem and sepsis still is the most dangerous problem. The effect of selenium and carnitine deficiency on the myocardium has led to appropriate supplementation of these in patients on long term TPN. Aluminium toxicity is emerging as a major cause for concern in long term TPN. The role of routine addition of heparin was questioned earlier, but the recent recognition of the problem of chronic pulmonary thromboembolic disease in long term TPN has justified the need for routine addition of heparin in TPN. The rote of streptokinase, ethanol and 0.1N HCL in unblocking the catheters due to blood clots, fat and mineral deposits has been well documented. Although the current trend is to use enteral nutrition whenever feasible, parenteral nutrition has its specific role and judicious use of both parenteral and enteral nutrition will benefit the patients. In future, substrate specific nutritional needs of the gut, liver and immune system, which act at cellular level, may be used to improve the outcome. Supplements like glutamine, arginine, branched chain amino acids, growth factors, omega-3 fatty acids, dietary RNA (Immunonutrition) and modified structured lipids have been tried, but studies conducted so far have not substantiated any advantages of such substitutes. However, there is no doubt that in the near future this art and science of nutritional support of the whole organism and of the key organ system will lead to the cellular level of nutritional support and provide optimal nutrition for all patients.

IMR SYMPOSIUM 2: MOLECULAR BIOLOGY IN TROPICAL DISEASES

Molecular approaches to the diagnosis of tropical diseases

FEG COX

Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, United Kingdom

The requirements of a diagnostic test are specificity, sensitivity, ease of performance and cost and most current techniques **suffer** from deficiencies in one or more of these areas. The gold standard is the direct identification of the causative organism and, if appropriate its isolation in culture or in cell lines. Such methods are useful, if not essential, for the diagnosis of an infection in an individual but are too expensive and time consuming for epidemiological surveys. The most widely used alternatives, immunodiagnostic techniques, can be used for the identification of antibodies in the serum or indirectly for the identification of protein or carbohydrate antigens in the circulation or in tissues. Although easy to perform and suitable for large scale application, most immunodiagnostic techniques sufferfrom problems of false positives and false negatives, cross reactivity, difficulties in distinguishing between patent and past infections and being expensive. There is an obvious need for improvement and the future of diagnosis lies in the development and use of molecular techniques particularly those

based on the detection of nucleic acids that can be isolated and amplified using the polymerase chain reaction (PCR). In essence, molecular techniques involve the use of primers that bind to, and can thus be used to identify, specific fragments of pathogen nucleic acids. The primers can be designed for specific-purposes such as the identification of a species, strain or variant. Such techniques permit the identification of minute amounts of material and are unlikely to give false positives. Molecular techniques also have the potential for automation and high-speed turnover. Currently, these techniques are in the developmental phase and tend to be expensive and to suffer from problems of reproducibility. Nevertheless molecular techniques have been used with encouraging results some of which will be discussed with special reference to parasitic infections. In addition, some of the problems inherent in developing and using molecular techniques for the diagnosis of tropical diseases will also be discussed.

Molecular approaches to tropical diseases research

Carlos M MOREL

Director, UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) World Health Organization, Switzerland

Tropical diseases research has undergone a profound change as molecular approaches have, increasingly, been incorporated into basic and applied laboratory, diagnostic, clinical and epidemiological investigations. Seen by many some years ago as "too sophisticated and therefore "not suitable for use in disease endemic countries", the science and technology of molecular biology have quickly become indispensable companions of the tropical diseases researcher. Although at first only the most advanced centres in the North were indeed privileged to use molecular biology approaches, these approaches have progressively found space in disease endemic countries - first in a few centres of excellence and now in a number of institutions where they are routinely used in basic and applied laboratory or field projects, as described in the presentation. The path from the first cloning of a parasite gene in the 80's to the imminent complete sequencing of several parasite genomes has taken less than 20 years - and as a result tropical diseases research will never be the same. But the so-called "molecular biology revolution" is far from completed: new information and knowledge accumulate at an ever increasing rate and will continue to profoundly impact on the way we think, interpret and do research in tropical diseases. Coping with this continuing revolution represents a real challenge for disease endemic countries but, as learned in the past, harnessing its power may open new avenues for the control of tropical diseases.

Human genetic factor in parasitic disease

Kenji HIRAYAMA

Department of Medical Zoology, Saitama Medical School, Moroyama, Japan

To clarify host genetic factors determining susceptibility to parasitic diseases, DNA polymorphism within human major histocompatibility complex (HLA) region was analyzed in the patients with Chagas disease (Trypanosoma cruzi infection), with Schistosomiasis japonica, and with cerebral malaria. In Guatemala, the frequencies of HLA-B35 and MICA-AS were significantly increased in the seropositives (Chagasic patients). The effects of two genes were synergistic on the susceptibility. In China, severity of hepatic fibrosis due to repeated Schistosoma japonicum infections was estimated by the pattern of ultra-sonography as grade 0 (n=44), grade I (n=81), grade II (n=99), or grade III (n=6). HLA-DRB I*1101 (Pc < 0.02) and HLA-DRB I*1501 (Pc < 0.02) were associated with protection and susceptibility to fibrosis. HLA-class II molecules might play a role in preventing or promoting fibrotic liver change after deposition with Schistosome eggs. In Myanmar, polymorphism of TNF-a promoter region was analyzed in the patients with cerebral malaria. TNF-a flanking region showed biallelic polymorphic sites at -238, -308, -857, -863, -1031, and there were 7 alleles (TNFP-A, B, C, D, M1, M4, M7). TNFP-D allele was significantly associated with cerebral malaria.

IMR SYMPOSIUM 3: ADVANCES IN THE CONTROL OF VECTOR-BORNE DISEASES

The global programme to **eliminate** lymphatic **filariasis** EA OTTESEN

World Health Organization, Geneva, Switzerland

Ten years ago, no one foresaw that in the year **2000** there would be a global programme to eliminate lymphatic filariasis (LF) that is already **2** years old, active in >20 of the **80** endemic countries and operating under a wholly new paradigm in public health - a paradigm affirming that **public/private** sector partnerships are essential in sharing both responsibilities and responses to global health problems. Principally responsible for this initiative have been: 1) *the development of tools* capable of effecting **LF** elimination (simple intervention regimens to eliminate blood microfilariae; simple, effective regimens for managing disease; simple, accurate diagnostic tools to define the presence of infection and to monitor programme success), 2) a new *understanding of the pathogenesis* of LF (including recognition that infection is acquired during *childhood*, first causing subclinical and then overt disease by parasite damage to the lymphatics and subsequent bacterial superinfection); and 3) *international commitment* that includes the largest-ever private sector drug donations (of albendazole from **SmithKline Beecham** and Mectizan [ivermectin] from Merck & Co., Inc.) as well as a political mandate from the World Health Assembly and appreciable humanitarian support from more than **20** governmental and non-governmental aid organizations working together in a partnership termed the Global Alliance to Eliminate Lymphatic Filariasis.

Recent research on Dengue vectors

Han Lim LEE

Division of Medical Entomology, Institute for Medical Research, Kuala Lumpur.

Dengue today still remains a public health problem in many tropical and subtropical countries. In the absence of any specific treatment and an effective vaccine to date, the control of dengue depends primarily on the interruption of disease transmission by the vectors, Aedes aegypti and Ae albopictus. Major advances in the control, surveillance and bionomics of these vectors in the past 5 years are reviewed. In the development of vector control technologies, studies were conducted to search for more effective control agents. Microbial control agent such as Bacillus thuringiensis H-14 (Bti) has been shown to be highly and specifically effective against dengue vectors and effective mass application techniques such as ultra-low-volume spraying of these agents have been developed and used. Simultaneous spraying of chemical insecticides especially the pyrethroids and Bti has further enhanced the control of vectors since both adulticiding and larviciding can now be combined into a single operation. The effectiveness and extended activities (larvicidal activity, wall residual activity) of new insecticides continued to be tested for their suitability in dengue control. Techniques for the rapid detection of possible emergence of vector resistance to chemical insecticides have been developed. A kit is now available for field use. In vector surveillance, ovitrap has been found to be an efficient tool in detection and monitoring the Aedes populations. Based on ovitrap data, a mathematical model incorporating entomological and epidemiological data was first developed and used in outbreak prediction. Molecular and immunological techniques were developed for the detection and monitoring of viral infection in the vectors. The most important finding in bionomic studies of dengue vectors was the discovery of the transovarian transmission of dengue virus from infected adults to the larvae. In other fields of study, a more recent study involved testing the antidengue activity of anti-viral drug, ribavirin and other drug on the development of dengue virus in Aedes aegypti adults. These voluminous research findings and data are now gradually incorporated into dengue control programme in order to effect a more favourable outcome against these vectors and the diseases.

Japanese encephalitis

N RAMAN

Malaysia

Abstract not available

PATHOLOGY SYMPOSIUM 1: LABORATORY INSTRUMENTATION

Testing at the point of care: issues and concerns

SF YAP

Department of Pathology, Faculty of Medicine, University of Malaya, Malaysia

Testing at the point of care, as an extension of the laboratory service, has been practised in various forms. The main objective of performing testing close to the patient is rapid turn around time (TAT) and immediate availability of test results. However, the practice of point of care testing (POCT) was relatively limited until the past decade or so. The increasing use of POCT in the 1990's was the result of two developments - (i) decentralisation of the healthcare service and (ii) major advances in technology. Point of care testing, as it is practised today, generally refers to the use of portable devices to perform biological testing at patient care locations. Operators of the service are largely clinical staff directly responsible for patient care. Superficially, **POCT** is a major improvement over traditional testing in central laboratories. It provides for patient and physician convenience, and improved patient care in the ambulatory setting. In hospitals, the use of POCT allows immediate therapeutic decisions, particularly in critical care areas. However, the fact that POCT is not widely used as an alternative to laboratory testing is indicative of the problems inherent in the service. The main issues are related to (i) problems in the maintenance of the quality of the service, (ii) difficulties in management of **POCT** and (iii) economics. The presentation will focus on these issues and the strategies that have been suggested to tackle these difficulties. The role of the laboratory in POC testing will also be addressed.

Static telepathology: an experience in a private laboratory setting Kai Soon CHAN

Malaysia

Static telepathology is defined as the electronic transmission of digitized ("static") gross or microscopic images for remote consultation, research or education. This paper describes the experience in using static telepathology in a private laboratory over a two-year period. The equipment, method, results and problems are described. The advantages and circumstances in which static telepathology would be useful are also discussed.

Microminiaturisation of laboratory analysers: "labs-on-chips"

Leslie C LAI

Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia

Microminiature devices are being developed for many applications including drug discovery, pharmacogenomics, forensic science, genetic testing, clinical chemistry diagnostic panels, point of care testing and separation science. The size of the chips varies but is typically 1 to 2 cm². They contain micrometer-sized structures within microlitre to nanolitre volume reaction chambers. Microminiaturisation has developed along several paths. Firstly, the demands of drug discovery programmes have stimulated the development of high throughput analysis using high density **arrays**

of microreaction wells on plastic plates. The volume of these wells may be as little as 50 nl for 6,500 well microplates. Secondly, surface microarrays have been developed comprising tens of thousands of 10-100 mm² reaction zones onto which individual oligonucleotides or cDNAs have been deposited or synthesized in situ. These biochip microarrays are proving to be invaluable tools, especially for the detection of genetic disease, infectious agents and expression analysis. A third type of chip exploits micromachined channels, chambers, filters, and other structures for defined analytical purposes, e.g. micrometer-sized channels etched in glass are effective for capillary electrophoresis, glass-capped silicon chambers can be used for polymerase chain reaction, and silicon filters are effective for isolation of white cells from whole blood. The integration of different structures on the same chip provides a combination of analytical functions. Biochip array technology was developed by Randox to enable simultaneous multi-analyte detection of a wide range of diagnostic parameters on a single patient sample, e.g. cardiac markers, tumour markers and drugs of abuse. The **Randox** biochip assays are based on immunoassay principles with chemiluminescence as the means of detection, using either competitive or sandwiched assay formats. These biochip assays are run on the **Randox** analyzer EVIDENCE. The applications of the multianalyte biochips coupled to the automated handling system (EVIDENCE) provide high sample throughput and may enable more rapid diagnosis. The ultimate goal of any microchip development effort is a fully integrated analytical system, incorporating sample preparation, biochemical reactions and detection as well as result analysis - "lab-on-a chip".

PATHOLOGY SYMPOSIUM 2: THALASSAEMIAS

Phenotypic diversity of a monogenic disease

Swee Lay THEIN

GKT School of Medicine, Department of Molecular Haematology, King's Denmark Hill Campus, London, United Kingdom

A major challenge in medical research is to relate genotype to phenotype. Since the early descriptions of sickle cell disease, the simplest of monogenic diseases it has become apparent that genotype at a single locus rarely predicts phenotype, the clinical phenotype can vary between families and even within families, affecting a different sub-set of organs with different ages of onset. I will focus on the inherited disorders of haemoglobin the **commonest** monogenic diseases, to illustrate the complexity of the contributing molecular mechanisms and to assess the problems one may encounter in **relating** genotype to phenotype in other common monogenic diseases such as cystic fibrosis. Understanding of the genetic interactions that determine phenotype in apparently monogenic diseases should help towards dissecting the complex interactions between the different genes that are involved in polygenic diseases. Such observations will be of major importance not only in predictive genetics and genetic counseling, but also in providing prognostic information for decision-making in novel and gene therapy programmes as they become available.

Rapid diagnosis of **Thalassaemias** using molecular techniques Jin Ai Mary Anne TAN

Department of Allied Health Sciences, Faculty of Medicine, University of Malaya, Malaysia

The inherited disorders of haemoglobin are the commonest single gene diseases. Homozygous or compound heterozygous states of these conditions result in severe anaemia with splenomegaly and skeletal modifications (β-thalassaerhia major), in severe haemolytic anaemia (sickle cell disease) and in hydropic foetuses dying during pregnancy or soon after birth (Bart's hydrops foetalis). Although present management of such conditions, with the exception of Hb Bart's hydrops foetalis, gives a probable life expectancy beyond the third of fourth decade, clinical and health complications in affected individuals pose a heavy load on blood transfusion and paediatric services. An alternative approach in addressing this problem is to offer efficient and economical molecular analysis and

prenatal diagnostic services for these disorders. Both deletional and non-deletional mutations produce a-thalassaernias. The a^o-thalassaernias are due to large deletions of the a-gene complex which can be identified directly by gene mapping. DNA analysis for molecular characterization of the a-thalassaernias began with Southern blotting and restriction enzyme mapping and identified the different single a-gene deletions (-a) and heterozygous α°-thalassaemia (αα/--). DNA amplification by the polymerase chain reaction allowed both -aa haplotypes and αα/-- genotypes to be diagnosed in either a single or multiplex PCR. DNA analysis for molecular characterization of the Pthalassaemias began with linkage analysis of **RFLPs** to normal and P-thalassaemia chromosomes in family studies. DNA amplification followed by restriction enzyme digestion was used to identify βthalassaemia mutations that either abolished or created a restriction site within the P-globin gene. The dot blot-allele-specificoligonucleotidehybridisation**technique** and AmplificationRefractory Mutation System allowed direct detection of point mutations, nucleotide insertions and deletions involved in β-thalassaemias. Molecular techniques have offered rapid, reliable and economical diagnostic tests for the molecular screening and prenatal diagnosis of the thalassaemias. Prevention of the severe thalassaemic syndromes will continue to be one of the more realistic means of reducing the incidence of these disorders.

Haemoglobin F switching and its therapeutic application

Swee Lay THEIN

GKT School of Medicine, Department of Molecular Haematology, King's Denmark Hill Campus, London, United Kingdom

The switch from fetal to adult haemoglobin synthesis occurs just before birth, but the switching process is not complete in that small amounts of **HbF** production (< 1% of total haemoglobin) persist into adult life. They are restricted to a sub-set of red cells termed F cells (FC) The values of HbF and FC in adults vary considerably with a continuous distribution that is substantially positively skewed, and studies have shown that these values are overwhelmingly genetically controlled (heritability=0.89). The factors known to influence HbF levels include age, sex and genetic determinants both linked and unlinked to the P-globin gene cluster. Against this background of its distribution in normal population, higher levels of HbF in adults have been observed in association with acquired conditions, e.g leukaemias, or as a direct result of an inherited disorder, e.g hereditary persistence of fetal haemoglobin (HPFH). Although increased levels of HbF are present in P-thalassaemia, the increases are limited and appear to be secondary responses to dyserythropoeisis and haemolysis However, there are individuals with sickle cell disease (SCD) and β -thalassaemia who have a genuine increase in HbF levels with a major beneficial effect. The ameliorating effect of HbF in SCD and β -thalassaemia has prompted several pharmacological approaches for the reactivation of HbF synthesis and although these have met with limited success, the fact that HbF synthesis can be reactivated at all in adults, is extremely encouraging. It is hoped that a better understanding of the control of haemoglobin switching might allow its manipulation and provide novel therapeutic approaches to the β haemoglobinopathies

PATHOLOGY SYMPOSIUM 3: CARCINOGENESIS

p53 in carcinogenesis

PL CHEAH

Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

p53 mutations have been documented in around 40% of cancers making it the most common genetic event in human malignancies. Located on chromosome 17p13, p53 encodes a 53 kilodalton modular nuclear phosphoprotein, which functions predominantly as a transcriptional regulator. p53 protein within a cell integrates signals arising from a wide range of cellular stresses and directs cellular responses through several downstream genes via its conserved domains viz N-terminal, SH³-binding,

sequence-specificDNA binding, tetramerization and C-terminal. Under normal circumstances of cell growth, p53 protein has a relatively short half-life, being mainly controlled through an autoregulatory loop in which Mdm-2 binds p53 and targets it for nuclear export and ubiquitin-dependent proteolysis. In times of cellular stress, p53 is phosphorylated by protein **kinases** at several sites, becomes stabilised, and acts via different pathways that ultimately lead to protection and adaptation of the damaged cell through growth arrest or apoptosis. In the event of mutational change or inactivation of the gene by virally-encoded proteins e.g. HPV E6, p53 protein can lose its protective and adaptive functions, allowing damaged cells to continue in the cell cycle. Missense point mutations within the DNA-binding domain (exons 5-8), form the most frequent alteration of the p53 gene in human cancers. Although much has been learnt regarding its role in carcinogenesis, including recent demonstration of "gain of function" mutants, existence of p53 polymorphisms, gene dosage effects and p53 homologues, many questions still remain unanswered for example it is still even unclear whether cell cycle arrest or apoptosis is the prime factor in oncogenesis.

Telomeres and telomerase in cancers

LM LOOI

Department of Pathology, Faculty of Medicine, University of Malaya, Malaysia

Telomeres are the ends of linear eukaryotic chromosomes that play essential roles in cellular replicative activities and maintenance of chromosomal integrity. Human telomeres consist of a hexameric sequence ³TTAGGG⁵ in tandem repeats of 100-1000s. It has been reported that human telomeres shorten by about 50-200bp after each round of normal somatic division, so that after 50 to 70 divisions, the loss of genetic material reaches a critical stage and the cells undergo senescence and eventual cell death. This hypothesis of progressive telomere shortening as a function of aging in vivo has been referred to as the "mitotic clock." Telomerase is a ribonucleoprotein, which is capable of synthesizing telomeric DNA onto chromosomal ends using a segment of its RNA component as a template. First discovered in Tetrahymena and other eukaryotes in 1989, it has been convincingly demonstrated in humans in 1995. Studies indicate strong telomerase activity in germ cells (ovary and testis) and various tumours but weak or no activity in normal somatic tissues. This has led to the notion that telomerase plays a key role in the neoplastic cell immortalization process by restoring telomere length. Furthermore, telomerase activity has been shown to be repressed in immortal cell lines at the quiescent phase or during cellular differentiation, providing the basis for a repression-derepressionmodel for telomerase regulation. A review of current literature shows that about 86% of tumours exhibit telomerase activity. Studies at the Department of Pathology, University of Malaya has also demonstrated telomerase activity in 20-60% of neoplastic tissue samples whereas nonneoplastic controls show almost no telomerase activity. That the differential presence of telomerase may provide a potential basis for anti-neoplastic chemotherapy has generated considerable excitement and optimism. The feasibility of using telomerase assay as an adjuvant marker of malignancy has also been mooted. Nevertheless, the telomerase mechanism does not appear to be ubiquitous and it is likely that there are alternative or co-existent mechanisms for cell immortalization.

$\label{lem:constraints} \textbf{Recent developments of detecting chromosomal translocations}$

PUTERI Jamilatul Noor

Haematology Division, Institute for Medical Research, Kuala Lumpur, Malaysia

The general outcome of chromosomal translocations in human cancer (leukemias and solid tumours) is gene fusion, which is easily detectable by cytogenetic and molecular methods. This paper will describe the two proven powerful methodologies that have been successful in land-marking chromosomal regions and genetic changes relevant to tumourigenesis. The molecular cytogenetic technique, in particular fluorescence *in situ* hybridisation (FISH) allows us to identify complex chromosome aberrations or subtle rearrangements limited by conventional karyotyping. This

technique can be applied throughout the cell cycle, in non-dividing cells, dead cells, fixed cells and archival specimens. Improved digital imaging and combinatorial fluorescence approaches have also been developed to increase the number of discernable probes resulting in multi-colour karyotyping, which include CGH, multiplex FISH, RxFISH and spectral karyotyping (SKY). On the other hand, PCR-based technology such as RT-PCR, competitive and real time RT-PCR, is useful for detection and quantification of specific fusion transcripts in neoplastic disorders. Diagnostic molecular marker such as AML1/ETO t(8;21) and NHL t(14;18) fusion transcript, has direct application by real time PCR for quantifying MRD levels in various malignancies with specific chromosomal translocations. In known translocation abnormalities, (e.g. AML) the use of poly/monoclonal antibodies as an investigating tool for identification of fusion proteins is widely used. Other new technologies are emerging such as laser-capturemicrodissectionand microarray gene chips which can offer quantitation of a wide panel of genes from clinical samples. The identification and molecular characterisation of specific chromosomal translocations or breakpoint regions as potential hot spots for genes will provide insights into tumourigenesis processes and offer new tools for diagnosis, prognosis and monitoring of cancer patients; in particular of remission and early relapse detection.

ANAESTHESIOLOGY SYMPOSIUM 1: ANAESTHESIA IN THE TROPICS

Pre-anaesthetic assessment/routine investigations

Siew Hian NG

Department of Anaesthesia & Intensive Care, Penang Hospital, Malaysia

The ultimate goal of pre-anaesthetic assessment of patients is to reduce the morbidity associated with anaesthesia and surgery. The goals of the assessment are: to educate the patient about anaesthesia, perioperative care, and pain treatment in the hope of reducing anxiety and facilitate recovery; to obtain pertinent information about the patient's medical history and physical and mental conditions; to determine which tests and consultations are needed and, guided by patient choices and the risk factors uncovered by medical history, to choose the care plans to be followed, and to obtain informed consent. Non-expensive multi-phasic batteries of laboratory tests have been used routinely to screen for diseases in asymptomatic patients undergoing surgery. Increasing evidence have shown that routine laboratory tests are not only ineffective in detecting diseases, they increase risk to the patients, increase medico-legal risks to the physicians and add cost. It is recommended that preanaesthetic assessment should be based on clinical judgement and any investigations guided by medical history and physical examination. A selective utilisation of routine examination can then accurately supplement the clinician's evaluation. In spite of agreed criteria, there have been errors in ordering diagnostic tests. Ironically, while the number of unnecessary tests has reduced **significantly**, there has been a corresponding increase in the percentage of tests which were not performed although clinically indicated. Since the risk of not performing indicated tests is greater than that of doing unnecessary tests and for maximal benefits, there is a need to educate the clinicians in the proper conduct of preoperative assessment.

Ethnic and cultural considerations in anaesthesia MOHAMED NAMAZIE Ibrahim

Department of Anaesthesioldgy, North West Armed Forces Hospital, Tabouk, Saudi Arabia

The homogenous nature of many nations has been gradually breaking down over the last half of the last century and has gained momentum in the last couple of decades. This will continue to be so in the foreseeable future with many restrictive barriers being lifted to allow free movement of people from country to country. Many nations are now being identified as multiethnic, multicultural and multireligious. This phenomenon has made it necessary for health care providers to understand and appreciate the interethnic differences ta be able to provide appropriate health care for their patients of different ethnicity. Genetic variations, cultural practices, dietary practices, environmental and

living habitats, can contribute to the disease patterns and variations that occur among the different ethnic groups. Interethnic differences due to genetic variations have also been found to be important factors accounting for interindividual variations in drug responsiveness and disposition. Interethnic differences have not received much attention in the practise of anaesthesia in Malaysia though we have been multiethnic for a long time. Some of the variations, for example, pain tolerance and experience in a certain group, have often been dismissed as a cultural phenomenon without any scientific basis. Recent investigations elsewhere have shown genetic and/or other molecular basis for drug disposition in different ethnic groups that could explain some of the clinical observations. This presentation will endeavour to highlight some of the ethic and cultural differences that have been documented. The importance of these differences should make us re-evaluate our current practice and individualise not only drug dosages but also our approach to patient care taking into consideration the many cultural practices and religious beliefs of the patient population we are dealing with.

Health economics
Nirumal KUMAR

Malaysia

Abstract not available

ANAESTHESIOLOGY SYMPOSIUM2: TROPICAL DISEASES – INTENSIVE CARE MANAGEMENT

Intensive care management of viral encephalitis Augustine YEW

Department of Anaesthesia and Intensive Care, Kuala Lumpur Hospital, Malaysia

Between September 1998 and June 1999, there was an outbreak of severe viral encephalitis in Malaysia associated with a mortality of 106 patients. This mysterious vicious killer is now known as Nipah virus, a newly discovered paramyxovirus. In general, the management of viral encephalitis requires a systemic approach, as its causes are so diverse. Along with a careful history of the symptoms, the physician must consider epidemiological features such as the season, geography and any insect or animal exposures. Some manifestations may influence likelihood of certain diagnoses for example; segmental myoclonus appears to be a common and prominent sign along with fever and headache in Nipah encephalitis. Computed tomography or magnetic resonance **imaging** should be performed prior to lumbar puncture. Diagnostic imaging is helpful in ruling **out treatable** causes of altered mental status and also may identify patients with increased intracranial **pressure** in whom lumbar puncture may be dangerous. Unless contraindicated, an early lumbar puncture should be performed especially if bacterial meningitis need to be ruled out. **From** a microbiologia standpoint, both serologic and virology studies are invaluable. Among them include detection of the virus via polymerase chain reaction, isolation from brain biopsy and antibody detection, An additional useful tool is electroencephalogram. Treatment strategies are tailored to the severity of the illness and specific antiviral therapy. Intensive supportive care is usually indicated in patients with encephalitis. Relatively few viruses can be treated with specific antiviral chemotherapy. Among them are acyclovir for Herpes simplex and Varicella zoster viruses, ganciclovir for Cytomegalovirus and amantidine for Influenza virus. Counseling of family members and next-of-kin with regards to brain death and care of the patient in those who survive but with neurological sequelae are important considerations.

ICU management of leptospirosis Lela MANSOR

Department of Anaesthesiology & Intensive Care, Hospital Kuala Lumpur, Malaysia

Leptospirosis should be considered in the differential diagnosis of a patient who presents to ICU with an acute vasculitic febrile illness associated with multisystem organ dysfunction, especially if there is preceding history of contact with animals. This is a zoonostic infection caused by the spirochete Leptospira Interrogans. Human, the dead end host, become infected when they come in contact directly or indirectly with the urine of infected animals. Increased prevalence is seen during the wet season especially following a flood. Two clinical forms of the disease occur: anicteric (90% of cases) and icteric (10%) but the initial presentation is the same in all patients. The disease follows a biphasic course, with an initial septic phase in the first 3 to 7 days, followed 10 to 30 days later with the immune phase. This phase is associated with some deterioration of body systems. The anicteric patient may then present with aseptic meningitis or with pulmonary infiltrates which may requite ICU care. Patients with icteric leptospirosis (Weil's Disease) have more severe manifestation with early onset of hepatic and renal failure associated with bleeding diasthesis and pulmonary haemorrhage and can present to ICU in prostration and circulatory failure. Management in ICU include ventilation, maintenance of the circulation, correction of bleeding diasthesis, renal support, liver support and cerebral protection if CNS is involved; while confirming the diagnosis and treating the underlying infection as well as preventing further complications and other nosocomial infections. Differential diagnoses such as dengue fever, malaria, typhus, viral hepatitis and bacterial septicaemia need to be ruled out. Diagnostic confirmation is usually by serological studies although cultures may be positive in the blood, CSF and urine. Penicillin is the antibiotic treatment of choice although erythromycin and Doxycycline have been used. Outcome depends on the severity and number of organs involved with high mortality expected when more than two organs fail.

Tetanus and intensive care management

Cheng Cheng TAN

Hospital Sultanah Aminah, Johor Bahru, Malaysia

Severe tetanus should be managed in ICU. Criteria for admission to ICU are.- (1) Generalised spasms, (2) Laryngospasm (3) Uncontrolled rigidity interfering with respiration (4) Autonomic instability. Management in ICU includes:- (1) Passive immunisation (2) Eradication of the organism by wound care and antibiotics (3) Suppression of effects of tetanospasmin by controlling muscle spasms and autonomic instability with diazepam and morphine or magnesium sulphate (4) Early tracheostomy (5) Supportive treatment with particular attention to nutrition. Steps should be taken to prevent nosocomial pneumonias, pressure sores, deep vein thrombosis, pulmonary embolism, gastric haemorrhage and contractures.

ANAESTHESIOLOGY 3: DEBATE – IS THERE A NEED TO REPEAT CLINICAL TRIALS IN TROPICAL COUNTRIES?

Abstracts not available

OBSTETRICS & GYNAECOLOGY SYMPOSIUM 1: INFECTIONS IN PREGNANCY

Intrauterine infection and preterm labour

Raman SUBRAMANIAM

Malaysia

Abstract not available

HIV in pregnancy: antenatal therapy

Verapol CHANDEYING

Department of Obstetrics and Gynaecology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Thailand

In 1994, Protocol ACTG 076 demonstrated that a three-part regimen of zidovudine (ZDV) could reduce the risk for mother-to-child HIV-1 transmission by nearly 70%. The regimen includes oral administration of 100 mg ZDV five times daily, initiated at 14-34 weeks" gestation and continued throughout the pregnancy, during labour, intravenous administration of ZDV in a 1-hour initial dose of 2 mg/kg body weight, followed by a continuous infusion of 1 mg/kg body weight/hour until delivery. Postpartum oral administration of ZDV to the newborn (ZDV syrup at 2 mg/kg body weight/dose every 6 hours) for the first 6 weeks at life, beginning at 8-12 hours after birth. Most perinatal transmission likely occurs close to the time of or during childbirth. The short-term safety of ZDV regimen and other regimens are now available, as a result of follow-up of infants and women enrolled in the various studies. However, the recent data concerning the animal studies of potential transplacental carcinogenicity assert the need for long-term follow-up of children with retroviral exposure in utero. These advances have important implications for maternal and child health. The clinicians considering the use of antiretrovirals in HIV- 1 infected women during pregnancy must take into account two separate but related issues: a) anti retroviral treatment of the woman's HIV infection, and b) antiretroviral chemoprophylaxisto reduce the risk for perinatal HIV-1 transmission. Alternative strategies, reduction of vertical transmissions, may be appropriate according to each country's policies and standard practices. The use of antiretroviral drugs for reduction of perinatal HIV-1 transmission may differ and will depend on local considerations such as availability and cost of antiretroviral drugs, assess to facilities for safe intravenous infusions among pregnant women during labour, and alternative interventions that may be evaluated. Therefore, providing antiretroviral therapy to HIV-1 infected women during pregnancy, whether primarily to treat HIV-1 infection, ro reduce perinatal transmission, or both, should be accompanied by a discussion of the known and unknown short- and long-term benefits and risks of such therapy for infected women and their infants. In the absence of data, drug choice should be individualized and must be based on discussion with the woman and available data from preclinical and clinical testing of the individual drugs. The benefits of antiretroviral therapy in a pregnant woman must be weighed against the risk for adverse events to the woman, fetus, and newborn. Although ZDV chemoprophylaxis alone has substantially reduced the risk for perinatal transmission, when considering treatment of pregnant women with HIV infection, antiretroviral monotherapy is now considered suboptimal for treatment; combination drug therapy is the current standard of care. More aggressive combination drug regimens that maximally suppress viral replication are now recommended. Although considerations associated with pregnancy may affect decisions regarding timing and choice of therapy, pregnancy is not a reason to defer standard therapy. This presentation focuses on antiretroviral chemoprophylaxis for the reduction of perinatal HIV transmission and a) reviews the special considerations regarding the use of antiretroviral drugs in pregnant women, and b) provides updated recommendations on antiretroviral chemoprophylaxis and other interventions for reducing perinatal transmission.

Hepatitis B and pregnancy

R GUAN

Singapore

Hepatitis B infection is a common public health problem in this region. The chronic infection rate is about 6 to 8% in Singapore and Malaysia. It is estimated that around 10% of pregnant women are chronically infected with this virus. About a third to half of them will be positive for **HbeAg**, indicating a highly infectious stage. Acute hepatitis B infection does **not affect** maternal morbidity or mortality, although hepatitis occurring in the last two months of pregnancy may cause premature delivery and vertical transmission of the virus to the baby. There is no increased incidence of congenital malformations, foetal wastage and intrauterine growth retardation in pregnancy complicated by acute hepatitis B. Chronic hepatitis B infection is associated with an increased incidence of infertility. Common obstetric complications include toxemia, hepatic failure, and post-parturn haemorrhage. Increased intra-abdominal **pressure** and therefore portal pressure increases the tendency of oesophageal variceal bleeding. 10-20% of pregnant women with hepatitis B cirrhosis might develop liver decompensationduring pregnancy. Management of liver complications during pregnancy is symptomatic. Anti-viral agents like interferon and lamivudine are contraindicated. Vertical transmission of infection is high if the pregnant mother is **HBeAg** positive and this can be prevented by intramuscular injection of **0.5ml** HBIG and an initiating dose of hepatitis B vaccination.

OBSTETRICS & GYNAECOLOGY SYMPOSIUM 2: SCREENING FOR CANCER IN WOMEN

Ovarian cancer screening

BK LIM

Malaysia

Ovarian cancer is one of the most expensive gynecological malignancies to treat with the least rewarding results. Despite the improvement in chemotherapy over the last 20 years, there's only a single digit improvement in terms of survival. The overall 5-year survival remains quite dismal at about 30%. Survival is a lot better in Stage 1 disease (80% 5-year survival). At least 75% of ovarian cancers are diagnosed at advanced stage in view of its "silent" nature. The "Holy Grail" in the treatment for ovarian cancer lies in the screening. Potential screening methods include ultrasound scanning (transvaginal or transabdominal) and serum CA125 measurement. Colour Doppler imaging has also been incorporated to identify abnormal blood flow to malignant tumours. Serum CA125 has been used in combination with ultrasound scanning or as an initial test followed by ultrasound if the levels are elevated (multi-modal screening). The aim of the entire exercise is to achieve a test of high sensitivity and specificity. The higher the sensitivity the greater the test, the less potential damage it'll cause as a result of unnecessary intervention. The largest multi-modal screening to date (22000) women), by Jacobs et al, reported 79% sensitivity (CI: 49%-95%) at one year. The proportion of ovarian cancers diagnosed at Stage 1 was 36%. The false positive rate was 0.1%. Smaller studies using transvaginal ultrasound (van Nagell 1995) and transabdominal ultrasound (Campbell 1989) have reported sensitivity of 89% and 100%, respectively at one year interval. The false positive rate was 1.3% and 3.5%, respectively. Overall, using ultrasound alone has higher false positive rates (1.2%-5.0%) compared to multi modal screening (0.1%-0.6%). Ultrasound and colour Doppler combination has false positive rates ranged from 0.3%-0.7%. The definitive diagnosis for ovarian cancer can only be made at laparotomy or laparoscopy. Based on an average incidence of ovarian cancer of 40 per 100000 the false positive rates will result in 30 to 120 surgical procedures carried out per cancer detected at annual ultrasound screening. For multi modal screening, between 2.5 to 15 procedures would be carried out for every cancer detected. Screening can generate a lot of anxiety and distress for patients who are tested positive. There will also be a significant number of surgical procedures carried out unnecessarily in the false positive group. For a population screening purpose, one must weigh the cost effectiveness of the screening programme against the effect on ovarian cancer mortality and also the adverse effects experienced by otherwise healthy women. There is

currently no strong evidence to support a routine screening programme for detecting ovarian cancer. Therefore, no screening should be carried out outside the context of clinical trials.

Screening for breast cancer

CH YIP

Department of Surgery, University Hospital, Kuala Lumpur, Malaysia

Breast cancer is the leading cause of cancer deaths in women in Malaysia. The best hope for improving survival is early detection, hence the importance of screening for this disease. Mammography, the most successful method of breast screening has a sensitivity of 80-90% and a specificity of 95%. Other methods such as breast self-examination and ultrasonography of the breast has been shown to be unreliable in detecting early lesions. The first randomised control study of screening mammography was undertaken by the Health Insurance Plan (HIP) of Greater New York from 1963 through 1967. This showed a 30% reduction in breast cancer mortality in the screened group at the end of 7 years. This was followed by similar studies in Sweden, Edinburgh and Stockholm, which showed a benefit in the screened group mainly in women aged 50-74 years. Based on these studies, in the 1980's, screening for breast cancer by mammography was advised for all women above 50 years old. However the appropriate interval between mammographic screening has yet to be determined, and it was felt that the best frequency was probably between 18-24 months, although the American Cancer Society recommendation was for yearly screening. In the 1990's controversy over whether there was benefit in screening younger women arose amid new reports that significant reduction in breast cancer mortality was also seen in women aged 40-49 years who were screened. Based on this, in 1997, the American Cancer Society extended their screening guidelines to include women from the age of 40 years. In January 2000, controversy again arose with a Danish publication in the Lancet, reviewing the methodological quality of 8 major screening trials and concluded that there was no reliable evidence that screening decreases breast cancer mortality However this paper was widely criticised by supporters of mammographic screening. What about population-based screening for breast cancer in Malaysia? Mammographic screening, the only proven method, is costly and involves manpower which is not readily available. The average size of breast cancer in the University Hospital Kuala Lumpur is between 4 and 5 cm and has not changed much in the last 6 years. Breast self-examination and clinical breast examination as a screening method, and ongoing health education programmes, so that women present with smaller tumours is more feasible than mammographic screening.

Endometrial cancer screening - current status

Pritam SINGH

Gynecology Associates Womens Medical Centre, Mount Elizabeth Medical Centre, Singapore

Endometrial cancer (EC) is a common female genital malignancy and in the majority is associated with a good prognosis though subgroups of women are at risk of more aggressive disease with poor prognosis. Screening of the general population is neither justified nor proven to be cost effective; both exfoliative cervical and endometrial cytology are unsuitable techniques for EC screening. Transvaginal (TV) ultrasonography has recently been evaluated to screen women with known risk factors for EC (age, obesity, post-menopausal status, nulliparity, anovulation, **HRT** usage) and is proving to be a feasible and sensitive screening technique. TV ultrasonography which measures endometrial thickness (double layer) both in asymptomatic post-menopausal women and those with post-menopausal bleeding identifies a high risk group (≥8mm endometrial thickness) in whom there is a very high likelihood of EC (20%). Endometrial thickness in post-menopausal women better discriminates patients at high risk of EC & complex hyperplasias then either presence or pattern of post-menopausal bleeding. TV color Doppler ultrasonography is able to detect important differences between benign and malignant endometrium and identifies both neovascularisation with abnormal blood flow patterns and differential flow indices (Resistance Index significantly lower in **ECs**) and

is also able to detect myometrial invasion. TV ultrasonography is a potential screening technique which identifies women P high risk of EC and TV color Doppler ultrasonography is able to identify those with EC and with myometrial invasion. TV color Doppler ultrasonography is thus an aid in tumor staging and identifies a subgroup with aggressive disease and poor prognosis. This in turn facilitates appropriate referral and tailoring of treatment with most efficient utilization of available resources and expertise to obtain optimal outcome in patients with EC. EC screening is appropriate for women with risk factors using conventional TV ultrasonography and to identify the subgroup with aggressive disease and poor prognosis TV color Doppler ultrasonography is an effective tool. These 2 ultrasonographic techniques hold promise for wider application as methods for EC screening in the future.

OBSTETRICS & GYNAECOLOGY SYMPOSIUM 3: ANAEMIASI HAEMOGLOBINOPATHIES IN PREGNANCY

Prenatal diagnosis for thalassaemia

E GEORGE

Unit Hematology, Department of Pathology, Hospital Universiti Kebangsaan Malaysia.

Prenatal diagnosis is done when a couple has thalassaemia trait, have a history of producing a child with beta-thalassaemia major or Hb Bart's hydrops fetalis and when hydrops fetalis is identified in a pregnant woman during antenatal check-up. Hb Bart's hydrops fetalis is nearly always the result of the co-inheritance of two α-thal 1 (a⁰) gene determinants where both a globin genes are deleted. The most common α^0 gene determinant in Southeast Asia is the -- SEA, which deletes 17.5-20 kb of the tt globin gene complex leaving \(\frac{1}{2} \) globin gene intact. The molecular basis for Hb Bart's hydrops fetalis is -- SEA/-- SEA/ ... SEA/ ... THAI, ... SEA/FIL. The most severe form of beta-thalassaemia is transfusion dependent and results from the homozygous state of β^0 ($\beta^0/+\beta^0$). In Asia, the common β^0 mutations are -28 (A to G), -29 (A to G), IVS 1-1 (G to T), CD 17 (A to T), CD 35 (-C), FSC 41-42 (-TCTT), F8C 71-72 (+A), -619 bp, -β^{FIL}, and FSC 8-9(+G). It is mandatory to get informed consent prior to atty procedure; the safety of the invasive procedure, accuracy of laboratory diagnosis, and abortion of the affected **fetuses** are areas where information need to be provided. Fetal sampling procedures depend upon gestational age of the fetus. Fetal DNA is obtained from chorionic villi (CV), amniocytes, and fetal blood (FB), at 10-12, 14-16, 18-24 weeks gestation respectively. Prenatal diagnosis is not recommended after 24 weeks gestation except for Hb Bart's hydrops fetalis. FB samples obtained with cordocentesis by experienced obstetricians are pure. In contrast CV samples always have a risk of maternal contamination. With FB samples both the phenotype and genotype of the fetus can be identified. Studies on CV samples provide only genetic information. Errors arise as a result of incorrect diagnosis in parent., non-paternity and contamination of fetal samples with maternal tissue/blood. In Asia, there is ethnic diversity, with a possibility of number of mutation combinations and where patients may come in quite late in pregnancy makes routine methods not feasible. Techniques that are used in DNA analysis are selected such that they are able to define a number of mutations simultaneously. Screening for DNA sequence variations may be identified by single strand conformation polymorphism (SSCP), denaturating gradient gel electrophoresis (DOGE), and chemical cleavage mismatch (CCM) and then the actual analysis of DNA done by two separate **PCR** analysis. If the DNA analysis is not informative by these latter techniques, DNA sequencing is done.

Management of **haemoglobinopathies** in pregnancy Qunasegaran PT RAJAN

Malaysia

Abstract not available

Anaemia in pregnancy

Kwee Boon NG

Tung Shin Hospital, Kuala Lumpur

The incidence of anaemia in pregnancy depends on the definition. Taking an arbitrary nidus of Hb concentration of 100 g/L, it is safely estimated that 10-15% of the local population are anaemic during pregnancy. The causes of anaemia in pregnancy are primarily physiological haemodilution and nutritional, although haemoglobinopathies, haemolytic anaemias and myeloproliferative disorders may also be found. Screening for anaemia should begin in early pregnancy with a thorough history and examination. A finger-prick Hb estimation can be done in suspicious situations at 28 weeks. Investigations for the anaemic patient generally include a FBC, PBF and perhaps serum assay for **TIBC**, folate and B12 together with a stool examination for occult blood and parasitic infestation. Other tests should ideally be done in consultation with a haematologist. Antenatal care and assessment of the fetus are routine with no additional monitoring necessary unless indicated. Management of anaemia should be jointly undertaken with the haematologist. Haematinics and dietary supplementation have been shown to improve the Hb in compliant antenatal patients. The cost and side effects of oral iron therapy are well tolerated and mild. Folic acid deficiency has been reported to increase the risk of fetal loss, fetal anomalies especially neural tube defects, preterm delivery and PET aside from megaloblastic anaemia. Iron deficiency has no associated adverse fetal outcome. The recommended minimal daily Fe and folate requirements in pregnancy are 100 mg and 0.6 mg respectively. The perinatal and maternal events in patients with physiological anaemia in pregnancy are highlighted in a prospective study performed in UHKL.

PUBLIC HEALTH SYMPOSIUM 1: HEALTH INTERVENTION IN THE NEW MILLENNIUM

Modifying cancer risk through behavioural changes

ZARIHAH Mohd Zain

Malaysia

Cancer is a world health problem, causing more than 6 million cases and 4 million deaths annually in 1980s and has now risen to 9 million and 5 million respectively. It is predicted that the toll will escalate further to 300 million new cases and 200 million deaths in the next 25 years, with almost two-thirds of these arising in developing countries. The disease pattern has been attributed to population aging and changes in living environment and lifestyle. Although major intrinsic cancer contributing factors like age and genetic predisposition are fixed, most other risks are quite largely changeable. This dreadful disease, cancer, develops principally as a consequence of conditions of life, i.e. exposure of individuals to carcinogenic agents in the atmosphere and in what people consume. Personal habits such as tobacco use and occupational exposure to carcinogens as well as certain biological factors such as hepatitis B infection, play particularly significant roles in the aetiology of cancer. Many of these factors can be exploited and hence prevent or delay the occurrence of cancer. Tobacco is the most widely disseminated carcinogen in the world. Its use in all forms is responsible for about 30% of all cancer deaths in developed counties and a rapidly rising proportion in developing countries. For public health reasons, the present and potential burden of tobaccoinduced cancer in Malaysia must be given immediate priority. There is a dire need to keep the prevalence of tobacco use especially cigarette smoking checked. Dietary modification is another approach to cancer control. In recent years, substantial evidence has pointed to a causative role of excessive dietary fat in certain cancers, and protective effect of increased intake of whole grains, fruits and vegetables. Eating habits that may inhibit the development of diet-associated cancers will also lower the risk of cardiovascular diseases. Alcohol may increase the risk of cancer of the oral cavity, pharynx, oesophagus and liver, hence control of alcohol consumption in the population is also necessary. Other known cancer risk factors that can be modified include occupational and environmental exposure to carcinogenic chemicals, hepatitis B infection, human papilloma virus infection, ionising and ultraviolet radiation. Knowledge regarding all these provides obvious and ample scope for action to reduce cancer burden.

Case control study: evaluation of impact

OMAR HASAN Kasule

Faculty of Medicine, UIA, Kuantan, Malaysia

The case-control methodology has been popular for 7 decades for preliminary evaluation of causal relations using small numbers of study subjects. It has also been used, inappropriately and extravagantly, for confirmatory large studies. It is destined to become even more popular for cheap and rapid identification of causal relations that can be confirmed later by molecular and other laboratory studies. It is an intuitive comparison of exposure in diseased and non-diseased subjects. The cases, all incident or newly diagnosed, are from the same population base as the controls to ensure comparability. Results of a case control study are set out in the familiar 2 x 2 table. The exposure odds ratio, Pr(E+/D+) I Pr(E+/D-) is computed as ad/bc with 95% confidence bounds. The case-control study design has 4 advantages that explain its popularity. 1. Easy estimation of the risk ratio using the odds ratio. 2. Economy: few subjects are adequate to answer epidemiological questions in a short time. 3. Compression of time: exposure information is obtained from history or records. 4. Convenience: study subjects are seen only once with no follow-up. The case-control design suffers from 7 disadvantages. (a) It gives an approximate parameter, OR, rather the real one, RR (b) It gives probability of exposure among the diseased, Pr(E+/D+), but real interest is the probability of disease among the exposed, Pr(D+/E+). (c) It is not possible to obtain a direct estimate of incidence or the prevalence because of sampling design constraints. (d) The time sequence between exposure and disease is not certain. (e) It is very vulnerable to information, selection, and confounding bias (f) It can not be employed to study multiple outcomes from the same exposure (g) historical information about exposures used in case-control studies can not be validated.

Management of occupational hazards in petroleum industry

ABU HASAN Samad

Esso Production Malaysia Inc., Menara Esso, Kuala Lumpur, Malaysia

Petroleum industry involves various activities in both the upstream and downstream sectors. Each facet of these activities carries its own risks and hazards to the workers, public and **environment**. These include physical, chemical, biological, ergonomics and psychosocial hazards. In Malaysia, the logistics of working in the middle of the South China Sea make the industry even more challenging. In line with OSHA Act **1994**, management commitment with workers involvement is necessary to ensure safe and healthy operations at all work sites. Occupational Health Management System and all hierarchy of hazards controls are in **place** and stewarded together with emergency preparedness for possible disaster. With these measures, the petroleum industry can continue to contribute to the country's economy without impacting the health and safety of the workers, public and environment.

PUBLIC HEALTH SYMPOSIUM 2: POPULATION AND ETHICAL ISSUES IN NEW PUBLIC HEALTH

Reassessing population expansion policy: global perspective

Raj KARIM

Malaysia

Abstract not available

How to develop an informed patient MOHD HISHAMUDDIN Harun

Medical Online Sdn Bhd, Malaysia

Consistent with Malaysia's Vision 2020 the healthcare vision of creating 1 mation of healthy individuals, families and communities will be realised by **promoting** a lifelong focus on wellness where individuals and families are empowered to play the major **role** in managing their health. Individuals must have greater knowledge of health issues, the capacity to make informed health decisions and the ability to play a central role in both health and illness management in order to fulfil this vision. The MSC Integrated Telehealth (telemedicine) project has been envisaged to support and strengthen the future health care system based on the healthcare vision. Telehealth will promote wellness through personal empowerment and responsibility for healthcare management via a protective lifelong plan. The two applications of the Telehealth project which will help to empower patients as to the management of their health is the Lifetime Health Plan (LHP) and Mass Customised/Personalised Health Information and Education (MCPHIE). The Lifetime Health Plan (LHP) is a health plan which is a network-based personalised health management of an **individual** based on electronic medical records. Mass Customised/Personalised Health Information and Education (MCPHIE) comprises the dissemination of tailor-made information and education to the individual and community via appropriate tools and media e.g. Personal computers, E-mail, web-ty, pamphlets etc. In order to develop such informed individuals, a multiple prang strategy needs to be developed which include: User-friendly interfaces/access points; Multiple delivery channels; Personalised information and education rather than generic; Interactive elements within the delivery services to attract individuals to participate in health-related events; Functional and easy to use LHP so that the individual sees it as a valuable tool for personal health management; Easy to access, high quality virtual health services (as compared to current physical service provision); Incentives to promote the use LHP - may be financial or non-financial; Promotion of programmes sponsored by Government, private sector, media, sports and NGO's to help entrench health-related issues and behaviour. The advent of Integrated Telehealth in Malaysia will greatly assist in developing informed patients who can make decisions regarding their health and be responsible for their health management. Services, resources and technologies will be structured to empower and enable patients to take the utmost advantage of online services. The challenge will be to motivate the individual to take appropriate action to lead a healthy lifestyle.

Radioactive contamination of food: magnitude and prevention HARRISON AZIZ Shahabudin

Food Quality Control Division, Department of Public Health, Ministry of Health, Malaysia

Everything in our environment, including food, contains trace amounts of natural radioactivity and this cannot be avoided. Drinking water, edible plants and animals and even dust in the air contain isotopes. Radioactive materials are particularly concentrated in some foods, thus consuming these foods would expose consumers to higher doses than average. Our food supply is king contaminated with contaminants and one of the major contaminants is radioactive isotopes. When food is contaminated with radioactive isotopes, the term radioactive food is used and this refers to accidental contamination from **nuclear** accidents and the like. Early inclusion of isotopes into the food chain had been demonstrated where increased radiation levels were found in leafy greens growing in the contaminated fields and in cow's milk. Rain becomes radioactive and soils are also contaminated, Animals grazing on contaminated fields will concentrate isotopes in their tissues and this will be passed on to the carnivores that feed on them. This paper will discuss the magnitude of radioactive contamination of food, giving emphasis to accidents that had occurred and would also suggest ways of prevention of such contamination.

Ethics in occupational health

Krishna Gopal RAMPAL

Department of Community health, Medical Faculty, Universiti Kebangsaan Malaysia, Malaysia.

Professional ethics should always determine the manner in which occupational health doctors practice. Like all doctors the occupational health doctor has a duty to do good, to do no harm or minimise harm and promote autonomy of the patient. They are bound to act according to their duties and rights (being duty driven) and on occasions is to act in a manner, which may not be what the patient wants but, which has the best overall consequences (public good vs individual good). The occupational health doctor, because of the unique role they play are constantly faced with a number of ethical problems. The nature of their practice places them in a "double agent" role being paid by employers to take care of employees. Questions are continuously raised about where their loyalty lie - the worker (their patients) or the employer (their client). They work in a social context which is riddled with competing interests coupled with unequal distribution of power between their patients and their clients. With emergence of "managed care" this issue is further compounded in their effort to provide the best possible care for their patients. In Malaysia it is all the more complex as there is no clear demarcation between the primary care they provide and the occupational health role they play. Some of the common issues faced by the occupational health doctor include: confidentiality of medical information, ownership of medical records, pressure to reduce sickness absenteeism and loss time injuries, company's trade and business secrets. Their professional autonomy is always being challenged. Ethical guidelines like those developed by professional societies overseas need to be drawn, adopted and communicated to occupational health practitioners in the country.

PUBLIC HEALTH SYMPOSIUM 3: HEALTH MANAGEMENT ISSUES OF THE NEXT CENTURY

Rewarding the health care staff

Ahmad TAJUDDIN

Malaysia

Background: All public employees are subjected to similar forms of rewards by the **Government**. Rewarding specifically to the health care staff of the Ministry of Health is generally not addressed by any circulars, programmes of systems holistically, having both objective as much as subjective elements in its process and implementation. It is both important we reward public healthcare employees in accordance with their **contributions**, and in **turn** provide incentives for continued and improved performance for the Ministry of Health. *Objective:* To understand the development and implementation of reward systems applicable for health care staff of the Ministry of Health. **Method:** This is a narrative paper that describes how systems relate to **personnel** satisfaction and organisational goals; followed by analysing the principles and processes involved in the development of the reward systems, and explained by the responsibilities of managers/supervisors in the development and administration of the reward systems. **Results:** Discussion of how rewards and reward systems relate to salary administration, human resource motivation, career progression (career development progression, performance planning and appraisal, promotion and transfers) role of organisational and supervision, teamwork (teams and self-managed groups), learning organisation, innovation, organisational climate, benefits and services are described. *Conclusion:* Key factors for a successful reward system and guidelines for rewarding are recommended. To achieve health care staff personal achievement and organisational effectiveness, performance management processes practices are of imperative importance. A critical success factor is to design a flexible and focused reward system to support this performance thus emphasising the linkages and ensuring the desired results.

Communicating during health crisis SULAIMAN Che Rus

Malaysia

Effective planning and communicating of risk to the public is an important component of managing any health crisis. The Ministry of Health has had numerous positive and negative experiences in the past of health crises such as the **Nipah virus** outbreak, the haze, and **Dioxin** contamination of imported food. Planning of risk communication involves identification of potential health issues, which are among others influenced by 'fright factors' and 'media triggers'. An analysis of communication situation involving internal and external stakeholders need to be undertaken. Communication objectives must be clarified and set. The "Dos's and Don'ts" in public presentation is discussed.

Benchmarking of public hospitals Syed Mohamed ALJUNID

Malaysia

In Malaysia, public hospitals are the main providers for in-patient services. As in most countries, inpatient care usually absorbed the highest proportion of funds allocated for health care. Hence, costmanagement efforts targeting at expenses spent for hospital care would bring significant improvement in overall efficiency of health care system. Benchmarking is a strategic tool, which could be utilised by public hospitals for the purpose of improving quality and efficiency. It is defined as a process of identifying, learning and adapting outstanding practices from other organisations to help the hospital its performance. Hospital managers can choose any of the four types of benchmarking to implement: best practice studies, cooperative benchmarking, collaborative benchmarking and competitive benchmarking. Forming a **benchmarking** team sponsored by influential practitioners in the hospital is the first step that needs to be taken in the benchmarking exercise. Finding suitable benchmarking partners can be problematic because public hospitals are organised at various levels with different facilities and staffing mix. Indicators for comparison include general performance indicators such as average length of stay, bed occupancy rate, turnover interval, cost per in-patient day, cost per admission and specific indicators such as cost per DRGs, peri-operative mortality rate, hospital acquired infection rate and mortality rate for specific operative procedures. For benchmarking to be successful, it is important that the benchmarking team must receive adequate support from all levels of staff in the hospitals. It is important that **benchmarking** code of conduct be observed at all time by all parties involved. Benchmarking exercise should be a continuing exercise and adequate time and resources should be allocated to implementation of changes.

Effective partnership in community based rehabilitation (CBR) SAMIAH YASMIN Abdul Kadir

Malaysia

Community Based Rehabilitation (CBR) was initiated by the World Health Organization (WHO) and has its beginnings in the 1970's. Over these past decades CBR has undergone tremendous evolutions and refinements and towards the new millennium CBR is being regarded as an appropriate model of disability service delivery in many developing countries. In the 1994 United Nations Joint Position paper, CBR is defined as a strategy within the realm of community development to facilitate rehabilitation, equalization of opportunities and social integration of all people with disabilities. In short, CBR requires combined effort of people with disability, their families and communities and the appropriate health, education and social authorities of the local government. With heavy emphasis on community involvement, implementation requires Participatory Rural Appraisal (PRA), which evolved on four tasks namely, (a) identification and gaining entry to the local community, (b)

determining the index of disability and existing support or facilities available in the community, (c) establishing conceptual framework, action strategies and coordinating resources within the community and finally, (d) provide feedback to all interested parties, instigate processes for action and develop structures and external supports. When PRA is appropriately employed, the burden of rehabilitation services will be shared among the community, non-governmental organizations and the local governmental bodies. PRA will also result in greater community awareness of disability issues, greater informal and community support for people with disabilities, more effective **networking** and coordination between community members, and a sustainable service model which is responsive to the needs of people with disabilities.

SURGERY SYMPOSIUM 1: COLORECTAL CARCINOMA

Technology and colorectal cancer in the new millennium John RT MONSON

Academic Surgical Unit, University of Hull, UK

The dawn of the new millennium presents an opportunity to consider the current and potential application of new technologies to the management of patients with colorectal cancer. New approaches to treatment such as laparoscopic surgery are already being widely used and the results from international randomised trials awaited with interest. Data will be presented demonstrating the safety and outcomes from a series of 524 laparoscopic resections. In addition, the results of a study considering resection margins in patients undergoing a laparoscopic total mesorectal excision for rectal cancer suggest oncologic safety. Survival at two years indicates no difference from patients undergoing traditional open surgery. The increased efficacy of imaging modalities offer considerable potential and techniques such as virtual colonoscopy are easily applied and may significantly alter the paradigm of colonic imaging and evaluation. An overview of the world experience in this technique in the detection of colorectal neoplasms will be presented. In the field of metastatic disease less invasive approaches include radio-frequency ablation of hepatic secondaries used at open surgery, laparoscopically or percutaneously. The use of **RFA** in this setting along with an overview of robotics on surgery will be discussed. Finally the potential use of telemedicine in the dissemination of surgical techniques and training will be reviewed.

Familial colorectal cancer

Akhtar QURESHI

Department of Surgery, International Medical University, Seremban, Malaysia

Colorectal cancer (CRC) is primarily a genetic disease with lesions being either somatically induced by environmental agents or inherited through the germline. CRC carcinogenesis is a process that takes several years and at multiple biologic levels, from the molecule and cell to tissue and organ. In the general scheme, certain environmental and host factors combine to influence the eventual formation of the carcinoma. It has long been recognised that colorectal cancer has a familial component. The calculated risk in first degree relatives for colorectal cancer is 1.78-2.67. The two commonest genetic diseases **referred** to include familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). **FAP** accounts for approximately 1% of colorectal cancers, and is due to the **APC** gene located at **5q21**. HNPCC, accounts for 5-10% of colorectal cancer patients. HNPCC is sub-classified into Type I, or site specific, and Type II or the cancer family syndrome. HNPCC is thought to be a result of DNA mismatch repair gene, resulting in the **hMSH2** gene on **2p** and **hMSH1** on **3p**. Several other genes implicated include the MCC and Ras genes. Less common familial colorectal cancer seen in Malaysia include the hamartomatous polyposis syndromes such as Peutz-Jeghers syndrome.

Transanal resection of cancer rectum Samuel TAY

Malaysia

Cancer of the rectum occurs in about 30% of all colorectal carcinomas. They are about equally distributed in all the three segments of the rectum. Surgery remains the mainstay of the treatment options and it can be classified as sphincter-saving operations or abdomino-perineal resection. Transanal resection is a form of sphincter-saving operation. The aim of surgery for cancer of the rectum is to eradicate tumour and to preserve near normal function of the anorectum. Palliation of symptoms is important when the above aim is not possible to achieve. Cancer of the rectum has very troublesome symptoms, in particular tenesmus and hematochezia. Transanal resection of the primary tumour gives good palliation of symptoms. It is a particularly good modality for the aged, frail and severely infirmed patient. Curative intent can be achieved if strict selection criteria are applied. The tumour should be not more that 3 cm in diameter, well differentiated in histology and there should not be any invasion of the lymphatics, blood vessels or the nervous tissues. Ideally there should not be any invasion of the muscularis propria. Tumours situated in the lower third of the rectum are most amenable to this procedure. However, a more sophisticated variant of this procedure called Transanal Endoscopic Microsurgery enables a higher rectal tumour to be excised transanally.

SURGERY 2: DEBATE - TRANSMISSIBLE DISEASES & THE SURGEON

Abstracts not available

SURGERY SYMPOSIUM 3: SURGICAL TRAINING FORUM

Surgical training needs in Malaysia: present and future Mahmud MOHD NOR

Department of Surgery, Hospital Kuala Lumpur, Malaysia

Prior to 1981, the training and certification of surgeons were by the Royal Colleges of Surgeons of United Kingdom. The number of surgeons trained was never adequate for the needs of the country even for general surgeons. Since the inception of local training by the Universities there has been substantial increase in the number and specialisations of Surgery. Despite this, the stock of surgeons at December 31, 1999 is well below 50% of the required number based on the target ratio of specialists to population. To compound this problem further there is a mismatch between the workload and number of private and public sector surgeons. Planning for the future needs of specialist surgeons will require a reliable database of private and public sector surgeons and the need for Private Hospitals to undertake training and be more involved in teaching and research. A well-coordinated system of planning and training is required to maximise every available facility in the country. There must be greater involvement of the profession and the private sector in this endeavour through the Academy of Medicine.

Surgical training - what's available in Malaysia Freda A MEAH,

Department of Surgery, Faculty of Medicine, Universiti Kebangsaan Malaysia, Malaysia

Prior to 1981, newly graduated doctors aspiring to be qualified general surgeons had to study independently and appear for the Fellowship Examinations conducted by the Colleges either in the United Kingdom or Australia. From 1981, UKM initiated a four-year Masters of Surgery (MS) programme in general surgery. By 1991, all the three universities (UKM, UM & USM) were offering

similar programmes. MS Surgery is a structured training programme spread out over a period of four years. Doctors who were not successful for selection to enter the programme or did not wish to join the MS Surgery programme may opt to take the U.K. Fellowship examinations. The FRCS programme consists of Part A and Parts B&C. From the year 2000, this programme in the U.K. has been changed and the new system now consists of Basic Surgical Training and 5 years of Higher Surgical Training. The local training programmes in the three universities follow a common syllabus. The time spent in general surgical units and the rotational postings in other specialty units varies from university to university. The timing of the Part I examination is the same for UKM and UM but USM has its own system. However, the Part II examinations for all the three universities are held at the end of the four-year training periods. Since 1996, the "open system" was instituted. This came about because the Ministry of Health directed that in order to prevent the shortage of "service" medical officers at the hospitals it was not possible to release all the selected candidates for training at the universities at the same time. The candidates are now trained as "on campus" at the universities or as "off campus" at the accredited hospitals. To date, 88 general surgeons have been trained by UKM, 25 by UM and 15 by USM.

Quantity & quality - is this achievable?

Abdollah SALLEH

Department of General Surgery, Hospital Selayang, Selangor, Malaysia

The need for training quickly many new specialists in various surgical specialties to meet the inadequate numbers at present may result in inadequately trained surgeons. The paper will discuss the current needs and training posts in terms of numbers. A study of yearly enrollments and cumulative number of trainees from the various universities in the Masters programmes will be presented. Opinions of both trainers and trainees with regards to adequacies of the cumculum, the number of trainers and degree of exposure to various case categories and procedures were sought through interviews. The Masters in Surgery programmes have become the main programme for the training of surgeons in Malaysia. All programmes appear to be very well structured to provide knowledge and skills in clinical patient care as well as research methodologies. Two main problems are apparent mainly the inadequate number of qualified trainers and the inappropriate proportion of trainees to cases. The differences in the training centres mean that training may not be as comprehensive as planned. Trainees in public heapitals may not be exposed to more complex conditions and the sophistication of their management. There is difficulty in placement of trainees for elective postings. Trainees in the open system face difficulties in getting guidance for basic sciences and for writing case studies, earrying out study projects and writing the thesis. In the universities the impression is trainees may have less frequent opportunities to be exposed to various procedures.

A trainee's perspective NOR **AISHAH** Taib **Malaysia**

Abstract not available

PAEDIATRIC SYMPOSIUM 1: NEONATOLOGY IN THE TROPICS

Ethical issues in neonatal intensive care

NY BOO

Neonatal Intensive Care Unit, Hospital Universiti Kebangsaan Malaysia

Newborn infants admitted to the neonatal intensive care units are usually critically ill. They cannot speak for themselves, nor express their wish. However, they often need urgent treatment to save their lives, and yet their prognosis are often uncertain. Neurodevelopmental handicaps among survivors of NICU patients are not uncommon. Although advances of technology has provided effective treatment for many illness, there are other which merely succeed in prolonging life. Furthermore, many of the treatment are painful, expensive and causing prolongation of suffering. Therefore, in the care of infants requiring neonatal intensive care, making ethical decision on the management of these infants is not as straightforward as just protecting life and health over economic and psychosocial costs. It is a rather complex procedure, touching on moral, religious, cultural and legal aspects of life. Some common neonatal problems requiring ethical decisions are: 1) Care of the extremely low birthweight infants of less than 1000 grams. Common questions raised are: "How small is too small and how much treatment and intervention are too much?" 2) Management of infants with severe perinatal asphyxia. When should treatment be withheld or withdrawn? 3) Management of infants with multiple or severe congenital malformations. Should they be treated? Sometimes withholding or withdrawing treatment in newborn infants does not necessarily result in death shortly. Instead it may cause poorer outcome owing to added consequence of **hypoxic** ischaemic brain damage and multi-system organ injuries. Many countries have drawn up legislation to balance between the right of life and withholding treatment of the **imperiled** infants. For instance the USA **government's** 1984 Federal Child Abuse Amendments stipulate, "treatment should be given to the **imperiled** infants except when chronically comatose, provision of treatment would prolong dying, or treatment would be futile in term of survival".

Oxygen and the sick neonates — too much of a good thing? CT LIM

Department of Paediatrics, Faculty of Medicine, University Malaya

Retinopathy of prematurity (ROP) remains a significant morbidity among very low birth weight infants. As high as 82% and 31% of extremely low birth weight infants have been reported to suffer from ROP of all stages and severe stages respectively. It is well established that the incidence of ROP is inversely related to the birth weight and gestational age of the infants. Numerous factors had been implicated in the actiology of ROP. Recent literature will be reviewed. Studies in the fifties demonstrated that significantly more acute and cicatricial ROP developed in infants who were exposed to high levels of $\mathbf{F_1O_2}$. However, despite careful monitoring of oxygen use, the incidence of ROP among extremely low birth weight infants (ELBW<1000g) did not reduce although its incidence in larger infants did. Moreover, recent studies showed that wide fluctuation of F₁O₂ levels in sick infants in the first two weeks of life was more predictive of severe ROP than the degree and duration of hyperoxia. In a multi-centre randomized clinical trial, Reynolds et. al. (N England J Med, 1998) demonstrated that the incidence of ROP among pre-term infants (birth weight ≤ 1250g or < 31 weeks of gestation) nursed in reduced ambient light within 24 hours of birth did not differ significantly from that of the control group. This study showed that light, a pro-oxidant factor does not play a role in the initiation of ROP. But there is still a concern whether it does contribute to its development. Blood transfusion and exchange transfusion have been identified as risk factors in the pathogenesis of ROP in several studies. It is possible that oxygen delivery to the immature retinae is improved by transfusion of adult haemoglobin leading to the retinal changes comparable to those resulting from hyperoxaemia. It has also been postulated that increased free iron reacts with various intermediates of oxygen, generating highly reactive oxygen free radicals. The role of vitamin E deficiency (an antioxidant) remains unclear. In a meta analysis of randomized clinical trails of vitamin E prophylaxis, Raju et. al. (J Paediatrics, 1997) found no difference in the overall incidence of ROP but a lower incidence of severe or stage 3+ ROP in the vitamin E-treated pre-term infants. However this was associated with higher incidence of necrotising enterocolitis, sepsis and intraventricular haemorrhage among treated infants. It had been observed by Saunders et. al. (Arch Opthalmol, 1997) that pre-term white infants had higher incidence of severe ROP (13% vs. 10%) and higher threshold ROP (7.8% vs. 3.2%) than black infants. This remains highly significant even after correcting for other compounding factors suggesting ethnic predisposition. Recent discovery of missense mutations in the N-D gene in infants with ROP further support genetic predisposition in the pathogenesis of ROP. (Norrie's disease is rare hereditary exudative vitreoretinopathy). Despite extensive research the pathogenesis of ROP remains elusive. It is conceivable that it is the more preterm and lower birth weight infants who are more likely to experience stormy neonatal period. Such infants are more likely to suffer from ROP.

The baby-friendly hospital initiative in Malaysia

Nyok Ling LIM

Department of Paediatrics Hospital Selayang, Malaysia

The WHO/Unicef Baby-Friendly Hospital Initiative (BFHI) was launched in 1991 to implement practices in hospitals that would protect support and promote breastfeeding. Since then the programme has supported training courses in breastfeeding counselling improving hospital practices and drafting of legislation to implement the International Code of Marketing of Breastmilk Substitutes. Malaysia launched the BFHI in 1993 and after 4 years had all 110 Ministry of Health (MOH) hospitals accredited with the BFHI status resulting in Malaysia being the 3rd country in the world to do so. BFHI largely abides by the 'Ten Steps to Successful Breastfeeding' which is a comprehensive set of guidelines in achieving breastfeeding targets. Education training and providing a supportive breastfeeding environment are essential elements of the **programme**, and to ensure success a certain amount of compulsion for hospital administrators was needed. The National Code of Ethics on the Marketing of Breastmilk Substitutes guards against negative influences from the milk industry. In the early stages of the programme some difficulties with hypoglycaemia in the low birth weight babies were encountered. It is also recognised that breastfed babies are more prone to severe jaundice especially those who have not been fed adequately. Prolonged jaundice, which is generally harmless, is also more prevalent. Though the BFHI concept has been well publicised and accepted, private and university hospitals have largely been unsuccessful in achieving the necessary standards. It is recognised however that breastfeeding is promoted in all these health facilities albeit in an 'optional or choice for mother' way rather than as a regulation as in the MOH hospitals. The rate of 'Ever Breastfed Infant' has increased from 78.0% in the early 1970's to 88.6% in 1997 according to a national survey, but comparative rates for subsequent breastfeeding are not yet available. The MOH is presently working out a programme for the monitoring and reassessment of the BFHI status.

PAEDIATRICS SYMPOSIUM 2: CONTROVERSIES IN CHILDHOOD NUTRITION

Feeding the preterm infant Wei Leng LIM

Sunway Medical Centre, Selangor, Malaysia

In preterm infants who are <1000g or critically ill, it is often difficult to start enteral feeding immediately after birth. Nevertheless, early introduction of enteral feeding is vital for its trophic effects on the gastrointestinal tract and physiological effects on gastrointestinal exocrine and endocrine secretion and motility. In infants <32-34 weeks, gavage feeding is the method of choice. Continuous nasogastric feeding does not have significant advantage over intermittent nasogastric feeding and may result in increased nutrient loss. Transpyloric or gastrostomy feeding should not be

used as they are associated with increased mortality in preterm infants. Human milk has nutritional advantage over formula milk. It results in better fat absorption, contains more taurine and cysteine, LCPUFA and has a greater bioavailability of trace elements. It also confers to the infant immunological and antimicrobial protection, and transfers breast milk hormones and growth factors. Randomized trials involving preterm infants have demonstrated a reduction in necrotizing enterocolitis, postneonatal infant mortality and higher developmental score at 18 months with human milk. However. the protein, sodium, calcium, phosphorus and magnesium content of human preterm milk is too low to meet the requirement of the growing preterm infant. Human milk fortifiers are used to correct these deficiencies and have been shown to improve growth rate, bone mineralisation, calcium and phosphorus balance. The use of human milk fortifiers is recommended in infants <2000g or <35 weeks gestation. If the mother decides against expressing breast milk or her milk supply is temporarily interrupted, preterm formula should be used. These formulae are designed to meet the theoretical needs of preterm infants and have been shown to improve growth rates and long term developmental score compared to standard term formula. More recently, amid concern about inadequate intake in the post-discharge preterm infants, follow-on preterm formula has been introduced. These formulae has composition that is intermediate between a preterm and term formula and has been shown to significantly improve growth and bone mineral content in infancy compared with those fed term formula after discharge. The maintenance of optimal nutrition for preterm infants is important as there is now increasing evidence that dietary manipulation have significant long term influence on their health, growth and neurodevelopment.

Refeeding the child with acute diarrhoea1 diseases: myths and facts Meng Kar OON

Department of Paediatrics. Hospital Universiti Kebangsaan Malaysia, Malaysia

The increasing widespread use of oral rehydration therapy (ORT) in the successful treatment of acute diarrhoea is a testimony of the application of science in solving medical problems. Guidelines relating to ORT from WHO, AAP and CDC and other bodies have gradually been taught to and accepted by healthcare givers and the community. Dietary treatment is an important but often poorly handled aspect of the overall management of childhood diarrhoea. There is much ad hoc and outdated approaches to refeeding. Myths and fallacies regarding refeeding are sadly ubiquitous within both health care personnel and the layman. Webster's dictionary defines myth as any fictitious story or unscientific account, theory or belief and fallacy as a false or mistaken idea, opinion, error in reasoning or flaw or defect in an argument. Some myths and fallacies regarding refeeding after acute diarrhoea include: the fear that refeeding infants during acute episodes might aggravate the diarrhoea. Thus the idea of fasting the child to provide 'bowel rest''. Others practice the gradual reintroduction of milk feeds after a period of fasting by gradually increasing the strength of diluted milk over several days. The routine changing of milk feeds to a soy based formula is very common, along with the use of specialized or hydrolysed milk formulas. These myths need to be corrected in the light of evidence from published studies that show these assumptions to be flawed. Controlled trials have demonstrated the efficacy and safety of continued feeding during diarrhoeal episodes with a variety of diets including standard lactose containing cow milk formulas, locally available diets and breast milk. These studies demonstrated that continued feeding did not increase stool output nor prolong diarrhoea. It was also shown that infants who were given prompt refeeding had less stool output and decreased duration of **diarrhoea**. There was also better weight gain in the recovery period. This paper will briefly elaborate on these facts to correct the myths that are prevalent.

Weaning and vitamin supplementation: when and what?

Christopher CM BOEY

Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

The term "to wean" means "to accustom to". It refers to the change from an all milk liquid diet to a varied diet using solid foods. Factors that influence the weaning process and the foods that are given include (a) the nutritional requirements of the infant, (b) the anatomical and physiological development of the mouth, teeth, gastrointestinal tract and the maturation of the infant kidney, and (c) the foods that are available in a community to supply nutrients. Weaning is usually done when the infant is at least 3 months old. Reasons why it is undesirable to introduce solid foods before three months of age include the following factors: infants have not developed the ability to bite or chew; infants are not yet ready to experiment with different types of foods; the infant gastrointestinal tract may be more vulnerable to infection and sensitization; the use of energy rich foods could lead to obesity. Reasons why weaning should not be delayed include the following factors: infants may not achieve an adequate nutritional intake on milk alone after 6 months; by 6 months, infants have started to develop a biting and chewing reflex which should be encouraged; about this age, the store of iron laid down in fetal life runs out. The foods given to infants must not be influenced by the known nutrient requirements of adults and the dietary guidelines based on them. The lecture will discuss some of the different types of foods given to infants in the first year of life, including the issue of vitamin supplementation. Suggested reading: (a) Pediatr 1974; 53:11, (b) Acta Paediatr Scand 1986; 75 (suppl 323):5-13, (c) Pediatr 1980; 65:1178-81, (d) Lancet 1988; 1:140-3, (e) Lancet 1989; 1:490, (f) Br J Nutr 1990; 64:13-22, (g) Acta Paediatr 1995; 84:733-41, (h) Acta Paediatr 1995; 84:512-5, (i) Major controversies in infant nutrition. Royal Society of Medicine, London. 1995, (j) Br J Hosp Med 1995; 53:567-9, (k) Singapore Med J 1998; 39:551-6.

PAEDIATRICS SYMPOSIUM 3: INBORN ERRORS OF METABOLISM

The sick infant: clues to look for

Yew Sing CHOY

Paediatrics Institute, Kuala Lumpur Hospital, Malaysia

Inborn errors of metabolism (IEM) are individually rare, but collectively numerous. It might appear that their diagnosis requires precise knowledge of a large number of biochemical pathways and their inter-relationships. As a matter of fact, adequate diagnostic approach can be based on the proper interpretation of clinical clues and the use of only a few simple clinical tests. A great diversity of signs and symptoms can lead to the diagnosis of IEM. In general, there are four groups of clinical situations in which physicians are faced with metabolic disorders: (1) Acute symptoms in the neonatal period or infancy, (2) Late-onset acute and recurrent symptoms such as coma, ataxia, vomiting and acidosis, (3) Chronic and progressive general symptoms involving mainly neurological and digestive systems, (4) Specific and permanent symptoms indicative of an inborn error of metabolism like cardiomy opathy, hepatomegaly, lens dislocation etc. Neonates and infants have a limited repertoire of responses to severe illness and at first glance present with non-specific symptoms such as respiratory distress, hypotonia, poor feeding, vomiting, diarrhoea, dehydration, lethargy, seizures, all symptoms which could easily be attributed to infection or some other common cause. But careful analysis of these symptoms with the help of a few basic clinical tests such as blood sugar, blood gas, electrolytes and urine ketones would help one in deciding for further diagnostic work up of IEM while carrying out urgent resuscitative management. Therefore, metabolic acidosis with raised anion gap, hyperlactacidemia, hypoglycemia with ketosis or without ketosis in a child with symptoms mentioned above warrants serious consideration for IEM. Some helpful clinical clues to suggest IEM in a child with encephalopathy include "normal" peripheral muscle tone which suggests relative hypertonia, axial hypotonia with limb hypertonia, large amplitude tremors and myoclonic jerks, abnormal urine and body odor. Occasionally, specific dysmorphia or malformation may suggest IEM, for example, syndactyly of second and third toes suggests Smith-Lemli-Opitz syndrome, a defect in sterol

metabolism; cerebral malformation in a child who has seizure from day one of life may suggest sulphite oxidase deficiency.

Inborn errors of metabolism, the role of newborn screening ROWANI MR

Department of Paediatrics, Clinical Genetic and Metabolic, School of Medical Sciences, Universiti Sains Malaysia, Malaysia

Newborn screening was initially introduced to prevent mental retardation in children through presymptomatic detection and early treatment. Newborn screening for congenital hypothyroidism, phenylketonuria and galactosaemia was carried out for this purpose and has now been implemented in most part of the world. The objectives of newborn screening has now expanded to include other health benefits such as prevention of physical disabilities, morbidities and mortalities and this include screening for conditions such as G6PD deficiency, sickle cell disease and congenital adrenal hyperplasia. Treatment is available for many Inborn Errors of Metabolism (IEM) including biotinidase deficiency, phenylketonuria, galactosaemia and homocystinuria. Without treatment the majority of classical phenylketonuric patient will be severely retarded but with early treatment most of them will have normal IQ. Biotinidase deficiency is easily treated with biotin but without treatment the majority of patient will develop severe neurological impairment. The benefits of newborn screening are not confined to treatable conditions. In non-treatable **IEM**, newborn screening may reduced the incidence of the disease through genetic counseling. The cost benefits of newborn screening for phenylketonuria and other IEM has been shown by many studies. The cost benefits as well as availability of treatment are one of the pre-requisite for newborn screening. However, the concept is now questioned as (1) it is difficult to measure the cost benefits of prevention of death and disability to the individual, family, community and the country. The value of preventing disability and death is not measurable (2) the availability of genetic counseling which is effective even when medical treatment is not available (3) the value of identifying diseases to the medical scientific communities and advancement of medical technologies (4) the role of screening in the planning of health services for the countries. The development of new technologies for newborn screening such as tandem mass spectrometry (MS-MS) warrant a review in the screening criteria for IEM. MS-MS allows rapid detection of more than 30 **IEM** using minute volume of blood in conditions previously difficult to diagnose. Radical changes in the screening criteria is expected.

Pitfalls in the laboratory diagnosis of inborn errors of metabolism Yew Sing CHOY

Paediatrics Institute, Kuala Lumpur Hospital, Malaysia

As most of the diagnostic biochemical tests for inborn errors of metabolism (IEM) are too slow for clinical management and too expensive, it is absolutely necessary to make clinical judgement based on the analysis of simple screening tests before deciding to initiate sophisticated investigations. However, there are several pitfalls in this respect. A normal or an abnormal result may fool one if guidelines are not followed and considerations not given in sampling, transportation, testing and analysis. Specimen collection is a very important step in the detection of metabolic disorders. In acutely ill patients, the blood and urine specimens on admission are likely to be most revealing and most appropriate for metabolic screening. It is a good practice to save these specimens from all patients in whom the diagnosis is unclear. Simple treatment such as iv. infusion of dextrose containing solutions may have actually treated many of the acute intoxication type of IEM. Many of the diagnostic biochemical changes and metabolites would have disappeared with such treatment. Therefore, it is advisable to collect blood for blood sugar, blood gas, electrolytes, lactate and ammonia, amino acids and an extra tube of blood taken and kept, prior to infusion of the fluids. The first urine passed should be sampled for reducing sugar, ketones and organic acids. Certain pitfalls such as difficult sampling and venous stasis may falsely raise the levels of ammonia and lactate.

Improper transportation and delayed testing would also give the same pitfall. Improper handling of specimen can result in artefactual changes in the amino acid contents of the blood. Unspun blood left at room temperature for example can show artefactual changes in ornithine and arginine. Hemolysis would also result in changes in certain amino acids. To minimize specimen artefacts, it is advisable to centrifuge the blood and separate the plasma or serum as soon as possible and keep frozen before transport. Beside acute sampling, early morning sample before feeding is preferred for most amino acid disorders. But postprandial sampling is more suitable for hyperammonemia screening since an elevation of ammonia may be intermittent and present only in the fed state. On the other hand, accurate and complete clinical information on the clinical status of the patient, any dietary manipulations and any medications are an indispensable prerequisite of optimal organic analysis. Many of these pitfalls can be avoided if there is good communication between the clinician and the laboratory biochemist.

OPHTHALMOLOGY SYMPOSIUM 1: MACULAR LESIONS

Pathophysiology of macular disorders

T Vasantha KUMAR

Department of Ophthalmology, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia

Essentially anything that alters the retinal pigment epithelium and Bruch's membrane can cause choroidal neovascularization (CNV). Most histopathologic studies of choroidal neovascularization have been performed in eyes with age-related macular degeneration (ARMD). The histopathologic feature common to many eyes that develop CNV is a break in Bruch's membrane. The capillary-like neovascularization originates from choroidal vessels and extends through these breaks. In ARMD, the CNV advances through a break in the outer aspect of Bruch's membrane and is located initially between the thickened inner aspect and the outer aspect of the membrane. The pathogenesis of CNV in various diseases may have similarities irrespective of the underlying disorder. Underlying pathophysiologic mechanisms in cystoid macula oedema, idiopathic macula holes, central serous choroidoretinopathy and idiopathic polypoidal choroidal vasculopathy would also be discussed as these represent the commoner of the macular disorders.

Fundal flourescein angiography in macular lesions

T Vasantha KUMAR

Department of Ophthalmology, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia

For more than a decade, **fundus** photography and flourescein angiography have proved to be extremely valuable techniques for expanding our knowledge of the pathologic anatomy and pathophysiology of various conditions, and have aided the diagnosis and monitoring of the treatment of retinal vascular and macular disease. This is particularly true for choroidal neovascular membranes from whatever underlying aetiology. Although macular lesions can be readily examined using direct and indirect ophthalmoscopy and slit-lamp biomicroscopy, flourescein angiography provides a valuable addition to these clinical techniques. It was never intended that flourescein angiography would replace these **techniques**, but it can clearly amplify their findings.

OPHTHALMOLOGY SYMPOSIUM 2: MEDICAL RETINA

Indocyanine - Green Angiography

Caroline CHEE

Singapore

Indocyanine-green angiography has revolutionized our perception of choroidal diseases and expands diagnostic capabilities and potential for treatment in many conditions. The peak absorption and emission of **indocyanine-green** (ICG) is at **800-850nm** (near **infra-red**), allowing it to penetrate through melanin pigment in the retinal pigment epithelium as well as blood. Its presence in the choroidal circulation can therefore be detected. ICG is 98% protein bound, and therefore leaks minimally out of the fenestrated choroidal vessels. It is therefore useful in delineating the choroidal circulation. Some of its functions include the detection of potentially treatable hyperfluorescent lesions under subretinal haemorrhages, hot spots within occult subretinal neovascularization, detection of idiopathic polypoidal choroidopathy and choroidal hyperfluorescence in central serous retinopathy. The use of ICG angiography in Asia is particularly significant as it giving us important information on the characteristics of age-related macular degeneration in our population.

Tissue plasminogen activator in submacular haemorrhage

Caroline CHEE

Singapore

Submacular haemorrhage can be associated with severe central visual loss especially if the **haemorrhage** overlying the fovea is thick. **This** is thought to result from degeneration of photoreceptors as a result of lack of blood supply from the choroidal circulation as well as toxicity from the breakdown products of haemoglobin. The use of intravitreal tissue plasminogen in combination with intravitreal gas and face-down positioning is a very effective method of clearing blood from the submacular area, displacing it away, inferiorly, and can result in very significant restoration of vision. This technique is effective within 2 weeks of the haemorrhage, and the long term prognosis for vision depends on the underlying cause of the haemorrhage. It is much less invasive than the surgical evacuation of submacular haemorrhage and allows early treatment of underlying pathology. It is of particular relevance in South-East Asia, where, in our experience, submacular haemorrhage is more common the Chinese and Malay populations than it is in Caucasians.

Laser therapy in ARMD

Caroline CHEE

Singapore

For many years, the only treatment for age-related macular degeneration (ARMD) shown to be effective by randomised controlled trials has been laser photocoagulation of well-defined choroidal neovascularization (CNV). Fundus fluorescein angiography is mandatory to identify treatable lesions and guide the treatment. Just last year, the results of photodynamic treatment (PDT) for classic choroidal neovascularization were published, and this showed that PDT helped to maintain vision in patients with subfoveal classic choroidal neovascularization. In PDT, aphotosensitizer dye, Visudyne, is injected intravenously and the subfoveal neovascularization is exposed to a very low power of diode laser which activates the dye, resulting in the release of free radicals which destroy the neovascular complex. Recurrence of the CNV is common, and re-treatment may be required up to 4 times a year. Other laser treatment strategies in age-related macular degeneration include laser to CNV adjacent to retinal pigmentepithelial detachments, laser to "hot spots" identified on indocyanine-green angiography and laser treatment for drusen. Under investigation is transpupillary thermoplasty treatment, which uses a long duration, large spot size diode laser to destroy occult neovascularization,

the type of exudative ARMD for which no effective treatment has been shown to **be** useful before. A type of ARMD seen frequently in our population is idiopathic polypoidal choroidal vasculopathy, and this appears to **be** effectively treated by laser photocoagulation with a much lower recurrence rate than choroidal neovascularization

OPHTHALMOLOGY SYMPOSIUM 3: SURGERY IN MACULAR LESIONS

Macular hole surgery
Bethel LIVINGSTONE

Malaysia

Abstract not available

Macular translocation surgery

Sze Guan ONG

Singapore National Eye Centre

Foveal translocation procedures have been used in recent years in the attempt to overcome blindness resulting from subfoveal choroidal neovascularisation. This condition is associated with significant central visual loss and is seen in age related macular degeneration as well as other conditions such as myopia, angioid streaks etc. Although recently photodynamic therapy with verteporfin has been shown to be beneficial, a surgical approach may still be indicated in some patients. The current techniques of macular translocation will **be** reviewed and discussed.

Retinal vein occlusions

Yoon Kee LAI

Malaysia

Retinal venous occlusive disease both branches (BRVO) and central retinal vein occlusion (CRVO) are the most common retinal vascular disorders after diabetic retinopathy. Macular dysfunction is encountered very often in both BRVO and CRVO. Two landmark studies ~ the Branch Vein Occlusion Study and the Central Vein Occlusion Study – have addressed this and other complications. The application of the results of these randomized studies to **our** clinical management is the basis of this presentation.

OPHTHALMOLOGY SYMPOSIUM 4: REHABILITATION IN ARMD

Cataract extraction in ARMD

P SINGH

Malaysia

Abstract not available

Non-optical aids in ARMD S ANUSIAH

Malaysia

Abstract not available

Optical aids in ARMD

Norhani MOHIDIN

Malaysia

Abstract not available

INTERNAL, MEDICINE 1: CARDIOVASCULAR SYSTEM

Cases studies. Abstracts not available.

INTERNAL, MEDICINE SYMPOSIUM 2 : SYSTEMIC LUPUS ERYTHEMATOSUS

Pathogenesis of systemic lupus erythematosus

AZIZAH MR

Institute for Medical Research, Kuala Lumpur, Malaysia

Systemic lupus erythematosus is a chronic inflammatory multi-system disease. The aetiology is thought to be multifactorial. Evidence suggests that a combination of aetiologic factors may play a critical role in the disease pathogenesis. Five groups of hypotheses proposing explanations for the aetiologic pathogenesis of SLE in humans will be considered: (1) failure of the mononuclear phagocytic system to clear immune complexes leading to stimulation of autoimmunity by autoantigens. Interaction of autoantibodies with circulating autoantigens results in the formation of soluble complexes which localize in the basement membranes of tissues These are normally removed from the blood by the mononuclear phagocytic system which appears to be defective in many patients with SLE, (2) aberrant polyclonal activation of B lymphocytes, resulting in autoantibody production, (3) abnormality of idiotypic networks, cross-reactive idiotypes on autoantibodies has led to the hypothesisthat a disturbance of the network of idiotypes and anti-idiotypes may stimulate autoantibody production, (4) the breaking of tolerance to autoantigens by antigenic mimicry by microbial antigens or by the interaction of viral antigens with host intracellular molecules. Abnormal lymphocyte stem cells, defective thymus function, and failure of peripheral suppressor mechanisms have been implicated in disease pathogenesis. What is the nature of the inciting antigens and why are there so many? Are they native component possibly altered making them immunogenic?, (5) viruses as a cause of disease, and (6) genetic susceptibility; genetic predisposition could depend on any number of variables; determination of antigens for which tolerance fails, the characteristics of autoantibodies that are **formed**, and the immune complex mechanisms.

Catastrophic anti-phospholipid syndrome (CAPS)

Morris WO

Malaysia

The antiphospholipid syndrome is characterized by recurrent fetal loss, arterial and venous thromboses, thrombocytopenia and circulating antiphospholipid antibodies. In 1992, an attempt to single out a

different and important group of patients was adopted by introducing the term "catastrophic" antiphospholipid syndrome (CAPS) to describe their potentially life threatening clinical course. characterized by acute multiorgan failure (3 or more organ system damaged). CAPS is an uncommon disorder characterized by widespread micro- and macrovascular changes due to intravascular thrombosis. This complication of the antiphospholipid syndrome is often fatal and recurrences are very rare. The differential diagnosis of CAPS includes thrombotic **thrombocytopenic purpura** (TTP) and this distinction may be difficult, but essential for appropriate therapy. Plasmapheresis is effective in both conditions, but anticoagulation, a mainstay in the treatment in the treatment of CAPS, may be disastrous in TTP. Precipitating factors include infections, trauma (surgical), drug administration and warfarin withdrawal. Pathogenesis of the CAPS seems dependent on a "**two-hit**" or "three-hit" hypothesis in patients already suffering from a hypercoagulable state. The systemic inflammatory response syndrome (SIRS) may be responsible for some of the clinical manifestations such as the adult respiratory distress syndrome (ARDS). The mortality is high, most patients dying as a result of a combination of cardiac and respiratory failure. Therapeutic options include high dose i.v. steroids, heparin, cyclophospharnide, i.v. globulin, and plasmapheresis.

Therapy of severe lupus nephritis (LN)

Norella CT KONG

Department of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Renal involvement occurs in about 40-80% of patients with SLE. There is **immuno-dysregulation** of apoptosis leading to the release of nucleosomes which may be the major autoantigen rather than the poorly immunogenic ds DNA. Nucleosome antibodies coupled with nucleosomes have a high affinity for the GBM resulting in LN. LN presents in many ways and various combinations thereof (WHO classification) are found on renal biopsy. Severe LN includes Classes III, IV and V and combinations of these. An aggressive therapeutic approach to severe LN especially in the past four decades have led to markedly improved patient and renal survival. The goals of treatment of severe LN encompasses remission induction, remission consolidation and remission maintenance in the short term PLUS prevention of progressive renal failure and minimization of drug toxicity in the long term. To this end, **lowdose** steroid-cytotoxic combinations are superior to high dose steroids alone. IV cyclophosphamide is presently considered the 'gold' standard although optimal dosage, dosing interval and duration of therapy remain controversial. At our institution, minipulse methylprednisolonè (250 mg for three days) followed by **lowdose** oral steroids and **lowdose** IV cyclophosphamide as induction therapy have shown equivalent efficacy to the NTH regimes. Azathioprine, cyclosporin A or even mycophenolate mofetil (except for costs in the latter two) may be preferable for chronic maintenance therapy. Plasmapheresis and IV immunoglobulins are useful adjuncts for refractory disease and especially in sick patients at risk for infection although they are expensive and less efficacious when used on their own. New forms and combinations of chemotherapeutic agents (eg mycophenolate mofetil and adenosine analogues), attempts to achieve immunological reconstituition with near-ablative chemotherapy (with or without bone marrow or stem cell rescue). In particular, prospects for specific immunotherapies are novel and promising. These include monoclonal antibodies directed against the various cytokines implicated in the aetiopathogenesis of SLE. An idiotypic antids DNA vaccine has successfully completed Phase I B evaluation. Ultimately, perhaps gene therapy for human SLE.

INTERNAL MEDICINE SYMPOSIUM 3: AGEING AND DEMENTIA

Clinical approach to dementia

KH SNG

Gleneagles Intan Medical Centre, Kuala Lumpur, Malaysia

The clinical diagnosis of dementia [American Psychiatric Association DSM IV-1994] requires the demonstration of impairment of short and long term memory together with one of the following i.e. disorder in abstract thinking, impaired judgment, higher cortical function disturbance and personality change. The memory and intellect impairment should have an affect on social and occupational performance. Exclusion of disorders of delusion is necessary. Cognitive or intellect impairment involve memory deficit, language impairment, visuospatial disturbances and altered ability in executive functions. Affective changes include irritability, lability, disinhibition, anxiety, delusions, hallucinations, apathy, withdrawal. Functional disturbances include inability in using instruments, daily living, incontinence and immobility as well as sleep, sex and appetite. Besides Alzheimer's disease, vascular dementia, AIDS, traumatic brain injury, drugs and alcoholism are other common causes of dementia. The entity of Minimal Cognitive Impairment has to be considered as a high proportion of patients develop dementia. The use of neuropsychological testings, laboratory tests and imaging studies enable further evaluation of the dementias.

Diagnosis of alzheimer's disease

P SRINIVAS

Division of Geriatrics, Department of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Alzheimer's Disease (AD) is a progressive neuropsychiatric disease characterised by a loss of memory and affective or behavioural disturbances. A diagnosis of AD is usually based on getting a detailed history from the caregiver, full physical examination, cognitive assessment, laboratory investigations (to rule out reversible causes of dementia) and neuroimaging in selected cases. Although memory loss for recent events is the cardinal feature of AD, language difficulties, complex task difficulties and behaviour problems secondary to depression and psychoses are often found. As no diagnostic markers are available presently for AD a good clinical assessment and diagnostic workup of older persons with cognitive impairment is essential for the accurate diagnosis of AD. Detecting AD in the early stages allows for better treatment strategies and planning of future care.

Management of alzheimer's disease

Philip JH POI

Division of Geriatrics, Department of Medicine, University Hospital, Kuala Lumpur, Malaysia

The management of the commonest neuro-degenerative disease in the elderly can be divided into the treatment of cognitive deficits, the management of neuro-psychiatric symptoms, and patient and carer support. The best symptomatic therapeutic responses in the treatment of cognitive deficits have been with drugs that increase cholinergic activity. In managing neuro-psychiatric or behavioural symptoms, it is important to consider physical causes, activity related behaviour, depression and delusions, before attributing the symptoms to the intrinsic nature of Alzheimer's disease. Pharmacological and non-pharmacological approaches should be considered. Neuroleptics and antidepressants should be used with care to avoid side effects. With limited therapeutic options available, the support of the carer and the patient is imperative to reduce carer burden and inappropriate early institutional placement.

NURSING SYMPOSIUM 1: NEEDLE STICK INJURIES AMONG HEALTH CARE WORKERS

Incidence of needle stick injuries among health care workers Jeya COOMARASAMY

Hospital Universiti Kebangsaan Malaysia, Malaysia

A prospective study was done over an 18-month period (January 1998-June 2000) to determine the incidence rate of needle stick injuries among health care workers and students attached to a teaching hospital. Data was analyzed according to occupation, the work place, the task in which the **worker/** student was involved and the environment of injury. There was a total of 94 sharp injuries during the period and 5189% were due to needle sticks. The highest three group of workers to sustain injury were staff nurses (35.5%), cleaners (22.5%) and doctors (15%). Most of the injuries were due to hollow-boreneedles and could have been prevented. In majority of the cases it was related to disposal mechanism and unsafe work practices. The study highlights the need for ongoing education. continuous emphasis on existing policies and procedures as well as continuous monitoring to ensure a safe work environment.

Factors contributing to needle stick injuries

TUMINAH Jantan

Hospital Kuala Lumpur, Malaysia

The use of needles in the hospital setting is unavoidable. Reviewing the reported cases of needle-stick injuries that occurred in Hospital Kuala Lumpur over the past four years (1996-1999) revealed that majority of the health care workers involved were the nursing **personnel** which include the staff nurse, assistant nurse and the student nurses (57.7%). The major contributory factors to needle-stick injuries were identified. Lack of experience and skill: 44.4% of staff nurses that had needle-stick injury were those with less than 3 years of working experience. The other factors are unsafe device, neglected needles, inappropriate use of needles and non-compliance to guidelines on handling of sharps such as overfilled sharps bin and recapping. The possibility of **unwarranted** phlebotomies could also be considered contributory. The reduction in the usage of needles, the modification of the work process and choosing device with safety features could be considered to reduce the incidences of needle-stick injuries.

Preventive measures for the control of needle stick **injuries** NORSIAH Mohamad Nor

Ministry of Health, Malaysia

Preventive measures should be observed diligently to prevent needle stick injuries among health care providers. Policies on prevention has been tabled by the Ministry of Health as a guideline for all health care providers. Disposable syringes and needles should be disposed in a puncture proof container immediately after use. All needles and syringes used should be sterile. Reusable **cannulaes** should be autoclaved. Used needles should not be recapped, bent or broken by hand. All health care providers should receive proper training and be trained periodically. Supervisors should develop standard operating procedures as a guideline and made known to the health care providers. Monitoring and record keeping will ensure compliance. All health care providers should adhere to the guidelines given to prevent incidence.

NURSING SYMPOSIUM 2: MANAGING AN OUTBREAK - A NURSING PERSPECTIVE

Managing an outbreak: Public Health Nursing Perspective 1997 Sibu experience AY WONG

Divisional Health Office, Sibu, Sarawak, Malaysia

In mid-1997, several children died in Sarawak, Malaysia, during an epidemic of enterovirus-71 (EV71) hand, foot and mouth disease. The children who died had a febrile illness that rapidly progressed to cardiopulmonary failure and the cause was not satisfactorily resolved. The unusual outbreak was **first** recognised in Sibu hospital where 20 out of 34 recorded child deaths occurred. As the emergence was so sudden everyone was stricken with uncertainty of the best action to be taken. The medical professionals were working very hard to save the children admitted to the hospital while the public health professionals did their best to assist in the investigations and the control programme. This paper aims at sharing the **public** health nursing experience during the crisis in Sibu. Public health nursing concentrated at vigilance of cases, intensifying health education on preventive measures and control measures. During the 1997 crisis in Sibu, the public health nurses played the key roles in the field investigation teams. Besides, they were also entrusted the responsibility to persuade the parents and relatives to give consent for the post mortem of all fatal cases. The 1997 Sibu outbreak experience is a priceless learning experience that has equipped and enabled the nurses to handle such outbreak more efficiently in the future as no one can be sure when the viruses will strike again.

Nursing experience in managing the Nipah virus epidemic RADZIAH Mohd. Sharif

Intensive Care Unit, University of Malaya Medical Centre, Malaysia

This study describes the nursing experience in managing the epidemic of Nipah virus in the University of Malaya Medical Centre (UMMC). The outbreak of Nipah virus started in Perak in late September 1998 and spread to Negeri Sembilan by late February 1999. With the increasing number of patients admitted to the hospital, the intensive care unit was not able to accommodate all the ill patients, but to expand the unit in a new area. The care of Nipah virus patients employed a multidisciplinary team approach and each member of the team (nurses, doctors and relatives) played a vital role. The nursing care was directed towards achieving the objectives of preventing potential complications, especially under these conditions where the mode of transmission was still uncertain. Patients with Nipah virus were separated from the other patients to avoid spread of infection and cross infection to other patients and health care staff. Standard and droplet precautions were practiced. Supportive care was the mainstay of treatment which included intensive care monitoring and the initiation of mechanical ventilation as needed for airway protection with the onset of neurological deterioration. Patients were observed intensely with regards to their general condition, complaints, and most importantly, their neurological changes - that is falling levels of consciousness which probably can increase intracranial pressure and reduced cerebral perfusion. Above all, total patient care was initiated to ensure comfort and to maintain hygiene at all times. The problems and difficulties faced by the nurses, the stress and anxiety of grieving relatives will be highlighted.

Management of infection in NICU Institute of Paediatrics, Kuala Lumpur Hospital FARIDAH Ahmad Shiek and Yon SAID

Institute of Paediatric, Kuala Lurnpur Hospital, Kuala Lumpur

Introduction: Nosocomial infection are a major problem in neonatal intensive care units. The prevalence, mortality and morbidity of baby with infection are noted to be increasing and management guidelines and practices has been formulated to improve infectious cases. **Aims:** The aim of this study is to determine the impact of these guidelines and practices on the NICU management of infectious

cases by comparing the trend of management of infectious cases before 1998 and 1999. **Design:** Prospective study from January 1st 1997 to December 31st 1999 by infection control nurse. **Setting: Neonatal** Intensive Care Unit (**KK9**) Kuala Lumpur Hospital, Kuala Lumpur. **Subjects:** Baby admitted to ward NICU from the ages of newborn until discharge or transfer out with the organism positive. **Results:** The total number of positive cultures in 1997 versus 1998 and 1999, were n=201 versus n=143 and n=113 respectively. More blood culture were sent in 1997 (n=1416) versus in 1998 (n=601) and 1999 (n=593). More death associated with nosocomial infection in 1997 (n=21) than 1998 (n=16) and 1999 (n=12). **Discussion:** The study showed that better results were obtained in 1998 and 1999 due to closer supervision of junior doctors in blood taking technique, tighter criteria for blood taking, and enforcement of infection control practices to all categories of staffs. **Conclusion:** It is showed that the management in N1CU recent years were in keeping with the current infection management guidelines and practices, with this direction, we hope to decrease the number of infections cases in the NICU.

NURSING SYMPOSIUM 3: EMERGING TRENDS IN CLINICAL NURSING

Palliative care in oncology department

ASMAH Sharif

Hospital Kuala Lumpur, Malaysia

Palliative care is a concept of interdisciplinary team approach coordinated by medical, nursing and allied health professionals who deliver an active holistic care to patients whose disease is not responsive to curative treatment. The main emphasis of care is to control symptoms and provide physical, psychological, social and spiritual support of patient and carer/family. The criteria of admission for any patient diagnosed as having advanced cancer is commonly severe pain, fatigue, dyspnoea, constipation and severe anorexia which require medical treatment and regular assessment. In addition, emphasis which include organising support services for assistance to the carer, respite care for the patients and **financial** support for the family will be attended to by the oncology team. It is particularly important to lessen a wide range of responsibilities and problems of the **family/carer** during the festive season or special occasion. During this period the respite care is delivered by the palliative care nurses in the ward. The aim is to give the opportunity for the family members to rest or celebrate festivals happily. Recognizing various religious beliefs amongst the patients, the religious groups are encouraged to visit patients with permission from the hospital medical welfare department. A space is provided for the **muslim** patients to perform their prayers, 5 times a day. Therefore spiritual beliefs will promote internal strength and acceptance of God's will in facing chronic disease. Alteration in comfort, related to pain from the cancer site and due to metastasis of disease indicates a focus on quality of life. Monitoring the severity of pain 24 hours by the nurses enable the doctors to prescribe appropriate doses of morphine at regular intervals and breakthrough intervals. Through education and counseling the nurses are not only reducing fear, anxiety and feelings of hopelessness in patients but also offering caring support. The proper method of using body mechanics while lifting and turning patients will be shown to the carer. At the same time skillful and aseptic techniques in procedures such as dressing, care of pressure areas and care of catheters will be taught sequentially. Therefore the above goals of palliative care will facilitate self determination among the interdisciplinary team to provide tender loving care for cancer patients.

Pain management

Poh Chin GAN

University Hospital Kuala Lurnpur, Malaysia

Pain is defined as "an unpleasant sensory or emotional experience, associated with actual or potential tissue damage, or described in **terms** of such damage" (International Association for the Study of Pain, 1979). My main focus is on post-perative pain management. The inadequacy of post operative

pain relief analyseics using the conventional intramuscular injections of opioids, showed a need to set up an organized Acute Pain Service. Therefore, in October 1992, the Acute Pain Service in University Malaya Medical Center was set up by Professor Ramani Vijayan, as a new patient service commitment, in keeping with the worldwide trend to improve the quality of pain relief following surgery. Various techniques had been introduced for the management of post-operative pain and the two most common techniques used are patient controlled analgesia (PCA) and epidural analgesia. Explanatory leaflets on the use of PCA given preoperatively by ward nurses, or explaining the epidural technique to patients undergoing moderate to major surgeries, have allay their fears of postoperative pain. Nurses occupy a unique position closest to patients in assessing and managing postoperative pain and are therefore the prime agents to deliver high quality pain care. By attending inservice training and following standardized procedures for nursing practice on the various pain relieving techniques, using assessment tools for pain rating and documentation of such observations in the observation charts, the ward nurses are then able to achieve good quality pain care. Successful assessment and control of pain depends on nurses establishing a positive relationship with the patient because nurses are the middle managers of patient pain relief. The role of the acute pain nurse is very important in providing continuity in patient care. Besides doing the APS round and collecting data, she conducts periodical teaching sessions to ward nurses a n d trouble shoots" any problems that may arise in the wards. In conclusion, it has created the potential for nurses to become Clinical Nurse Specialist in this field in the future to come.

Wound management

SITI HAZAIMAH Md Shahit

Jabatan Pengurusan Kejururawatan, Hospital Universiti Kebangsaan Malaysia, Malaysia

Various case studies are done on patients with open wounds e.g. diabetic foot, pressure ulcer and infected wound in different patient care environments. The management of wounds especially large ones requires a multidisciplinary panel of experts. The introduction of modem dressings are cost-effective, since they reduce nursing time spent changing dressings and patients are comfortable and appreciate being mobile.

FREE PAPER PRESENTATIONS

The TEL-AML1 translocation in two pediatric cases of acute lymphoblastic leukemia

GILL HK1, TEN SK2, DHALIWAL JS1, TAN SK3, ROSHIDA H3, YASMIN A4, ZUBAIDAH Z2, NASURUDDIN BA1, YONG ASM5, CHANG KM5, HISHAMSHAH16, ENI J6, PURUSHOTAMAN V5, and HO CML6

'Immunology Division, Institute for Medical Research, 'Haematology Division, Institute for Medical Research, 'Department of Pathology, Kuala Lumpur Hospital, 'Blood Bank, Kuala Lumpur Hospital, 'Clinical Haematology Unit, Kuala Lumpur Hospital & 'Paediatric Institute, Kuala Lumpur Hospital, Malaysia

The **TEL-AML1** translocation was detected in two pediatric cases of acute lymphoblastic leukemia. Case 14 was a **three-year-old** boy with a **WBC** of 5.0 **x** 10°/1 who was diagnosed with ALL-L1, while case 28 was a five-year-old girl with a WBC of 22.1 **x** 10°/1 who was also diagnosed with ALL-L1. The karyotype of case 14 was **46XY**[3] and that of case 28 was **46XX**[4]/46XX, -5,add(9q),+mar[2]. Immunophenotyping of case 14 classified the case as CALLA-ALL with co-expression of the **CD13**/CD33 myeloid antigens. RT-PCR on RNA from both cases generated a 464 base pair (bp) fusion product **which sequencing** confiled as the TEL gene joined to **exon** 2 of the AML 1 gene. Case 28 also displayed a minor band of **the** 425 bp shorter fusion product in which the TEL gene is joined to **exon** 3 of the AML1 gene. A less intense band of the reciprocal **AML1-TEL** translocation was also detected in both cases. The presence of the fusion transcript was also comed by fluorescence in **situ** hybridization (FISH). In case 14, FISH further revealed that a proportion of the cells with a **TEL-AML1** fusion signal showed an associated loss of the non-translocated **TEL** gene.

Effects of palm oil vitamin E on vas deferens contractility and testosterone level. HAMZAH FH¹, HAMID A¹, NEW KHH² and KHALID BAK³

Departments of Anatomy', **Physiology**² and Medicine³, Faculty of Medicine, National University of Malaysia, Kuala Lumpur, Malaysia

The objectives of the present studies were to determine the effects of vitamin E deprivation and supplementation on the contractility of the vas **deferens** and plasma testosterone (T) levels. Groups of male Wistar's rats were subjected to treatment with **0**, **30** and 120 **mg/kg** diet palm oil vitamin E for a period of up to 20 weeks. Measurement of body weight (BW) and T levels were canried out at weeks **0**,**4**,**8**,**12**,**16** and 20. Vas **deferens** contractility and testicular weight (TW) were measured at 20 weeks. The results revealed that palm oil vitamin E significantly increased the vas **deferens** contractility in a dose dependent manner. BW and TW of rats treated with 30 and 120 mg vitamin E differ significantly from vitamin E deficient rats at week 20. Response of T to vitamin E appears to follow dose levels. T values are highest in rats receiving 120 mg and lowest in rats receiving **0** mg vitamin E. However, the difference in T between rats receiving 0, 30 and **120mg** vitamin E are insignificant. We therefore concluded that palm oil vitamin E caused an increase in the BW, TW and contraction of the vas **deferens** in male rats. The dose dependent effects of palm oil vitamin E on T however needs to be tested further using higher doses and longer treatment periods.

A partially purified specific antigen of *Parastrongylus cantonensis* for immunodiagnosis of human parastrongyliasis

Praphathip EAMSOBHANA

Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

To isolate a 31-kDa specific antigen from Parastrongylus cantonensis for immunodiagnosis of human parastrongyliasis, the crude extract of P. cantonensis was fractionated by gel filtration chromatography in Sephacryl S-200 HR. The antigenic components of the peak fractions were determined by sodium dodecyl sulphatepolyacrylamide gel electrophoresis and immunoblot analysis using serum from a patient with parasitologically confirmed parastrongyliasis. Pooled fraction which contained an immunodominant antigen with molecular weight of 31 kDa was used in an indirect enzyme-linkedimmunosorbentassay (ELISA) for detecting of the specific antibody of *P. cantonensis*. Three distinct protein peaks were obtained when the crude extract of *P. cantonensis* adult worms was passed through a Sephacryl S-200 HR column. The 31 -kDa diagnostic antigen of *P. cantonensis* was present in the first elution profile as revealed by immunoblotting. The band of 31-kDa antigenic component reacted strongly with parastrongyliasis serum. A semipurified fraction from the first elution peak was used in ELISA for detecting specific antibody to the 3 1-kDa antigen of P. cantonensis. A total of 200 serum samples was used in the study. Of these, 25 sera were from patients with parastrongyliasis. Fifteen sera each were from patients with gnathostomiasis, toxocariasis, filariasis, paragonimiasis and cysticercosis. The control group consisted of 100 serum samples from normal healthy individuals. The sensitivity and specificity of the ELISA were 100% and 98.87%. respectively. The Sephacryl S-200 fraction containing an immunodominant antigen of 31 kDa, appears promising as a diagnostic reagent in the ELISA for human parastrongyliasis.

Serological profile of *Toxoplasma gondii* antibody among **HIV** positive and negative cases: retrospective review of indirect immunofluorescence antibody test (IFAT) **results**

RADEN Shamilah RH, LOKMAN Hakim S, NOR AZIAN MN, MALKITH K and YUSRI MY.

Division of Parasitology, Institute for Medical Research, Kuala Lumpur, Malaysia

The Division of Parasitology, IMR, received a total of 2,554 samples for the diagnosis of toxoplasmosis by **IFAT** in the year 1995-1997. Out of these samples, 729 (28.5%) were from HIV

positive cases. **IgG** titre of 1:64 was considered as highly suggestive of current infection (positive result). The positive rate among HIV positive and HIV negative patients was 31.3% and 24.3% respectively (p<0.001). The positive rate among HIV negative patients was highest among the Malay (27.0%) followed by the Indians (25.6%), Chinese (21.4%) and others (19.8%)[p=0.001]. Similar trend was noted among HIV positive cases with higher positive rates but the proportion of positive titre increased significantly among the Malays (42.1%, p<0.001), but not among the Indians (30.8%, p=0.645), Chinese (22.0%, p=0.934) and others (24.3%, p=0.827). Significantly more male had positive titre (26.3%) than female (21.8%) among HIV negative cases (p=0.024) but not among HIV positive cases (31.8% and 28.3% respectively, p=0.457). The *anti-Toxoplasma* antibody titre increases significantly with age ($\mathbf{r_s}$ =0.1, p<0.001) among HIV negative but not among HIV positive cases ($\mathbf{r_s}$ =-0.4, p=0.114).

Damage to endothelial cells of rat aortae consequent to consumption of rat chow mixed with 20% w/w of soya bean oil, palm oil or ghee for a prolonged period.

MERICAN Z1, FADZIL H2, AZILAH AJ3, HATIJAH M4, FAIZAH O5 and KHALID BAK5

Faculty of Applied Sciences', Universiti Teknologi MARA, Department of Biomedical Science?, Department of Pharmacy, Faculty of Allied Health Sciences, Universiti Kebangsaan Malaysia, Electron Microscope Unit³, Universiti Putra Malaysia and Departments of Anatomy and Medicine⁵, Medical Faculty, Universiti Kebangsaan Malaysia.

Consumption of saturated oils increase low density lipoproteins while consumption of polyunsaturated oils increase the formation of **lipid** peroxidation products. Such increases may result in endothelial cell injury. The effects of consumption of 3 oils of varying degrees of saturation on endothelial cell surface structure of rat aortae were studied using the scanning electron microscope. 3 groups of 5 rats each group were fed with either **20%w/w** of soya bean oil, palm oil or ghee mixed with rat chow for a period of 18 months. A control group of 5 rats was fed rat chow only. The rats were then sacrificed and their aortae isolated and processed for viewing under the scanning electron microscope. The study showed that the aortae of rats fed with the three types of oils showed abnormal alignment of endothelial cells, enlarged endothelial cells and holes and craters on their surfaces to about a similar extent when compared to each other. These changes were minimal, if any, in the aortae of control rats. The study suggests that too much oil in the diet whether saturated or polyunsaturated over a prolonged period of time is damaging to endothelial cells.

Clinical and serological disease expression and HLA types in early and late onset disease of Malaysian patients with systemic lupus erythematosus

AZIZAH MR*, AINOL SS**, KUAK SH*, KONG NCT**, NORMAZNAH Y* and RAHIM MN#

*Institute for Medical Research, Kuala Lumpur, ** Faculty of Medicine, Universiti Kebangsaan Malaysia, and # Faculty of Allied Sciences, Universiti Kebangsaan Malaysia, Malaysia

Systemic lupus erythematosus (SLE) is a chronic disorder of the immune system with heterogeneity of clinical and immunological manifestations. Age has been suggested to modify disease expression. In this study we have attempted to study 13 patients with late onset (40 years and above) and 121 with early onset disease (below 40 years) to determine whether age-related differences in disease expression exist. We found that patients with late onset disease initially presented with pericarditis (31% vs 3%, P<0.005) Arthritis, renal involvement and hemolytic anemia were also common presentationsthough not statistically significant. However, there was a lower incidence of malar rash (31% vs 57%, p<0.05) in the late onset group. During the disease course, there was a lower incidence of mucocutaneous symptoms especially malar rash (p<0.005) and psychosis (p<0.05) in the late onset group. Serological parameters were similar in both groups. There was a significant increase of HLA-DQA1*0103 in patients with a later onset disease (pcorr=0.004). In this study, we have shown several differences of organ involvementat presentation and in the course of the disease between two groups of patients with regard to age at disease onset. The data also shows the influence of the HLA

type on the age of disease onset. These findings suggest that our subgroup of late onset patients experience a milder disease and that the risk conferred by the HLA-DQA1*0103 is significant only among the later onset disease

A new simultaneous chromatographic method for quantification of sulfadoxine and pyrimethanime and its application in clinical pharmacological studies.

NW SIT, SM MANSOR, S RAMANATHAN, PL LEE, PL OLLIARO and V NAVARATNAM

Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

Recently, evaluation of the possibility of combining sulfadoxine/pyrimethamine with artemisinin derivatives has been pursued, in order to prolong its lifespan and to curtail the development of malaria resistance. A sensitive and reproducible chromatographic method with ultraviolet detection for simultaneous determination of sulfadoxine and pyrimethamine has been developed. Plasma (0.25ml) was extracted using a DSc-18 Bond Elute cartridge. Separation of the compounds was achieved on a C., Nucleosil column using gradient elution with acetonitrile-acetic acid (1%; pH3.2). Calibration curves for sulfadoxine and pyrimethamine were linear (r>0.99) in the range of 0.05-80mg/0.25ml and 0.025-4mg/0.25ml plasma respectively. Mean recoveries for sulfadoxine and pyrimethamine were 86.2% and 92.9% respectively. The minimum detectable concentration of sulfadoxine and pyrimethamine were 50 and 25ng respectively using 0.25ml of plasma. The withinday and day-to-day coefficient of variation (C.V.) for sulfadoxine (0.7-30mg/0.25ml) were from 2.0-3.2% and 6.7-8.3% respectively and the corresponding C.V. for pyrimethamine (0.15-3.5mg/0.25ml) were from 5.9-7.7% and 8.3-9.2% respectively. Six healthy normal volunteers were given a single oral dose of Fansidar'' (25mg/kg of sulfadoxine and 1.25mg/kg of pyrirnethamine). Plasma samples were collected at various time intervals and stored at -70°C pending analysis. The mean C_{max} , mean T_{max} and mean AUCo-t for sulfadoxine were 245.1mg/ml, 13.50hr and 54.7mghr/ml respectively. The corresponding values for pyrimethamine were 1.2mg/ml, 1.25hr and 59.1mghr/ml respectively. The mean $t_{1/2}$ for sulfadoxine and pyrimethamine were 219hr and 82hr respectively. In conclusion, the method was found to be simple and reliable and has been successfully applied in a clinical pharmacokinetic study.

Comparative pharmacokinetic study of two rectal formulations of artesunate in healthy normal volunteers

S RAMANATHAN, SM MANSOR, PL LEE and V NAVARATNAM

Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

We compared the pharmacokinetic properties of two different rectal formulations of artesunate (ARS) in twelve healthy normal male Malaysian volunteers. The study consisted of two phases. In the first phase, subjects were given 200mg of ARS (formulation 1). After the washout period, the subjects were crossed-over with 200mg of ARS (formulation 2). Blood samples were drawn before and after treatment at appropriate time points. Blood samples were centrifuged and plasma were separated and frozen at -70 °C pending analyses. Plasma concentrations of artesunate and dihydroartemisinin were determined simultaneously by HPLC with electrochemical detection. Comparison of pharmacokinetic parameters of artesunate after formulation 1 (F1) and formulation 2(F2) administrations showed statistically significant differences in $AUC_{0+}(AUC_{0+}F1: 598\pm413 \text{ nghr/ml}; F2: 266 \pm 142 \text{ nghr/ml}, p<0.04)$ and $C_{max}(C_{max}F1: 402.2\pm277.2 \text{ ng/ml}; F2: 161.9 \pm 110.4 \text{ ng/ml}, p<0.01)$ but no changes in $T_{max}(T_{max}F1: 1.31 \pm 0.59 \text{ hr}; F2: 0.91\pm0.64 \text{ hr})$. However, for dihydroartemisinin neither AUC nor C_{max} were significantly different between the two rectal formulations. In conclusion, this study demonstrated that for the same dose size, rectal formulation 1 was better absorbed and thus had higher availability when compared to the rectal formulation 2. The test medications were well tolerated and no side effects were observed in all subjects.

The prevalence of diabetic peripheral neuropathy in an outpatient setting M OMAR and CY CHIA,

Primary Care Department, University of Malaya, Kuala Lumpur, Malaysia

This study was undertaken to estimate the prevalence of clinical peripheral neuropathy among outpatient diabetic patients and to evaluate their risk factors for developing peripheral neuropathy. It was a cross-sectional study of 134 diabetes mellitus patients who attended the Primary Care Clinic, University Hospital, Kuala Lumpur. The patients were interviewed for their demographic data, past and present **medical/surgical** history, social history, personal habits and symptoms of peripheral neuropathy. Foot examination and clinical neurological tests were conducted and the presence of peripheral neuropathy was assessed. The main outcome measures were the Neuropathy Symptom Score and the Neuropathy Disability Score. The prevalence of diabetic peripheral neuropathy was found to be 50.7%. Peripheral neuropathy was related to the age of the patient and the duration of diabetes but does not seem to be significant related to diabetic control. To conclude, there was a high prevalence of peripheral neuropathy amongst the diabetics in this study. These patients developed peripheral neuropathy at a younger age and shorter duration of diabetes.

Pateint's perception of food induced asthma N NIVEDITA

Hospital Muar, Johore, Malaysia

To what extent does diet affect asthma control? The answer is as yet not clear as there appears to be a wide gap between patient's perception and scientifically proven roles. 20-60 % of athmatics report food as trigger factor while only 2.5 % react to double-blind placebo controlled challenges. The *aim* of this study was to determine: the frequency, type and sources of dietary advise being offered to patients, the prevalence of dietary modification, whether dietary changes were perceived to be of benefit and the type and sources of **food/beverage** reactions that people perceive they have experienced. *Method:* 212 asthmatic attending the out patient and medical follow up clinics of Hospital Muar & Hospital Tangkak were interviewed using a special "food and asthma" questionnaire. *Results:* Dietary advise had been offered to 83.5 % of patients while 92.9 % had tried to modify their diet. Dietary restriction was the most common dietary modification. Where dietary restriction had occurred 95 % of patients perceived that this had improved their asthma control. The most common source of dietary advise was from friends and relatives. 92.9 % reported that specific food induced asthma. *Conclusions:* We confirmed that asthmatics perceive diet to be important in their asthma control and that dietary modification is common despite lack of objective evidence. The influence of diet and asthma requires more research, evaluation and clinical attention.

Bilateral adrenal masses presenting as pyrexia of unknown origin H OMAR, SURESH RL, H ABDULLAH, J SUBRAMANIAM and I MERICAN

Malaysia

A 45-year-old man with a background history of diabetes mellitus for six years presented with pyrexia of unknown origin of two months associated with loss of weight of ten kilograms and loss of appetite. General examination revealed palatal ulcer measuring 1 x 2 centimeters. There was hepatomegaly of four centimeters below the right costal margin which was smooth and non tender Regional lymph nodes were not enlarged. Preliminary haematological examination revealed haemoglobin 13.7g/dL, a white cell count of 8.3x10 ⁹/uL and platelet count of 275x10³/uL. Erythrocyte sedimentation rate was 62mm in one hour. Random blood sugar was 9.lmmol/L. Liver function revealed elevated alkaline phosphatase 508 u/L and alkaline transaminase of 173u/L. Ultrasound revealed suprarenal masses measuring 2-3 centimeters. Further imaging with CT scan revealed bilateral adrenal masses with no evidence of calcification. Diagnosis was finally established

by punch biopsy of the palatal ulcer. Histology showed inflammatory cells and histiocytes with numerous histoplasma organisms. The patient was commenced on Itraconazole, which is a definitive treatment for histoplasmosis. The patient has exhibited clinical improvement and has gained weight. Serial CT scans of the adrenal are being performed to look for resolution of adrenal enlargement.

Contrast media nephropathy after coronary angiography: Penang GH experience CHONG S, LO S, Norella KONG, IDRIS M, GHAZALI R $\,$ and ONG LM $\,$

Malaysia

Background: Coronary artery disease is a major cause of mortality. Coronary angiography is increasing in volume. Contrast media nephropathy (CMN) remains a common cause of hospital acquired renal failure. The frequency of CMN and the predisposing factors are not well established. Objectives: (i) To determine the frequency of CMN after coronary angiography at Penang GH (ii) To identity die predisposing factors in CMN in our local populations. Design & Methods: 140 consecutive patients undergoing coronary angiography using nonionic monomeric low osmolar contrast medium were prospectively studied. CMN is defined as a rise in serum creatinine ≥ 20% of baseline in the early post exposure period. Renal profiles were performed on days 0, 1, 3, 5 and 10. Demographic characteristics, comorbid conditions and the volume of contrast medium used were recorded. Results: From June 99 - Dec 99 in Penang GH, 140 patients underwent coronary angiography. The mean age of these 140 patients was 55.11 ± 14 years. Mean volume of contrast medium used was 124.32 ± 87.35 mls 38 or 27.14% of these 140 patients developed CMN. The mean increase in serum creatinine in die CMN group was 59.61 ± 41.86 mmol/L. The mode day of creatinine peak was day 3. Pre-existing chronic renal failure (CRF) (p=0.036) and hypertension ≥ 10 years (p=0.017) were significantly associated with CMN. Diabetes mellitus alone, diabetes mellitus with preexisting CRF, proteinuria, proteinuria with DM, volume of contrast medium, calcium channel blocker, age and sex were not associated with CMN. Conclusions: The frequency of CMN is high in our study cohort despite the use of low osmolar nonionic monomeric highly hydrophilic contrast medium. Pre-existing CRF and hypertension ≥ 10 years were highly associated with CMN.

Rapidly progressive glomerulonephritis(RPGN) and diffuse alveolar haemorrhage syndrome SUGANTHIC, SOEHARDYZ, WONG M, FAUZI AR, NADZRI M, ROSLANH, JEFFRI H, *PHANG KS, **WAN MUHAIZAN and Norella KONG CT

Department of Medicine, *Department of Radiology, **Department of Pathology, Universiti Kebangsaan Malaysia, Malaysia

"Uncommon presentations of a common disease are more common than the common presentation of an uncommon disease." We report here a recent case of a 26-year-old Chinese male who presented with the pulmonary-renal syndrome. Anti GBM antibody disease (Goodpasteur's) and Wegener's granulomatosis were our initial differential diagnoses. After urgent exclusion of an infective cause, highdose methyl prednisolone and lowdose IV cyclophosphamide were started. Prior to renal biopsy, he showed a remarkable response to therapy with loss of lung infiltrates, increasing urine output, reducing severity of gross haematuria and stabilization of renal function. Lupus screen was negative. Blood for Anti-GBM, p-ANCA and c-ANCA antibodies were sent. Renal biopsy showed cellular crescentic glomerulonephritis. 5 out of 15 glomeruli were globally sclerosed. The rest showed fresh cellular crescents with capillary tuft collapse. There was moderate tubulointerstitial disease. The blood vessels were normal. Immunofluroresence showed 'full-house' staining. In particular, there were strong (3+) granular deposits of lgG and C, along the GBM, and + lgM, IgA, C, and fibrin. Thus this patient appears to have crescentic seronegative lupus nephritis and the unusual but well documented lupus alveolar haemorrhage syndrome. Prognosis is guarded.

Bartter's and Gitelman's syndromes - a life time search

Norella KONG CT, ROSMAN AR, ABD HADI J, JEYABALAN V, CHEONG IKS, FARIDAH I and Khalid BAK $\, . \,$

Department of Medicine, Universiti Kebangsaan Malaysia, Malaysia

Hypokalaemic metabolic alkalosis and nomotension are an uncommonly encountered syndrome complex. Over an 18 year period, our Department has been referred many cases of persistent severe hypokalaemia with the presumed diagnosis of renal tubular acidosis for management. We report here 3 patients with confirmed Bartter's syndrome and 1 patient with Gitelman's syndrome. The pathophysiology of these two conditions reside in the renal tubule. Bartter's syndrome can be simply understood as unopposed action of a 'loop diuretic' on the loop of Henle's. Gitelman's syndrome can be simply understood as unopposed thiazide action on the distal tubule. The approach to investigation and treatment thus becomes more rational.

Detection of renal artery stenosis by magnetic resonance angiography (MRA) SOEHARDY Z, SUGANTHI C, TOH ST, CHIA H, JEYABALAN V and Norella KONG CT

Malaysia

Objective: To review MRA's as a non-invasive investigational tool for renal artery stenosis (RAS). Design & Method: MRA (kidneys) was available at the Hospital UKM from Aug 1999. All MRA's of kidneys performed between Aug 1999 - end July 2000 for clinically suspected RAS were reviewed. These were then followed by renal angiography, the current 'gold' standard for confirming this condition. Results: In the one year period under review, a total of 38 MRA's were performed for this indication. There were 20 males and 18 females. 18 were Malays, 18 Chinese, and 2 Indians. 8 studies were positive for RAS. A bimodal pattern was obvious – patients were of a younger age group with suspected/known congenital or other nonatherosclerotic lesions of the renal arteries versus the majority who were older in whom atherosclerotic disease predominated. In addition to hypertension, the latter group also presented with a high frequency of diabetes and dyslipidaemia. Conclusion: MRA is a reliable non-invasive imaging modality for the detection of renal artery stenosis in the majority of patients. However, it proved unreliable for the follow-up of younger patients who have undergone previous surgical intervention for non-atherosclerotic lesions. Further experience with this imaging modality is required at our Centre.

Impediment of malaria resistance with concomitant administration of artesunate and sulfadoxine-pyrlmethamine: pharmacokinetic perspectives

SM MANSOR, S RAMANATHAN, NW SIT, M MURALITHARAN, ARA RASHID, PL OLLIARO and V NAVARATNAM

Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

Combination chemotherapy of antimalarials has emerged as a promising approach in the battle against malaria resistance. One of such combinations is concomitant oral administration of artesunate (4mg/kg) and Fansidar® (25mg/kg of sulfadoxine/1.25mg/kg of pyrimethamine). We have evaluated the pharmacokinetic parameters of sulfadoxine, pyrimethamine, artesunate and its active metabolite, dihydroartemisininin 12 healthy normal Malaysian volunteers. All subjects were initially administered a single dose of artesunate and twenty fours later, each subject either received a single dose of Fansidar® or combination of artesunate and Fansidara. All subjects were crossed over after the washout period of 53 days. Plasma samples were collected at various time intervals and stored at 70 °C pending analyses. Artesunate and dihydroartemisinin concentrations were determined by high-performance liquid chromatography (HPLC) with electrochemical detection in the reductive mode whereas sulfadoxine and pyrimethamine concentrations were determined simultaneously by HPLC with ultraviolet detection. There were no significant differences in the pharmacokinetic parameters

(Cmax, Tmax, AUCo-t and t,,) of sulfadoxine and pyrimethamine in subjects who received Fansidar® alone or in combination. Similarly, administration of Fansidar® did not affect the pharmacokinetics of artesunate and dihydroartemisinin in healthy volunteers. The test medications were well tolerated in all subjects. The effectiveness of this combination should be further evaluated in malaria patients of different degree of severity.

Factors contributing to poor compliance with anti-TB treatment among tuberculosis patients

SYED HATIM Noor, ABDUL RAHMAN Isa, NORAINI Bakar, *MOHD ROBI Mahmod Department of Community Medicine, School of Medical Sciences, Universiti Sains Malaysia, and *Chest Clinic, Department of Medicine, Hospital Kota Bharu, Kelantan, Malaysia

Tuberculosis is making a comeback. It has become a resurgent public health problem in developing countries in the tropics and is the leading cause of death from any single infectious agent. Noncompliance to anti-tuberculosis treatment is the most serious problem in TB control. A **cross**-sectional study was conducted to investigate the determinants of poor compliance with **anti**-tuberculosis treatment among tuberculosis patients in Kota **Bharu**, Kelantan, Malaysia in 1999. A total of 390 patients were included in the study of which 130 were Tuberculosis (TB) patients who defaulted treatment and 260 were those compliant to treatment. Data collection was done by interviewing the patients and collecting clinical and laboratory data from their medical records. Using multiple logistic regression method, patients who were not on DOT, lived far distance to the health facility, were intravenous drug users and were Human lmmuno-deficiency Virus (HIV) positive had statistically significantly higher odds of being non-compliant. Patients should be given treatment under direct supervision with special attention to IVDU and **HIV** positive groups. Anti-TB treatment should be accessible to patients at the nearest health **center** from their residence. Interventions with health education programs emphasizing the benefits of treatment compliance should be implemented by large-scale multi-centered studies.

Social support during labour in a district hospital JAPARAJ RP and *GOH YS

Hospital Teluk Intan and *University Hospital, Kuala Lumpur, Malaysia

Continuous social support has been shown to be very beneficial to the labouring mother and her baby in most western countries. Our study was done to assess the benefits of social support and also the perception of the labour ward staff about the presence of companions in the labour ward of the district hospital. This was a prospective controlled study done in Hospital Seri Manjung from 1st September 1998 till 31" October 1998. All low risk nulliparous women who presented to the labour ward in spontaneous labour were recruited. The women were divided into 2 groups. The study group had a companion of their choice during labour and the control group went through labour without any social support. The labour ward staff was also asked through an anonymous questionnaire about their perception of social support during labour at the end of the study period. One hundred and ten patients were recruited during the study period. Fifty-one patients had a companion during labour and fiftynine had no companions during labour. Seventy one percent of the study group chose their husbands as their social support. The average length of labour was 562 minutes in the study group and 567 minutes in the control group. The average pain score was less in the study group (3.9 vs. 4.2 in the control group). The number of Caesarean sections was almost similar in the study group and the control group (4% and 3% respectively). There were fewer babies admitted to the SCN from the study group compared to the control group (6.1% and 10.2% respectively). All 21 nurses and 5 doctors managing the labour ward felt that both the patient and her companion benefited from the practice of having a companion during labour. Continuous social support during labour is beneficial to the mother, baby and probably the companion as well.

Babies born before arrival: a study at Hospital Bersalin Kuala Lumpur SIVA Ahcanna, SC LOO and FS MAK

Obstetrics and Gynaecology, Hospital Bersalin Kuala Lumpur, Malaysia

Objective: To establish the prevalence of babies born before arrival at the local hospital, to identify the risk factors for birth before arrival and the outcome in terms of morbidity and mortality associated with such births. *Design:* A prospective case control study in Hospital Bersalin Kuala Lumpur. Each baby born before arrival and its mother was compared with the next born in the hospital matched for gestation and birth weight. Subjects included all babies (and their mothers) born before arrival from 1st January 1999 till 31" December 1999. Demographic, social and obstetric features of the mothers, perinatal mortality rates and patterns of perinatal morbidity were the main outcome measures. Results: 231 (0.97%) of 23895 deliveries were before amval at hospital (BBA group). Mothers who delivered before arrival at hospital were significantly more likely to be single, to have received no antenatal care, to be of higher parity and were more likely to come from a socially disadvantaged groups (immigrants). There were 10 maternal complications observed (7 retained placenta, 2 postpartum hemorrhage and 1 mortality) in BBA group. Numbers of admission to neonatal intensive unit was higher (15.4%) compared to control (10%). Perinatal mortality rate associated with BBA was 4.7% (11of 231). There were 3 neonatal death and 8 stillbirths in BBA group. *Conclusion:* Babies born before arrival has higher perinatal mortality and morbidity compared to the control group. Improved antenatal education could potentially reduce the incidence of BBA and its adverse consequences. Community outreach programs to identify childbearing age groups, health education, drug rehabilitation, and education to utilize health services for prenatal care may help reduce the problem of out-of-hospital deliveries.

Sudden maternal deaths in Malaysia

RAVINDRAN Jegasothy

Department of Obstetrics & Gynaecology, Seremban Hospital, Malaysia

Sudden maternal deaths defined as the death of a mother within 24 hours of delivery, abortions or operative termination of the pregnancy were analysed nationally for the years 1995 and 1996 in order to determine the remediable factors in both the clinical and resource areas. There were 131 sudden maternal deaths out of the 636 maternal deaths recorded during the study period (20.6%). Postpartum haemorrhage accounted for the majority of the cases. In only 20 out of 74 deaths from PPH was there a notation that a red alert had been activated. The other main causes were obstetric embolisms, trauma and hypertensive disorders of pregnancy. There was a disproportionately increased risk of sudden maternal deaths in the Chinese and the 'other bumiputra' racial groups. The Chinese often seek treatment in the private sector and this finding could be reflective of weaknesses in that sector in handling obstetric emergencies. In the present series of 19 Chinese patients who died suddenly, 13 delivered in the private sector. Out of this, eight patients were transferred to the government sector only to succumb very shortly thereafter. However the death rates in the other East Malaysian races classified together as 'other bumiputras' was far higher than the West Malaysian races. There was no relationship to parity but 65.8% of the mothers had never used any form of contraception. The proportion of mothers excluding the primigravida who had no obstetric risk factors in the pregnancy that led to death was 16.8%. Fourteen mothers died in transit while being transferred to another facility. The majority of the mothers delivered vaginally. Twenty mothers died after a caesarian section. Of these, only three had a regional anaesthetic. The findings of this review of sudden maternal deaths emphasises the fact that caregivers in obstetrics need to be forever vigilant. There needs to be a long term view of staffing needs in the labour wards in order to ensure continuity of experienced and trained staff in these wards which need to provide intensive care to the mothers.

Bllateral hypogastric artery ligation - a 5 year experience

S VIJAYARANI and SUMITA Prabhakar

Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia

Postpartum haemorrhage is the leading cause of maternal mortality in Sabah. When medical management of the haemorrhage had failed, hysterectomy is the standard surgical procedure for life threatening haemorrhage, which removes the offending organ. The loss of the uterus may not be acceptable to young women of low parity and may lead to several social problems. Hence, an alternate uterine conserving surgery is necessary. Aim: To study the effectiveness of bilateral hypogastric artery ligation in women of low parity in controlling postpartum haemorrhage. Materials & Methods:-During the period May 1995 to May 2000, 38 women underwent bilateral hypogastric artery ligation at Queen Elizabeth Hospital by the authors. All of these women were less than Para4 in whom routine medical management of postpartum haemorrhage had failed and had required surgery. Since all of them were young women of low parity, bilateral hypogastric artery ligation was done instead of hysterectomy in order to conserve the uterus. The transperitoneal approach for ligation of the anterior division of the hypogastric arteries used. Duration of follow up of these patients ranged from 5 years to 6 months. Results: Postpartum haemorrhage was successfully controlled in 33 patients (86.8%). Only 5 patients (13.2%) required hysterectomy due to persistent haemorrhage. There was no mortality, no serious complication encountered during the procedure. No untoward sequelae of the procedure was noted on follow-up of these patients. Conclusion: Hypogastric artery ligation is effective in controlling postpartum haemorrhage in women of low parity in whom uterine conservation is desirable.

Preliminary experience with the new wonder drug for ovarian cancer

DEEPIKA Monga, SACHCHITHANANTHAM K, KUMARARAJAH AT, **HARIKRISHNA** S, and THAM SW

Department of Obstetrics and Gynaecology, Melaka Hospital, Malaysia

Cancer of the ovarian epithelium is the leading cause of death from gynaecological cancer. At the time of diagnosis, the majority of women with the disease have involvement of one or both ovaries, with peritoneal implants outside the pelvis. Chemotherapy with surgery remains the cornerstone of treatment. So far, options have been limited to platinum based compounds and alkylating agents. Newer consensus statements have emphasized the role of the "wonder drug" paclitaxel in improving outcome and survival. However use of this has been associated with neutropenia, hypersensitivity reactions and alopecia. This prospective **study** was carried out on 20 women with ovarian cancer, who received carboplatin with either cyclphosphamide or paclitaxel. The two groups were compared in terms of demographic data, type and stage of tumour, side effects and complications. There was no significant difference in demographic profile, stage of tumour and in side effects. Two women in the paclitaxel group had neutropenia after the first course, which stabilized to values between 3.4 and 5.2 x10³ subsequently. There was no case with hypersensitivity reaction, which may be due to improved tubing material supplied, or dexamethasone premedication. This preliminary study shows no major side effects with the use of paclitaxel. Further studies with larger numbers studying long term outcome are in progress.

A new cure for an old problem

SACHCHITHANANTHAM K, DEEPIKA Monga, TAN MN and YOW CM

Department of Obstetrics and Gynaecology, Melaka Hospital, Malaysia

Vaginal candidiasis is the commonest reason for women to attend gynaecology clinics, and compliance to medication remains an important factor in management. The efficacy, safety and tolerance of a single oral 150 mg dose of fluconazole was studied for the treatment of vaginal

candidiasis in non-pregnant women. Twenty-two women with candidiasis proven by microscopic examination, with no coexistent infection, were treated with a single oral dose of 150 mg fluconazole. Symptoms (dyspareunia, pruritis, discharge), signs (erythema, excoriations, oedema) and vaginal swab culture were reviewed on days 1,7 and 14. Full blood count, liver function tests and renal profile were assessed on days 1,14 and 35 as a measure of safety of the drug. Compliance to treatment was 100%. Discharge was the commonest symptom (100%) followed by pruritis (86.3%) and erythema (72%). All these were significantly reduced 14 days after treatment (54.5%, 27.2% and 13.6% respectively). Vaginal erosion, burning sensation, dyspareunia and vulvovaginal oedema were also significantly reduced by day 14 of treatment. Liver function tests and renal profile did not show any deterioration on day 14 or day 35 after treatment. Oral fluconazole in a single dose of 150 mg is safe and effective in the treatment of vaginal candidiasis, and compliance to this dose is excellent.

A rare case of SSPC - pre and intraoperative diagnostic dilemma SACHITHANANTHAM K, DEEPIKA Monga and ANANTHAN E

Department of Obstetrics and Gynaecology, Melaka Hospital, Malaysia

Serous surface papillary carcinoma (SSPC) is a rare malignant tumor originating from the surface epithelium of the ovary. Only 26 cases have been reported as obtained through extensive literature search. This tumour is characterized by macroscopically normal ovaries accompanied by diffuse peritoneal dissemination. Diagnosis of SSPC is difficult preoperatively or even intraoperatively. We report a rare case of SSPC in which an apparently well woman developed **ascites** and shortness of breath, and ultrasound and CT Scan failed to reveal a primary source of carcinoma. Detailed GIT investigation revealed no abnormality. Laparotomy revealed **ascites** and diffuse peritoneal seedlings, but no obvious primary source. TAHBSO was performed despite relatively looking normal ovaries and to our surprise histopathological examination revealed SSPC. She is currently on adjuvant chemotherapy with carboplatin and paclitaxel and is doing well. This case is being presented in view of rare incidence and difficulty in preoperative diagnosis and management.

Does epidural analgesia affect labour outcome on nulliparous women: a randomized, controlled, prospective trial

NAZRI Y, SATBER K and T P BASKARAN

Maternity Hospital Kuala Lumpur, Malaysia

Objective: The aim of this study was to determine the effect of epidural analgesia on nulliparous women in labour. Study design: A 6 month randomised controlled study from 1st January till 30th June 2000 centered in Maternity Hospital Kuala Lumpur. All normal term nulliparous women in active spontaneous labour with the fetus in cephalic presentation were randomized to receive either intramuscular opioids or epidural analgesia. Results: A total of 100 women were randomly assigned to receive epidural analgesia. Maternal age, race, gestational age and cervical dilatation at admission and at first analgesic dose did not differ between the groups. There were no significant differences in the rate of spontaneous vaginal delivery (69.5% vs 68.3%), the overall caesarean delivery rate (19.0% vs 19.4%) and operative vaginal delivery (11.5% vs 12.3 %). The epidural group had a significant prolongation in the second stage. There were no significant difference in the first stage duration and requirement for oxytocin augmentation. Conclusions: Epidural analgesia resulted in a significant prolongation of the second stage of labour but does not prolong the first stage and does not increase the rate of operative delivery or caesarean delivery.

The knowledge and attitude of women towards emergency contraception in Kuala Lumpur: questionnaire survey.

NAZRI V. KAMALJIT K AND BASKARAN T P

Department of Obstetrics and Gynaecology, Maternity Hospital Kuala Lumpur, Malaysia

Objective: To study the level'of knowledge and attitude towards emergency contraception in a group of postnatal women in Hospital Kuala Lumpur. Design: Structured questionnaire study. Setting: 200 women in postnatal ward at Maternity Hospital Kuala Lumpur were randomly selected for this study in July 2000. 220 questionnaires were distributed and 200 were completed. Results: A total of 140 women (70%) were ignorant of the existence of emergency contraception. 60 women (30%) who knew about emergency contraception but do not use it, gave risk-taking behavior as the main reason (50%). Women who were educated beyond secondary level (70% versus 30%) were more likely to have heard about emergency contraception. Younger mother (< 25 years) had heard about emergency contraception more compared to older mother. No statistically significant difference in knowledge and attitudes among the ethnic groups were found. Conclusun: There is a need to improve women knowledge on emergency contraception through education. Majority of the women who were included in the study suggest that the medications used in the emergency contraception should be non prescription items, repackaged as single-use packs and be easily available.

Persistent pulmonary hypertension of newborn successfully treated with inhaled nitric oxide J ROHANA, NY B 0 0 and SC YONG

Neonatal Intensive Care Unit, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Persistent Pulmonary Hypertension of the Newborn (PPHN) has a high mortality and morbidity rate. Intravenous magnesium sulfate has been used locally to treat PPHN with variable success. We report a term baby girl who developed PPHN secondary to Meconium Aspiration Syndrome (MAS). She was commenced on inhaled nitric oxide following failure of magnesium sulfate therapy. The PPHN reverted 1 hour after starting treatment. She received inhaled nitric oxide for 7 days. There was no adverse effect related to the therapy. She was discharged home well on the 14th day of life. The patient's progress, treatment protocol, monitoring of treatment and adverse effects will be discussed.

Lifestyles of children with special needs 3: facilities for children with special needs in Malaysia WAN ASMA WI, HASHAMI B, NORIZAN AM, AB RAHIM WA, RASHIDAH AW AND MUSTAPHA E

Department of Paediatrics, School of Medical Sciences, Universiti Sains Malaysia. Kelantan, Malaysia

The purpose of the study is to study the available facilities for CSN in Malaysia. This is a **cross**-sectional multi-centre study of existing facilities conducted between May 1999 and March 2000 in Malaysia using a structured format asking various aspects of the facility. Five hundred and eighty eight facilities under study and 425 (72.3%) responded. Of the 588 facilities, 194 (33%) were CBR, 62 (10.5%) were CLBR and 332 (54.8%) were integrated and special schools. Of the 425 responded, 108 (25.4%) from CBR, 56(13.2%) from CLBR and 261 (61.4%) from integrated and special school. A total of 9080 CSN were **attending** 425 available facilities. There were 2362 children attending the CBR, 1101 were attending CLBR and 5617 attending integrated and special schools. There are four categories of CSN which include children with Down syndrome (DS), Mental retardation (MR), Cerebral palsy CP and others. Of the 9080 CSN attending the responded facilities; there were 1740 (19.2%) children with Down syndrome, 903 (9.9%) children with cerebral palsy, 2975 (32.8%) children with mental retardation and 3462 (38.1%) children with other problems There were 5383 (59.3%) boys and 3695 (40.7%) girls. In conclusion, we have identified a total of 588 available existing facilities throughout Malaysia with 72.3% response rate. Highest respondent from the CLBR (90.3%) followed by school (78.6%). Among the 42.5 respondents attended by 9080 children.

Majority of Down syndrome attending the CBR and CLBR as compared to more children will mental retardation attending schools. These findings provide those who concern regarding the types and number of available existing facilities including the CSN using these facilities.

Aminoacidopathies in Hospital Universiti Sains Malaysia

ROWANI MR 1,2,3, SARUDDIN A2 AND MARINI I3

'Department of Paediatric and ²Metabolic Laboratory, School of Medical Sciences, Universiti Sains Malaysia and ³Clinical Genetic and Metabolic Service, Hospital Universiti Sains Malaysia

The review was conducted to evaluate factors determining the outcome of cases of aminoacidopathies seen at Hospital Universiti Sains Malaysia from August 1997 through July 2000. Seven (7) infants was included in the study. Factors affecting prognosis was reviewed. They include severity at presentation, age of diagnosis, age of starting treatment, availability of treatment and mortality. Diagnosis among the seven cases include arginase deficiency (2 case), citrullinemia (2 cases), methylmalonic acidaemia (1 case), maple syrup urine disease (1 case) and phenylketonuria (1 case). All cases were Malay. There were 6 male and one female. 4 cases presented with encephalopathy. 3 were investigated because of family history of specific IEM. The mean age of diagnosis was 132 day. The delayed diagnosis was due to inavailable diagnostic facilities for IEM at the time of admission. Diagnosis is based on aminoacid analysis, organic acid analysis and enzymic assay. Due to the cost of treatment, only one cases received complete treatment while the rest received partial treatment. In all cases except one, appropriate treatment was delayed due to difficulties in obtaining the relevant drugs and special diet. 4 cases died. Of the three who survived, one was on full treatment, The rest received partial treatment. Management of aminoacidopathies needs to be improved by (1) establishing services for diagnosis and monitoring of patient (2) ensuring drugs and special diet are easily accessible. The timing of diagnosis and treatment is an important prognostic factor.

Neonatal Lupus Syndrome

FAUZI AR and NCT KONG

Department of Medicine, UKM Hospital, Malaysia

We present here a case of neonatal lupus erythematosus presenting with complete congenital heart block (CCHB). The mother was totally asymptomatic and had positive anti-Ro and anti-La autoantibodies (anti SSA and anti SSB antibodies respectively). On examination she did have a photosensitive rash over the face and neck. She was diagnosed as **Subacute** Cutaneous **I,upus** Erythematosus. The child is now 2 years old and on regular paediatric review with no necessity for a pacemaker at the present time. Congenital complete heart block (CCHB) in infants born to mothers with SLE is associated with the presence of the anti-Ro and anti-La antibodies. However, the mothers of these affected infants usually suffer either a mild disease or are asymptomatic except for the presence of the anti-Ro anti-La antibodies. Over the years other presentations of neonatal lupus have also been noted in these infants viz, liver, skin and bone marrow involvement. It is postulated to be due to placental transfer of maternal **IgG** autoantibodies which react with the specific organs. Most organ involvement are reversible except for CCHB which is due to irreversible fibrosis of the conducting tissue of the kart.

Molecular analysis of Salmonellosis due to drug-resistant Salmonella bovismorbificans

Kwai-Lin THONG¹, CC M BOEY² and SD PUTHUCHEARY³

'Institute. of Biological Science, Faculty of Science, 'Departments' of Medical Microbiology and 'Paediatrics, Faculty of Medicine. University of Malaya, Kuala Lumpur, Malaysia

Aim: To investigate a case of recurrent salmonellosis in a 3 month-old child due *Salmonella bovismorbificans* and *Salmonella matopeni* by using pulsed-field gel electrophoresis (PFGE) and antibiotic susceptibility analysis. **Method:** Molecular typing was done by **analyzing** DNA band patterns of isolates of *S. bovismorbificans* and *S. matopeni* after digestion of chromosomal DNA with infrequently-cutting restriction endonulceases **xbaI**, **AvrII**, **SpeI** and **XhoI** and separation of DNA fragments using PFGE. The isolates were tested for susceptibility to antibiotics by standard disk diffusion procedures for measuring resistance. **Results:** PFGE clearly distinguished the two serovars and that the recurrent infection was shown to be associated with variant forms of **Salmonella bovismorbificans** The chromosomal changes detected among sequential isolates of **S.bovismorbificans** appeared to be associated with the varying antibiogram patterns.

Application of molecular typing methods for Salmonella species.

Kwai-Lin THONG

Institute of Biological Science, Science Faculty, University of Malaya, Malaysia

Typhoid fever and other salmonellosis remain an important public health problem in developing countries. Reports of the emergence of multidrug resistant <code>Salmonella</code> spp in the Indian subcontinent and other Asian countries is a cause for concern. Hence there is a renewed interest to better understand the epidemiology of <code>Salmonella</code> spp and the characterization of strains in different epidemiological settings depend largely on the utility highly precise typing tools. The objective of the paper is to discuss the application of a variety of molecular-based techniques to assess its usefulness in subtyping <code>Salmonella</code> spp , in particular, <code>S. typhi</code>. The strengths and weaknesses of genomic fingerprinting will be discussed. The different discriminatory levels observed in each of the typing technique indicates that there is "no gold standard typing method for epidemiological studies of <code>S. typhi</code>.

The molecular basis for the Hepatitis B virus e-minus phenotype in local isolates YAP SF, WONG PW and CHEN YC

Department of Pathology, University of Malaya, Malaysia

The hepatitis B virus (HBV) e-minus phenotype is frequently reported in chronic HBV carriers. This phenotype is generally the result of a point mutation (1896 $T\rightarrow A$) in the pre-core region of the virus, which result, in the failure of production of the HBe antigen (HBeAg). The basis for this is the introduction of a stop signal at codon 28 of the pre-core sequence. Results of our previous study have shown that two thirds of our HBeAg negative patients carry the mutant virus. In other words, only 2/3 of the e-minus phenotype is due to the pre-core mutation; in 1/3 of the cases with the e-minus phenotype, no pre-core mutation is detectable. In order to determine the basis of the HBe minus phenotype in this group, we sequenced the pre-core region, inclusive of the promoter sequence, of 8 virus isolates. In 5 of these 8 specimens, we identified a paired mutation (1862A→T and 1864G→A) at the second AT rich region of the core promoter sequence. This region controls the transcription of pre-C mRNA; the paired mutations at this location have been reported to decrease transcription and therefore HBe synthesis. However, viral replication is unaffected. This double mutation is therefore the basis for the interference of **HBe** production in 5 of our cases. It is interesting to note that in 4 out of the 5 cases, the virus is a wild type variant. In another case, a point mutation (1815T \rightarrow C) was found at the pre-core start codon (ATG \rightarrow ACG) resulting in failure of HBe production. However, we did not find any mutations in the precore/promoter to explain the e-minus phenotype in the remaining 2 cases (25%).

Hepatitis B genotypic variation in local isolates and its association with the Hepatitis B virus pre-core mutation

YAP SF, WONG PW, CHEN YC, *ROSMAWATI M and **WONG NW

Departments of Pathology & *Medicine, University of Malaya, and **Loh Guan Lye Specialists Centre, Penang, Malaysia

The objective of this study was to determine the hepatitis B virus (HBV) genotype in local isolates, and to relate the genotype to the pre-core mutant status. HBV with 1858T (CCT at codon 15) is classified as the wild type (WT) virus and HBV with 1858C (codon 15: CCC) is considered the WT variant. The pre-core mutant is due to an 1896G \rightarrow A point mutation, which results in the introduction of a stop signal at codon 28 of the precore gene, and thus failure of HBe production. Further, this region includes an encapsidation sequence (E) that is necessary for reverse transcription of the virus genome and for virus encapsidation. E is comprised of a number of inverted repeats that form a stem loop by base pairing which include the 1896-1858 G-T pair (WT) or G-C pair (WT variant). It follows that WT virus is likely to acquire the 1896G \rightarrow A point mutation, which results in stabilisation of the stem loop. In this study, 31 clinical specimens from known chronic HBV carriers who were previously screened for the pre-core mutant (MT) by specific hybridisation were analysed. The gene sequence of the isolates was determined by cycle sequencing. Overall, 15 out of 21 isolates (71.4%) determined as non-mutant by hybridization analysis were WT virus (codon 15 CCT). The dominance of the WT virus is consistent with the frequent occurrence of the pre-core MT in our chronic hepatitis patients -39.4% in HBe positive and 66.7% in HBe negative cases (unpublished data). Further all isolates of the mutant HBV were found to carry T at nt1858. Conversely, none of the WT variant virus (codon 15 CCC) were found to have the $1896G \rightarrow A$ point mutation.

Tubercular lymphadenitis: changing spectrum of disease S AHIAWAT, K RAMACHANDRAM, *RAVINDER S Ahlawat and *M FAUZI

Departments of Pathology and *Medicine, Hospital Tengku Ampuan Afzan, Kuantan, Malaysia

Tuberculosis (TB) is the main infectious killer of this decade, superimposed on HIV-AIDS pandemic. Not only has TB re-bounded, its clinical pattern and morphological pattern is considerably different. Lymph nodal TB is the commonest mode of extra-pulmonary TB presentation. A definitive and accurate diagnosis of TB lymph node (TBLN) is important because effective drug therapy is freely available. FNAC is the first line of investigation for an enlarged LN at HTAA. We find FNAC useful as it is quick and obviates the need for surgical excision. Its utility is further improved when combined with staining for AFB and culture for mycobacterium on FNAC material. This study was planned to assess the usefulness of FNAC for diagnosis of TBLN, to review the morphological and clinical spectrum of disease and its response to treatment. 56 cases of TBLN were diagnosed between January 1999 to June 2000. Only those cases which were clinically and therapeutically proven to be TB were included. These include HIV positive and HIV negative cases. Morphological spectrum, clinical presentation, response to treatment and clinical outcome were compared in both groups.

Periodontal treatment needs in diabetics – a Malaysian perspective ED SAMUEL

Periodontic Specialist Clinic, Ministry of Health, Seremban, Malaysia

Periodontal disease is an important oral complication in diabetic patients. If untreated, it can lead to progressive tooth loss and a reduced quality of life in these individuals. Recent studies showed that carefully managed periodontal therapy can improve the metabolic control of diabetes as well. The aim of this study was to examine the treatment needs of a sample of Malaysian diabetics and determine the need for a preventive screening programme for early detection, counseling and referral. 95 dentulous diabetics referred from the Diabetic Clinic, Medical Outpatient Department, Hospital

Seremban were interviewed, examined and their periodontal treatment needs assessed using the Community Periodontal Index of Treatment Needs (CPITN) by one periodontist. 96.8% of the random sample were Type 2 diabetics (NIIDM), 53.7% were female, 43.2% were of Indian ethnic origin and 66.8% were aged between 45 to 64 years. Only 10.5% were on regular dental follow-up. Treatment needs based on the CPITN ranged from TNO (0.0%), TN1 (0.0%), TN2 (4.2%), TN3 (27.4%) to TN4 (68.4%). All patients hence required oral hygiene instructions and scaling, while 68.4% also required specialist attention due to advanced disease. These findings highlight the dire need for a preventive periodontal screening programme for early detection and referral in this group of high risk patients.

Elderly presentations to a GP clinic

CHAN Sook Ching and TEOH Long Chee

Department of Primary Care and Public Health, Perak College of Medicine, and Klinik Teoh, Batu Gajah, Perak, Malaysia

The pattern of presentation of the elderly to the health care provider in the community provides essential information to determine the needs and management of the elderly. This study looked at the morbidity patterns of elderly patients presenting to a general practitioner's (GP) clinic. A questionnaire was filled by the attending physician on all elderly patients aged 60 and above presenting to the GP clinic over a 3 month period between 1st January to 31st March 2000. Of 612 elderly patients in the study period there were 42.6% males and 57.4% females; 61.7% were in the 60-69 age group with 12.4% over 80 years of age. Majority were Chinese (88.7%) and most (91.7%) were old patients registered with the clinic. The top 10 most common presentations included upper respiratory tract infections (21.6%), hypertension and diabetes mellitus (18%), gastritis/dyspepsia (5.1%), backache (4.6%), gout (2.6%), anxiety (2.5%), acute gastroenteritis (2.3%), osteoarthritis of the knees (2.3%), and dizziness (2.1%): Injuries as a group was among the top 5 presenting complaint. These were mainly soft tissue injuries and sprains.

Homocysteine concentrations in medical students in University Putra Malaysia

A MOHAN and G DURAISAMY

Faculty of Medicine and Health Sciences, University Putra Malaysia

Total homocysteine (tHcy) levels in young Malaysians were determined to study the distribution in the different sexes, ethnic groups and age. Hyperhomocysteinearniahas been gaining prominence as a strong, graded independent risk factor for atherosclerotic (cardiovascular) diseases. It has also been implicated in the etiology of neural tube defect. Hyperhomocysteineamia has usually been defined as the tHcy value above 15µmol/L. Sera from 90 (39 males; 51 females) medical students collected for routine health screening was assayed for tHcy using the Axis Homocysteine Enzyme Imrnuno Assay (EIA) kit (Axis-Shield Diagnostics, UK). The age of study subjects ranged from 19 to 32 years. The calibration curve was estimated using a logistic curve fit. The tHcy values were adjusted for the twenty-four hour delay in separation of the sera, as the constant leak of homocysteine from the red blood cells cause an increase in the tHcy values. Data was analyzed using SPSS version 7.5. The mean tHcy was 11.35µmol/L (Range 2.14 to 23.56 µmol/L). Males had a higher mean than females (12.43 \texttt{\texttt{\texttt{mmol/L}}} vs.10.52 \texttt{\texttt{\texttt{\texttt{\texttt{\text{ferrence}}}} among mean values for Malays (11.14 μmol/L), Chinese (11.90 μmol/L), Indians(11.66 μmol/L), and others(10.92 μmol/L). There was a rising trend with age with a mean of 10.64 µmol/L for subjects aged 19 to 12.45 µmol/ L for subjects aged 20, but the differences were not statistically significant. The mean tHcy (11.35 μmol/L) was found to be higher than that of a previous Malaysian study (10.4 μmol/L). The cut off point for hyperhomocysteineamia may be higher than 15 μmol/L if the method of arbitrarily setting the tHcy value of the 95th percentile was employed. This study is a pilot study prior to future research on a larger scale to look at age, race and gender-specific intervals for total homocysteine levels.

Intersectoral colaboration in health programmes: Perak state experience

Elangovan SUBBIAH

Perak State Health Department, Ipoh, Malaysia

The purpose is to share with participants the Perak experience in successfully organising various intersectoral collaboration health programmes. Full committment from the administrators is the most important factor in ensuring success in these programmes. A liasion person is essential to co-ordinate all the activities. A cordial working relationship between the organisers and the mass media is essential. Among the agencies were the Diabetic Association, The Rotary Clubs, Sathya Sai Organisations, Palliative Care Society, Malaysian Red Crescent Society, St. John Ambulance, St. Vincent De Paul Society, private hospitals, government agencies and others. Health awareness programmes, community participation and smart partnerships were the essence of these campaigns. All the programmes achieved tremendous response. There was a great deal of awareness created as a result of good publicity from the mass media. Donations in many forms were received. The number of pledges from organ donors was very encouraging and the palliative care unit was visited by many volunteers and donors. Health promotion and community participation which are components of the Vision of the Ministry of Health, Malaysia can be achieved if these programmes are planned properly and carried out by a team of committed people.

Nutritional status among aborigines in Hulu Selangor district

NOOR HAYAATI AR, ZALEHA MI and OSMAN A

Department of Community Health, Medical Faculty, University Kebangsaan Malaysia

The main purpose of the study was to determine the problem of iodine deficiency disorders (IDD) among the aborigines living in the district of Hulu Selangor. In this study their nutritional status was measured in 4 villages, namely Kuala Kerling, Gerachi, Pertak and Bukit Manchong. All villagers between 4 to 65 years old were taken as subjects which is the mean of age was 19.0 ± 315.0 . It was found that for Bukit Manchong 57.3% (751131) malnutrition, 23.7% (311131) normal and 19.21% (25/131) overweight: for Gerachi, 43.8% (28/64) malnutrition, 32.8% (21164) normal and 23.4% (15/ 64) overweight: for Kuala Kerling. 29.7% (11/37) malnutrition, 48.6% (18137) normal and 21.6% (8/ 37) overweight: for Pertak: 19.7% (12161) malnutrition, 42.6% (26161) normal and 37.7% (23161) overweight. The most frequently eaten freshwater fish among the 4 villages was 'ikan putih'. Sea fish and seafood was not commonly consumed by the 4 communities. All the subject studied took sweetened condensed milk and eggs as their main source of dairy product. In the meat.group, chicken was the most popular source of food. Rice and tapioca were the most frequently eaten food under the cereal group in Kerling, Pertak and Gerachi while Bukit Manchong took rice and flour as their main source of cereal. Since banana and papaya were self grown by the communities, they were the most available fruits in the 4 villages. Cassava was the most popular vegetables taken by the subject in all studied areas. Ground and green nuts were highly consumed by all subjects. Although the dietary pattern of the Orang Asli in the urban fringe area is somewhat similar the urban community, they still took considerable amount of goitrogenic food such as tapioca and cassava. This might be one of the .contributing factor of **goiter** existence in these areas.

Globalization: the effect on health of the urban community

ZALEHA MI, MOHD. RIZAM AR and OSMAN A

Department of Community Health, Medical Faculty, University Kebangsaan Malaysia

This cross-sectional study was aimed to determine the perception of the urban community towards **globalisation** in health sector and its effect on their life. A total of 627 respondents from 6 conveniently-selected locations were interviewed using guided questionnaires. Kuala Lumpur and

Johor Baharu represented the city area, Kota Baharu and Langkawi represented the municipal council area, and Bentong and Kuala Selangor represented the district council area. Only 13.1% respondents really understood the meaning of globalisation, however, more than 50.0% were aware of the economic development and world health. A total of 90.7% respondents claimed to have heard of corporatization in health sector, but only 38.3% agreed the benefits of corporatization and only 23.0% agreed for the health sector to be corporatized now. Majority of the community (75.9%) felt that corporatization will increase service charges and only 1.4% felt that it is profitable to the workers. If health services had to be corporatized, 35.9% respondents suggested that the installment payment scheme should be introduced. Only 8% respondents suggested the use of health insurance scheme. The understanding of telemedicine and MSC existence were still low among the respondents, only 29.1% have heard of it, in which only 65.7% of them really understood the matter. In term of respondents' preparation towards IT era, only 23.6% owned personal computer and 19.9% used it regularly. A total of 75.9% respondents have never used internet and among the users, less than 50.0% used it at least twice a week. The use of internet as a media to gain health information and e-commerce were still too low (only 0.3%). Majority of the respondents (71.8%) did not agree to use interest as treatment guidelines. In this globalization era, 48.3% respondents felt that alternative medicine need to be urged, however the extensive incoming of alternative medicine should be strictly restricted. Therefore, in succeeding the country's vision, great effort from multiple bodies are needed to upgrade the knowledge and practice of the urban community on globalization.

Incidence and management of congenital anorectal malformations in Sabah-an eight year review

RAJAH S, BASKARAN TP, CHIAN TP and THAY KT

Division of Paediatric Surgery, Queen Elizabeth Hospital Kota Kinabalu, Sabah, Malaysia

The incidence of Congenital Ano Rectal Malformations (CARM) is high in Sabah. A significant number of parents prefer to avoid colostomy due to fear of difficulties in taking care of a baby with colostomy and several socioeconomic problems. *Aim*: To analyse the incidence of CARM in various ethnic groups, the type of lesions, the feasibility of avoiding colostomy and the results.

Material and Methods: 237 babies with CARM were referred to our unit between January 1992 to December 1999. 187 babies who underwent surgery and were followed up for a minimum period of 6 months were included for study. The clinical findings and results of investigations, parental preference, operative findings and the outcome were analysed. Results: 45% out of 112 male babies and 70% of the 75 female babies were found to have low type of anomaly. Anoplasty was performed for 58 patients, 34 patients underwent Anal Transposition and simple outback for 2 babies. The site, size and functional results of the anorectum and the rate of complications were comparable to that of staged reconstructions. Conclusion: Colostomy can be avoided in 50% babies with Congenital Anorectal Malformations. High incidence CARM in Sabah is partly due to more number of foreigners seeking treatment. It is cost effective and ideal to refer all babies with CARM to the Specialist Paediatric Surgery Centre before colostomy.

A national survey of adult inguinal hernia surgery JABAR MF, SHAKER ARH, MOISSINAC K and GUL YA

Deportment of General Surgery, University Putra Malaysia, Malaysia

Introduction: The ideal repair for inguinal hernias should be cost effective, relatively pain-free with few complications and a low recurrence rate. The aim of this study was to determine methods of inguinal hernia repair in Malaysia in view of the recent technical and surgical advances. Methods: A questionnaire based national survey involving 132 general surgeons of specialist grade and above. Type of inguinal hernia repair employed was determined especially in relation to the use of mesh and laparoscopic surgery. Results: Ninety responses were obtained (68%). Open mesh repair was employed by 29% of surgeons. Cost of mesh (39%), unfamiliarity with the technique (18%) and

perceived low rates of recurrence with conventional methods (15%) were the main factors that prevented adoption of this method. Day case and in-patient surgery; was solely employed by 3% and 59% of surgeons respectively. Repairs under local or regional anaesthesia were adopted by 62% of surgeons. Some 21% of surgeons audited their hernia repairs. Surgeons from academic institutions (86%) and those with specialist experience of less than 10 years (67%) were more likely to utilise the open mesh repair. Laparoscopic hernia repair was employed by only 4% of surgeons. *Conclusions:* Open mesh hernia repair is a relatively popular technique in Malaysia though the overall uptake is evidently low in comparison to Western series. The major factors hindering this form of repair include cost related factors and unfamiliarity with the technique. Laparoscopic hernia repair has yet to make an impact based on the current survey.

The predictive indicators for surgery in patients with acute non-variceal upper gastrointestinal haemorrhage

K RAVINDRAN, NC LIEW, K MOISSINAC and Y GUL

Department of Surgery, Faculty of Medicine and Health Sciences, University Putra Malaysia, Malaysia

Objective: To determine the predictive indicators for surgery, in patients with acute non-variceal upper gastrointestinal haemorrhage (NVUGIH). Method: A retrospective cross sectional study was made in patients admitted to the General Hospital Kuala Lumpur in 1998 with evidence of NVUGIH on oesophagogastroduodenoscopy (OGDS). A standardized proforma was used to collect patient information on demographic data, clinical presentation, haemodynamic parameters, clinical and endoscopic findings, treatment modality and outcome. All NVUGIH cases that were stomach or duodenal related were included. All neoplastic and oesophageal related cases were excluded. Data analysis was done using the Statistical Package for Social Sciences (SPSS version 9.0). Binary logistic regression analysis was done using the SPSS software. Result: 121 patients were studied, of which 10 underwent surgery (8.3%). The number of patients who had peptic ulcer (PU), gastritis/ erosions (G) and both (PU+G) were 55(45.5%), 39(32.2%) and 27(22.3%) respectively. For those who underwent surgery, 6 (60%) had PU while the remaining 4 (40%) had both PU+G. No patients that required surgery had gastritis/erosions alone. Independent predictors of surgery were transfusion requirement of greater than 4 units of blood (df=1, p<0.01), presence of stigmata of recent haemorrhage (df=1, p<0.01), age of above 70 years (df=1, p<0.01) and clinical evidence of continuous bleed (df=1, p<0.01). Of the three factors, continuing bleed was the best predictor for the need for surgery ($r^2=0.35$), followed by presence of stigmata of recent haemorrhage ($r^2=0.23$). Conclusion: Transfusion requirement of greater than 4 units, presence of stigmata of recent haemorrhage, age above 70 years and evidence of continuing bleed can predict the need for surgery in acute NVUGIH patients. These predictive factors provide a guideline and can help in the planning of surgical intervention in NVUGIH patients.

Role of surgery in the management of thoracic infections

Simon VENDARGON and WONG Poo Sing

Cardiothoracic Surgery Unit, Sultanah Aminah Hospital, Johor Bahru, Malaysia

Objective: 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. We studied the role of surgery in this group of patients at Sultanah Aminah Hospital, which is the regional centre for thoracic surgery for Southern Peninsula Malaysia and East Malaysia. *Methods:* A retrospective review of records of 247 patients who underwent thoracic surgery since the unit's inception in November 1996 to March 2000 was conducted. *Results:* Sixty-three (25%) patients underwent surgery for thoracic infection, of whom 38 (60%) were male and 25 (40%) were female. The mean age is 33.1±20.1(40 days to 69 years). Fourteen patients were less than 12 years old and 3 patients in this group were less than 1 year old. Twenty-six patients (41%) underwent decortication

for empyema thoracis (3 tuberculosis, 12 bacterial and 11 had no organisms demonstrated). **Twenty**-nine patients (46%) underwent lung resection for bronchiectasis, aspergilloma, cryptococcus neoformans and various solitary nodules of infective origin. Four patients (6%) had video-assisted thoracoscopic surgery for pleural biopsy (all tuberculosis). Four patients with mediastinal lymphadenopathy had cervical mediastinoscopy and biopsy of mediastinal lymph nodes (all tuberculosis). Two patients had rib resection (one for chronic tuberculous empyema and another had post-pneumonectomy empyema), 1 patient underwent thoracoplasty (chronic bacterial empyema) and 1 patient had thoracotomy to close a bronchopleural fistula as a result of massive air leak secondary to massive lung abscess. There were three perioperative deaths, of which 2 were unrelated to the primary procedure. *Conclusion:* Criteria for refemng patients with thoracic infections for surgery differ depending on whether a centre performing thoracic surgery is available or not. These patients should be referred early to reduce the prolonged course of their disease. Although the spectrum of thoracic disease in our hospital has a varied aetiology, thoracic infections form a significant part of **our** thoracic work.

Audit on emergency vascular admissions to the vascular surgical unit, Hospital Kuala Lumpur.

K NORMAYAH, H HANIF and AA ZAINAL

Vascular Surgical Unit, Department of Surgery, Hospital Kuala Lumpur, Malaysia

Background: It has been generally accepted that the quality of service declines as the quantity increases. We feel that the number of emergency vascular admissions are high and some of these patients may not require emergency or out-of-hours admissions but instead be admitted as elective cases after investigations. More referrals to the Vascular Clinic would reduce inappropriate emergency admissions. *Methods:* A prospective study involving all patients who were admitted as an emergency vascular case to the Vascular Surgical Unit, HKL from 1st September 1999 to 31st December 1999. The cases were assessed by the consultant in charge and the head of unit with regards to the appropriateness of emergency admission. Results: Vascular cases constitute 21.0% (176 cases) of total admission and 62.5% (110 cases) of these patients were admitted as emergency cases. There were 26 cases (24.0%) that were classified as inappropriate. On further analysis, 13 of these cases (50%) did not have a vascular condition. Reasons for these inappropriate admissions were no prior consultation, imaging studies not available at refemng hospital, incorrect clinical evaluation given or they came from outstation. Conclusion: The workload of the unit's staff can be reduced if a significant number of inappropriate admissions are prevented, by increasing the awareness of the general or non-vascular surgeons with regards to vascular disease. Consultation via telephone prior to referral can also reduce inappropriate admissions.

A review of consecutive abdominal aortic aneurysm managed surgically in the Vascular Unit Hospital Kuala Lumpur

YM MAZRI, H HANIF and AA ZAINAL

Vascular Unit, Department of Surgery, Hospital Kuala Lumpur, Malaysia

Background: With an increasing elderly population in our country, the incidence of abdominal aortic aneurysm (AAA) is increasing. Ruptured abdominal aortic aneurysm (AAA) is a disease with a grave outcome. A mortality of more than 50% has been reported even in the best centres. The aim of this study is to determine local demographic data of AAA and its postoperative immediate outcome of cases surgically treated in Vascular Unit, Hospital Kuala Lumpur. **Patients and Methods:** This is a retrospective study of AAA managed surgically in Vascular Unit HKL from 1993 to 2000. The data were obtained from a vascular data registry and operation theatre book. These data then were entered into an Excel spreadsheet. Their demographic distribution, comorbid conditions, size of the AAA and postoperative immediate outcome were evaluated. **Results:** Two hundred and thirtynine consecutive patients were included in the study. There was a male preponderance with 204 patients (85.4%) **145** patients (60.7%) underwent elective AAA repair and **94(39.3%)** as emergency.

Median age of presentation for elective cases was 67 years and for emergency cases was 69 years. From 145 elective patients, 111 (76.6%) were male and 34(23.5%) female, and from 94 emergency cases, 85(90.4%) male and 9(9.6%) female. Overall male:female ratio was 8.6:1. Majority of our patients were Malay (65.3%) with Chinese and Indian contributing 25.1% and 38% respectively. However, complete records were only available in 226 cases and this was used for further evaluation. Hypertension was observed in 98 patients, DM in 6 and IHD in 50 patients. Median size of AAA in elective cases was 6cm and for emergency was 7cm. Mortality for elective cases was 8.0% and for emergency was 46.6%. From 88 emergency cases, 47 presented with hypotension and pallor, and mortality in this group was 26(55.3%). Conclusion: AAA is not an uncommon disease in this country. Elective AAA repairs can be done with acceptable mortality. In emergency cases a higher mortality is observed. Hypotension and pallor on presentation will indicate an even poorer prognosis.

Survival is not the sole criteria of appropriateness of surgical treatment in differentiated thyroid cancer

A SAROJAH and AN HISHAM

Breast and Endocrine Surgical Unit, Department of Surgery, Hospital Kuala Lumpur, Malaysia

Background: Controversy continues regarding the optimal extent of primary surgery in most patients with differentiated thyroid cancer (DTC), mainly in those who are at minimal risk with good prognostic criteria. Patients and Methods: 3 patients diagnosed with DTC more than a decade ago and had defaulted treatment were seen in our clinic over the last 2 years. Results: There were two females and one male patient with a mean survival of 18 years (range 12 to 25 years). Two patients with papillary thyroid cancer did not have any surgical intervention. The other patient diagnosed with follicular thyroid cancer had 2 previous operations, the nature of which is not unknown. She had radiotherapy and chemotherapy. These three extraordinary cases have not been reported for their long-term survival. Their decision to default initial treatment revealed that survival is not the sole criteria to determine the extent of primary thyroid surgery. As such total thyroidectomy should be considered in view of loco-regional control, pressure symptoms, adjuvant treatment, monitoring of recurrence during follow up and for cosmetic reasons. Conclusions: Observations from our preliminary study showed that survival is not the sole criteria to determine the extent of thyroid surgery in DTC. Long-term survival can still be achieved even without surgery. Hence total thyroidectomy should be considered in the management of DTC for reasons other than survival.

Newly diagnosed cases of breast carcinoma in HUKM - is age an important factor? MS HASLIZA, A NORLIA, MJ SHUKRI, T SHALIZAN, AY JASMI, FA MEAH, NA SHARIFAH*, MA SITI AISHAH' and MA ZULFIQAR"

Departments of Surgery, Pathology* & Radiology**, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

156 cases of newly diagnosed carcinoma of the breast seen in the Department of Surgery, Hospital Universiti Kebangsaan Malaysia from July 1997 till June 2000 were reviewed. These women were divided into 2 large groups according to their age at the time of diagnosis. Group A (n=130) were above 40 years old and Group B (n=26) were 40 years old and below. The factors that were studied were age at diagnosis, age at menarche and menopause, age at first pregnancy, use of oral contraceptive and fertility pills, duration of breast feeding, family history of malignancy, and type, grading, receptor status and staging of the tumours. It was noted from this review that the majority of patients in the younger age group had a high tumour grade (more than 50 %) and the reverse was true for the older age group. There was no significant difference between the two groups for the other variables.

Malignant gastric stromal tumours: a clinico-pathological review of 14 cases AY SHAHROL, AY JASMI and *S SWAMINATHAN

Departments of Surgery and *Pathology, Faculty of Medicine, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Background: Gastro-intestinal stromal tumours are a group of intramural tumours formerly known as leiomyoma and leiomyosarcoma. Gastric leiomyosarcoma or malignant gastric stromal tumour is an uncommon disease, and the optimal treatment has not been established. Aim: To review the clinical and pathological aspect of gastric stromal tumour managed by the Department of Surgery, Universiti Kebangsaan Malaysia. Materials & Methods: A retrospective and prospective study was conducted to present the experience of managing 14 patients with gastric stromal tumour during a 10-year-period between 1990 and 1999 at the Universiti Kebangsaan Malaysia. Data from clinical records and histology reports were analysed. **Results:** The most common symptoms were abdominal pain (71%), anorexia (57%), weight toss (57%) and maelena (28%). The tumour was located commonly in the body (84%) and fundus (36%) of the stomach. The tumours were diagnosed by endoscopy, ultrasound, computed tomography and contrast examination. Definite histological diagnosis was made preoperatively in 11 of 14 patients. All patients underwent resections except one patient with severe ischaernic heart disease. Operation ranged from wedge resections to partial and total gastrectomy. Two of the cases already had liver metastases. Resection was potentially curative in 12 cases, with one having a recurrence. On evaluating the histology, there seemed to be no significant correlation between the size of tumour and the number of mitoses with the clinical behaviour of gastric stromal tumour. Conclusions: Gastric stromal tumours are still uncommon and their clinical behaviour unpredictable. Since they do not response to other modes of therapy, it is recommended that complete excision should be attempted whenever possible.

A study on the effect of breast cancer and sexuality among Kuala Lumpur (Malaysia) breast cancer survivors

TAN Tang Peng

Monash University, Sunway Campus, Petaling Jaya, Selangor, Malaysia

While some shy 'fortunates' hunch to hide what plentiful they have, some thrust forth their chests in vain, to lift what little they have. The effects of breast cancer on sexuality is a double taboo in many cultures for the victims as well as some health professionals. A study on 30 Malaysian breast cancer survivors and 10 husbands was conducted to study the effects of the mutilating surgery on sexuality including body image. Findings show that body image and sex life related to breast cancer and its associated treatments were not a top priority during counselling sessions by professional as well as voluntary breast cancer survivors. 88% women and 100% husbands were more womed about the danger posed by cancer rather than the removal of breast(s) which were rated 42% and 50% respectively. 63% husbands were also worried about losing their wives to cancer than their women losing their breast(s)! This study shows great implications on the need for trained breast cancer nurses or general nurses not to evade the issue on sexuality during counselling sessions, although this is not expressed by the breast cancer survivors during the initial counselling period, when fear of the disease itself overpowers everything else. This study done for the first time here enlightens them about their feelings in comparison with the other survivors on such sensitive issues, as sexuality, sex life, body image, etc.

A study of an excellent organisation

ABDUL RAHIM Abdullah, ZAILAN Adnan, ROSLAN JOHARI Mohd Ghazali, RUHANA Mahmod, JAYALETCHUMY Thuraisingham and ABDUL HALIM Ahmad

Institute of Health Management, Hospital Tengku Ampuan Afzan, Kuantan, Pahang, Malaysia

This study was started in November 1998 after a preliminary visit earlier. The decision to study HTAA was the aftermath of HTAA winning the ultimate Prime Minister's Quality Award (Public Sector) and also to meet the request of top management to ensure management best practices are continually **disseminated** and where possible emulated. The study revealed HTAA success factors in key process areas based on the generic TQM concept, namely: i. Leadership, ii. Strategic planning, iii. Teamwork, iv. Patient Satisfaction, v. Quality Assurance, vi. Innovation, vii. Performance evaluation. The study was done through relevant document reviews, self administered questionnaire survey of patients and staff, focus group discussion of heads of departments and units, and interviewing the hospital director. HTAA did very well in all the key process areas above - patient satisfaction (6.4 from maximum score of 7) and strategic planning (6.2) scored highest and performance evaluation (5.9) scored the least. A survey of the wards showed both patients and staff agreed on the wards being noisy and the rest room facilities were somewhat not to expectations. Nevertheless, the past and current studies of organizations that have achieved similar awards for excellence have also mainly looked at inputs and processes. Hospitals must deliver services in the form of positive outcomes and generation of satisfaction. Achievement of accreditation this year (2000) is certainly a step towards this direction. Excellent organizations certainly must have all these. Besides having strategies, structure and systems in place, clear purpose, quality processes and committed and motivated staff are necessary ingredients for success. In summary, it is proposed that a more comprehensive organizational assessment will require outcome evaluation to be done. In particular, the impact of hospitals in key result areas of a health care system of the population served and whether the hospitals are moving towards fulfilling the goals of the health care system and hospitals of the future.

The practice of the Ministry of Health's corporate culture among nurses

Azizun ABDUL AZIZ

Lembaga Jururawat Malaysia

A cross-sectional descriptive study was carried out to determine the nurses' awareness, level of knowledge of the 3 core values of MOH corporate culture, and their perception of whether corporate culture was practiced in **their** place of work. A self-administered questionnaire was used to gather information from 10% of all categories of nurses in all the Hospitals in Selangor, 3 districts each in the states of **Perak** and Selangor and Hospital Kuala Lumpur. It was found that the awareness and knowledge of nurses on the corporate culture core values in MOH was high as 91.3% of them had heard of the corporate culture movement, and 72.1% were able to name all the 3 core values of caring, teamwork and professionalism. Only 49.6% of nurses said they had been trained **in** corporate culture. However, training did not seem to be the only source through which the nurses obtained their knowledge on the core values of corporate culture as only 54.3% of those who were able to name the 3 core values correctly, were trained. The relationship between the level of knowledge of nurses and the **training** of oorporate culture values as well as the practice of rites and rituals of corporate culture needs to be explored further.

A study to identify the factors as to the underutilization of health facilities for the taking of pap smears among eligible women

FATIMAH Hj Dolmat

Jabatan Kesihatan Negeri Kelantan, Malaysia

The districts of Bachok and Pasir Putch are among the ten districts in the State of Kelantan with the majority of the population being Malays (99.5%) and the rest Chinese and Thais (0.5%). Estimated number of women aged between 20-60 years in the district of Bachok is 2,200 while in Pasir Puteh it is 2,000. There are 6 Health Centres and 22 Rural Health Centres in the district of Bachok while Pasir Puteh have 5 Health Centres and 17 Rural Health Centres. All these centres provide maternal and child health care including family planning services and pap smear taking. Data have shown that the positive pap smear reading for the district of Bachok in 1997 was 10 out of 520(21.6%) smears taken and in 1998, 4 out of 704 (30%). Targets were 2,400 eligible women for both years. While in the district of Pasir Puteh in 1997 was 9 out of 1,600 (66.6%) and in 1998, 3 smears out of 500 smears taken. Targets being 2,600 for both years. Almost all the women with positive smears were having cancer of the cervix at stage CIN 1 or 2. Based on the above data a study or analysis have to be carried out to identify the factors contributing to the underutilization of the health facilities for the taking of pap smear among eligible women age between 20 - 65 years old. This study will allow us to find out regarding the taking of pap smears from the socio demographic factors and the attitude and knowledge of the husbands with regards to pap smear taking. With findings from the study recommendations can be made to increase the utilization on the health facilities to detect cervical cancer at an early stage in order to decrease the mortality and morbidity rate of cervical cancer.

Nursing: choice of a career

NORZIDA Yusuf

Kolej Kejururawatan Alor Setar, Kedah, Malaysia

Nursing is a profession carried out with care, empathy and compassion. Nurses assist individuals, families and communities to develop self-reliance in promoting health, preventing diseases, maintaining and restoring life in order to enhance the quality of living. This preliminary research was done to assess the current situation in our country as to the reasons why there is a shortage of nurses and also the reluctance of school leavers to choose nursing as their first choice of career. So far, there is very limited literature or research being carried out overseas on **this** topic as this applied more to our local settings. From our findings, there is indeed a need for us to do more researches if we are to promote and to encourage more people especially **school** leavers to choose nursing as their first choice of career.

Are.nurses overworked?

Bella PUVOK

Hospital Queen, Kota Kinabalu, Sabah, Malaysia

In general, nurses claim that **they** are overworked. The perceived contributing factors include the expanded roles introduced by the Ministry of Health and probably made worse by insufficient existing number of staff who are outnumbered by the increasing workload. The researchers therefore, decided to carry out a time motion study in an attempt to find out whether nurses are really overworked or otherwise. The study was carried out in three selected KKIA in the state of Sabah and the findings showed that **1635.7** hours **(85%)** were spent on nursing functions while the remaining **298.04** hours **(15%)** were on non-nursing function. It was also found that the nurses had actually spent **3.68** times more on non-nursing function than that to the expanded scope of the Family Health Programme.

POSTER PRESENTATIONS

Acute pain service in Hospital Melaka - a three-year survey (1997-1999) V SIVASAKTHI

Department of Anaesthesiology, Hospital Melaka, Malaysia

The effective and safe management of pain after surgery requires an organised institutional approach. Melaka Hospital is an 860-bedded hospital with a full compliment of surgical specialities. From 1997 to 1999, the Acute Pain Service managed 1155 patients. 31.8% were males and 68.2% were females. Their ages ranged from 7 years to 85 years. General surgical patients were 43.8%, obstetric & gynaecological patients were 41.7% and orthopaedic patients were 14%. The main indications were post operative pain relief in 98.2%, trauma pain relief in 1.6% and bums in 0.2%. Regional blockade was used via thoracic route in 0.6% and lumbar route in 28.7% of patients. Disconnection of epidural catheters was the most common problem (8%). Serious complications included hypotension (0.8%), inflammation (0.9%). backache (5.6%), motor deficit (9.4%) and sensory deficit in 2.4%. Visual analgesia pain score (VAP) were <2 at rest and <3 on coughing. Patient Controlled Analgesia (PCA) was used in 70.7% of patients. 100% of these patients were on demand boluses. There were no major complications due to PCA. Common complications were nausea and/or vomiting 23.3%, pruritus 5%, respiratory depression 0.3% and urinary retention 2.5%. We conclude that an APS can provide good analgesia and have a low incidence of major complications.

Pulmonary embolism - a case series study in Hospital Universiti Kebangsaan Malaysia CHOY Yin Choy

Department of Anaesthesiology, Faculty of Medicine, Universiti Kebangsaan Malaysia

Pulmonary embolism is a complication of venous thrombosis. It is a major cause of morbidity and mortality, but a condition that is highly preventable and, when diagnosed, very effectively treated. The clinician must maintain a high index of suspicion at all times in the patient at risk for this entity, keeping in mind that overall only about one-third of the patients suspected of having pulmonary embolism actually turn out to have it. A strong suspicion alone is not enough to warrant initiation of treatment, as a clinician must confirm with appropriate studies that venous thrombosis or pulmonary embolism is present. Deep vein thrombosis itself is still an underestimated and often unrecognised disease despite being far from rare and in spite of its severe complications and often debilitating sequelae. It is a disease, which is becoming more frequent due to increased life expectation, the larger number of operations on elderly patients, and the increased frequency of limb injuries. General and specialised surgery is often hampered by this complication. This has raised interest in a more detailed knowledge of the mechanisms leading to DVT, and the correct employment of the latest equipment which enable diagnosis to be made and daily monitoring of the disease during its evolution. But the greatest efforts must be reserved for preventive measures in order to achieve a statistically significant reduction in the incidence of the disease in operated patients. It is to be hoped that a greater awareness of thromboembolic diseases will allow this to be achieved in the future. A series of mortalities from pulmonary embolism in Hospital Universiti Kebangsaan Malaysia had been reviewed and the relevance and methods of prevention will be discussed.

Topical lignocaine and thiopentone for the insertion of laryngeal mask airway; a comparison with propofol

Angeli QUAH*, YS LEW* and Nurulhuda TAN*"

*Department of Anaesthesia & Intensive Care, Hospital UKM, Kuala Lumpur and **Department of Anaesthesia, Hospital Pulau Pinang, Malaysia

Conditions for insertion of a laryngeal mask airway (LMA) in 50 adult patients who received either thiopentone 5mg/kg preceded by 40 mg of topical lignocaine spray to the posterior pharyngeal wall or propofol 2.5mg/kg alone were assessed in a randomised, single-blinded trial. All the patients were pre-medicated with 7.5mg midazolam and received fentanyl lmg/kg before induction. Conditions for LMA insertion were graded as good or poor; occurrence of gagging, coughing and laryngospasm are considered as poor inserting conditions. There was no significant difference in inserting condition found between the two groups of patients. Both groups did not demonstrate any changes in heart rate but propofol-induced patient had significant hypotension at 5 and 10 minutes post induction. We conclude that lignocaine spray to posterior pharyngeal wall prior to thiopentone induction provide acceptable LMA inserting condition and better haemodynamic stability when compared with propofol induction.

TTVA for a patient with lung bullae MD RAHA, ZK AMIR and HMA SAFIAH,

Department of Anaesthesiology, Hospital Tengku Ampuan Afzan, Pahang, Malaysia.

This case is to illustrate the use of TIVA (total intravenous anaesthesia) for a patient with a lung bullae who underwent right maxillectomy. He was ventilated by SIMV mode throughout the 4+hour operation. This technique was chosen to avoid using nitrous oxide and minimizing risk of rupturing the lung bullae. Patient was induced and intubated under inhalational technique using Sevoflurane. For maintenance, continuous infusion of Propofol, Midazolam and Morphine were used to achieve adequate surgical relaxation. Postoperatively, he was electively ventilated and extubated the next day.

Anaesthetic incident monitoring study in Hospital Tengku Ampuan Afzan, Kuantan AY LUTFI and HMA SAFIAH

Department of Anaesthesiology, Hospital Tengku Ampuan Afzan, Pahang, Malaysia

This study was conducted to identify the common anaesthetic incident, at Hospital Tengku Ampuan Afzan, and its causes with the intention of remedying any shortcomings. A total of 151 incidents were reported during June 1998 and April 2000. The incidents were reported using a prepared form based on that produced by the Australian Patient Safety Foundation. All the data collected was analysed using the Australian Incident Monitoring Study software version 1.00L The Airway incident category had 93 reports, the most difficult intubation making up 23.8% of the total Airway incident. This was followed by an equal number of reports for Circuitry and Pharmacological incidents i.e.14.6%. Inexperience, inadequate pre-op assessment and error of judgment were the leading cause of the incidents. Having additional training with emphasis on equipment checking and maintenance was suggested as corrective strategies to overcome future incidents.

Predicted effect compartment concentration of propofol at loss of the eyelash reflex TA LIM and K INBASEGARAN

Anaesthesiology Unit, Universiti Putra Malaysia, Malaysia

Introduction: The aim of this study is to determine the effect compartment concentration of propofol at induction of anaesthesia. Methods: 54 patients, ASA I -II, participated in the study. All patients in did not receive any premedication or opioids pre-induction. Patients in Group I received a bolus dose of 2 mg/kg; patients in Group 2 received an infusion at 1500 mg/hr -1, while patients in Group 3 received a bolus of 30-50 mg followed by an infusion at 1500 mg/hr. The time at loss of eyelash reflex was noted. The effect compartment concentration was simulated using the pharmacokinetic models reported by Marsh *et. al.* and Wakeling *et. al.* Results: Median concentrations at which loss of eyelash reflex occurred were 1.79 ug.ml⁻¹ in group I, 1.85ug.ml⁻¹ in group II, and 1.93 ug.ml⁻¹ in group III. The median concentrations were not significantly different between groups. Conclusion: Predicted effect compartment concentration of thiopentone at induction is the same regardless of whether it is given as a bolus or by infusion.

Co-induction of anaesthesia with thiopentone and propofol: synergistic or additive TA LIM and K INBASEGARAN

Anaesthesiology Unit, Universiti Putra Malaysia, Malaysia

Introduction: The aim of this study is to determine whether thiopentone and propofol act synergistically by comparing their effect compartment concentrations at induction of anaesthesia. Methods: 21 patient, ASA I -II, participated in the study. All patients in did not receive any pre-medication or opioids pre-induction. Patients received a bolus of 75 - 125mg of thiopentone followed by an infusion of propofol at 1500mg/hr. The time at loss of eyelash reflex was noted. The effect compartment concentrations of thiopentone and propofol was then simulated. Earlier studies at the Unit revealed median concentrations of 1.84 mg/ml and 11.00 ug/ml at loss of eyelash reflex for propofol and thiopentone respectively. In this study, predicted thiopentone concentrations were converted to equivalent propofol concentrations by multiplying by a factor of [1.84 / 11]. This was then added to the simulated propofol concentration. Results: Median propofol equivalent concentrations at which loss of eyelash reflex occurred was 1,72 mg/ml. This concentration was not significantly different from the concentration derived in the earlier study. Conclusion: Concurrent administration of thiopentone with propofol results in an additive hypnotic effect.

Susceptibility pattern of Malaysian isolates of rnethicillin-resistant Stuphylococcus aureus (MRSA) against commonly used antibiotics

NORAZAH A, KOH YJ, ROHANI MY and 'LIM VKE

Bacteriology Division, Institute for Medical Research, Kuala Lumpur and 'Department of Microbiology, Faculty of Medicine, National University of Malaysia

Methicillin-resistant *Staphylococcus aureus* (MRSA) that are multiply resistant to several groups of antibiotics is becoming **increasingly** common in most parts of the world. This study was conducted to determine the antibiotic susceptibility of MRSA strains isolated in Malaysian hospitals against commonly used antibiotics. A total of 685 MRSA strains were isolated from Malaysian hospitals throughout Malaysia for the duration of 1997 until 1999. These strains were tested against erythromycin, cotrimoxazole, tetracyline, gentamicin, fusidic acid, rifampicin, ciprofloxacin, chloramphenicoland vancomycin by a disc diffusion method as recommended by National Committee for Clinical Laboratory Standards (NCCLS). The resistant rates of MRSA to the non-beta lactam antibiotics were as follows: 99.1% resistant to tetracycline, 99.4% resistant to erythromycin, 98.8% resistant to gentamicin, 99.1% resistant to cotrimoxazole, 82.8% resistant to ciprofloxacin, 25.5% resistant to chloramphenicol, 7.7% resistant to fusidic acid and 7.6% resistant to rifampicin. All were

sensitive to vancomycin. If the antibiotics are grouped together, 97.7% of MRSA were resistant to erythromycin, cotrimoxazole, tetracycline and gentamicin; 81.3% resistant to erythromycin, cotrimoxazole, tetracycline, gentamicin and ciprofloxacin; 4.5% resistant to all tested antibiotics except chloramphenicol and vancomycin and 0.1% resistant to all except vancomycin. Multiantibiotic resistant MRSA is clearly a significant problem in Malaysia. While the sensitivity of the MRSA strains to other antibiotics was generally low, good activity against MRSA is still retained by fusidic acid and rifampicin. The high resistance to commonly available antibiotics limits therapeutic options. Strict infection control and surveillance should be exercised to curb the spread of these multiresistant strains. Newer choices of antibiotics should be looked into for the treatment of MRSA infections.

Determination of oxidase activity in relation to insecticide resistance in the mosquitoes vectors of public health importance

NAZNI WA, 'KAMALUDIN MY, LEE HL and SA'DIYAH I

Entomology Division, Institute for Medical Research, Kuala Lumpur, Malaysia and *Ministry of Health, Brunei Darulsalam

Mosquitoes from field and laboratory collection were used to determine the oxidase activity in relation to insecticide resistance. The adult Aedes aegypti, Aedes albopictus and Culex quinquefasciatus were exposed to 5% malathion and 0.75% permethrin, while the larvae of these species were exposed to a range of concentrations of malathion, permethrin and temephos. This was conducted to obtain the LC50 values of the field strains. In a separate test these mosquitoes were exposed to piperonyl butoxide prior to exposure to insecticides. This was conducted to determine the level of oxidase, an enzyme which is involved in detoxification of insecticides, thus causing resistance. The enzyme activity was determined by measuring the optical density of the biochemical reaction. From the study conducted Ae. aegypti Ae. albopictus and Culex were resistant to malathion, temephos with a resistance ratio ranging from 1.55-5.35. After exposure to the synergist, piperonyl butoxide, the resistance ratio reduced by 4 folds in the larvae of Ae. albopictus against temephos. Thus, indicating that oxidase is involved in the resistance mechanism against permethrin. Aedes albopictus was tolerant against malathion with 80% mortality after 1 hr exposure. Cx. quinquefasciatus showed 75% mortality after exposure to malathion but 100% mortality after exposure to permethrin. The esterase and mixed function oxidase levels in the adult and larvae of Aedes aegypti, Aedes albopictus and Cx. quinquefasciatus was high compared to the laboratory strains. This indicates that resistance mechanism of esterase and mixed function oxidase is involved in these mosquitoes.

Susceptibility of *Culex sitiens* to Japanese encephalitis virus in peninsular Malaysia INDRA Vythilingam, KRISHNASAMY M and TAN Swee Heng

Entomology Division, Institute for Medical Research, Kuala Lumpur, Malaysia

Japanese Encephalitis (JE) virus was isolated from *Culex sitiens* for the first time and was reported as a possible vector of JE virus in Peninsular Malaysia in 1994. Thus the susceptibility of *Cx sitiens* to JE virus was studied in the laboratory together with *Aedes togoi* as the control mosquito. The mosquitoes were provided with an infected blood meal, after which they were maintained with sugar solution for 12 days. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was carried out on the mosquitoes. *Cx sitiens* was highly susceptible to the virus and was found positive after day 12. The role of *Cx sitiens* in the transmission of JE virus in P. Malaysia is discussed.

Polymerase chain reaction for detection of *Legionella pneumophila* DNA in urine samples NORMAZNAH Y¹, NORHATIAH ML¹, SANIAH K¹, NOOR RAIN A¹, SABIHA P², NORAZAH A¹ and ROHANI MY¹

Institute for Medical Research, Kuala Lumpur and ²Faculty of Medicine, UKM, Malaysia

Legionella pneumophila is a common cause of nosocomial and community-acquired pneumonia, particularly among patients with impaired host defence. The mip gene is known to encode a virulent protein of L. pneumophila and studies have shown that it is a promising target for use in the detection of the organism. Detection of the *mip* gene have been previously done on environmental samples, serum and respiratory secretions. In the present study, polymerase chain reaction was applied for amplification of mip gene on urine samples collected from suspected cases of legionellosis. DNA was extracted from urine samples using the Geneclean II Kit (Bio 101, Inc. USA). Primers Lpm-l and Lpm-2 amplifying the specific sequence of the mip gene were used in the PCR. Twenty five cycles of PCR amplification on a total PCR mixture of 25 µl was carried out using 2400 Perkin Elmer Thermo Cycler. Positive amplification gave a product size of 630 bp that was detected by gel electrophoresis and ethidium staining. The positive strain (11920) obtained from PHL, Colindale was used as positive control. Out of 20 urine samples tested, 12(60%) gave positive PCR amplification products. Specificity of the mip gene for L.pneumophila has been reported by several previous studies. From the study it has been shown that Legionella DNA could be detected in urine of infected patients. The ease of obtaining urine samples from patients compared to serum or respiratory secretions makes this technique a feasible and useful test for diagnosis of *L.pneumophila* infection.

Leishmaniasis among Bangladeshi immigrant workers in Cameron Highlands ABDUL HALIM Abdullah, LOKMAN Hakim S, NORASHIKIN M, YUSRI MY and AHMAD DASUKI AG

Division of Parasitology, Institute for Medical Research, Kuala Lumpur, Malaysia

The main objective of this study was to determine the seroprevalence of leishmaniasis among Bangladesh immigrant workers. Finger prick bloods were collected from farm workers in the Cameron Highlands. Serum samples were analyzed for *anti-Leishmania* using Melotest Leishmaniasis Ab ELISA Kit. Five mL of venous blood sample was taken from those with significant raised antibody titre in heparinized tube and centrifuged. Smears were made from the buffy coat and stained with Giemsa and examined under microscope for Donovan's bodies. A portion of the buffy coat was inoculated into the culture medium. Parasite DNA was extracted from the remaining buffy coat and amplified by polymerase chain reaction (PCR) using specific primers targeted at *Leishmania donovani*. Out of 72 specimens, 28.7% of the samples showed evidence of exposure to *Leishmania infection*. Out of these, 12.5 % and 5.6% were potentially active and most likely to be active infection respectively. The correlation between *in-vitro* culture, microscopy and PCR with antibody titre will be discussed.

Extra-intestinal amoebiasis: serological, biochemical and haematological profiles of patients admitted to Hospital Kuala Lumpur.

LOKMAN HAKIM S, *SURESH R. LACHMANAN, **DOSHI PS, **SINGH H, 'NORASHIKIN M and *ISMAIL I

Division of Parasitology, Institute for Medical Research, Kuala Lumpur, *Department of Medicine, Hospital Kuala Lumpur and **Department of Surgery, Hospital Kuala Lumpur

The results of counter immuno-electrophoresis (CIEP) test for extra-intestinal amoebiasis were reviewed. The rate of positive cases increased steadily from 17.0% in 1994 to 25.6% in 1997 and then started to decline to 22.0% in 1999. In 1998-1999, 195 serum samples were tested. The Orang Asli (OA) had the highest positive rate (62.5%), followed by the Malays (22.0%), Indians (21.0%), Chinese (20.3%) and 13.8% among others (x^2 , p=0.004). The positive rate was significantly higher

among male (27.6%) compared to 12.5% in female (x^2 =9.22, p=0.002). The proportion of positive cases increases with age group (r_s =0.2, p=0.03), with highest rate among those 21-30 year old (x^2 =8.10, p=0.02). Out of 151 known clinical summaries from 178 cases in 1999, 49.7% (75) presented with clinical liver abscess, 40 (53.3%) of which confirmed by ultrasonography. Fever and abdominal pain were the commonest presentation. Among those with solitary liver abscess, 62.8% were positive for amoebiasis as compared to only 18.1% among those with multiple liver abscess (x^2 , p=0.03). Biochemical and haematological profiles were essentially normal with slight elevation of white blood cell counts.

HLA antigens in Malay patients with systemic lupus erythematosus association with clinical and autoantibody

AZIZAH MR* AINOL SS**, KUAK SH*, KONG NCT**, NORMAZNAH Y* and RAHIM MN#

* Institute for Medical Research, Kuala Lumpur, ** Faculty of Medicine, Universiti Kebangsaan Malaysia, #Faculty of Allied Sciences, Universiti Kebangsaan Malaysia, Malaysia

We have studied the frequency of HLA-DR, -DQA, -DQ13 and -DPB alleles in 56 subjects with systemic lupus erythematosus (SLE) and compared them to 59 ethnically matched healthy controls by the method of modified PCR-RFLP to determine the role of the HLA class II genes in determining disease susceptibility and whether any significant clinical and immunological correlation existed with various HLA antigens. We found a strongly significant association of the DR2 and DQB1*0501 and DOB1* 0601 (p corr=0.03, K =3.83, p corr=0.0036, rr =4.56 and p corr=0.0048 and rr =6.0 respectively). However, there was also a weak increase of DQB1* 0201 and DQB1*0901 with a weak decrease of DQA1*0601 and DQB1*0503 and *0301 which were all found not to be significant after corrections for multiple comparisons made. This could have occurred by chance. We found a significant positive association of renal involvement with DR2 and DQB1*050l, arthritis with DR8, malar rash with DOB1*0501, oral ulcers with DOB1*0601, alopecia with DOB1*0501. However, there was a non-significant increase of DQB1*0503 in patients with photosensitivity. Significant associations were also found in patients with antism/rnp antibodies; DOB1*0601, DR2 to antiro/1a antibodies, and DR2, DOB1*0501 and *0601 to antibodies to dsDNA. There was no specific DR, DQ or DP association in patients with age of disease onset below 30 years or those at or above 30 years. Our data suggests the role of the HLA class II genes in confemng disease susceptibility to SLE and the heterogeneity in clinical and autoantibody expression.

The association of major histocompatibility complex genes and susceptibility to systemic lupus erythematosus among the Malaysian Chinese population

AZIZAH MR*, AINOL SS**, KUAK SH*, KONG NCT**, NORMAZNAH Y* and RAHIM MN# .

*Institute for Medical Research, Kuala Lumpur, ** Faculty of Medicine, Universiti Kebangsaan Malaysia and #Faculty of Allied Sciences, Universiti Kebangsaan Malaysia

To determine whether the HLA class II genes, HLA-DR, DQ and DP, carry increased risk to the development of systemic lupus erythematosus (SLE), we have studied the frequency of HLA-DR antigens and HLA-DQA and DQB, and DPB alleles among 70 Malaysian Chinese patients with SLE and compared them to 66 ethnically healthy controls by the modified PCR-RFLP technique. The HLA-DR antigens did not show any significant association with SLE. However, a significantly increased frequency of HLA-DQA1*0102 was found among the patients (43.6 vs 33.3%, p=0.004) and even after correction showed significant result (p corr=0.03, RR=3.39). HLA-DQB1*0501 and 0601 were found increased among the patients and remained significant even after correction was made (RR=4.55 and 4.22 respectively). HLA-DPB1*0901 was also significantly associated with the disease and carries a relative risk of 4.58. Our findings suggest that the DQB1*0501, 0601 and HLA-DPB1*0901 genes may contribute towards determining SLE disease susceptibility among the Malaysian Chinese.

Stability of artesunate in aqueous solutions of physiological significance K SATHASIVAM, S RARNANATHAN, SM MANSOR, NK NAIR and V NAVARATNAM

Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia

Artesunate, a water-solublederivative of artemisinin is rapidly biotransformed to its active metabolite, dihydroartemisinin following oral or intravenous administration. In view of this, a study was conducted to investigate the hydrolysis of artesunate in seven buffer solutions at pH 1.2-7.4 at 37°C and ionic strength of 0.5. The catalytic rate constants for hydrogen ion and water were estimated to be 14.1 x 10⁻³s⁻¹ and 1.79 x 10⁻⁵s⁻¹ respectively. The order of reaction with respect to [H], m was 0.42. The non-integral value of m usually implies the existence of some intermediate formations during hydrolysis of artesunate. These values adequately describe the hydrolysis at 37°C in the pH range of 12–7.4. The pseudo first order rate constant as a function of temperature at pH 12 and 7.4 obey the Arrhenius equation. In conclusion, data from this study can he used to predict the stability of artesunate over a wide range of pH and temperature conditions.

Development of a new procedure for dissolution profiles of artesunate suppository K SATHASIVAM, S RAMANATHAN, SM MANSOR, NK NAIR, PL OLLIARO and V NAVARATNAM Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

To date, there is no dissolution method available to **determine** the dissolution profile of artesunate from suppositories. This study describes a newly developed dissolution procedure for analysis of artesunate suppositories. *In vitro* dissolution profiles of artesunate from the suppositories were examined by means of basket (Apparatus I, USP XXII) and paddle (Apparatus 11, USP XXII) methods. The dissolution profiles were also studied using a modified paddle method in all cases. The dissolution medium used was **900mL** of deaerated phosphate buffer (pH7.4 and 37M.1°C) and the speed of rotation was **100rpm**. Ten milliliters of test solution was removed at appropriate time-points. In the basket method, 75% of the drug was released after 16 hours. Whereas in the paddle method, the dissolution profile could not be determined as the capsule floated after 2 hours. The paddle method was then modified, by using a stainless steel helix and mesh. 75% of the drug was released after 12 hours. In the absence of the mesh, 75% of the drug was released after 10 hours of operation. However, when 0.05% of sodium doedecyl sulphate was added, 80% of the drug was released after 6 hours. Under the same conditions, the basket method took 12 hours to release 80% of the drug, In conclusion, the modified paddle method with 0.05 % of sodium doedecyl sulphate was adopted for artesunate suppository developmental studies

Chromatographic analysis of pyronaridine and its related substances for application in product development

S KARUNIAH, SM MANSOR, S RAMANATHAN, NK NAIR, PL OLLIARO and V NAVARATNAM

Centre for Drug Research, Universiti Sains Malaysia, Pulau Pinang, Malaysia.

The antimalarial pyronaridine is effective against chloroquine-resistant *Plasmodium falciparum* and is less toxic than chloroquine. To date, no high performance liquid chromatography (HPLC) and thin layer chromatographic (TLC) methods for determination of pyronaridine and its related compounds in raw material, finished products and clinical samples have been reported. New TLC and HPLC methods with fluorescent detection have been developed for this purpose. HPLC separation was performed using reversed phase C., Partisil column. The mobile phase used was methanol-0.05M acetate buffer (50:50;v/v) adjusted to pH 4.0. TLC separation was carried out using pre-coated silica gel TLC plates with fluorescent indicator. The mobile phase consisted of benzene-methanol-diethylarnine (80:20:1 v/v). Three peaks B, X and Y were observed when the raw material was analyzed using the HPLC method. The relative percentages of B. X and Y were 5.5, 54.3 and 40.2% respectively. TLC analysis also showed the presence of three compounds. In addition refluxing the

raw material in water converted X to Y. Column chromatography was then used to separate Y from B. NMR and MS data indicated that Y was pyronaridine. The relative percentages of B, X and Y in the finished products were 25.5, 29.7 and 44.8% respectively. Preliminary analysis of a plasma sample from a Thai patient administrated with **6mg/kg** pyronaridine base shows 1 peak, which corresponded to Y. In conclusion, the methods were found to be sensitive and suitable for application in the developmental studies of pyronaridine and its related substances.

Drug compliance among hypertensive patients - self-report versus pill-count. M ISMAIL, R KRISHNAN and Y SHAHJAHAN.

Primary Care Medicine Department, University Malaya Medical Centre, Kuala Lumpur, Malaysia.

Medication compliance is an important medical process, and useful methods are needed to measure compliance in clinical practice. A study was conducted to assess medication-taking behaviour among 129 ambulatory hypertensives, using both pill counts and patient's self-report in a hospital-based primary care clinic. The non-compliance rate with medication was 19.4%. Higher compliance was associated with male sex and longer duration of hypertension, and low compliance with patient's perceived side effects from the medication, previous used of traditional medication and history of stopping anti-hypertensive medication while taking other non-hypertensive drugs. Variables such as age, ethnic group, marital status, level of education, adequacy of blood pressure control, complexity of drug regimen and history of prior hypertension related admission, family history of high blood pressure, stroke or heart attack, patient's knowledge of hypertensive complication, patient's attitude towards treatment, their social support and satisfaction with the health services were not found associated with compliance. Patient's verbal self report as a measure of drug compliance was found to be moderately sensitive and specific (sensitivity 63.5%, specificity = 52%). In conclusion, it is possible to identify non-compliance by relatively simple means and ascertain certain factors associated with poor compliance.

Continuity of care: provider continuity and its influence on diabetic patients NIK SHERINA Hanafi and Christina TAN

Department of Primary Care Medicine, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

This study was undertaken to assess the degree and influence of provider continuity amongst diabetic patients attending a Family Practice Clinic. A cross-sectional survey of 166 patients and retrospective chart audits were carried out. Outcome measures were the Provider Continuity Index, demographic characteristics, clinical parameters as well as patients' perceptions and **selfcare** behaviours. The Usual Provider Continuity Index (UPCI) ranged from 0.18 to 1.00 with a mean **HbA**_{le} value of 8.7%. The majority of patients perceived that having a regular doctor was important and reasons for this are discussed. *Conclusion:* Health care providers should consider the element of continuity of care in planning and carrying out health activities. The physician-patient relationship remains a primary bond, which may influence patients' health status.

Achalasia of 'the cardia: a one-year review in Kuala Lumpur Hospital S GANESANANTHAN and ST KEW

Department of Medicine, Kuala Lumpur Hospital, Malaysia

Background: This study is to review achalasia of the cardia in our practice. **Methods:** Fourteen cases of achalasia that underwent standard oesophageal manometry from mid 1999 till mid 2000 were reviewed. **Results:** The average age was 51f18 (range 27-73) years with 7 males and 7 females. There were 9 Malays, 4 Chinese and 1 Indian. All the cases presented with dysphagia to liquids and

solids. Symptoms of regurgitation (10 patients), heartburn (4 patients), weight loss (4 patients), nocturnal cough (1 patient) and retro-sternal chest discomfort (1 patient) was noted. Duration of illness before diagnosis was 7±6 (range 1 - 20) years and their presenting weight was 51±16 (range 35-86) kg. Two patients, were referred for reassessment of dysphagia following treatment with Botulinium toxin injection and myotomy respectively, were excluded in the subsequent analysis as the diagnosis was previously made. A definite diagnosis of achalasia was made radiologically in 8 patients. There were 4 patients with megaoesophagus and one epiphrenic diverticulum. There was no pseudoachalasia noted in this series. Manometry demonstrated aperistalsis in all patients with one vigorous achalasia based on manometric criteria. The manometric assembly failed to pass through the lower oesophageal sphincter (LOS) in 3 cases and hence the LOS was not assessable. Two cases demonstrated normal LOS pressure with adequate relaxation. All the cases underwent pneumatic dilatation after discussion of risk and benefit. *Conclusion:* Achalasia, a primary oesophageal motility disorder is not uncommon and has a varied presentation. Ideally the diagnosis is made based on a good history, endoscopy, barium swallow and manometry.

Medication errors during prescribing and dispensing of drugs. SALMIAH MA, DOREEN L and MERICAN Z.

Faculty of Applied Sciences, Universiti Teknologi MARA, Malaysia

Errors in prescriptions have occurred but fortunately they have remained minimal. The mistakes can be made by either the prescriber or the dispenser of drugs both of whom can play a role to reduce this minimal level further. The study for prescription and dispensing errors was done in a hospital for a period of one year. Errors in prescriptions and during drug enquiries and dispensing were studied by looking out for (a) different drugs whose spelling are almost alike, (b) drugs that sound almost alike, (c) misspelling of drugs resulting in dispensing a drug whose spelling is closer to that of another drug, (d) misreading of decimal points in prescriptions and (e) misinterpretation of abbreviations used in prescriptions. The study showed that mistakes occurred in all these types of categories. Clarityne was mistaken for clarinase and marvalon was mistaken for mersilon. De-nol and daonil sound almost alike and an enquiry by telephone has led to wrong dosage being told to the doctor. Similarly, gliclazide was heard over the phone as glipizide. Doxorubicin was heard as daunorubicin. Buscopan was written as buscophan by the prescriber and dispensed as busulphan. Prednisolone 25mg was dispensed as prednisolone 2.5 mg. Neupogen written as GCSF was mistaken for leucomax (GM-CSF) and imovane was mistaken for imuran. Scratchy and unclear handwriting played a major role in causing these errors. It is imperative that clear legible prescription writing be given greater emphasis than presently and clarity in handwriting and speech be treated as equally important as being knowledgeable. The use of abbreviations should have stopped long ago

Endoscopic sphinterotomy: an audit

SURESH R Lachmanan, S GANESANANTHAN, R KANANATHAN, J ONG, M SINGH, I MERICAN and ST KEW

Department of Medicine, Hospital Kuala Lumpur, Malaysia

Introduction: Endoscopic sphincterotomy (ES) at endoscopic retrograde cholangio-pancreatography (ERCP) along with subsequent stone extraction have become an accepted therapeutic modality for common bile duct (CBD) stones. It is also essential in ascending cholangitis and has shown to improve outcome in gallstone induced acute pancreatitis. Objective: Audit of ES in terms of indications, technique and cofinplications. Methodology: Analysis of 25 consecutive cases who underwent ES. Results: The mean age of patients was 52.24 years (Range: 19-80 years). They were made up of 13 males (52%) and 12 females (48%). The ethnic breakdown was Malays (60%), Chinese (32%) and Indians (8%). The commonest indications in descending order were choledocholithisasis 17 cases (68%), followed by gallstone induced acute pancreatitis, 4 cases (16%), ampullary tumours with lower CBD obstruction, 2 cases (8%), primary sclerosing cholangitis

with multiple liver microabscesses and a dominant CBD stricture, 1 case (4%) and oriental cholangitis with an intrahepatic stone and recurrent cholangitis, 1 case (4%). Bile duct access was gained in all cases allowing for decompression of the biliary system. Access was gained by sphincterotomy alone in 20 cases (80%) and in 5 cases a precut pappillotomy was required as a prelude to a sphincterotomy. Major complications encountered include minor bleeding (defined as bleeding which is easily controlled with simple haemostatic measures) in 6 cases (24%) and acute pancreatitis in 2 cases (8%), which was self limiting in nature. No perforation was encountered in this series. Out of the 17 cases with choledocholithiasis, successful stone extraction was carried out in 12 cases at first instance (70.6%). In the remainder of cases due to multiplicity of stones and large stone size, partial extraction alter biliary decompression was achieved initially. This was followed by stenting of the CBD. These cases are subjected to a subsequent ERCP to achieve stone extraction, of which success has been achieved in 3 cases (17.7%) and another 2 are awaiting ERCP. Conclusion: ES is a safe procedure and the advent of new lithotripsy methods will broaden its application. Choledocholithiasis can now be successfully treated endoscopically in 85 to 90% of cases with an acceptable complication rate. Although still experimental, extracorporeal shock-wave lithotripsy, electrohydraulic lithotripsy and laser lithotripsy hold the promise of even more effective endoscopic stone removal.

An audit on Chronic Hepatitis C cases seen in the outpatient clinic in Hospital Kuala Lumpur SURESH R Lachrnanan, R KANANATHAN and Ismail MERICAN

Department of Medicine, Hospital Kuala Lumpur, Malaysia

Objective: To assess the characteristics and management of Hepatitis C cases in Hospital Kuala Lumpur. Methodology: 106 consecutive Hepatitis C cases seen between 1990 and 2000 were analysed retrospectively. This database comprises data on patient characteristics, risk factors, clinical features, virology screen and management including types of treatment and treatment outcome and complications. Results: Hepatitis C cases accounted for about 2.1% of cases seen in the hepatobiliary outpatient clinic in that period. The mean age of patients was 40 years (Range: 16 to 63 years). They were made up of 73.34% males and 26.66% females. The main method of transmission was blood transfusion (49%) with an ethnic breakdown of Chinese (44.1%), Malays (39.3%), Indians (15.6%) and others (1%). Other risk factors include intravenous drug abuse (13.1%) and sexual transmission. Risk factors could not be identified in 35% of cases. Half (50%) of these patients were asymptomatic. The commonest symptom, fatigue was seen in 40.7% of patients. Other symptoms were yellow sclera and loss of appetite. The commonest physical finding was hepatomegaly, which was present in 19.81% of patients. The majority or 84.9% of patients had elevated alanine transaminases, while the remaining 15.1% exhibited persistently normal transarninases despite testing positive for the virus. Hepatobiliary ultrasound was requested in all patients. Ultrasound was performed in 78.3% of cases. The rest of the cases had defaulted alter their first or second clinic visits and hence the scans had not been performed on them yet. Liver biopsies were performed in 58.5% of patients and uniformly showed chronic active hepatitis. Complications seen include oesophageal varices (11.3%) and hepatocellular carcinoma (2.8%). A total of 35% of patients underwent treatment with either 6 or 12 months of interferon (IFN). End of treatment response was seen in 46% of cases and sustained response in 10.1%. The combination of IFN + ribavarin was administered in 17 patients who failed to respond to IFN monotherapy. Sustained response was seen in 5(56%) of 9 patients who have completed follow up. **Conclusion:** Chronic Hepatitis C is a potentially treatable condition and combination therapy has increased sustained response rates. Further improvements in response are expected with the introduction of PEG interferon in combination with ribavarin.

Chronic Hepatitis B in Hospital Kuala Lumpur SYED R, NG KG, SURESH RL and MERICAN I

Department of Medicine, Hospital Kuala Lumpur, Malaysia

Objective: Hepatitis B is the most common cause of acute and chronic liver disease and hepatocellular carcinoma worldwide. The World Health Organization estimates that by the year 2000 there would be 400 million cases of Hepatitis B worldwide. This study was undertaken in order to establish a database of Hepatitis B cases in Hospital Kuala Lumpur. Methodology: One hundred cases were randomly selected and analysed. These cases are currently being followed up in the Hepatology clinic in Hospital Kuala Lumpur. *Results:* The hundred cases comprised of Chinese (55%), Malays (36%), Indians (4%), Bidayuhs (2%), Syrian (1%), Bangladeshi (1%) and Indonesian (1%). The mean age of the patients was 40 years old, of which 73% were males and the remaining 27% were females. Vertical transmission accounted for 37% of the total cases while horizontal transmission accounted for 14%. In the remaining 49% the mode of transmission could not be established. The commonest modes of horizontal transmission were blood transfusion (6%), sexual transmission (4%), tattooing (2%), needle prick injury (1%) and acupuncture (1%). There was one patient (1%) co-infected with Hepatitis C. Chronic Hepatitis B was largely detected through targeted screening of individuals based on risk factors. At presentation, 48% of cases were HbeAg positive. Sixty percent of cases with HbeAg positivity exhibited elevated alanine transaminases (ALT), of which, 27% have levels exceeding twice the upper limits of normal. 14% of cases showed natural seroconversion of HbeAg positivity to HbeAg negativity. 74% of cases had ultrasonographic examination, of which 37 % were normal. In 23% of cases, cirrhosis was noted with 2% also having underlying hepatocellular carcinoma, 7% had fatty liver and 7% had gallstones. All cirrhotic patients were closely monitored with regular evaluation of liver function, alpha fetoprotein, prothrombin time and serial ultrasound examination. 78% underwent endoscopic examination of which 45% had oesophageal and 25% had portal hypertensive gastropathy. Patients who were eligible for treatment received interferon, famciclovir and lamivudine. The three patients who had interferon therapy showed end of treatment response but only one has shown sustained response so far (one remains on follow up and the other has relapsed. Four out of patients on famciclovir completed treatment but none showed end of treatment response. Lamivudine treated patients are still on follow up. *Conclusion:* Hepatitis B is a significant problem and close follow up and monitoring of patients is required to institute appropriate treatment and to detect complications at a treatable stage.

Biopsy-proven lupus nephritis - The Renal Unit, Universiti Kebangsaan Malaysia (UKM) Norella KONG CT, *PHANG KS, JEYABALAN V, CHEONG IKS, SEGASOTHY M and *Wan MUHAIZAN

Department of Medicine, * Department of Pathology, UKM, Kuala Lumpur, Malaysia

Objective: To review the experience of the UKM Renal Unit in biopsy- proven lupus nephritis (LN). Design & method: Renal biopsies were subjected to both HPE and immunofluoresence examinations from Jan 1982. Hence we reviewed only those renal biopsies performed between Jan 1982 - April 1997 and analysed those from patients with LN. Results: 140 of the then registered SLE patients underwent a total of 187 renal biopsies. There were 120 (85.7%) female patients and 20(14.3%) males. Their mean age was 28.7 ± 9.3 years (range 12-52). There were 63 (45%) Malays, 70 (50%) Chinese and 7 (5%) Indians. Nephrotic syndrome (43.3%) was the commonest clinical presentation followed by asymptomatic proteinuria ± microscopic haematuria in 26.2%, AGN/ARF in 18.7% and CRF/ESRF in 4.3%. 7.5% of the biopsies were performed predominantly for follow-up of the initial active disease following therapy. Diffuse proliferative LN (46%) was the commonest histological class (WHO) encountered followed by membranous nephropathy (25.7%) and focal proliferative LN (19.3%) respectively. Crescentic LN (≥50% glomeruli affected) occurred in 17.1% of the biopsies. Hypertension was present in 56.7% and renal failure in various combinations in 46% of the patients. At the time of review, 30 (21.4%) of the patients had died from infections, renal failure or acute lupus crises in that order. 62.1% have serum creatinines in the normal range (62-133 umol/l), 7.1% with

stable mild-moderate CRF (se creatinine >133<250 umol/l) and 13 (9.3%) have either severe CRF/ESRF or were on chronic renal replacement therapy. *Conclusions:* Our experience mirrors that of most renal units. With new improved dialysis1apheresis facilities, we believe patient mortality and renal outcome can be further improved in patients with severe LN.

Serum interleukins as new serum markers of disease activity in Systemic Lupus Erythematosus

AINOL SS, KONG NCT, IDRIS M, MOHAMED AL, RAHIM N* and AZIZALL MR**

Faculty Of Medicine, *Faculty Of Allied Health Sciences, Universiti Kebangsaan Malaysia and **Institute for Medical Research, Malaysia

Cytokines are postulated to induce the production of the autoantibodies that characterise SLE, a disease of relapses and remissions. Serum levels of IL-6, IL-10, sIL-2R and IL-1ra were prospectively measured in 134 SLE patients and correlated with disease activity. The latter was measured using the Lupus Activity Index (LAI). 134 patients with a female: male ratio 9: 1 (age range of 14-69 years) were studied to assess disease activity. 81 (60.4%) patients had active disease and 53 (39.6%) were in remission (LAI < 0.5). Of the four interleukins, serum sIL-2R and IL-lra showed high correlation with disease activity. The median serum slL-2R level in active disease was 178 pg/ml vs 131 pg/ml in active disease (p=0001; r=0.251, p=0.004). The median serum sIL-LRA level in active disease was 300 pg/ml vs 225 pg/mil in quiescent disease (p=0.003; r=0.0258, p=0.003). Although patients with active disease had a higher mean serum level of L - 6 than those in remission $(4.22 \pm 1.25 \text{ pg/ml})$ vs $2.48 \pm 0.8 \text{ pg/ml}$) this was not significant (p=0.3) serum L - 6 levels on its own did not correlate with disease activity. However serum L-6 in conjunction with slL-2r and IL-1ra was significantly correlated with disease activity (B=0.01, p=0.03). The mean serum IL-10 levels in active and inactive disease were not significantly different (5.61 \pm 1.7 pg/ml vs 1.77 \pm 0.7 pg/ml; p=0.2). Serum IL-10 also did not correlate with disease activity whether on its own (r=0.054, p=0.5) or when assessed in conjunction with the other interleukins (B=0.0044; p=0.4). We conclude that serum sIL-2r and IL-Ira are potential new serum markers for disease activity in SLE. Sequential monitoring of these may be superior to currently measured serological parameters for predicting lupus flares.

Establishment of an in vitro cell culture system for human Hepatitis B virus infection

WANG Suk Mei¹, Andrea Lisa HOLME¹, SEOW Heng Fong¹ and ABDUL MANAF bin Ali²

'Immunology Unit, Department of Clinical Laboratory Science, Faculty of Medicine and Health Science, Universiti Putra Malaysia, Selangor, Malaysia and ²**Department** of Biotechnology, Faculty of Food Science and Biotechnology, Universiti Putra Malaysia, Selangor, Malaysia

Hepatitis B virus (HBV) causes acute and chronic hepatitis and is an aetiological agent for hepatocellular carcinoma. It is still a major public health problem with currently 300 million HBV carriers worldwide. Although much information is known about HBV, still the knowledge of the virus is by no means complete. Historically, the major obstacle in the study of HBV has been the inability to infect animal model system due to strict virus-host range. It has been suggested that the tissue and species specificity of HBV infection may be due to the preferential attachment of the HBV envelope proteins onto the plasma membrane of human hepatocytes that lead to viral entry and replication. Many potential cellular receptors have been shown to interact directly or indirectly with all three virus envelope protein - small (S-HBsAg), middle (M-HBsAg) and large (HBsAg). The direct involvement of human Annexin-V, a calcium-dependent-phospholipid-binding protein in the initial step of HBV infection has been reported (Gong et. al., 1999, Hepatol. 29:576). The aim of this study is to establish an *in yitro* cell culture system that will continuously produce sufficient HBV by episomal replication. To facilitate the penetration and internalization of HBV, the expression of Annexin-V was enhanced using dexarnethasone and by transfection of two liver cell lines, Chang liver and HepG2 cells. Total RNA was isolated from dexamethasone treated and untreated HepG2, a human hepatoma cell line and Chang liver, a human liver cell line. First strand cDNA was amplified

via reverse-transcription polymerase chain reaction (RT-PCR) using primers based on published human Annexin-V cDNA sequence. The results indicated that dexamethasone has no significant effect on up-regulation of Annexin-V mRNA expression. The cDNA product was cloned into a plasmid, pTarget for transfection of Chang and HepG2 cell lines. The assay of the outcome of the Annexin-V transfected cell lines via Western Blot is in progress. The effect of up-regulation of Annexin-V on susceptibility to HBV infection will be investigated via immunofluorescent staining and polymerase chain reaction. The establishment of an *in vitro* cell culture system which is susceptible to HBV infection and replication is very important because it is an essential tool for the development of new antiviral strategies against Hepatitis B virus infection and for studying the molecular events in viral replication.

Intravitreal ganciclovir in CMV retinitis SENGAL Vathani, GOMATHY A and C LEE

Hospital Kuala Lumpur, Malaysia

Purpose: To review the response of patients with ocular CMV infection to intravitreal ganciclovir. **Method:** 8 patients (11 eyes) were given weekly intravitreal ganciclovir **2mg/0.1ml** for varying periods between October 1999 and July 2000. **Result:** All 11 eyes responded well while on treatment. However, two eyes had reactivation. One subsided with treatment while the other underwent vitrectomy. One eye became blind secondary to CRAO. **One** patient passed away and another defaulted follow-up. Those eyes in a resolved state are on fortnightly intravitreal ganciclovir presently. **Conclusion:** Intravitreal ganciclovir is effective in treatment of CMV retinitis however reactivation has been noted and compliance is a problem.

A new approach to diagnose bronchial asthma

DHRUBA Chakraborty

Department of Human Biology, International Medical University, Kuala Lumpur, Malaysia

The dermatoglyphic characteristics of subjects with bronchial asthma when compared with control group revealed significant differences. The whorls were increased in bronchial asthma patients, but there were little changes in atd angles between normal and bronchial asthma. The observed changes suggest a marked participation of genetic factors in the aetiology of bronchial asthma, and they can be explained by laws of developmental mechanics of the papillary line during embryogenesis. Dermatoglyphics, a non-invasive method could serve as a screening indicator for the follow-up of individuals in threatened families.

Endothelial dysfunction in patient with cardiovascular risks ANNUAR R, NAWAWI H, NORAFAEDAH MH, NORAZIAN and YUSOFF K

Heart Centre, UKM, Malaysia

Background: Endothelial dysfunction is a feature of early stage atherosclerosis and is associated with cardiovascular risk. Recently, the probability of this abnormality as a risk marker or surrogate end point in the management of cardiovascular disease has been discussed. In this study we try to assess the endothelial function of patients with hypercholesterolaemia, newly diagnosed hypertension who are asymptomatic of coronary artery disease and compare them with normal persons. **Method and results:** Non-invasive method in detection of endothelial function was used. With a **7.5MHz** linear transducer and 2D Echocardiography **Sonos 5500** diameter of brachial artery and the flow velocity were measured at rest, during reactive hyperaemia with increased flow (endothelial-dependent dilatation) and after sublingual spray of glyceryl trinitrate (endothelial-independent dilatation). The **58** subjects comprised 20 patients with high total cholesterol **8.5±0.6mmol/1.** LDL

 5.9 ± 0.6 mmol/l, HDL 1.3 ± 0.1 mmol/l, 20 newly diagnosed hypertension within 6 months and 18 control subjects. The mean age for patients with hypercholesterolaemia, newly diagnosed hypertension and control was 44.9 ± 2.9 , 42.6 ± 1.5 and 43.6 ± 1.0 years respectively.

Result of	`endothelial	dysf	unction	study

MEAN ± SE					
	Control	Hypercholesterolaemia	Hypertension	P,	P_2
Age (year)	43.6± 1.03	44.9f2.9	42.6f1.5	0.88	0.93
Males	9(27.3)	11(33.3)	13(39.4)	0.63	0.73
Baseline vessel size (cm)	0.39±0.01	0.36±0.02	0.35±0.02	0.67	0.32
Flow-mediated dilatation (%)	12f1.8	4.9±0.6	5.7±1.4	0.005	0.001
GTN induced dilatation (%)	28.6±3.6	30.6± 3.8	20.1f 2	0.8	0.23
Hyperaemia	105±8.4	132.1±9.8	112.9f8.5	0.102	0.81

P,=for comparison of controls and hypercholesterolaemia, P, = for comparison of controls and hypertension.

Conclusion: Asymptomatic patients with hypercholesterolaemia and newly diagnosed hypertension have impaired vasodilatory effect secondary to hyperemia which is endothelial dependent but normal vasodilatation after sublingual spray of GTN which is endothelial independent (smooth muscle dependent). Endothelial dysfunction appears to occur early and to the same extent any patients with hypercholesterolaemia and hypertension. This observation may have important implication on the future management strategies for these patients.

A clinical profile of patients with unstable angina. NORLAILA M, A RAPAIEE and KHALID Y

The Heart Centre, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Better understanding of the pathophysiology of acute coronary syndrome has led to new developments in managing these patients. A thorough overview of our own set of patients with unstable angina is important in providing them with the most up to date care and to enable adequate provision of care for them. Aim: To define the clinical profile of patients who present with unstable angina Subjects and Methods: This observational study includes 275 patients admitted to Coronary Care Unit, HUKM from 1st January 2000 until 31" July 2000. The patients were provided with standard therapy for unstable angina. Demographic data, coronary risk factors, management strategies and outcomes of these patients were ascertained. **Results:** The 275 patients with a mean age 58.8 ± 10.6 years (74.9) 0% males) were made up of 42.2 % Malays, 33.1% Chinese and 22.9 % Indians. Hyperlipidaemia, hypertension and diabetes mellitus were present in 77.8 %, 72.7 % and 58.9% respectively. Three quarter of them had more than two risk factors. A past history of acute myocardial infarct or unstable angina was present in 24.7 %, and 26.2 % respectively. 23.3 % had heart failure on presentation and 75.6 % had ECG changes (ST or T wave changes). OT dispersion was not prolonged. 98.2% of our patients were in Braunwald's Class IIIB. The therapy include intravenous nitrates (78.5%), aspirin (96.4 %), b-blockers (87.6%), calcium channel blockers (22.2 %), unfractionated heparin (47.5 %) and on low molecular weight heparin (52.5 %). There was no significant rise in Troponin T in relation to the onset of chest pain (p>1.2), presence of more than two risk factors (p = 0.640) and ECG changes (p=0.52). All patients were stabilized and discharged home after an average hospital stay of

3.5 days. *Conclusions:* There was a high prevalence of coronary risk factors and poor risk prognostication in the patients admitted to our set-up. In diagnosing unstable angina, history and high index of suspicion still remain as essential components.

Continuation of pregnancy after midtrimester Gemeprost administration - a case report S VIJAYARANI

Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia

A 27-year-old G,P, was referred to our hospital for aplastic anaemia and an unplanned pregnancy at 11 weeks of gestation. She was diagnosed as aplastic anaemia 3 years prior to this by bone narrow biopsy and had been counselled for tubal ligation, which she had refused. She had declined oral contraceptive pills also and was lost to follow-up until this pregnancy. She was counselled at length about the risks of continuation of the pregnancy. She agreed for termination of the pregnancy, which could not be performed immediately due to want of platelets in the hospital. She requested to go home and returned only at 18 weeks of gestation requesting for a termination. 5 Cervagem pessaries were inserted at 3 hourly intervals but there were only mild irregular uterine contractions and no change in the cervical score. Patient was reluctant for further Cervagem insertion and after consultation with the haematologist the pregnancy was allowed to continue. A detailed anomaly scan at 20 weeks was reported as normal. At 33+ weeks, the patient complained of decreased foetal movements. The CTG was abnormal and the umbilical artery blood flow was reported as abnormal by Doppler ultrasound. A LSCS was done under platelet cover. There was moderately thick stale meconium. Surgery was uneventful. An active baby girl of 1.9kg was delivered. Mother and baby are currently doing well. This case is being reported for its rarity. There has been only one such case reported in the English literature so far.

Menarche in a 2-year-old - cause for alarm? DEEPIKA Monga, SACHCHITHANANTHAN and SURINDAR Singh

Department of Obstretrics & Gynaecology, Hospital Melaka, Malaysia

Precocious puberty, or menarche / thelarche before 8 years of age, is a cause of alarm for parents and the young child. Commonly due to hypothalamic /pituitary causes, it may occasionally be secondary to an oestrogen secreting tumour of the ovary. We present a rare case of a 23-month-old girl presenting with menarche and thelarche of 3 months' duration. Extensive work-up, including CT scan brain and serum hormone levels revealed no abnormalities. The FSH & LH levels were in the prepubertal range. Ultrasonography of the abdomen revealed a single unilocular cystic mass, 7cm in diameter, with no solid areas or papillary projections. Laparotomy with unilateral salpingo-opherectomy was performed. Histopathological examination revealed a follicular cyst - a possible benign cause of the precocious puberty, which has subsequently subsided since surgery. This case is presented in view of the very young age of onset and rare cause of precocious puberty.

Molecular renditions of the **glucose-6-phosphate** dehydrogenase gene amongst selected babies delivered in Kajang **District** Hospital.

HIDAYAH NI*, SALIM AM*, MATSUOKA H", IWAI K", YOSHIDA S'* ARAI M** et. al.

*Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia, **Kuala** Lumpur, Malaysia and **Department of Medical Zoology, Jichi Medical School, Japan

A cross-sectional study was undertaken in the Kajang District Hospital between 1st January, 1999 to 31st December, 1999 to determine the distribution of glucose–6-phosphatedehydrogenase deficiency amongst babies delivered in **Kajang** District Hospital as well as the type of glucose-6-phosphate gene defect amongst selected babies with the deficiency. Out of 5396 babies delivered in the hospital and

screened for the deficiency, 152 were found to have either intermediate or complete deficiency of the enzyme. The majority of those with intermediate or complete enzyme deficiency were Malays. Of the 152 enzyme deficient babies, 6 male babies were randomly selected to undergo further genetic studies. Ethical clearance from the National Ethics Committee as well as written consent from the parents were obtained prior to further analysis by the polymerase chain technique and direct gene sequencing to determine the gene sequence and identify the molecular defect. Out of the 6 selected babies, 3 were Malays, 1 Chinese and 2 Aborigines (Orang Asli). The glucose b-phosphate dehydrogenase (G6PD) variant for two Malay babies corresponded to that of the international variant "Mahidol" while the third Malay subject had the G6PD variant Viangchan. Studies by Quek et. al in 1996 also showed that G6PD Mahidol is common amongst the Malays. DNA sequencing of the Chinese respondent at exon 12 showed a change in nucleotide from G→A at locus 1388 which corresponded with the variant Kaiping. The result of the analysis of the Orang Asli babies at exon 6 showed a change in nucleotide C→T at locus 592. The name of the international variant for this defect was 'Coimbra''.

An unusual presentation of a B-cell non-Hodgkin's lymphoma MAHFUZAH Mohamed, ENI JURAIDA Abdul Rahman, HISHAMSHAH Ibrahim, Caroline HO

*ARNI Talib and WAHIDAH Abdullah

Department of Paediatrics, Paediatric Institute, Hospital Kuala Lumpur and *Department of Pathology, Hospital Kuala Lumpur, Malaysia

Non-Hodgkin's lymphoma is one of the commonest childhood solid tumours in Malaysia. Although the abdomen is the commonest site of presentation for B-cell non-Hodgkin's lymphoma, many other unusual primary sites have been reported before. These unusual sites more often than not have misled us from the diagnosis. We report a 13-year-old Malay girl who presented to the gynaecology team with a left jaw mass, menorrhagia and painful breast lumps. Biopsies from the jaw, breast lumps, anterior lip of the cervix and endometrial **curettings** all showed similar histopathological findings. She showed remarkable response following chemotherapy.

Intussusception in infants and children: a review of 129 cases from a single institution S RAJAH, G RAMESH, N JOSEPH, MG FLORA, CK LIM and K DAMIAN

Division of Paediatric Surgery, Queen Elizabeth Hospital, Kota Kinabalu, Sabah, Malaysia

The incidence of intussusception in infants is high in Sabah. This study is to analyse the incidence of intussusception among various ethnic groups in Sabah, age, sex distribution, pathology and management. *Patients and Method:* 129 patients treated in our unit during January 1992 to December 1999 were divided into two groups. Group 1 (65 patients) treated during the first half of the study (1992-1995) and the rest (64 patients) as Group II. 105 patients, 59 from group I and 46 in group II were treated surgically. 34 patients, 21 in Group I and 13 from Group II required resection of gangrenous bowel. Hydrostatic reduction was possible in 6 patients from Group I and 18 patients from Group 11.72% of patients were under one year of age and the male:female ratio was 2:1.50% patients were Kadazan and 25% were Chinese. Ileocolic intussusception was 52% and caeco-colic was found to be high (34%). One child died due to septic shock and another patient required prolonged ICU care. One bowel perforation was encountered during barium enema reduction. *Conclusion:* The incidence of intussusception is high among Chinese in Sabah. Caeco-colic intussusception is more common than the reported incidence in the literature. Increased awareness, early referral, improvement in health and facilities and posting of more specialists can reduce the number of infants with intussusception requiring surgical treatment.

Expression of p53 and bcl-2 proteins in uterine cervical carcinomas SITI-AISHAH MA, NOR SALMAH, SHAHRIN ISKANDAR AW, SH KWAN, FATIMAH S and ABD AZIZ Y*

Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia and *Department of Obstetrics & Gynaecology., Gleneagles Intan Medical Centre, Kuala Lumpur, Malaysia

The present study was to examine the pattern of expression of p53 and bcl-2 in archival material from patients with invasive cervical carcinomas. Eighty-three surgical cases of cervical carcinomas were immunostained with monoclonal antibodies to p53 and bcl-2. This study included 69 squamous cell carcinomas, 12 adenocarcinomas and 2 adenosquamous carcinomas. Expression of bcl-2 was found in 30.1%(25/83) invasive cervical carcinomas, 34.8%(24/69) of squamous cell carcinomas and only 8.3%(1/12) of adenocarcinomas. In contrast, expression of p53 was seen in 83.1%(69/83) invasive cervical carcinomas; 88.4%(61/69) of squamous cell carcinomas, 58.3%(7/12) of adenocarcinomas and 50.0%(1/2) of adenosquamous carcinomas. Bcl-2 positivity was found in 14.8, 35.7 and 42.9% of grade 1 (G1), grade 2 (G2) and of grade 3 (G3) respectively, compared to p53 where expression was seen in 85.2, 88.1 and 71.4% of G1, G2 and G3 respectively. Lymph node metastases were observed in 40.0 and 80.0% of bcl-2 and p53-positive carcinomas respectively. In staging, bcl-2 was expressed in 33.3, 35.7 and 8.35% of Stage I (SI), Stage II (SII) and Stage III (SIII) respectively while p53 was positive in 76.2, 85.7 and 100% in SI, SII and SIII respectively. This study showed expression of p53 occurred more frequently as compared to bcl-2 in uterine cervical carcinomas.

Diagnosis of inborn error of metabolic disease in Malaysia MY ZABEDAH, AKD PERTIWI, YS CHOY *, M SITI AISIAH, S SUWAJI and I ZAKIAH

Biochemistry Division, Institute for Medical Research, Jalan Pahang, Kuala Lumpur. "Paediatric Institute, Hospital Kuala Lumpur.

Inborn Error of Metabolic Diseases (IEMD) are single gene defects which cause abnormalities in the synthesis or catabolism of proteins, carbohydrates or fats. They are rare individually but collectively common and incidence or clinical manifestations are extremely variable between different disorders and populations. In Malaysia, diagnosis of IEMD was a problem clinically as well as laboratorically because of unawareness about the prevalence/incidence of the disease and unavailability of the laboratory facilities to confirm clinical diagnosis and screening results. Under the Dasar Baru program we were able to set up a number of specialised diagnostic tests using High Performance Liquid Chromatography and Gas Chromatography - Mass Spectrometry to confirm some of the commonest amino acidopathies and organic acidurias. Out of 470 samples received from all over the country from June 1999 till June 2000 from cases suspected IEMD clinically, 24 cases of IEMD have been confirmed biochemically. Out of these 24 cases, 7 cases of Maple Syrup Urine Disease (MSUD), 4 cases of tyrosinemia, 8 cases of Urea Cycle Defects (UCD), 3 cases of methylmalonic acidemiu (MMA), 1 case each for Non-ketotic hyperglycinemiu (NKH) and Propionic acidemia were diagnosed biochemically. The common presenting features noted were lethargy (50%), seizures (50%), poor feeding (46%) and septicaemic-like illness (42%). Persistent unexplained metabolic acidosis occurred in all cases of MSUD, MMA and Propionic acidemia while all cases with UCD presented with hyperammonemia. Consanguinity of the parents was found in 7 of these cases (29%), history of neonatal death of the siblings occurred in 6 cases (21%) and history of similar illness of IEMD in other live siblings occurred in 3 cases (13%). Our experience shows the importance of specialised biochemical tests and good team work between the referring clinicians and laboratory staff in diagnosing IEMD. Furthermore, diagnosis does not require extensive knowledge of biochemical pathways or individual metabolic disease but understanding of the broad clinical manifestation of **IEMD** and high index of clinical suspicion by the attending clinicians based on the presenting features and preliminary or routine laboratory results.

Cathepsin D expression in hydatidiform mole AR HAYATI and MJ SURYANI.

Department of Pathology, Faculty of Medicine, Universiti Kebangsaan Malaysia

The difference in the expression of cathepsin D, which is an estrogen-induced protease, was studied between the trophoblastic cells of hydatidiform moles and spontaneous abortions in order to elucidate their possible roles in the process of invasion and metastasis of the disease. *Method:* This was a study done on 30 cases of complete moles, 23 cases of partial moles and 20 cases of abortions. The formalin-fixed paraffin embedded tissues were stained with rabbit anticathepsin D polyclonal antibody using the labeled Streptavidin Biotin method. The intensity of staining were assessed and compared in the three categories of lesions. *Result:* The irnmunoreactivity for cathepsin D was noted in both the syncytiotrophoblasts and cytotrophoblasts in all three lesions. Light microscopic examination consistently showed intensive and more extensive staining for cathepsin D in complete moles as compared to abortions. Statistical analysis revealed a significant difference in the expression of cathepsin D in the syncytiotrophoblasts, cytotrophoblasts and the villous stromal cells between complete moles and abortions. *Conclusion:* The presence of cathepsin D in a significantly higher amount in complete moles in comparison to abortions suggests the importance of its role in the control of trophoblastic and stromal cell activities and may be involved in the process of tumour invasion and metastasis.

T-cell receptor gene rearrangement in **non-Hodgkin's** lymphoma. NH HAMIDAH, AR FARIDAH, O AINOON, SK CHEONG, NH NORAIDAH and SC PEH'

Department of Pathology, Faculty of Medicine, HUKM, Universiti Kebangsaan Malaysia and Department of Pathology*, Faculty of Medicine, Universiti Malaya, Malaysia

Gene rearrangement studies have become an important diagnostic tool in the diagnosis of lymphoproliferative diseases. In our effort to establish the technique of detecting T-cell receptor (TCR) gene rearrangement for the diagnosis of T-cell malignancies in our laboratory, we have used a PCR-based technique suggested by Trainor et al. We report here our experience in using this technique where we found that results could only be obtained with modification of the method. The modification was in the separation of the first PCR primer mix (Mix I) into two separate mixes (Mix Ia & Mix Ib). Similarly the second primer mix (Mix II) was also separated into two mixes (Mix IIa & Mix IIb). In this study we used the Touchdown and Step-down PCR technique. This technique involved incremental annealing temperature decreases in progressive cycles designed to bracket the melting temperature of the reaction. We performed this technique on samples of DNA extracted from paraffin embedded lymph node tissues from 11 cases of known T cell lymphomas. Our results showed that when the samples were subjected to the original method, there were amplifications only in 4 cases with Mix I and none with Mix II. With modification of the method, amplifications of TCR gene were observed in 7 cases with Mix Ia, 3 cases with Mix Ib and 3 cases with Mix IIa, i.e. all the 11 cases of T cell lymphomas showed amplification of the TCR gene, confirming their monoclonality. In conclusion, we have successfully amplified the TCR gene for determination of TCR gene rearrangement and monoclonality by modification of an established technique. We found this technique useful for the diagnosis of T cell malignancies.

DNA damage in diabetic patients with microalbuminuria

ZARIDA Hambali, Sze Kiat SIM, HAIZA Onn, ROZITA Rosli, She Kin LIM*and ZURAIDAH Hanim Ibrahim*

Department of Clinical Laboratory Sciences, Faculty of Medicine and Health Sciences, UPM and *Medical Department, Hospital Kajang, Selangor, Malaysia.

Elevated oxidative stress is considered to be a likely cause of atherosclerosis and has been implicated in the development of diabetic complications. In this study single cell gel electrophoresis or Comet assay is used to detect DNA damage in diabetic patients with rnicroalbuminuria and to relate the DNA damage with severity of rnicroalbuminuria. Fasting blood samples were collected from 33 normal control and 73 non-insulin dependent diabetic patients for the determination of fasting blood glucose (FBG), glycated haemoglobin (HbAlc) and DNA damage. Microalbuminuria was detected using Micral-Test II. Patients were grouped into four groups, based on the findings of microalbumin in the urine test: negative, 20 mg/dl, 50 mgldl and 100 mgldl. No DNA damage was seen in normal control and diabetic patients with negative urine test. However low DNA damage was detected at rnicroalbuminuria marked 20mg/dl, high and complete DNA damage were detected at microalbuminuria marked 50 mg/dl and more. Mean value of DNA damage was significantly higher in diabetic patients with microalbuminuria of more than 20 mg/dl (p < 0.01). There were correlation seen between DNA damage, FBG and HbAlc. No significant differences in the mean values of FBG and HbAlc between the diabetic groups. This study suggests that DNA damage occurs early in diabetic patients with rnicroalbuminuria. The DNA damage occurs with the development of rnicroalbuminuria, and even before overt microalbuminuria detected.

Glucose-6-phosphate dehydrogenasedeficiency neonatal screening by routine semiquantitative and the quantitative assay methods

O AINOON, YH YU, SK CHEONG, NH HAMIDAH and NY BOO*

Departments of Pathology & Paediatrics*, Faculty of Medicine, HUKM, Universiti Kebangsaan Malaysia.

The aim of this study was to determine whether the currently employed G6PD screening semiquantitative technique could only detect neonates with severe enzyme deficiency and not the partial deficient cases. We performed both the semi-quantitative fluorescent spot test (routine) and a quantitative G6PD enzyme activity assay on cord blood samples from 976 (669 Malays; 307 Chinese) neonates in HUKM. The neonates were diagnosed as G6PD deficient by the routine test when spotted blood showed absence or minimal fluorescence. 3.1 % of the Malay and 3.6% of the Chinese neonates were diagnosed as G6PD deficient by this method. With G6PD enzyme assay, the mean value of G6PD activity for Malay (335 males and 334 females) and the Chinese neonates (163 males and 144 females) were 14.8 u/gm Hb and 14.3u/gm Hb respectively. The upper limit of partial G6PD deficiency (60% of the mean value) for the Malays and the Chinese neonates were 8.8 u/gm Hb and 8.5 u/gm Hb respectively. The upper limit for severe G6PD deficiency (20% of mean value) for the Malays and Chinese neonates were 2.96 u/gm Hb and 2.86 u/gm Hb respectively. Using these cut off points we found that 7.1% (70 of 976) of the neonates were diagnosed as G6PD deficient. Twenty-six (3.8%) Malays and 12 (3.9%) Chinese neonates who had enzyme activity >2.86< 8.5 u/ gm Hb and >2.96< 8.8 u/gm Hb (partial deficiency) respectively were not diagnosed as G6PD deficient by the routine test. Their mean G6PD activities ranged from 3.2 - 8.6 u/gm Hb with a mean value of 7.0 u/gm Hb for the Malays and 3.7 - 8.2 u/gm Hb with a mean value of 6.0 u/gm Hb for the Chinese. They were all female neonates. Thus, by using the enzyme assay 7.1% neonates were diagnosed as G6PD deficient (total and partial deficiency), as compared to 3.3% (total deficiency) by routine screening. In conclusion, we find that the semiquantitative method could only detect cases with total G6PD deficiency but not the partially G6PD deficient females. We feel that the fully quantitative G6PD assay should be recommended for screening of newborns for G6PD deficiency in order to diagnose female heterozygotes as they are also susceptible to severe haemolysis.

Anti HCV reactive donors at the Blood Services Centre, Hospital Kuala Lumpur

RAJA ZAHRATUL Azmar R Shabudin, YASMIN Ayob and FARAIZAH Abd Karim

Blood Services Centre, Hospital Kuala Lumpur, Malaysia

In 1998, out of 70,637 donations, 483 (0.68%) were found to be anti-HCV reactive by Enzyme Immune Assay (EIA). 153 were positive by Recombinant Irnmunoblot Assay (RIBA); 167 were negative and 164 were indeterminate. Data from 325 blood donors which who were anti HCV (EIA) reactive in the Blood Services Centre, 8 were analysed. 235 (78%) came for counseling, 146 (45%) were RIBA positive, 7% (231325) were RIBA negative and the remaining 48% (1561325) were RIBA indeterminate. They were more likely to be new donors, male, Malay and age between 21-30 years old. 35% of those with RIBA positive that came for counseling had raised ALT whereas among the RIBA indeterminate donors, majority 74.1% had normal ALT. Among the anti HCV EIA reactive donors with RIBA positive there was a significant number with history of injecting drugs (17%) and 15% have history of transfusion. The association of these risk factors and raised ALT is stronger with EIA reactive RIBA positive donors. The data suggests that donors with risk behaviour are still donating blood and efforts must be made to educate potential donors. A large number of EIA reactive and RIBA intermediate donors require Nucleic Acid testing to determine their status which would help in counseling and management of this category of donors.

Impact of donor deferral for nvCJD in Malaysian blood donors

NORRIS Naim, FARAIZAH Abdul Karim and YASMIN Ayob

Pusat Perkhidmatan Darah, Hospital Kuala Lumpur, Malaysia

Creutzfeldt-Jakob Disease (CJD) is one of a series of transmissible spongiform encephalopathies affecting both animals and human, with prion protein identified as the probable infectious agents, whose route of transmission include ingestion, parenteral administration and intracerebral inoculation. The new variant CJD (nvCJD) is a different entity from sporadic CJD which can be acquired by an unknown route. Theoretically, it is possible that a reservoir of incubating cases of nvCJD exist among population of high risk areas like the United Kingdom. Hence, several countries have excluded potential blood donors who have visited the United Kingdom for a period of more than 6 months between 1980 to 1996 from donating. The aim of our limited survey is to assess the proportion of our blood donor who would otherwise be deferred if we decide to implement a similar policy or guideline. Method: The survey was conducted in the National Blood Service Centre (NBSC) Hospital Kuala Lumpur. Participants were blood donors (regular and first time donors) who donated at the centre itself and at mobile clinics organised by NBSC throughout the Klang Valley. The questionnaire handed out was completed by 412 donors. **Findings:** Of the 412 donors, 39 (10.26%) reported to have been to the United Kingdom between 1980 to 1996, 16 or 4.2% spent an accumulative time of more than 6 months. With an annual collection of 72,000 units of blood, deferral of 4.2% of donors would results in a potential loss of 3,000 units of blood annually for the National Blood Service Centre, Hospital Kuala Lumpur. Conclusion: With relatively limited scientific evidence of nvCJD transmission through blood and blood products, changing the current policy in donor recruitment to combat the nvCJD 'crisis', would not only be unnecessary but also represents a potential loss of an already scarce resources.

Microangiopathic hemolytic anemia due to cryofibrinogenemia in a patient with systemic lupus erythematosus

SK CHEONG, SAW FADILAH, O RAUDHAWATI, SC SUGANTHI*, AVM KALAICHELVI and NCT KONG*

Department of Hematology and Transplantation, MAKNA-HUKM Cancer Institute, Department of Medicine*, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur

Cryofibrinogenemia refers to the presence of an abnormal cold-precipitable protein in the plasma. It is usually associated with malignancy, thromboembolism, collagen vascular disease, or infections. The most common clinical presentations of cryofibrinogenemia are cold intolerance, acrocyanosis, skin necrosis and ulcer. The peripheral blood count is usually normal and hemolysis is rarely seen. We describe a 44-year-old Chinese woman who presented with severe anemia and thrombocytopenia one year after the diagnosis of systemic lupus erythematosus (SLE). Livedo reticularis, Raynaud's phenomenon and petechial rashes were evident on examination. Microscopic examination of the peripheral blood revealed erythrocyte fragmentation, red cell rouleaux formation, platelet clumps and pinkish precipitates between the red cells. Further tests confirmed the presence of cryofibrinogen. The patient was treated with 3 cycles of plasmapheresis that resulted in the resolution of the skin lesions, MAHA, platelet clumping and cryofibrinogenprecipitates. This report describes an uncommon association between cryofibrinogenemia and MAHA that was successfully treated with plasmapheresis.

Characterization of the Metronidazole resistance strains of *Helicobacter* pylon' isolated from dyspeptic patients

H SALASAWATI, A JASNI3, D AL AMIN3, A AMINUDDIN2, N MAZLAM2, M NORHAYATI4, H ALFIZAH1 and M RAMELAH1

'Departments of Medical Microbiology and Immunology, ²Medicine, ³Surgery, and ⁴Parasitology and Entomology, Universiti Kebagsaan Malaysia, Malaysia.

The main purpose of the study was to investigate the genotypic characteristics of metronidazole resistance strains of Helicobacter pylori (H. pylori) isolated from dyspeptic patients. Methods used include isolation of *Helicobacter pylori* from biopsies of the gastric antrum obtained from patients who underwent endoscopy for dyspepsia at the Hospital Universiti Kebangsaan Malaysia. Gastric antral biopsies were subcultured onto blood agar plates which were then incubated at 37°C, under microaerophilic conditions for 5 days. *H. pylori* strains were identified by their colonial morphology, Gram stain appearance, oxidase and urease positivity. The sensitivity of H pylori isolates to metronidazole was determined using Epsilometer agar diffusion gradient test (E-test) method on Mueller-Hinton agar plus 10% horse blood. Susceptibility to metronidazole was defined as Minimal Inhibitory Concentration (MICs) of ≤8mg/L and resistance to metronidazole was defined as MIC of ≤16 mg/L. DNA fingerprints of metronidazole resistance strains of H. pylori were generated by random amplified polymorphic DNA (RAPD). Susceptibility testing carried out on Helicobacter pylori strains showed that 40.54% of the strains were resistant to metronidazole with all the resistant strains showing MICs >256 mg/L. Analysis of RAPD - PCR patterns obtained with strains isolated from different dyspeptic patients revealed great diversity at the genomic level with each isolate presenting a unique profile. About 40% of H. pylori strains isolated from patients with dyspepsia were resistant to metronidazole. Although genotyping by random amplified polymorphic DNA is unable to discriminate between susceptible and resistance strains of H. pylori isolated, these results are important in determining patients who failed to respond to treatment. Identical or different RAPD profiles of the isolates strain will enable us to differentiate between relapsed and reinfection.

Glucose-6-phosphate-dehydrogenasemutations in Malays

O AINOON, YH YU, SK CHEONG, NH HAMIDAH and NY BOO*

Departments of Pathology and Paediatrics*, Faculty of Medicine, HUKM, Universiti Kebangsaan Malaysia.

We performed DNA analysis on 90 cases of male Malay G6PD-deficient neonates born in HUKM as part of our continuing effort to characterise the molecular defects of G6PD deficiency in the various ethnic groups. Mutations were detected by established PCR-based techniques and DNA sequence analysis. We have successfully established the mutations in 41 out of the 90 cases of Malay G6PD deficiency and we present here our findings. We found 18 % (17 of 90) were mutation G>A at nt 871 (G6PD Viangchan), 11.1% (10 of 90) were mutation G>A at nt 487, 7.7% (7 of 90) were mutations C>T at nt 563 (G6PD Mediterranean), 2.2 % (2 of 90) were mutation G>T at nt 1376 (G6PD Canton) and 1.2% (1 of 90) of each mutation C>T at nt 1360 (G6PD Chinese-2) and G>A at nt 1361 (G6PD Andalus). All these molecular variants except G6PD Viangchan, G6PD Chinese-2 and G6PD Andalus have been previously found to occur among Malay G6PD-deficient individuals (unpublished data). It is interesting to note the high frequency of G6PD Viangchan among the Malays. We have also found that 50% (43 of 90) of the cases showed presence of additional mutation C>T at nt 1311, a silent mutation commonly seen among the Mediterraneans together with mutation C>T at nt 563. This mutation has also been reported to be a site of polymorphism in many populations. In our group of neonates mutation 1311 is not associated with 563 mutation since only 2 of the 7 neonates with mutation 563 had the 1311 mutation. In conclusion, our studies showed that at least 7 alleles account for 45% of Malay G6PD deficiency in this group of neonates. Fifty five percent of Malay G6PD deficiency remained to be characterised and they may be caused by other known mutations or novel mutations. Our findings suggest that mutation 563 in the Malays may have arisen independently from G6PD Mediterranean in Europe and our finding support the fact that nt 1311 is a common polymorphic site.

Apoptosis-related proteins in cervical carcinoma: what do they mean?

PL CHEAH and LM LOOI

Department of Pathology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Since the recognition of apoptosis or "programmed cell death" in the 1970s, there has been much progress in the understanding of its role in the development and homeostasis of an organism. It has also become evident that failure of programmed cell death may contribute to tumourigenesis. The bcl-2 gene family, made up of at least 16 different proteins, plays an important role in determining apoptosis with some members of the family facilitating and others obstructing apoptosis. Bcl-2 and Bax are respectively the prototypes of anti-apoptotic and pro-apoptotic members of the bcl-2 gene family. 16 LSIL, 22 HSIL, 39 invasive carcinoma (28 squamous and 11 adeno/adenosquamous carcinoma) and 15 benign cervices were immunohistochemically studied for Bcl-2 and Bax expression to provide some insight into the roles of these proteins in cervical carcinogenesis. Immunohistochemical expression of both proteins were scored based staining intensity (1:light; 2:moderate; 3:strong) and percentage of cellular staining (1:1-25%; 2:26-50%; 3:51-75%; 4:>75%). Mean Bcl-2 score was highest in HSIL (2.7) compared with benign squamous epithelium (0.8), LSIL (1.0) and invasive carcinoma (1.3) while **Bax** appeared to show a progressive increase from LSIL (3.0) through HSIL (4.7) to attain the highest score in invasive carcinoma (7.6). The reasons for upregulation of the antiapoptotic Bcl-2 at the crossover from preinvasive to invasive cervical carcinoma remains unclear but may be associated with protection of the cell from programmed death so as to allow time for acquisition of new cellular properties which lead to permeation of the basement membrane. Why Bcl-2 is subsequently downregulated in overtly invasive cervical carcinoma is equally perplexing and needs further clarification. Bax expression on the other hand appears to progressively increase with increased aggressiveness implying an increasing propensity for cell turnover from LSIL to HSIL and invasive carcinoma.

PCR detection of HPV in formalin-fixed,par n-embedded cervical carcinoma in a Malaysian population

PL CHEAH, MH NG, LM LOOI and *V SIVANESARATNAM

Departments of Pathology and Obstetrics and Gynaecology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

affi

The human papillomavirus (HPV) has been aetiologically associated with cervical carcinoma, a cancer which remains an important problem in Malaysian women. A study was conducted at the Department of Pathology, University of Malaya Medical Centre to determine the prevalence of HPV among cases of cervical carcinoma diagnosed for the first time using the polymerase chain reaction (PCR), Formalin-fixed, paraffin-embedded tissues of 43 cases of invasive cervical carcinoma were subjected to amplification of the ubiquitous human beta-globin gene to assess quality and quantity of the extracted DNA template. Only on successful amplification of the human beta-globin gene, the cases were further amplified using primers to HPV 6b, 11, 16 and 18. Cases which did not demonstrate any of the four above specific HPV types, were then subjected to PCR using MY09/ MY11 consensus primers to HPV L1 ORF. 35 cases exhibited human beta-globin gene amplification. Of these, 28 were squamous, 5 adeno and 2 adenosquamous carcinoma. In the squamous carcinomas, **HPV** 16 was detected in 13, HPV 18 in 2 and HPV 6b in 1. HPV 16 was the only specific type detected in 3 adenocarcinomas. 1 adenosquamous carcinoma showed HPV 18. HPV L1 consensus primers PCR demonstrated positive HPV DNA in 10 squamous and 1 adenosquamous carcinoma. Overall, HPV was detected in 31(88.6%) cases. HPV 16 was the most common type and was detected in 45.7% of the cases. HPV 18 was found in 8.6% of cases. Interestingly, a case of nonkeratinising squamous carcinoma exhibited HPV 6b, a type usually associated with low-grade dysplastic lesions rather than overt malignancies in the cervix. The finding of a HPV prevalence of about 89% in cases of cervical carcinoma in this study lies within the range reported from other populations (75% in Algerian cases of cervical carcinoma to 100% in cases from Guinea, Thailand and Poland).

Detection of hemoglobinopathies using an automated cellulose acetate electrophoresis system YM CHIN. FARIDAH M and SAPIAH R

Division of Hematology, Institute for Medical Research, Kuala Lumpur, Malaysia

Hemoglobinopathies is not uncommon in Malaysia. There are two main types of thalassaemia in our population, a and β thalassaemia which is due to the absence or reduction in the synthesis of the a and β chain respectively. a thalassaemia due to gene deletion is common in South East Asia. Depending on the number of a genes deleted the a thalassaemias can be classified into a thalassemia 1, a thalassemia 2, Hb (hemoglobin) H disease and hydrop fetalis. The other types of hemoglobinopathies commonly seen in our population are heterozygous and homozygous P-thalassaemia, HbE, HbS, HbE-P thalassaemia and Hb Constant Spring. The objective of this study is to use an automated cellulose acetate electrophoresis (CAE) system, the Microtech 672PC, Interlab, to detect the common hemoglobinopathies in the Malaysian population. The CAE system would be compared to a high performance liquid chromatography (HPLC) system. Both systems can detect most of the common hemoglobinopathies. Compared to the HPLC system, the CAE system can detect HbH, is more economical and can perform analysis faster than the HPLC system. CAE system can analyse a total of 60 samples in less than 3 hours compared to the HPLC system which can analyse a total of 100 samples at the rate of 6.5 minutes per sample. The disadvantage of the CAE sy'stem is that it requires the preparation of hemolysate which takes about an hour.

An antigen detection dipstick colloidal dye immunoassay for field diagnosis of brugian filariasis in humans residing at an endemic district of Peninsular Malaysia

AM ROSLAINI*, A WAN OMARY, O SULAIMAN, S YUSOF*, MS FATMAH* and G ISMAIL*

*Department of Clinical Laboratory Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; *Department of Parasitology and Medical Entomology, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

The aim of this study was to validate a dipstick colloidal dye immunoassay (DIA) for antigen detection which we have developed for field diagnosis of brugian filariasis. Dipsticks were prepared from rabbit polyclonal antibody against excretory-secretory antigens of *Brugia malayi* coated nitrocellulose membrane mounted on acetate strips that served as the assay capture matrix. The same antibody absorbed to a commercial palanil navy blue colloidal dye particles commonly used in textile industry served as antigen detecting reagent. The performance of DIA was compared with that of a previously described sandwich-ELISA. In the DIA, 69 of 70 sera from microfilaremic individuals were deemed to contain **filarial** antigens when screened at a dilution of **1:50**. End titres were 1:10 to 1280. The specificity of both assays was >95 % but their sensitivity was remarkably different. The inverse geometric mean **endpoint** dilutions for 20 antigenemic sera were 64.98 in Sandwich-ELISA and 452.55 in the DIA. As the DIA is simpler, rapid, inexpensive and not requiring sophisticated instruments its use under field condition of tropical countries is recommended.

Parasitological and immunological detection of active cases of brugian filariasis and dirofilariasis in some Malaysian reservoir animals

AM ROSLAINIX, A WAN OMARY, CK LOW*, JG VIVIAN*, 0 SULAIMAN*and MY ABD. HAMID**

#Department of Clinical Laboratory Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; *Laboratory Animal Resource Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia; and **Department of Veterinary Services, Seri Iskandar Bota, Perak, Malaysia

The aim of this study was to ascertain the prevalence of both the brugian filariasis and dirofilariasis in various reservoir animal hosts that live in close association with man and therefore likely candidates for **zoonotic** transmission. This study was carried out at Perak Tengah district from April 1996 through December 1999. Microfilaremia was detected and species determined from **giemsa**-stained blood smears of these animals. Serologically, two rapid antigen dipstick colloidal dye immunoassays (DIA) for brugian filariasis and dirofilariasis were used. The animals screened were 150 domestic cats, 100 dogs and 90 long-tailed macaque monkey, *Macaca fasicularis*. Parasitologically, 7 (4.67%) cats were positive for *Brugia malayi*, 18 (12 %) for *B. pahangi*, 6 (4 %) for *Dirofilaria* repens and 9 (6 %) for *D. immitis*. Only 3 (3 %) dogs were positive for *B. pahungi and* none for *B. malayi*. 54 (54 %) dogs were positive for D. *immitis*. 3 (3.33 %) monkeys were positive for only *B. malayi*. Serologically with the DIA, 15 (10 %) and 8 (5.33 %) cats were positive; 4 (4 %) and 60 (60 %) dogs were positive and 4 (6 %) and 2 (2.22%) monkeys were positive for brugia and dirofilarial antigens respectively. As *D. immitis* and *D. repens* were common in dogs and cats respectively, more human infections with Dirofilaria spp. can be expected.

Lymphocyte subsets in β-thalassaemia majors

SK CHEONG, GK AKRAM, NH HMIDAH, SIVAGENGEI K and RAHMAN J *

Department of Pathology and Pediatrics*, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

P-thalassaemia majors are known to be susceptible to recurrent infections. We carried out a study to ascertain whether this may be due to alteration in the quantity of the circulating lymphocyte subsets. Lymphocyte subsets were studied in 45 P-thalassaemia majors, age between 1 to 22 years. Flow

cytometry using three colour absolute count method was used with a panel of monoclonal antibodies consisting of CD3 (T-Cells), CD3/CD4 (helper /inducer cells), CD3/CD8 (suppressor /cytotoxic cells), CD19 (B-Cells), CD 16+56 (Natural killer cells). The patients were divided into four groups, according to the presence or absence of the spleen and whether or not under chelation therapy. The results show that patients that are not splenectomized but under chelation therapy have lower total lymphocytes and CD4 cells. This finding indicates that in order to avoid reduction in CD4 cells in b-thalassaemia major while on chelation therapy, it may be necessary to carry out a splenectomy.

Successful pregnancy in a patient with acute promyelocytic leukemia S K CHEONG, SAW FADILAH, MAL AMIR, S SHARANPAL and AAR ALAWIYAH.

Department of Hematology & Transplantation, MAKNA-HUKM Cancer Institute, Hospital Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Acute promyelocytic leukaemia (APL) in pregnancy is a rare event, with fourteen cases so far reported in the literature. Management of APL during pregnancy represents a difficult problem because of the associated coagulopathy and the potential teratogenic and mutagenic effects of the chemotherapeutic agents. Even though all-trans-retinoic acid (ATRA) has been shown to induce complete remission in most cases of newly diagnosed APL, its effectiveness in pregnancy has yet to be confirmed. We report a case of APL successfully treated with ATRA during the second trimester of pregnancy. Treatment with ATRA alone resulted in haematological remission on day 25 of therapy with no significant adverse effect. A healthy baby girl was delivered by Cesarean section at 34" week of gestation. Although ATRA is known to exhibit severe teratogenic effect during the first trimester of pregnancy, it seems to be reasonably safe during the second and third trimesters. However, close monitoring for fetal cardiac complications in particular **arrhythmias** is mandatory throughout the pregnancy.

Frequency distribution of Hepatitis C virus genotypes in Malaysia SF YAP, PW WONG and 'NW WONG

Department of Pathology, University of Malaya and *Loh Guan Lye Specialists Centre, Penang, Malaysia

The objective of this study was to determine the frequency distribution of the hepatitis C virus genotype among local subjects. Previous investigation using a specific priming amplification method (Okamoto) demonstrated that about a third of our isolates belong to genotype 3a, another one third belong to type 1 (with approximately equal proportion of 1 a and 1b), 10% were of mixed genotypes and 20% could not be classified. In order to ascertain the genotype of the latter group, consecutive specimens received in the laboratory for HCV detection were analysed. Specimens that were positive for HCV RNA were genotyped using a reverse lineblot assay (INNOLiPA). Using this method, 6 types and numerous subtypes including types 1a & 1b, types 2a/c & 2b, types 3a-c, types 4a-h, type 5a and type 6a can be distinguished. Till date, a total of 36 specimens have been tested. Genotypes 1 and 3 make up the large majority (88.9%) of the isolates, with genotype 1 constituting 41.7% and genotype 3a, 47.2%. It is significant that most of the type 1 isolates were of subtype 1b. Of the remaining cases, 1 was a type 2 isolate and 3 were of mixed genotypes, of which 2 were la+1b. None of the isolates analysed belong to type 6, which is reported to be common in South East Asia. Information on the HCV genotype is important for the appropriate treatment for chronic hepatitis C. It is generally accepted that types 2 & 3 infection are associated with good response to antiviral drugs, whereas type 1b is associated with poor response. The results show that 33.4% of our cases were infected with the type 1b virus. This group of patients should be identified to allow the dosage and schedule of anti-viral therapy to be adjusted accordingly.

Raised telomerase activity in neoplastic tissue compared to non-neoplastic tissue supports its role in neoplastic cell immortalization

MH NG, LM LOOI and PL CHEAH

Department of Pathology, Faculty of Medicine, University of Malaya, Malaysia

It is known that normal somatic cells undergo telomeric shortening with every round of cell replication, so that eventually the loss of genetic material reaches a critical stage and the cells undergo senescence and eventual cell death. Unlike normal cells, neoplastic cells have the unique ability to proliferate indefinitely. This study was conducted to investigate whether telomerase, an RNA-containing enzyme that restores the telomere length, may have a role in the neoplastic cell immortalization process. Fresh tissue samples taken from excision specimens received by the Department of Pathology, University of Malaya Medical Centre were investigated for telomerase activity. These comprised 33 breast lesions (10 infiltrating breast adenocarcinoma, 13 fibroadenoma and 10 non-neoplastic breast tissue), 27 colonic lesions (17 colonic adenocarcinoma and 10 nonneoplastic colonic mucosa) and 46 cervical lesions (24 cervical carcinoma and 22 non-neoplastic cervical tissues). Telomerase activity was detected using a technique which combines Polymerase Chain Reaction and Enzyme Link Immunosorbent Assay (TRAP-ELISA) methodologies. Telomerase activity was found in 6 (60%) of 10 breast carcinomas, 6 (46%) of 13 fibroadenomas, none of the 10 non-neoplastic breast samples, 3 (17.6%) of 17 colon carcinomas and none of the 10 nonneoplastic colonic mucosal samples, 14 (58%) of 24 cervical carcinoma and 3 (13.6%) of 22 nonneoplastic cervical samples. It appears that neoplastic tissues possess a higher telomerase activity than non-neoplastic tissue. This finding supports a contributory role for telomerase in tumourigenesis, but nevertheless does not exclude alternative or co-existent mechanisms for cell immortalization. The feasibility of using telomerase assay as an adjuvant marker of malignancy should also be investigated.

Mycetoma in Sudan, a challenging health problem: an overview NAGEEB SULAIMAN SAEED

National Health Laboratory, Khartoum, Sudan

Mycetoma is a serious health problem in Sudan, being more prevalent in the central region (myetoma belt) and commonly affecting males at the peak of their productive age with a significant socioeconomic impact. In spite of effective chemotherapeutic regiments there are still major challenges in the management of these case. Over 400 new cases are seen in hospitals with significant under reporting, most commonly seen in the age group 20 - 40 years with duration of illness ranging from 3 months to 30 years. Many of these patients are subjected to repeated surgery with 80% recurrence rates. Most patients tend to seek medical advice late, many with bone involvement. M:F is 5:1. It is common among low socioeconomic groups of agricultural workers, woodcutters and herdsmen. Partial deficiency in CMI has been demonstrated in many of them. It commonly affects the feet (70%) and hands (12%). In 10% of cases other parts of the body are affected including the head. Only 18% of patients present with pain which is usually due to secondary bacterial infection. Most of patients present with swelling, discharging sinuses with grains and deformities. Both eumycetoma and actinomycetoma are common. Bone involvement is seen more with actinomycetoma. The disease spreads locally through the subcytaneous tissues, in 1-3% spread is through lymphatics specially with actinomycetoma. The causative organisms are Madurrella mycetomatis (71.4%), Streptomyces somaliensis (18%), Actinomadura madurae (5.3%), Actinomadura pelliteri (2.7%) 2.6% of cases are caused by Nocadia baziliensis, Curvularia lunata or Aspergillus nidulans. Diagnosis depends on clinical findings, radiological, histopathological and mycological studies including serology. Immunodiffusion (ID) and counter current immunoelectrophoresis (CIE) are used in diagnosis and follow up of patients under treatment. Recently ELIZA has been used with high levels of sensitivity and specificity though the relatively high cost makes a barrier for routine applications. Most of the clinical trials for use of chemotherapy in mycetoma were carried out in Sudan. In spite of the establishment of good therapeutic regimens many patients are still subjected unnecessarily to

mutilating surgery and amputations, mostly because the cost of drugs or because of the too late presentation of many patients with bones already involved. Actinomomycetoma usually shows good response to chemotherapy (90%) provided that bones are not involved. The commonly used drugs are streptomycin in combination with dapsone, cotimoxazole or uphadoxine/pyrimethamine or rarely rifampicin in resistant cases. In case of eumycetoma response to chemotherapy is usually slow and may need surgical **debulking** of large swellings. Ketoconazole, itraconazole and combinations of procaine penicillin with griseofulvin have shown to be effective. Serological follow up of all patients who had chemotherapy is important to avoid clinical relapses. Most of mycetoma patients are poor and illiterate and cannot afford the costly drugs and show poor compliance with treatment and hence poor response. Many of them are subjected to repeated surgery with high relapse rates and subsequent deformities and disabilities and later on amputations with bad reflections on families.

Pilot sanitary survey of a popular tourist beach S SITHAMPARAM, S AMBU, USHA DEVI, WM LOH, PC LEE and M NAWI

Environmental Health Research Centre, Institute for Medical Research, Kuala Lumpur, Malaysia

Port Dickson was chosen for this study because it is a popular tourist destination on the West Coast of Peninsular Malaysia. The UN Report on the State of the Planet states that home to two billion people, coastal areas play a vital economic role and also feel the full brunt of human impact (Time-Earth Day, April-May 2000), 'Exposure to faecal pollution through contaminated recreational water leads to detectable health effects of varying nature and severity and there is growing evidence of a dose-response relationship linking faecal pollution with both enteric and non-enteric illness. Available evidence also indicates that pollution-related health effects occur at levels of faecal indicator bacteria which are encountered in recreational waters world-wide and which may be substantially below the prevailing legal standards in many parts of the world' (WHO 1998). A sanitary inspection, water quality determination and data analysis and interpretation are essential elements in characterising the microbiological safety of water in recreational areas' (Monitoring Bathing Waters, edited by J Batram and G Rees, WHO 2000). Initial surveys were successfully carried out and the results of initial analyses have indicated that there are several 'hot-spots'. Besides conducting a sanitary inspection along the eight mile beach at Port Dickson, the EHRC team also measured-the physical parameters of several storm-water drains and coastal waters. These parameters included pH, temperature, salinity, turbidity, dissolved oxygen and Chemical Oxygen Demand. In addition, the extent of microbiological contamination in the coastal waters of the eight mile was determined using indicators such as E. coli, Enterococci and Clostridium perfringens. These were analysed using colilert and enterolert test kits and membrane filtration methods.

Epidemiology of geriatric patients in the female orthopaedic ward of Hospital Seremban Hing Kock SHONG

Orthopaedic Department, Seremban Hospital, Malaysia

The aim of this study was to obtain a statistical database of the epidemiological pattern of the problem so as to assist in the development of prevention, management and post hospitalization home care of the geriatric population. A retrospective **patient/records** study of patients above the age of 60 years was carried out between July 1999 and December 1999 in Seremban Hospital. The age distribution ranged between the 6" and 7" decade (79%). Racial distribution showed Malays and Chinese dominating (45% and 42% respectively) The major reasons for admission were trauma, degeneratic diseases, infection and malignancy. The generatic diseases mainly involved the spine and knee, osteoporosis as an aetiological factor was inferred in 50% of the patients admitted. An admission rate of nearly 20% of the admission (to the female orthopaedic) reflects gravity of the problem. With the continuous increase in the population and life expectancy this figure is expected to increase. The study demonstrated the magnitude of the problem, the demographic scenario and aetiological epidemiology of geriatric population in a small scale. A further in depth study is recommended and

with detailed statistical analysis of the findings a comprehensive geriatric care programme can be formulated to address this rising problem.

Acute mesenteric ischaemia: the need to be aware MEHESHINDER Singh and D BALASINGH

Malaysia

Acute mesenteric ischaemia is a life threatening surgical condition with a high mortality rate. A delay in diagnosis combined with the premorbid condition of the patient is usually responsible for its poor outcome. We report a case of a 42 year old man with an acute mesenteric occlusion due to embolization from a mural thrombus.

Antimicrobial prophylaxis in elective colorectal surgery HL LEE, MF JABAR, K MOISSINAC and YA GUL

Department of General Surgery, University Putra Malavsia

Introduction: Inappropriate and prolonged antibiotic use has brought unanticipated complications including the emergence of resistance, allergy and toxicity. The aim of this study was to determine the pattern of prophylactic antibiotic administration in Malaysia in elective uncomplicated colorectal surgery. Methods: Questionnaires were distributed to 132 surgeons of specialist grade (national & private healthcare). Questions pertaining to the type, timing and duration of antibiotic administration were assessed. Audit of wound infection rate together with the presence of and adherence to specific guidelines were also determined. Published evidence was used as gold standard in analysing the data. Results: The response rate obtained was 68% (n=90). Although the literature supports the administration of a single dose of intravenous antibiotic for prophylaxis, 72% of surgeons employed more than a single dose. Six surgeons (7%) administered both prophylactic oral and intravenous antibiotics, the remainder employing intravenous antibiotics only. Thirty-nine surgeons (43%) claimed that their protocol was evidence based. Personal preference was cited in 20% of responses while 32% based their antibiotic administration policy on hospital guidelines. Only 24% of surgeons audited their wound infection rate. There was no significant difference in the antibiotic dosage regimen between national, private and university academic institutions. $X^2=0.315$ (p=0.854). Conclusions: The above results suggest that a significant proportion of surgeons administer antibiotics inappropriately in elective colorectal surgery. Personal preferences, failure in adhering to guidelines and exercising evidence based medicine and failure to filter information to support staff are likely factors in explaining this phenomenon.

Audit of patients undergoing major limb amputation at the vascular surgical unit in Hospital Kuala Lumpur

KS TAN, H HANIF and AA ZAINAL

Vascular Surgical Unit, Department of Surgery, Hospital Kuala Lumpur, Malaysia

Objective: To determine the pattern of major limb amputation at the Vascular Unit in Hospital Kuala Lumpur. **Design:** A prospective study. **Methods:** All patients who underwent major limb amputation between 1 January 2000 and 30 July 2000 at the Vascular Unit in Hospital Kuala Lumpur were included into the study. **Results:** Twenty patients underwent major limb amputation during this period. The age range was from 29 to 82 years. The median age was **56.2.The** male to female ratio was **3:1.** Fifty percent of the amputees were Malay, 40% Indian and 10% were Chinese. The indications for amputation were critical limb ischaemia, non-healing venous ulcer and vascular injury secondary to motor vehicle accident. Forty percent of these patients were referred from hospitals situated outside the Klang Valley, 20% were in-hospital referral whereas only 10% of these

cases admitted through the Casualty Department. Primary amputations were performed in 12 patients (60%). Only 40% of these patients underwent some form of revascularization for limb salvage with eventual secondary amputation. The BKA: AKA ratio was 1:1.2. Forty percent of amputees had diabetes mellitus with a similar percentage of smokers. *Conclusion:* Majority of the patients that required vascular reconstruction was referred to the Vascular Surgical Unit at the stage of advanced ischaemia. This was supported by the high rate of primary amputation.

End stage achalasia of the cardia with megaoesophagus: experience in the surgical management of 5 cases

AY JASMI and A NORLIA.

Department of Surgery, Faculty of Medicine, Universiti Kebangsaan Malaysia, **Kuala** Lumpur, Malaysia.

Background: Standard management of achalasia of the cardia includes balloon dilatation as well as a cardiomyotomy. However, when a long standing achalasia has resulted in a megaoesophagus i.e. end stage achalasia, measures other than some form of oesophageal resection will not provide good results. Aim: Review of the surgical management of 5 cases with end stage achalasia and rnegaoesophagus. Patients: Between 1995 till date, 5 cases of persistent and recurrent achalasia were referred for further management. **Results:** There were 2 males and 3 females with one Chinese and the others Malays. Their ages were 50, 47, 29, 37 and 51. All presented with a long history of dysphagia. The first 2 patients underwent repeated balloon dilatation and subsequently a Heller's cardiomyotomy. Both developed recurrent symptoms a few months after surgery. Barium swallow showed rnegaoesophagus. The 50 year old lady then underwent a subtotal oesophagectomy, however, postoperatively she developed pulmonary complications and died in ICU. The 47 year old gentleman underwent a subtotal oesophagectomy and has remained well till now. The young 29 year old man, had a failed balloon dilatation and the barium swallow showed rnegaoesophagus. He underwent a successful subtotal oesophagectomy and was discharged well. The 37 and 51 year old females both had megaoesophagus shown on barium swallow examinations and were subjected to an almost total oesophagectomy. In all cases the stomach was used as an oesophageal substitute. Conclusions: For end stage achalasia of the cardia with rnegaoesophagus, balloon dilatation or a cardiomyotomy is unlikely to succeed and oesophageal resection appears to be the most appropriate treatment.

The colonic J-Pouch

MEHESHINDER Singh, DAVARAJ Balasingh and AKHTAR Qureshi

Departments of Surgery, Hospital Seremban & International Medical University, Seremban, Malaysia.

Bowel function after an ultra low anterior resection is improved by reconstruction of a neorectum with a reservoir capacity. The aim of the study was to analyse the clinical and functional outcome in two groups of patients following a low anterior resection. Seventeen patients with a low rectal cancer, mean age (range) 57.1 (39-74) years underwent an ultra low anterior resection with a straight coloanal anastomoses. Eight other patients, mean age (range) 53.4 (42-67) with a low rectal cancer had an ultra low anterior resection with a colonic J-pouch coloanal anastomoses. All patients had a defunctioning loop ileostomy, There was no significant difference in fecal urgency in both groups at 1 and 6 months post closure of the defunctioning loop ileostomy. (no pouch=4; pouch=0) (p=n.s.). However, there was a significant difference in the number of bowel motions in a day in patients who had a straight coloanal anastomoses as compared to those with a colonic J pouch. This difference was seen only at 1 month post closure of the stoma (no pouch=5.2; pouch=2.3) (p=0.476) and not at 6 months (no pouch = 3.5; pouch=1.4) (p=n.s.). We conclude that the colonic J-pouch is superior to the straight coloanal anastomosis at 1 month post closure of stoma. At 6 months there is no difference between the two groups.

Intussusception in Seremban Hospital

SUDIRMAN A, MEHESHINDER S, DAVARAJ B, SUBRAMANI V, RAMESH J and QURESHI A

Departments of Surgery, Seremban Hospital and International Medical University, Seremban, Malaysia

Intussusception remains a leading cause of intestinal obstruction and bowel necrosis in early infancy and childhood. Less invasive procedures in the management of intussusception have recently been introduced in Seremban Hospital and we report our early experience. We retrospectively analyzed all patients presenting with intussusception to our hospital over a period of 5 years from 1995-1999. We analyzed demographic data as well as modes of management. Barium reduction was introduced to our **center** in 1997. There were a total of 43 cases with 11 patients having barium-attempted reduction as the initial treatment. The commonest age group was 6-24 months. There was a marked predominance in males with ratio 3:1, and was more common in Malays (80%). The commonest presenting symptoms were rectal bleeding (76.7%) and vomiting (83.7%). Duration of symptoms for more than 48 **hrs** and presence of small bowel obstruction were predictors for the need of bowel resection. In the barium reduction group, only 5 (45%) were successfully reduced, while the remaining 6 patients required a laparotomy. We conclude that the barium reduction of intussusception is worthwhile. We hope that with time, our success rates will further improve.

Colorectal cancer in Malaysia

SAGAP I, JAYARAMM, A GUNN, NAIDOO, M RAJ, JASIAH Z, HARBACHAN S, D LOPEZ, KT ONG, DAVARAJ B and QURESHI A

Malaysian Society of Gastroenterology & Hepatology, College of Surgeons of Malaysia

Colorectal cancer is the third commonest cause of cancer deaths in Malaysia. Data from the Ministry of Health of Malaysia confirms an increase in colorectal cancer admission rates from 8.1% in 1987 to 11.9% in 1995 (MOH 1995). We analyzed data of all colorectal cancer patients in Malaysia presenting in the year 1998. A questionnaire was sent to all hospitals in Malaysia dealing with colorectal cancer patients. Data on a total of 396 patients was collected. We analyzed the age, sex, racial distribution and location of the colorectal cancer. A summary of the data is tabulated below.

Race	n	Mean Age	% under 40 years	% under 50 years
Malay	143	54.8	12.40	27.26
Chinese	180	62.3	6.93	17.55
Indians	16	55.2	10.67	24.70
Indigenous	57	50.7	16.84	32.96

We conclude that colorectal cancer appears to be commoner in the **Chinese**, while the Malay and Indigenous people appear to present with colorectal cancer at an earlier age. Overall colorectal cancer appears to present at an earlier age in Malaysia than in published western data.

Training in colonoscopy

RAZMAN J. SAGAP I and QURESHI A

Department of Surgery, Hospital UKM, Kuala Lumpur, Malaysia

Colonoscopy is now considered to be the investigation of choice in the inspection of the colon. Both diagnostics as well as therapeutic colonoscopy, are important parts of the surgeon's armamentarium. Training in colonoscopy is an important part of the MS (UKM) programme. We analysed the **training** of MS (UKM) candidates in the art of colonoscopy. During the period of 1998 to 2000, 16 MS

(UKM) candidates rotated through the colorectal unit for a 3 month period each. The unit performed on average 20 colonoscopies per week. All candidates had been trained in OGDS. The training involved removal of the colonoscope in a minimum of five patients, followed by supervised insertion. All colonoscopies were supervised by a specialist surgeon. The results are summarised in the table below:

Colonoscopies Performed	Candidates	Considered Proficient
40-49	10	8
50-59	4	3
>60	2	1

In conclusion, the MS (UKM) colonoscopy training programme is in line with the MSGH guidelines on training in endoscopy. Mere numbers of colonoscopy procedures performed is insufficient for certification. Certification in colonoscopy must include ce cation of competence by the supervisor.

Colonoscopy in Seremban Hospital

LC TAN, MEHESHINDER S, NADESAN S, BALASINGH D and QURESHI A

Departments of Surgery, Hospital Seremban & International Medical University, Serernban, Malaysia

The investigation of choice for diseases of the colon is colonoscopy. Flexible fibreoptic colonoscopy while available in most major centers, has only recently been introduced to Seremban Hospital. With this introduction in 1996, we have analysed the initial 589 colonoscopy procedures. We looked at indications, findings and major complications of the procedure. The male to female ratio was 300:289. The racial distribution of Malays: Chinese: Indians: Others was 217:226:144:2. The completion rate was 51%, with poor bowel preparation (n=85) and obstructing lesions (n=35) being the commonest pathological causes of incomplete colonoscopy. The commonest indications were altered bowel habit (n=207), rectal bleeding (n=131) and abdominal pain (n=90). Colorectal cancer was noted in 85 patients. Other common findings included polyps (n=35), diverticula (n=34) and colitis (n=34). There were no major complications. There was no mortality. Since the introduction of diagnostic colonoscopy to Seremban Hospital, there has been a gradual increase in the colonoscopy workload, with concurrent improvement in skill, and no major morbidity.

A review of breast cancer and fine needle aspiration cytology in Seremban Hospital Paul SELVINDOSS, NADESAN S, BALASINGH D and QURESHI A

Departments of Surgery, Hospital Seremban & International Medical University, Seremban, Malaysia

Breast cancer is a common malignancy seen in Malaysia. However there is a paucity of data on breast carcinoma. We analysed a total of 64 patients who were diagnosed to have carcinoma of breast, from July 1995 to July 1999. A further 413 patients were also studied for an analysis of fine needle aspiration cytology (FNAC). Data collection was performed by reviewing patient case records and also by personal interview, Malays (n=34) accounted for the majority of breast cancer patients, followed by Indians (n=15) and Chinese (n=15). The commonest age group affected was 41 to 50 years. The absolute sensitivity of FNAC was 69.8% and complete sensitivity was 98.4%. The specificity of FNAC was 81%. Mastectomy with axillary clearance was the commonest surgical procedure and chemoradiotherapy the commonest adjuvant therapy. Breast carcinoma is a common malignancy seen in Seremban Hospital. FNAC is a good diagnostic modality due to its high sensitivity and specificity.

Effectiveness of radio message to increase early antenatal checkup Lei Hua CHANG

Jabatan Kesihatan Negeri Sarawak, Malaysia

Pregnant women coming late for their first antenatal checkup is high (82.6%) at Klinik Kesihatan Ibu dan Anak Miri. Health education talks were given irregularly in the clinics on the importance of coming early for antenatal checkup. Many years back, the pregnant women were advised to register only after 20 weeks of pregnancy. It was only in the early 1990's then the women were advised to come for antenatal checkup before 12 weeks of pregnancy. The objective of the study is to evaluate the effectiveness of radio message as an intervention to increase the percentage of pregnant women coming early for antenatal checkup. This is a Quasi-Experimental Study where we compare nonrandomised control group (KKIA Bintulu) and the experimental group (KKIA Miri). Convenience sampling was used. A total of 800 pregnant women (400 from KKIA Miri and 400 from KKIA Bintulu) who came for their first antenatal checkup were interviewed using structured questionnaires during the pre and post intervention. Intervention was carried out by introducing health education through local radio regarding the importance of antenatal checkup before 12 weeks to the population in Miri for a period of one month. The findings showed that in Miri before intervention, the working women came early for their first antenatal checkup compared to housewives who came early after the intervention. Ignorance was the main reason why the pregnant women came late for their checkup which showed clinical significance decrease after the intervention. This study revealed that radio message may not be one of the most effective measures to create awareness on the importance of early antenatal checkup. The uses of other methods and allowing more time for intervention might achieve optimum results.

Implementation of clinical practice guidelines on the care and management of Diabetes Mellitus Type II

SAFIAH Bt Salleh

Hospital Batu Pahat, Johor, Malaysia

It was found that the number of admissions of diabetic patients is high in Hospital Batu Pahat. This prompted the group to study the implementation of health education aspect on the Clinical Practice Guidelines in the care and management of Diabetes Mellitus Type II in that hospital. The method used for the study is a descriptive cross-sectional based on three components. The study was conducted for three months i.e. from the middle of November 1999 till middle of January 2000. Firstly, is on the availability and accessibility of the CPG book to the doctors and paramedics in the Medical and Surgical wards of the hospital. This was done through a drafted checklist. Secondly, is on the extent of knowledge patient gained from receiving health education given by health personnel using the CPG book. All diabetic patients aged between 18 to 80 years old admitted during the three months period were interviewed using structured questionnaires. Thirdly, is to evaluate the extent of usage of the CPG by nurses working in the **Medical/Surgical** wards selected for the study. This was done through self-administered questionnaires on completion of the study on the patients. From the study it was found that the CPG book was available in 3 out of the 5 wards. Only 28.8% of the 64 patients interviewed received full health education on topics listed in the CPG Diabetes Mellitus Type II. The result was very unsatisfactory which contributes to factors such as language barrier, poor understanding and others. 50% of the Staff Nurses were not using the CPG book when giving health education to the patients due to time constraint, unavailability, unaware and no proper training. Therefore it is recommended that a proper place should be identified to keep the CPG book so that it will be available and accessible at all times. Uncontrolled diabetic patients are referred to the Diabetic Clinic for appropriate health education to be given by trained personnel. Training of all Staff Nurses on the usage of CPG book is also recommended so that they will have a sound knowledge when giving information to the patient.

Study of knowledge, practice and proficiency towards breast self-examination (BSE) among women attending child health clinic and antenatal clinic at Klinik Kesihatan Bota Kiri, Perak Meng HOOK

Pejabat Kesihatan Kinta, Perak, Malaysia

The purpose of this study is to determine the knowledge, practice and proficiency among women towards breast self-examination (BSE). The specific objectives are to:- (1). Determine the level of knowledge among women regarding risk factors in breast cancer, (2). Determine the level of knowledge regarding BSE, (3). Determine the practice of BSE. (4). Identify the reasons for not complying with the recommended interval. (5). Determine the level of proficiency in performing BSE, (6). Correlate knowledge of BSE to actual practice. During the one-month period, there were four antenatal and child health clinic sessions where total data 50 were collected. (Women who have been taught about BSE). The analysis of data was based on:- (1). The relationship between sociodemographical characteristics (age and educational level) and the score from the knowledge, frequency and proficiency of BSE, (2). The relationship between knowledge and the practice of BSE, proficiency level and practice at recommended interval. The study has demonstrated that about half of the respondents have good knowledge of BSE. However, only 2% have good knowledge of breast cancer risk factors. The number of participants who performed in the preceding 12 months is 96%. Although reported performance is high, it is sad to note only 18% of the respondents performed BSE monthly at recommended interval, 70% just performed occasionally and 4% never practiced and 8% practiced more that once a month. The reason for not complying with the recommended interval is that they have forgotten. Only 10% of them have good level of proficiency of BSE. 48% had moderate score while 42% had poor score. Hence, it can be concluded that the women who participated in the study are not performing BSE satisfactorily in terms of frequency and proficiency. In order to improve this situation, nurses are required to emphasize more on effective teaching of BSE. Meanwhile, BSE must be advocated as a self-care habit for women which may help to save their lives in future years through early detection and intervention of breast cancer.

Integrated Daily Clinic System SITI ZUHAIDA Binti Hussein

Putrajaya Health Clinic, Malaysia

Sepang was the first district in Selangor to introduce the "Integrated Daily Clinic System" (IDCS) since March 1998. Its introduction was the initiative of the management with the intention of improving certain quality of healthcare services and optimizing the utilization of human resource. With this system, all health services are made available on all days for the whole family. It involves the rescheduling of all clinic sessions of maternal and child health services where appointments are given from Monday till Friday. Other than the emergency and new cases, follow-up appointments are given according to the client preference and health needs. The workload is equally distributed throughout the week and no overcrowding of client at any clinic day. Through this system, it facilitates the maximum utilization of manpower. It improves the rescheduling of the staff roster and work process. Finally, it aims to give a better client and staff satisfaction based on The Eight Health Service Goals.

Quality of life in the elderly ZAHRAH Saad

College of Nursing Melaka, Malaysia

Aging is not simply a later life but a life-long event from the time of birth to infancy, childhood, adolescence and adulthood. This can be seen from the increase in the percentage in the proportion of the elderly in the total world population. Vital statistics also shows that by the year 2000, the world

population of elderly will have grown to 600 million with an increase in the life expectancy. Like any other developing countries, Malaysia's population has also been affected by an increase in the aging population. This existing and impending large number of elderly people has led to the need to plan programmes for their future physical, mental and social well-being. However, these programmes are still at the infancy stage because of the existing extended family structure. This study on the quality of life in the elderly was conducted in 1997 in an urban area in Mergong, Kedah with 400 participants using questionnaires and interviews. Here, the researchers will like to share her findings, which were conclusive at that time. However, more research need to be carried out to ensure that the elderly have access to the comprehensive health care services and at the same time to involve the community in the care and rehabilitation of the elderly in the near future.

An exploration of the factors influencing willingness to leave home for continuing education Goot Kooi WONG

Kolej Kejururawatan Alor Setar, Malaysia

This survey study was designed to explore the factors influencing a group of staff midwives' willingness to leave home for continuing education. The sample consisted of 15 staff midwives from the hospital 'X' in Northern Peninsular Malaysia. The research used quantitative and qualitative data collected by questionnaire method. The data revealed similar results to the existing literature regarding the factors influencing continuing education. Majority of the staff midwives supported professional and personal factors as the relating reasons. However, minority of them disagreed on some of these factors. The problems cited by them were personal factors such as accommodation, family commitments, age, monetary, transport and transferable after the course. The results were discussed in relation to various studies done. Limitations of the study were identified. Implications for the CPE were noted and some recommendations were proposed.

Penilaian tahap jaundis neonatal dikalangan bayi-bayi baru lahir di Daerah **Bentong** Ah Eng SEE

Pusar Kesihatan Daerah Kuantan, Pahang, Malaysia

Jaundis bagi bayi baru lahir adalab satu masalah yang sering berlaku dikalangan bayi pada minggu pertama kelahiran. Adalah dianggarkan sebanyak 75% daripada bayi yang baru lahir akan mendapat jaundis ini temasuk fisiologikal dan patologikal jaundis. Keadaan jaundis yang temk akan melibatkan komplikasi kekal termasuk kecacatan otak dan anggota. Ini boleh dielakkan dengan pengesanan jaundis diperingkat awal. Di daerah **Bentong**, kejadian jaundis neonatal yang **teruk** adalah masalah yang serius kerana terdapat kejadian jaundis neonatal yang temk adalah tinggi dan menunjukkan peningkatan. Kumpulan HSR Negeri Pahang menyedari ibu-ibu di daerah Bentong kurang kesedaran tentang jaundis neonatal. Untuk mempertingkatkan pengetahuan dan kesedaran dikalangan ibu-ibu hamil terhadap jaundis neonatal 2 buah klinik telah terlibat dalam kajian ini iaitu Kinik Kesihatan Bentong sebagai kumpulan intervensi manakala KK Karak adalah kumpulan kontrol. Saiz sampel bagi KK Bentong adalah 100 ibu hamil dan 93 ibu hamil bagi Kimik Karak. Semua ibu ditemurah dengan menggunakan soal selidik. Kajian ini menunjukkan 49% ibu di KK Bentong terdiri daripada kaum Cina dan di KK Karak 32.2% kaum India. Di Bentong mempunyai lebih banyak kampung baru Cina manakala di Karak, terdapat banyak ladang dan pekerjanya terdiri dari kaum India. Kajian ini menunjukkan kumpulan intervensi selepas diberi ceramah secara intensif, 100 responden dari KK Bentong dapat mengenalpasti sekurang-sekurangnya 1 tanda jaundis dan membawa bayi mereka ke hospital untuk menjalankan ujian serum bilirubin. Manakala di KK Karak, 59.1% ibu dapat mengenalpasti sekurang-kurangnya 1 tanda jaundis dan 31.1% ibu boleh mengambil tindakan yang betul. Daripada kajian ini, adalah dicadangkan supaya pendidikan kesihatan yang lebih kerap dan cara-cara yang telah digunapakai dapat diimplementasikan kepada semua ibu-ibu di daerah Bentong dan disemua kemudahan kesihatan di Negeri Pahang.

Amalan perancang keluarga di kalangan ibu berisiko tinggi di Hulu Terengganu LIJAH Abdullah

Jabatan Kesihatan Negeri Terengganu, Malaysia

Amalan perancang keluarga yang berkesan masih merupakan masalah yang besar di daerah Hulu Terengganu. Pada tahun 1999, 6 kematian ibu bersalin telah berlaku di daerah ini. Dari bilangan tersebut 5 darinya adalah dari gulungan ibu-ibu berisiko tinggi dimana hanya seorang sahaja yang pernah mengamalkan perancang keluarga. Kajian ini dilakukan di daerah Hulu Terengganu untuk mengkaji sebab-sebab ibu berisiko tinggi tidak mengamalkan perancang keluarga. Seramai 200 pasangan ibu berisiko daripada semua klinik kesihatan diseluruh daerah ini telah dipilih sebagai sasaran, Pilihan dilakukan secara persampelan sistematik (sistematic sampling). Borang soal-selidik digunakan sebagai alat untuk mengutip data. Borang-borang yang berlainan antara suami dan isteri diedarkan untuk diisi sendiri oleh mereka, kemudianya dikutip semulla oleh pemungut data yang terdiri dari jururawat dan Pengawas Kesihatan Awam. Borang-borang tersebut dibentuk berdasarkan dari hasil perbincangan kumpulan **berfokus** (Focus Group Discussion) yang telah dilakukan di daerah Hulu Terengganu dan Kuala Terengganu. Hasil kajian telah mendapati 26% sahaja ibu-ibu tersebut yang mengamalkan perancang keluarga secara berkesan. Pengetahuan tentang konsep sebenar perancang keluarga **amat** rendah dikalangan ibu-ibu **ini** dan pasangan masing-masing menyebabkan mereka tidak mengamalkan perancang keluarga. Berbagai alasan yang telah diberikan untuk tidak mengamalkan malah 27.5% dari suami memberi alasan sebagai pil yang dimakan tidak hancur, 12% - 13.5% suami dan isteri mengatakan yang ia dilarang oleh agama, 4.5%-14% suarni dan isteri mengatakan mereka mahu anak ramai, 24.5% dari isteri pula takut kesan sampingan dan 24.5% lagi isteri mengatakan mereka dilarang oleh suami atau mertua. Jarak rumah ke kemudahan kesihatan, kemudahan pengakutan dan taraf pendidikan mereka tidak memberi pengaruh kepada mereka untuk mengamalkan perancang keluarga. Ini telah didapati dimana 68.6% ibu-ibu ini tinggal kurang dari 2 km dari kemudahan kesihatan, masih tidak mengamalkan manakala sejumlah 45.8% yang menpunyai kenderaan sendiri juga tidak mengamalkan perancang keluarga. Walaupun suami-isteri ini mempunyai pendidikan, mereka masih tidak mengamalkan. Dari aspek komunikasi, didapati sejumlah 75.6% pasangan yang mengamalkan pernah berbincang tentang perancang keluarga manakala hanya 49.1% pasangan yang tidak mengamalkan pernah berbincang tentang ini. Kesimpulannya, pengetahuan yang jelas tentang konsep sebenarnya perancang keluargadan pentingnya perbincangan antara suami-isteri mengenal perkara ini adalah antara faktor-faktor terpenting dalam amalan perancang keluarga bagi ibu-ibu berisiko tinggi, di daerah Hulu Terengganu. Oleh itu satu strategi yang baik hendaklahdibentuk, seterusnya dilaksanakan sepenuhnya untuk memberi penjelasan dan pendidikan kepada komuniti supaya amalan ini dapat dipertingkatkan.

Tinjaun ke atas pendapat ''local preceptors'' dan segi beban kerja dan kepuasan dalam penglibatan latihan klinikal

RAHMAN A Razak

Jabatan Kesihatan Negeri Kedah, Malaysia

KKM memperkenalkan program "Local **Preceptor" pada** tahun 1997, **iaitu** sejak adanya latihan Pendidikan Jarak Jauh di kalangan jururawat. Program ini di wujudkan di semua hospital yang ada pelatih PJJ termasuk di Hospital Alor Setar dan Hospital Petani. Walaupun program ini **baru** tiga tahun di perkenalkan tetapi **sering** terdengar **rungutan** dikalangan "Local Preceptor" yang merasakan tidak puashati kerana **beban** kerja yang bertambah. Oleh yang demikian satu kajian telah di buat untuk meninjau pendapat mereka **tentang** program ini. Rekabentuk kajian adalah 'descriptive **cross**-sectional' dengan menggunakan 'self administered questionnaire' kepada semua 60 orang 'Local Preceptor' dan kedua-dua hospital. Hasil kajian didapati 70% dan respondan adalah berbangsa Melayu dan lebih kurug 51.2% daripada mereka ini berumur 46 tahun keatas. Telah didapati 68.7% respondan telah bertugas sebagai 'Local Preceptor' lebih dari 3 tahun. Dan segi **beban** kerja 61% daripada 'Local Preceptor' telah menyelia 6 dan lebih pelatih pada sesuatu masa dan hanya 39% menyelia kurang daripada 6 orang pelatih pada satu masa.

Do nurses possess mathematical proficiency?

FAIZAH bt Mohd Ghazali

College of Nursing Ipoh, Perak, Malaysia

No function in nursing is more important than safe administration of drugs. It demands both accuracy and care. Therefore this study was set to look into the computation skills in drug dosages calculation among registered nurses in Hospital Ipoh. The study also sought to examine the correlation between computation performance and the predictors: age, pre entrance mathematical score, and years of experience. Twenty-six registered nurses were selected for the study using convenience random sampling. The qualitative and quantitative data were collected using a set of questionnaire. The questionnaire consists of three parts: personal particulars of respondents, respondents' behaviour towards error, and test on computation. The computation test composed of multiplication, conversion and problem solving. The results were analysed by mean of percentage, frequency, mean and beta value. The results revealed that conversion errors were major. Personally nurses revealed that they have done drug errors before. The results also revealed that there was a significant relationship between poor performance in computation and pre entrance mathematics score.