

The International Congress of Pathology & Laboratory Medicine 2018: Frontiers in Diagnostic Pathology, organised by the College of Pathologists, Academy of Medicine of Malaysia and was held at Connexion Conference & Event Centre – The Vertical at Bangsar South on 28-30 June 2018. Abstracts of K. Prathap memorial lecture, plenary, symposium and paper (poster) presented are as follows:

K. PRATHAPMEMORIALLECTURE: EVOLUTIONANDADVANCEMENT OF BREAST CANCER MANAGEMENT: THE PATHOLOGIST’S CONTRIBUTION

Jane Dahlstrom

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Anatomical Pathology at ACT Pathology, The Canberra Hospital*

Breast cancer management is an inevitable intertwining between multiple disciplines. Pathologists remain largely responsible for making the diagnosis that determines a patient’s management and prognosis. Simple morphology based classifications and tumour grading are now being complemented by exploration of disrupted cell pathways with the use of immunohistochemistry and molecular techniques that enable us to better predict cancer progression and response to treatment. This talk will explore how our understanding of breast cancer has evolved and how this has been central to the evolution and advances in breast cancer management.

PLENARY 1: RISK ASSESSMENT

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Risk management is defined as ‘the systematic application of management policies, procedures and practices to the tasks of analysing, evaluating, controlling and monitoring risk’ (*ref: ISO*). Healthcare organisations have a responsibility to ensure the health and safety of their staff and their patients. Risk assessment is an integral part of an organisation’s occupational health and safety management plan and enables organisations to make an informed decision on the necessary measures needed to eliminate or minimise the risk of harm to those who may be affected.

Risk assessments should be done before new processes or activities are introduced and before changes are introduced to existing processes or activities. A risk assessment involves risk identification (recognition of hazards and risk factors), risk analysis and evaluation (assessment and characterisation of the hazards and determination of the level of risk) and risk control (determination of appropriate ways to eliminate the hazard or control the risk when the hazard cannot be eliminated). Once the risks have been identified, the organisation must implement control processes as well as continuously monitor and modify them, to ensure that risk is maintained at a clinically acceptable level.

Clinical laboratory tests must be accurate and reliable as they account for over 70% of medical decisions. In the clinical laboratory, errors can occur at any stage in the laboratory testing process and harm can occur to patients, laboratory staff and hospital staff. Clinical laboratories must conduct a comprehensive risk assessment to identify vulnerabilities in the pre-analytical, analytical and post-analytical aspects of laboratory testing. Guidelines from agencies such as the Clinical and Laboratory Standards Institute (CLSI) are available to assist clinical laboratories on risk assessment, including how to develop, implement and maintain a quality control plan for medical laboratory testing, so as to mitigate potential errors that can occur during the laboratory testing process.

PLENARY 2: THE BIOLOGICALAND CLINICAL SIGNIFICANCE OF STROMAL-EPITHELIAL INTERACTIONS IN BREAST CANCER

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There is increasing evidence that an aberrant tumour microenvironment facilitates cancer development, progression, and responses to treatment. This talk discusses recent advances in our understanding of how cancer epithelial cells interact with their microenvironment and how this knowledge can be exploited clinically.

PLENARY 3: VIRAL HEPATITIS: THE WAY FORWARD

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Medical Microbiology Department, University of Malaya Medical Centre.

In 2015, the global prevalence of HBV infection was 3.5% with 257 million living with HBV infection. Most of the burden of disease from HBV infection comes from infections acquired before the age of 5 years. Since the availability of the HBV vaccine in 1982, it has been 95% effective in preventing infection and the development of chronic disease and liver cancer. When the World Health Assembly recommended the inclusion of hepatitis B vaccine in the EPI in 1992, coverage in infants increased from 1% in 1990 to 84% in 2015. In a continuous effort to further improve seropositivity and compliance, new HBV vaccine formulations have been produced. With regards to management of chronic hepatitis B patients, serum HBsAg quantification is increasingly being used to predict disease activity and monitor treatment response in chronic hepatitis B. Even so, it is not a substitute for HBV DNA. With improved understanding of the relative roles of cccDNA and integrated HBV DNA, new light has been shed on the interpretation of HBsAg levels in different phases of chronic hepatitis B. The recent ability to measure serum Hepatitis B core related antigen (HBcrAg) also allows one to monitor the natural course of chronic HBV infection and possibly predict HBeAg seroconversion.

With regards to hepatitis C in 2015, an estimated 71 million persons are chronically infected, with an overall global prevalence of 1.0%. The continuous evolution of screening tests for HCV infection has now resulted in the availability of the 4th Generation assays that detect both anti-HCV and HCVcAg. The assays helped increase the sensitivity and shorten the window period between onset of HCV infection and detection of anti-HCV by almost one week. However, these assays cannot differentiate HCV exposure from chronic HCV infection. The use of HCVcAg test alone may also be applied as a one-step screening test since HCVcAg appears earlier than anti-HCV. With regards to the future use of HCV genotyping, the 2016 WHO Hepatitis C treatment guidelines still provide recommendations on the preferred and alternative DAA regimens by HCV genotype. However, as pangenotypic regimens become more readily available, genotyping may no longer be required.

Despite these recent advances, many who are infected with HBV and/ or HCV remain unaware of their infection & therefore frequently present with advanced disease & may transmit infection to others. The key reasons for the low rate of hepatitis testing include: limited facilities or services for hepatitis testing; lack of effective testing policies or national guidelines; complex diagnostic algorithms; and poor laboratory capacity & quality assurance systems. Even with scaled-up interventions, mortality due to viral hepatitis still increased by 22% from 2000 to 2015. Hepatitis B and C account for 96% of all hepatitis mortality. Thus, in 2016, the World Health Assembly endorsed the Global Health Sector Strategy on viral hepatitis 2016-2021 that calls for the elimination of viral hepatitis as a public health threat by 2030 by reducing new infections by 90% and mortality by 65%.

PLENARY 4: FROM DNA TO MOLECULAR MEDICINE - GENE THERAPY IS NOW

John Rasko AO

Sydney Medical School, University of Sydney. Gene and Stem Cell Therapy Program, Centenary Institute. Cell & Molecular Therapies, Royal, Prince Alfred Hospital, Sydney.

The field of genetics originally provided insights into disease pathogenesis. More recently genomic medicine has facilitated improved prognostication, reproductive choices and therapeutic drug options. The challenge of realising the full potential of genetic understanding has been in overcoming the hurdles of efficient gene therapy. Since the first human clinical trial using gene technology in 1989, there have been over 2400 approved clinical trials worldwide. A few dozen clinical trials have been undertaken in Australia representing just over 1% of the trials worldwide. The overwhelming majority of human clinical trials involves short-term gene expression or random integration of a therapeutic gene. Emerging technologies require controlled development in compliance with safety, regulatory and GMP requirements.

More precise gene targeting tools were first described in the early 2000s. Targeted gene editing or replacement using Zinc Finger Nucleases or TALENS have been tested in about a dozen clinical trials since 2009. These include attempts to delete the CCR5 protein on T cells (completed 2015+) and therapeutic ZFN-mediated genome editing in mucopolysaccharidosis (recruiting 2016+) and the haemophilias (recruiting 2016+). The pace of clinical development has accelerated over nearly three decades of gene therapy. However within this context, it's worth noting that the first ever (controversial) use of CRISPR to delete PD-1 in a lung cancer patient was administered in October 2016.

Highlights in the clinical gene therapy field will be discussed with special reference to haemophilia, thalassemia, blindness and cancer.

PLENARY 5: SCIENCE AND THE COURT OF LAW

Roger Byard

University of Adelaide, Forensic Science SA in Adelaide

Numerous problems arise in the assessment of inflicted trauma as there is often little reliable experimental data to help in evaluating cases. Clinical manifestations may be nonspecific and histories may be unreliable and are often designed to protect the perpetrator rather than to provide a clear explanation of the events leading to the injury or death. This means that cases of inflicted trauma that present to court are among the most challenging, particularly in terms of determining mechanisms, predisposing factors, time frames and the degree of force involved.

Involvement of forensic pathologists in experimental work in the laboratory may, however, be one way to answer some of these questions. Examples that will be discussed include i) the development of an anaesthetized sheep model of traumatic brain injury which has enabled the rapid assessment of intracranial pressure and brain oxygenation following closed head injury, and ii) the demonstration of markedly reduced cerebral free magnesium concentrations after blunt cranial trauma in alcohol-intoxicated rats.

The first study shows such a rapid alteration in intracranial pressure following blunt head trauma that a “lucid interval” would seem unlikely. The second model confirms that moderate to severe alcohol intoxication may predispose the brain to a worse outcome following injury by reducing brain free magnesium levels. Both of these studies and other research that will be discussed have provided very useful data to assist courts in evaluating particular features in cases of trauma, and other forensic issues.

PLENARY 6: INVESTIGATING HAEMOSTATIC DISORDERS IN THE DIGITAL AGE

Michael Laffan

Department of Haematology at Imperial College, London, UK. Hammersmith Hospital Haemophilia Centre.

For many years the diagnosis and management of haemostatic disorders has relied on phenotypic characterisation in the coagulation laboratory. This has generally been successful for the major disorders such as haemophilia and the platelet disorders such as Glanzmann’s thrombasthenia which have easily identified phenotypes. However, there are many limitations to this approach. Firstly, in disorders such as VWD and dysfibrinogenemia, the phenotype may be difficult to adequately capture due to limitations of the tests. Secondly, many molecules active in coagulation, such as tissue factor, and thrombomodulin, are not easily accessible by analysis of blood samples. Thirdly, the complexities of platelet production and function are not revealed by standard platelet function analyses. This is particularly problematic because it exposes patients to the risk of inappropriate treatment due to misdiagnosis as ITP or failure to recognise important syndromic features such as renal failure and risk of malignancy.

Digital technology has allowed the application of new sequencing techniques to haemostatic disorders to both complement and in some cases supersede laboratory testing. This is exemplified by the UK NIHR Bioresource Rare Bleeding and Platelet Disorders project (BRIDGE-BPD) which has applied a combination of systematic phenotyping, a Thrombogenomics array of 79 Tier 1 coagulation-active genes and whole exome/genome sequencing to address these problems. This has been successful in identifying novel BPD genes (including *RBM8A*, *NBEAL2*, *SRC*, *DIAPH1*, *TPM4*, *ABCC4* and *KDSR*) and extensively replicating abnormalities in BPD gene discoveries by other groups (*C6ORF25*, *CYCS*, *RNU4ATAC*, *STIM1*, *RASGRP2*, *ETV6*, *ACTN1*); providing a genetic diagnosis for a significantly larger group of patients. All results are reported after MDT review using algorithms for prioritising of variants. Results are made public by depositing in ClinVar to support the improvement of reference catalogues.

SYMPOSIUM

1A: DESMOPLASTIC SMALL ROUND CELL TUMOUR: IMMUNOHISTOCHEMICAL AND MOLECULAR PROFILES

Tan Geok Chin

Department of Pathology, Universiti Kebangsaan Malaysia

Desmoplastic small round cell tumour (DSRCT) was first described by Drs Gerald and Rosai in 1989. It is a rare, highly aggressive, intraabdominal, poorly differentiated malignant neoplasm that predominantly affects children and young adults. There is a male predominance. Most do not survive more than 3 years after diagnosis. Extra-abdominal cases have been reported. Its immunohistochemical profile is unusual with co-expressions of epithelial, mesenchymal, myogenic and neural markers. Histologically, it composed of undifferentiated small round cells with a desmoplastic background and could be confused with Ewing sarcoma, blastemal predominant Wilms tumour, alveolar rhabdomyosarcoma and neuroblastoma. Due to the unusual immunohistochemical characteristic and similar morphologic features with other childhood tumours, it can be a diagnostic challenge. Recently, the WT-1 amino-terminus and carboxy terminus antibodies have been shown to be able to distinguish DSRCT from Ewing sarcoma and Wilms tumour. DSRCT typically shows a selective positivity towards WT-1 carboxy-terminus, while WT-1 amino-terminus is negative. In contrast, Ewing sarcoma is both WT-1 amino and carboxy terminuses negative, and Wilms tumour is both WT-1 amino and carboxy terminuses positive. The typical gene rearrangement in DSRCT is the translocation EWS1-WT1: t(11;22)(p13;q12).

1A: FORENSIC ASPECT OF NEONATAL DEATH

Khairul Anuar Zainun

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Losing a neonate unexpectedly at a very tender age is a loss of no other. The death is devastating and tragic to the parents and communities. The grief may last forever.

Sudden and unexpected neonatal death in many jurisdictions around the globe warrants a proper and thorough investigation. Investigating process by relevant authorities may vary depending on different aims and requirements of respective laws of the land. More often than not, this investigating process involves performing postmortem examination, an important procedure where pathologists can play a crucial role. In Malaysia, the Inquiries of Death of the Criminal Procedure Code (CPC) is the main law that outlines thorough investigation process of sudden, unexpected death including death of neonates. Like in sudden, unexpected death of adults, the most important aim of the law is ascertainment of the cause and manner of death. Postmortem examination whenever required is performed towards answering various inherent forensic issues of each case.

One of the most common forensic aspects of neonatal death requiring postmortem examination by the investigating authority is establishing the medical cause of death for sudden, non-suspicious cases. This approach is also in line with the need to address preventable deaths as recommended by World Health Organization (WHO). Other challenging issues are associated with fatal abuse, potential livebirth and neonaticide, medical negligence, concealment of birth in abandoned body and neglect. These issues invariably related to other common laws namely Penal Code and Child Act 2001.

1A: OCULAR PATHOLOGY: BEAUTY IS IN THE EYE OF THE BEHOLDER.

Wan Azura Wan Yaacob

Anatomic Pathology Unit in Hospital Selayang, Malaysia

The talk will cover a potpourri of interesting Ocular Pathology cases seen in Hospital Selayang. These cases range from inflammation, benign lesions, corneal dystrophies to tumours.

1B: CHALLENGES AND PERSPECTIVES OF EXPANDED NEWBORN SCREENING IN MALAYSIA

Ngu Lock Hock

Genetics Department, Hospital Kuala Lumpur

Inborn errors of metabolism (IEMs) are phenotypically and genetically heterogeneous disorders caused by defects in cellular metabolism. Some IEMs are amenable to treatment, with promising outcomes: among them are amino acid and organic acid disorders and fatty acid oxidation defects. Population-based neonatal screening of IEM has become a mandatory public health strategy in most developed and some developing countries due to the advancement of the analytical technology. Early diagnosis allows pre-symptomatic treatment that is crucial in preventing morbidity and mortality. Between June 2006 and December 2008, 30,247 newborns from 11 major public hospitals in Malaysia were screened for 27 inborn errors of amino acid, organic acid and fatty acid metabolism in a pilot study. The detection rate of IEMs in this study was one in 2,916 newborns. This study provided sufficient scientific evidence for the implementation of expanded newborn screening in Malaysia. However, this is yet to be a reality due to the many challenges and obstacles. The currently existing newborn screening programme of G6PD deficiency and hypothyroidism utilises cord blood. We therefore need a new/concurrent system if we want to implement expanded newborn screening programme. Due to the lack of awareness and knowledge among the general public, health professionals and policy makers, expanded newborn screening programme is often not viewed as a priority among many competing health initiatives.

1B: EXPERIENCE IN ESTABLISHING REFERENCE INTERVAL FOR PEDIATRIC AGE GROUP

Loh Tze Ping

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The clinical utility of quantitative laboratory results is an exercise of comparison. In the case of diagnosis, the result of a patient is compared against certain reference values. For monitoring, the patient result is compared to her past results for trending. Reference intervals describe the percentile limits of a reference population. They are used to inform clinicians of results that deviate significantly from the reference population, and have increased probability of disease. In other words, they flag 'abnormal' results. Reference intervals are critical interpretative tools that must accompany any quantitative laboratory results for clinicians to make clinical judgement. Derivation of paediatric reference intervals is an area of high activity in laboratory medicine. Nevertheless, they are challenging to derive directly from healthy children given the operational, ethical and resources required to perform such activity in this unique population. In this talk, we will explore the different approaches that are used to obtain paediatric reference intervals, including the direct approach and indirect approach. We will also discuss some global initiatives in this area.

UPDATES ON PAEDIATRIC LABORATORY MEDICINE

A child is not a small adult. Children are wonderful beings that grow, develop and adapt to their environment rapidly. In a short span of their life, they grow from being totally dependent on others for daily living to being fully independent by adolescence. Along this journey, there are illnesses and diseases that can threaten their healthy growth and maturation. These conditions include infectious diseases and inherited disorders. In this session, we will examine some of the recent advancements in technologies such as next-generation sequencing and mass spectrometry laboratory techniques, and how they are being applied in paediatric laboratory medicine to advance the care for this precious population.

1B: MARKERS OF NEONATAL SEPSIS

Julia Omar

Department of Chemical Pathology, Hospital Universiti Sains Malaysia, Kubang Krian, Kelantan, Malaysia.

Neonatal sepsis is a major cause of neonatal deaths. Early diagnosis is essential to reduce morbidity and mortality. Although isolation of the causative microorganisms by blood culture has been the golden standard method for its diagnosis, the result is ready only 24-72 hours after the sampling. Various hematological indices had been utilized to screen for sepsis, most were neither highly sensitive nor specific. A number of biomarkers have been studied for the diagnosis but no gold standard has been identified. The properties of an ideal diagnostic biomarker include excellence in sensitivity and negative predictive value as well as excellent specificity and positive predictive value. Biomarker levels should change early in the disease course and remain altered for a period of time, to give an opportunity for clinicians to measure these biomarkers to optimize clinical management, monitor disease progress, and guide antimicrobial treatment.

Biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), haptoglobin, fibrinogen, proteomic markers in amniotic fluid, inflammatory cytokines (including interleukin 6, interleukin 8, and tumour necrosis factor α), and cell surface markers (including soluble CD14 subtype [presepsin], and neutrophil CD64) were studied to detect early onset of sepsis among neonates. Any other recent developments? Several steps are still needed to facilitate the use of biomarkers: the harmonization of protocols and the formulation of the use in single or multiplex format. In -spite of these developments, identifying a biomarker for neonatal sepsis still remains a challenge.

1C: DIAGNOSTIC APPROACH TO PAEDIATRIC THROMBOSIS

Paul Monagle

Department of Paediatrics and Paediatric Haematologist, The University of Melbourne, Royal Children's Hospital.

This will be a case based discussion of the relevant diagnostic strategies for a variety of common paediatric thrombosis. Use of the appropriate imaging modality is critical to minimise both false positive and false negative diagnosis. In addition the role of blood test such as D dimers and thrombophilia assays in paediatric thrombosis will be discussed.

DIAGNOSTIC CHALLENGE IN PAEDIATRIC BLEEDING DISORDERS

Acquired bleeding disorders in children are common and include vitamin K deficiency, disseminated intravascular coagulation, liver disease and massive transfusion to name a few. This talk will discuss the Interpretation of laboratory tests and how to use tests to guide therapy. Clinical assessment of the patient remains a critical tool.

1C: NEONATAL SEPSIS

Zurina Zainudin

Neonatal Intensive Care Unit, Hospital Serdang

Neonatal sepsis is a term used to designate a systemic bacterial infection within the first 4 weeks of life. It is the substantial cause of morbidity and mortality among the neonatal population. Despite the advanced in neonatal care, neonatal sepsis continues to be a common and significant healthcare burden, especially in very low birth weight infants (birth weight < 1500g). The incidence varies between high-income compared to low and middle income countries.

Neonatal sepsis has been classified as either early or late onset depending on the age of onset and timing of the sepsis episode. These also implies the different in the presumed mode of transmission and predominant organisms. Early onset sepsis is defined as onset of sepsis within the first 72 hours of life. It is most often results from the vertical transmission of bacteria from mother to infants during the antenatal or intrapartum period. The most common organisms associated with early onset neonatal sepsis are Group B streptococcus and *Escherichia coli*, with the latter being the major pathogen in premature infants. Clinical manifestation of late onset sepsis usually appear after 72 hours of life and is mainly associated with organisms acquired from the ex-utero environment such as coagulase-negative staphylococci.

The clinical manifestations of neonatal sepsis are non-specific ranges from subclinical to severe manifestations of focal and systemic disease. Clinically, it is almost impossible to differentiate symptoms and signs caused by sepsis and that is caused by other systemic illnesses. Therefore early diagnosis and prompt treatment for neonatal sepsis remains a challenge.

2A: MOLECULAR DIAGNOSTIC PATHOLOGY –THE MALAYSIAN EXPERIENCE

Pathmanathan Rajadurai

Sime Darby Medical Centre, Subang Jaya.

The implementation of molecular techniques as part of the diagnostic armamentarium of the practising pathologist has been a recent transformative event. It has become clear that the 21st century tissue pathologist must recognise and actively participate in extracting as much information as possible from patient material that rises far above conventional light microscopy. The uncovering of molecular mechanisms that underpin the pathogenesis of disease (especially neoplasia), and the development of precision medicine and targeted therapy has necessitated this development. Although molecular laboratory techniques have been deployed for a long time as part of research initiatives in the public and private sectors, and some molecular diagnostic analyses have been outsourced overseas, the establishment of a local molecular diagnostic services in Malaysia has been a relatively recent development.

Recognising the need to meet these diagnostic challenges, a molecular diagnostic facility was setup in the Subang Jaya Medical Centre about 20 years ago. The challenges of establishing, maintaining and continuing to stay abreast of the rapidly changing frontiers of such a high-end service will be presented.

2A: MOLECULAR & GENETIC BASIS OF SUDDEN DEATH

Roziana Ariffin

Genetic Lab, Dept of Genetics, Hospital Kuala Lumpur.

Sudden and unexplained death may be the first appearance and a premier indication of an unidentified hereditary cardiac disease. Research endeavors showed that cardiac disease is one of the biggest and a paramount cause of sudden death notably in 40 years old and above group. While coronary heart disease compounded with genetic factors, environmental and lifestyle are the most common causes of sudden cardiac death (SCD) in people over 35 cardiomyopathies, congenital heart disease, channelopathies, myocarditis and substance abuse are the common cause of death in the younger population. Advancements in genetic technologies and tools now permit better molecular scientific exploration to help unravel the relevant etiology and the identification of families at risk. Arrhythmic disorders causing sudden death, the long QT syndromes (LQTS), Brugada syndrome, hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular dysplasia (ARVD) among others will be described. The role of directed genetics testing in patient and family screening, and the future impact of genome-wide screening on propensity of sudden death will be explored.

Despite identification of many causal genes, many SCD due to inherited arrhythmia susceptibility cannot be explained by the known mutations thus warrant further investigation to delineate additional un-identified gene and other possible genetic changes. Contemporary strategies including exome and whole genome sequencing may be valuable to bring this information to light. Comprehending the mechanisms responsible for incomplete penetrance, by identification of modifier genes, will also contribute to decode the intricate and dynamic relationships between genotype and phenotype. Ultimately, Early diagnosis of the condition can maximize optimal medical therapy. Genetic testing can discover the disease causing gene/mutation, therefore identify at risk family members. Cure is not possible, but correct management can prevent SCD.

2A: ADVANCES IN MOLECULAR PATHOLOGY: HONG KONG EXPERIENCE

Annie NY Cheung

Department of Pathology, The University of Hong Kong.

In the recent decades, there is a belief that our fate lies not in our stars but in our genes. Indeed, molecular pathology and genetic analysis has been increasingly applied in daily medical practice. We are now applying molecular pathology in a wide spectrum of practice in Hong Kong. It is important for screening of diseases, from prenatal diagnosis to assessing risk of subsequent development of diseases including cancers. It has become crucial ancillary tool for diagnosis of solid and haematological malignancies with characteristic genetic aberrations. Molecular pathology can predict response to drug, particularly molecular targeted therapy. It has become an indispensable tool in identifying micro-organisms responsible for infection. It is important for matching of transplant donor and recipients. The application in forensic science is vast. To safeguard the interest of patients and upkeep the quality of molecular pathology service in Hong Kong, enormous collaborative effort has been applied to training of pathologists and accreditation of pathology laboratories.

Structured training in molecular pathology is introduced into the six-years training of different specialties of Pathology by the Hong Kong College of Pathologists. Accreditation of training centres has been conducted. Moreover, a post-specialty fellowship in Genetic and Genomic Pathology is being established by the College. Accreditation of pathology laboratories on the clinical practice of molecular pathology is also quite commonly conducted involving international and local accreditation bodies.

2A: THE DANGERS OF PREDATORY JOURNALS

Roger Byard

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Predatory journals are electronic journals that have no credibility in their field but will guarantee online publication for a fee. They use certain techniques to make themselves look credible such as having a title or a logo that are very similar to legitimate journals, and may have recognized academics listed on their editorial boards without their knowledge or consent. Although these journals may claim high impact factors they are not derived from recognized sources. There were 18 in 2011, 477 at the end of 2014, and 923 in 2016, with the majority charging significant APCs (article publishing charges). It has been suggested that there are more “British Journals of . . .” based in Pakistan than there are now in the United Kingdom.

Some of these journals may exist for only a matter of weeks. In forensic circles there has always been a problem in dealing with aberrant theories that are at odds with the mainstream literature. In the past this material was often introduced into court without the imprimatur of peer-reviewed, or any, publication. It is now possible with the advent of predatory journals, however, that even the most bizarre theories with inadequate or no scientific validation could be published. To the courts these papers would appear to be no different to those published in legitimate journals, and without a clear knowledge of a particular journal's reputation and process, may be difficult to exclude. It is of concern that predatory journals may be used in future to legitimize fringe theories and to validate bogus experts. Predatory and unethical publishing on such a global scale is a relatively recent phenomenon designed to bypass normal peer-review, to make money for the “publishers” and to create instant CV's for authors. This has a direct effect by undermining “public trust in the validity of peer-reviewed and scientific publication”. It is also of concern that members of the public seeking information on the internet will have no way of determining how valid the source of (mis)information is. While this strikes at the very heart of traditional academic practice, how we deal with this threat is yet to be established. Also how we identify such publications when they are presented in court or as part of a legal opinion for rapid assessment is another issue that has not yet been widely discussed.

PEDIATRIC DEATHS – ESSENCE OF QUALITY AUTOPSY

In addition to full death scene examination and medical history review, the autopsy in cases of unexpected infant and childhood death must be carried out in as comprehensive a manner as possible, utilizing accepted protocols. For example, the International Standardized Autopsy Protocol (ISAP) was developed to assist specifically with infant autopsies. All stages of the autopsy that are specified in protocols, including external examination, radiology, internal examination, histology, microbiology, toxicology, electrolyte/metabolic studies, and molecular/genetic studies, have been shown to have diagnostic yields. The usefulness of CT and MRI examinations, in particular for infants is well recognised but has not been extensively evaluated. Use of protocols has significantly increased the accuracy of diagnosis, with more infant deaths due to dangerous sleeping environments and drug effects now being identified. Protocols also help to standardize variations in practice that may occur even among pathologists within the same institution. A complete external examination should include the anogenital region, ears, mouth and nares (with an otoscope), and should be conducted in good light, as soon as possible after death. The pattern of lividity should be noted and photographed and any dysmorphic features documented, along with any injuries (explained or unexplained). Bruises are always a concern and raise the possibility of inflicted injury. A full skeletal survey in infants and the very young should be conducted, ideally by trained pediatric radiographers, looking for occult bony trauma. Although it is well-recognized that a ‘babygram’ is of limited use in these circumstances it has also been reported that 30% of American pathologists still preferentially use them over skeletal surveys. There is still considerable room for improvement in our evaluation of these cases.

2B: REFERENCE INTERVALS: WHAT'S NEW?

Wong Moh Sim

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A reference interval (or reference range) is a set of values that includes upper and lower limits of a laboratory test based on a group of otherwise healthy people (*ref: labtestsonline.org*). The values in between these limits may depend on factors such as age, gender and specimen type (such as blood, urine, spinal fluid) and are influenced by situations such as exercise and fasting. Reference intervals are essential for clinical laboratory test interpretation and patient care. Clinical laboratories may adopt reference intervals from manufacturers, from other laboratories or use existing patient data. They may also conduct their own studies.

Reference intervals are derived by statistical calculations typically using parametric and non-parametric approaches. When determining reference intervals, it is important to define the reference population. For many tests, reference intervals include the values that are statistically analysed and reported for the middle 95% of the reference population. Clinical laboratories report patient test results along with their corresponding reference intervals. It is the responsibility of clinical laboratories to employ reference intervals that are appropriate for their methodologies and the population they serve. Both clinical laboratories and clinicians should thus be aware of the advantages and caveats associated with the use of reference intervals for their respective populations.

ANALYTICAL INTERFERENCE: AN UPDATE

An analytical interference is defined as the effect of a substance present in the sample that alters the correct value of the result (*ref: National Center for Biotechnology Information, NCBI*). Interfering substances may be endogenous or exogenous. Depending on the site of the interference in the reaction, interfering substances may cause falsely high or falsely low results in one or more assay systems, which may lead to inappropriate clinical interpretation and intervention and compromise patient care.

Common endogenous interferents include haemolysis, lipaemia, hyperbilirubinaemia and paraproteinaemias. Exogenous interferents include drugs and chemical additives incorporated into blood collection devices to prevent or promote coagulation or preserve certain blood constituents. Many automated clinical chemistry systems are able to provide quantitative measurements of haemolysis, bilirubinaemia, and lipaemia and these can be reported as serum indices in patient reports. Common endogenous interferents in immunoassays include autoantibodies and human anti-animal antibodies which can interfere with the reaction between analyte and reagent antibodies. Exogenous interferences can occur due to pre-analytical variation, matrix and equipment reactions.

Guidelines have been established for the evaluation of effects of interferents on clinical laboratory analytical methods. Laboratories should comply with these guidelines, to assess the impact of common interferents on their respective methods and ensure that the results they report are accurate and reliable.

2B: THE PROMISES AND PITFALLS OF CELL THERAPY

John Rasko AO

Sydney Medical School, University of Sydney. Gene and Stem Cell Therapy Program, Centenary Institute. Cell & Molecular Therapies, Royal, Prince Alfred Hospital, Sydney.

Immunotherapies including checkpoint inhibitors and CAR-T cells have captured the attention of many scientists, physicians and cancer sufferers. The convergence of substantial incremental technical advances towards combined cell and gene therapy has led to improved clinical outcomes in immune deficiencies, haemoglobinopathies, immunotherapies and other inherited diseases. However in parallel with objectively proven therapies 'stem cell tourism' has become a billion dollar industry with increasing examples of false claims. Embryonic and induced pluripotent stem cells have been mired in controversy and clinical development has been forestalled. We reported an analysis of the global distribution of more than 400 unique businesses marketing stem cell-based interventions. Many of these online entities promote clinical applications of 'stem cells' beyond present-day standards of care. These data should be of immediate concern to governments and ethicists being lobbied to amend laws governing the manufacture, distribution and clinical use of human cell-based medical products. Unregulated, untested or unsafe stem cell 'therapies' place the field at a difficult crossroad. Blurring the lines that distinguish evidence-based cell therapies from those that are not remains a fundamental public health concern.

2B: UPDATE IN THALASSEMIA DIAGNOSIS

Suthat Fuchareon

Thalassemia Research Center, Mahidol University, Nakornpathom, Thailand.

Laboratory diagnoses of thalassemias and abnormal hemoglobins require a combination of tests including the measurement of red cell indices by automatic blood cell counter, hemoglobin analysis including the quantitation of Hb A₂ and Hb F. The automatic HPLC and capillary zone electrophoresis (CE) system is used for hemoglobin analyses. These automatic systems give both qualitative and quantitative analysis of hemoglobin components in the same run with good precision and reproducibility and help us to do both prenatal and postnatal diagnosis of thalassemia within a few minutes. Both systems give a good correlation with some caution in the interpretation because under the CE system Hb E is clearly separated from Hb A₂. This affects the amount of Hb A₂/E, especially in case with alpha thalassemia gene interaction. However, almost all of these techniques work well only with beta-thalassemia, not alpha thalassemia.

Alpha thalassemia 1 (alpha⁰-thalassaemia) heterozygote is suspicious in subjects with hemoglobin levels more than 10 g/dl, with low MCV (MCV ~65-70 fl), normal hemoglobin typing, A₂A, and hemoglobin A₂ is less than 3.5%. There is no clue for alpha thalassemia 2 (alpha⁺-thalassemia) heterozygote and very difficult to diagnose double heterozygote of beta-thalassemia and alpha thalassemia. We have developed an immunostrip test for the detection of Hb Bart's in adult blood. The strip is sensitive enough to detect small amount of Hb Bart's in many alpha thalassemia genotypes such as alpha thalassemia 1 heterozygote, homozygous alpha thalassemia 2, Hb H disease. The identification of different thalassemia syndromes can be revealed by the ratio of intensities between alpha/beta-globin chains and alpha/beta-mRNA ratios. However, none of these tests can accurately diagnose specific thalassemia genotype. Specific thalassemia mutation can be carried out by DNA analysis. Many DNA techniques have been used for point mutation detection. For the last few years there is a development of DNA chip technology and DNA MassArray has been developed and use for prenatal diagnosis at early stage of development. All of these techniques have some advantage and disadvantage. We highly recommend all service labs to use the technique(s) they are most familiar with and most economic one for their daily use. Recently next generation sequencing (NGS) has been introduced for mass screening of thalassemia in south China. Out of 20,222 individual (a total of 10,111 couple) traditional screening/molecular testing methods failed to detect 35 at-risk couples but identified by NGS method. The NGS-based approach identified both common and rare, annotated and novel variants in carriers with and without thalassaemic trait phenotypes. This has significantly improving the detection of carrier status and the detection rate of at-risk couples.

2C: PTEROPINEORTHOREOVIRUSES: THE NEGLECTED EMERGING ZOOONOTIC RESPIRATORY VIRUSES

Chua Kaw Bing

Temasek Lifesciences Laboratory, Singapore.

Pteropineorthoreoviruses are of up and coming important emerging bat-borne zoonotic viruses causing acute respiratory illnesses in human, especially in the Southeast Asia region. The viruses belong to a group of non-envelope double-stranded, segmented RNA viruses within the genus *Orthoreovirus* under the family *Reoviridae*. The prototype species, Nelson Bay virus, was first isolated in 1960s from the heart blood of a fruit bat, *Pteropus poliocephalus* captured in New South Wales, Australia. The second type species, Pulau virus was isolated from urine samples of *Petropushypomelanus* collected in Pulau Tioman in 2000. Melaka virus was the first type species isolated from human with severe acute respiratory illness. Following which, isolates of more type species were reported from both humans and fruit bats in this part of tropics and subtropics inclusive of China.

The prevalence of virus spillover in the affected region is indicated by a seroprevalence study in Tioman Island where 13% of residents were positive against the virus. A seroprevalence study conducted in Vietnam revealed a positive rate of 4% (12/272). The virus was detected in the respiratory secretion of 17% of patients with acute upper respiratory tract infection seen in a suburban outpatient clinic of peninsular Malaysia.

Up-to-date, only acute respiratory illnesses with evidence of limited human to human transmission but no fatality had been recorded. However, experimental study in mice shows the virus was able to cause severe lung infection leading to interstitial pneumonia and death within 7 days after intranasal inoculation. Given high mutation and evolution rate of RNA viruses and constant spillover, its public health importance should not be ignored.

2C: MOLECULAR DIAGNOSIS OF INVASIVE FUNGAL INFECTIONS

Fairuz Amran

Medical Bacteriology and Mycology, Institute for Medical Research (IMR).

One of the greatest challenges in the management of invasive fungal infections (IFI) is making accurate diagnoses in a timely manner. Conventional methods are not sensitive enough and time consuming. Various non-culture methods have been used to augment accurate identifications of invasive fungal pathogens which include immunodiagnostics and molecular diagnosis.

There has been a growing number of molecular techniques developed to improve diagnosis of IFIs. These techniques are more sensitive and offer quicker and earlier diagnosis compared to conventional methods. Fungal genome amplification using conserved oligonucleotide primers followed by sequencing is a particularly promising method for identification of fungal pathogens and have been found to be reasonably cost effective and reliable. One such situation where PCR followed by sequencing is valuable is when there is evidence of IFI on histopathological examination of a formalin fixed and paraffin embedded (FFPE) tissue but culture is negative. Although PCR may not provide a 100% sensitive yield due to the challenges in extraction of DNA and impairment of DNA quality by the formalin fixation and paraffin embedding, it does provide major improvement in species identification in many cases of IFI. Knowledge on infecting species is a useful guide for better management of IFIs where early targeted antifungal treatments could be instituted and this may eventually lead to better clinical outcomes.

2C: RESPIRATORY VIRUSES: THE ROLE OF MOLECULAR DIAGNOSIS

Jamal I-Ching Sam

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Respiratory viruses are an important cause of respiratory morbidity and mortality worldwide. These include both established and emerging pathogens, such as avian influenza and MERS-coronavirus. Conventional diagnostic methods such as immunofluorescence and culture are not widely available, so that most viral infections remain undiagnosed. The increasing availability and affordability of molecular testing, which may even be at point of care, has led to greater likelihood of making viral diagnoses more quickly. Theoretical advantages of molecular diagnosis include improved laboratory safety, earlier institution of infection control measures, reduced use of antibiotics, and faster discharge. However, cost-effective and clinically-relevant utility of these technologies at a given site requires close discussion between laboratory and clinicians, particularly with regards to the advantages, clinical impact and limitations of molecular diagnosis.

2C: DIAGNOSTIC CHALLENGES IN THE DIAGNOSIS OF EXTRAPULMONARY TUBERCULOSIS

Siti Suraiya Md Noor

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Tuberculosis (TB) affects one-third of global population in developing countries, with annual estimates of 9.0 million new cases and 1.5 million deaths. Extrapulmonary tuberculosis (EPTB) accounts for 10-25% of all TB cases worldwide. The definitive diagnosis EPTB is often delayed or even missed due to insidious clinical presentation, difficulty in obtaining an adequate sample for confirmation, poor performance and limited choice of diagnostic tests. Culture, the classical gold standard for tuberculosis, suffers from tedious technical and sampling constraints in EPTB cases. In this review current diagnostic options for the main

forms of EPTB will be discussed. The discussion on the opportunities and challenges in the microbiological diagnosis of EPTB and various attempts to find a new gold standard test for EPTB also will be explored.

3A: THE PLACENTA AS A WITNESS TO STILLBIRTH

Jane Dahlstrom

College of Health and Medicine at the Australian National University (ANU). Anatomical Pathology at ACT Pathology, The Canberra Hospital

In 2015 it was estimated that 2.6 million babies were stillborn. A detailed placental pathological examination is one critical component of stillbirth evaluation given the placenta's essential role in maintaining the pregnancy. This talk is case based and discusses placenta related causes of stillbirth in the context of the updated terminology proposed in the Amsterdam Placental Workshop Group Consensus statement.

ERROR AND ERROR REDUCTION IN DIAGNOSTIC PATHOLOGY

Diagnostic error in surgical pathology occurs. It can be pre-analytical, analytical or post-analytical. This talk is case based and will discuss contributing factors to errors, and means for error avoidance including: value of knowledge, experience and training; need for clinical history and clinical correlation; use of ancillary studies; necessity for standardization of procedures and terminology; and the importance of case review.

3A: MOLECULAR BASIS OF FAMILIAL HYPERCHOLESTEROLAEMIA IN MALAYSIA

Livy Alex

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Familial hypercholesterolaemia (FH) is an autosomal dominant disorder characterised by elevations in total cholesterol and low-density lipoprotein cholesterol (LDLc). Development of FH can result in the increased risk for premature cardiovascular diseases (CVD). FH is primarily caused by genetic variations in *Low Density Lipoprotein Receptor (LDLR)*, *Apolipoprotein B (APOB)* or *Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9)* genes. Majority of the known FH mutations were discovered in the Caucasian population, and we noticed there are limited reports of FH mutations in the Asian population. To gain better insights, we investigated the association of previously reported genetic variants that are involved in lipid regulation in our Malaysian study cohort.

A total of 1536 polymorphisms previously implicated in FH were evaluated in 141 consecutive patients with clinical FH (defined by the Dutch Lipid Clinic Network criteria) and 111 unrelated control subjects without FH using high throughput microarray genotyping platform. Fourteen SNPs were found to be significantly associated with FH, 11 with increased FH risk and three with decreased FH risk. Of the eleven SNPs associated with an increased risk of FH, only one SNP was found in the *LDLR* gene, seven in the *APOB* gene and three in the *PCSK9* gene. SNP rs12720762 in *APOB* gene was associated with the highest risk of FH (odds ratio 14.78, $p < 0.001$). Amongst the FH cases, 108 out of 141 (76.60%) have had at least one significant risk-associated SNP. Our study added new information and knowledge on the molecular basis of FH amongst Asians. SNPs with high odds ratio may serve as potential markers in risk prediction and disease management.

GENETIC AND NON-GENETIC RISK FACTORS FOR CANCERS IN MALAYSIA

The interaction between genes, environment, and lifestyle ultimately cause cancers to occur. Genetic risk factors and non-genetic risk factors both play a crucial role in aggravating cancer development. With the addition of each factor, the risk of the disease increases. We can control some of the risk factors (lifestyle factors) but not others (genetic factors). While it is difficult to determine exactly how much influence any single risk factor possesses, we can estimate the percent of a disease or trait that is due to genetic factors (heritability) and the percent of a disease or trait that is due to non-genetic factors, like lifestyle and environment.

We studied five cancers in Malaysian population and investigated the combined effect of genetic and non-genetic risk on the development of the disease. Non-genetic risk factors can be grouped into two different categories: environmental and lifestyle risk factors. Examples of environmental risk factors are sun exposure, air quality, and job-related hazards. Lifestyle risk factors are diet, exercise, smoking, and alcohol consumption. Family history is often the best risk factor because it ties together both the genetic and non-genetic risk factors. Many significant non-genetic risk factors were identified for their association with breast, colon, ovarian, nasopharyngeal and prostate cancers in our studies. Environmental and lifestyle risk factors analyses of our study were consistent with previously published reports, with the exception of cigarette smoking and alcohol drinking, both of which did not reach statistical significance. In Malaysia, overconsumption of salt-cured foods, and red meat were found associated with cancer risk. Regular consumption of salt-cured food gave very high OR (OR=3.43).

3B: FORENSIC SAFETY PRECAUTION

Mohd Shah Mahmood

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The word safety describes conditions we would all wish for ourselves, whether at work or daily activities. Safety is often being neglected and not put in place, and will only be realised and appreciated after an incident has occurred. The importance of safety in the workplace cannot be over-emphasised and this applies to both the employers and employee. The employers must show a duty of care to their employees as well as fulfil the legislative requirements on safety; while the employees must be well trained in handling hazardous substances and to ensure related Standard Operating Procedures are in place.

Forensic medicine services are also prone to the unexpected risks of exposure to hazardous agents during our daily routine work. Often, with limited information available, we would not know exactly what we are handling until we conduct the post-mortem examination.

Appropriate PPE need to be worn when handling cases suspected to contaminated with hazardous agents. Safety precaution is also very important in handling CBRNE (Chemical, biological, radiation, nuclear and explosive) cases. Risk assessment and decontamination is vital in this type of cases. Therefore, safety precaution in forensic practice is essential and failure to adhere to safety protocol and decontamination of the bodies may expose dangerous risks to anyone handling the body from recovery at the scene, forensic examination and funeral.

3B: EPIDEMIOLOGY, CLINICAL PRESENTATION AND POST MORTEM CHARACTERIZATION OF PATIENTS WITH PLASMODIUM KNOWLESI MALARIA INFECTION.

Azlin Muhammad

Department of Parasitology & Medical Entomology in Medical Faculty UKM.

The epidemiology of malaria has undergone a significant change over the last decade with *P. knowlesi*, formerly a relatively unknown simian parasite rapidly becoming the most predominant malaria species to infect humans in Malaysia. *P. knowlesi* is a zoonotic malaria parasite, transmitted between non-human primate hosts by *Anopheles* mosquitoes and causing infections in humans where the parasite, vector, primate host and human converge.

Although there were a number of studies conducted in the past years to determine its epidemiology and clinical manifestations, there is still much more that needs to be known about this 5th human malaria parasites. *P. knowlesi* seemed to be more or at least at par with *P. falciparum* in terms of their virulence and ability to cause severe disease in human, especially in adults.

This talk describes the clinical findings of *Knowlesi* malaria cases including several fatal cases in Malaysia. The discussion includes the differences or similarities in their epidemiology and clinical features including post mortem reports. The morphology of parasites, their severity and also management of the cases will also be covered.

3B: VALUES OF MICROBIOLOGICAL CULTURES IN POST-MORTEM INVESTIGATIONS

Syafinaz Amin Nordin

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There has been much discussion on the use of post-mortem microbiology in forensic pathology. Results from post-mortem microbiological cultures may be useful in determining the cause of a sudden death, when an infection is suspected from the clinical information, or when there are signs of infection at autopsy. Contamination of samples during post-mortem procedures and post-mortem translocation pose challenges when interpreting the microbiology results. Therefore, factors such as the interval between death and specimen collection, methods of sampling and sampling sites should be considered when interpreting the results.

A good communication between the forensic pathologist and the microbiology personnel is also important with respect to sample processing in the laboratory. Information pertaining to the specimens, case history and autopsy findings would facilitate the microbiological testing and interpretation.

3C: RECENT UPDATE IN HEMOGLOBINOPATHIES

Suthat Fuchareon

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Alpha-, beta-thalassemia and some abnormal hemoglobins such as Hb E and Hb Constant Spring (Hb CS) are common in most Asian countries. The complex gene-gene interaction between alpha and beta thalassemia leads to many thalassemia disorders such as homozygous beta-thalassemia, beta-thalassemia/Hb E, Hb H disease and Hb Bart's hydrops fetalis. The clinical features result from chronic anemia and iron overload. The mainstay of treatment for thalassemia major is regular blood transfusion to maintain adequate levels of the hemoglobin concentration. Iron overload is secondary to either multiple blood transfusions or increased iron absorption or the combination of both. Iron overload may be assessed by serum ferritin and MRI technique. In the absence of iron chelation death from iron-induced heart failure occurs by the mid-teenage years. Iron chelator such as

desferrioxamine and the oral iron chelators (deferiprone and deferaxirox) is indicated in those patients with severe iron overload. Previously the cure for thalassemia is by stem cell transplantation. This will need appropriated HLA match donor and follow by immunosuppressive treatment for certain period. Even haploidentical stem cell transplantation has been introduced, however, this is not widely accepted as standard treatment yet. Recently gene therapy with autologous CD34+ cells transduced with lentiviral vector reduced or eliminated the need for long-term red-cell transfusions in 22 patients with severe β -thalassemia without serious adverse events related to the drug product. All the patients have been followed up from 15-38 months. This will be the future hope for thalassemia patients worldwide.

3C: CLINICAL IMPLICATIONS OF CYTOGENETICS, FLUORESCENCE IN SITU HYBRIDIZATION (FISH) AND MOLECULAR TESTING IN CHRONIC MYELOID LEUKEMIA PATIENTS

Ravindran Ankathil

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Chronic myeloid leukemia (CML) provide an illustrative disease model for both molecular pathogenesis of cancer and rational drug therapy. The pathogenesis of CML involves a characteristic genetic abnormality, the fusion of *ABL1* gene in chromosome 9 with *BCR* gene in chromosome 22 resulting in the Philadelphia (Ph) chromosome which is the hallmark of CML. The fused *BCR/ABL1* gene encodes the p210 KDa BCR/ABL fusion oncoprotein which is a deregulated, constitutively active tyrosine kinase that promotes growth and replication and CML pathogenesis. The introduction of imatinib mesylate (IM), a BCR/ABL1 targeted tyrosine kinase inhibitor (TKI) drug, has revolutionized CML therapy and is the first line gold standard drug for CML treatment.

In all phases of CML and its treatment, conventional cytogenetic analysis in conjunction with fluorescence in situ hybridization (FISH) can serve as powerful tools for the diagnosis, prognosis, risk stratification and monitoring of therapeutic success. At diagnosis, conventional cytogenetic analysis uses light microscopy to identify the Ph chromosome by analyzing the GTG-banded bone marrow metaphases. This method will also identify any chromosome aberrations in addition to t(9;22) including complex or variant translocations involving 3 or 4 or more chromosomes. Following the initiation of TKI therapy, current NCCN and ELN guidelines recommend that cytogenetic analysis be performed at 3- to 6- month intervals after treatment initiation. FISH has greatly enhanced the accuracy and efficiency for cytogenetic analysis. Using dual colour *BCR/ABL1* fusion gene probes, FISH measures the proportion of interphase nuclei with the characteristic *BCR/ABL1* fusion and can be performed even in non-dividing cells from peripheral blood or bone marrow. FISH is especially important for cells of CML patients with inadequate or inferior quality metaphases or those with variant Ph translocations.

Monitoring the response to CML therapy is a continuum that begins at diagnosis and carries on serially throughout the entire course of treatment. Significant advances in technologies to detect *BCR/ABL1* positive cells have now refocused therapeutic goals on cytogenetic and molecular endpoints. Several different methods are used to assess cytogenetic or molecular response during CML treatment. Complete cytogenetic response (CCyR) is defined as the absence of detectable Ph metaphase cells which is a clinically important prognostic marker in CML patients. In comparison with conventional cytogenetics, FISH testing helps to analyze higher number of cells. However, secondary or additional chromosome abnormalities that may arise at later stages of treatment will not be detected by *BCR/ABL* dual probe alone. Cytogenetic testing has the advantage of detecting additional chromosome abnormalities which may have prognostic value and so FISH testing should not be considered to be a replacement for conventional cytogenetics.

3C: THE PROBLEM OF VON WILLEBRAND DISEASE

Michael Laffan

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Von Willebrand disease presents clinicians and pathologists with a large number of diagnostic problems. Firstly, the range of VWF plasma levels is the widest for any coagulation factor and also varies considerably in an individual from day to day, tending to obscure the boundaries between normal and abnormal. Secondly, the principal functional role of VWF is reliant on the effect of shear stress, which is difficult to reproduce in laboratory assays. Thirdly, the complex structure of the von Willebrand factor (VWF) molecule and its multiple interactions give rise to a wide range of abnormalities so that no single laboratory assay can adequately assess them all. Finally, although VWF can be readily measured in plasma samples, the contribution of the platelet, endothelial and extravascular pools are not easily accessed for measurement and so their importance is largely unknown. The problem of assaying VWF activity has led to numerous different approaches, but the wide range of abnormalities in different forms of VWD has meant that they have all encountered problems of detection in some cases. This also presents problems for monitoring therapy and the best approach to clinical management is still unresolved. Addressing these numerous problems requires careful application of several laboratory analyses and sometimes recourse to genetic testing to complete a practical and useful diagnosis.

4A: RECENTS UPDATES IN GYNAECOLOGICAL PATHOLOGY

Annie NY Cheung

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Updates on pathology of the female genital tract particularly that highlighted in the 2014 WHO classification, will be discussed. Related to ovarian serous borderline tumour, “invasive implants” should be diagnosed as low-grade serous carcinoma while non-invasive tumour with micropapillary pattern and moderate cytologic atypia exceeding an area of 5 mm should be classified as non-invasive low grade serous carcinoma. A new category of seromucinous tumours has been created, characterized by mixture of serous and mucinous and other cell types. Urothelial / transitional cell carcinoma is now recognized as high grade serous carcinoma. Squamous cell carcinoma is moved to the monodermal teratoma category. A simplified two-tier classification on endometrial hyperplasia, “hyperplasia without atypia” and “atypical hyperplasia”, is introduced. Endometrioid intraepithelial neoplasia (EIN) is considered as an alternative term for atypical hyperplasia. High grade endometrial stromal sarcoma is reintroduced under uterine sarcoma while the term “undifferentiated uterine sarcoma” is adopted to replace “undifferentiated endometrial sarcoma” since it may arise from endometrium or myometrium.

At the lower female genital tract, a two-tier system of low- and high-grade squamous intraepithelial lesions (SIL) is introduced for the cervix, vulva and vagina. This is considered to be histologically more reproducible than the three-tier cervical (vulva, vagina) intraepithelial neoplasia (-IN) 1 to 3. Mucinous carcinoma, gastric type, is a recently introduced entity incorporating cases of minimal deviation adenocarcinoma (adenoma malignum). Differentiated vulval intraepithelial neoplasia (VIN) is defined as HPV-negative squamous intraepithelial proliferation with abnormal keratinocyte differentiation and basal cell atypia. It is believed to be associated with keratinizing squamous cell carcinoma, lichen sclerosus and lichen planus. No reliable biomarker is currently available. The entity superficial myofibroblastoma is also introduced. Under gestational trophoblastic disease, “abnormal (non-molar) villous lesions” refer to various lesions with histological features resembling partial mole. More emphasis on genetic profiles of hydatidiform mole is made.

4A: IGG4 GASTROINTESTINAL DISEASE UPDATE

Lim Kiat Hon, Tony

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A brief discussion of the criteria and disease spectrum of IgG4 with some references to local studies will be made. Clinical, serological and histological features and evaluation of diagnostic problems will be summarised.

4A: LYMPHOMA DIAGNOSIS IN BONE MARROW TREPINE

Noraidah Masir

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In the assessment of patients with lymphoma, bone marrow trephine studies may be performed for primary diagnosis or as a staging procedure. Trephine biopsy allows examination of cell distribution pattern and extent of tumour infiltration. It also provides material for immunohistochemistry and molecular studies. WHO classifications broadly categorised lymphomas into B cell, T cell and Hodgkin lymphomas with more specific entities within each group. In a well-prepared sample lymphomatous infiltrates can be detected by morphologic and immunohistochemical assessment. Assessment of trephine however is complicated by the fact that characteristic architectural patterns seen in lymph nodes involved by lymphomas are not present in the bone marrow. Having an organised approach to the examination of the biopsy by routine H&E stain and immunohistochemistry, accurate lymphoma classification can be achieved in most instances. In addition, molecular studies need to be performed in selected cases when necessary.

4B: PRIMARY IMMUNODEFICIENCY (PID) AS A CLINICAL & LABORATORY ENTITY: CHALLENGES AND MILESTONES FOR MALAYSIA

Lokman Mohd Noh

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Primary immunodeficiency (PID) was reported as early as in 1977 (YH Thong) in Malaysia followed by the next waves in 1986. The predominant group are combined immunodeficiency and predominant antibody deficiency. There are more SCID (severe Combined Immunodeficiency) than XLA (X Linked Agammaglobulinemia) in our cohort. The most dramatic increase was after 2007 with more trained clinician immunologists returning to the universities. PID in Malaysia is grossly underreported as in other countries; for a population of almost 32 million, Malaysia would have 26,000 PID based on the estimate of 1:1200 for a population of a country (R Buckley). The lack of awareness leading to a delayed diagnosis with its subsequent morbidity & mortality remains the most ominous health threat. Overcoming them in a country with limited resources and expertise in PID remains an immense challenge.

As PID as a branch of Clinical Immunology, being both a clinical and laboratory discipline, it behoves upon the sole

clinician immunologist of the era then to develop the laboratory immune investigations as part of patient care. The author was fortunate to have an immunopathologist and later a PhD immunologist in UKM to assist him in developing the laboratory investigations. IMR's division of Serology came to the fore provided with its first flowcytometer in the country. The next phase of developing tertiary immune tests was in USM's Advanced Medical & Dental Institute, USM Bertam. We are now able to refine PID diagnosis towards improving patient care as well as to enrich translational research. The total patients referred up to 2016 was 363; with 235 suggestive of PID. With the availability of WES (whole exome sequencing) at UMBI UKM, newer novel entities has emerged; CARD 14 deficiency, a Primary Ciliary Dyskinesia presenting as Hyper IgE deficiency syndrome, which to the best of our knowledge had not been reported before.

4B: UPDATES ON THE DIAGNOSIS OF AUTOIMMUNE NEUROLOGICAL DISEASES.

Masita Arip

Allergy & Immunology Research Centre, Institute for Medical Research (IMR), Kuala Lumpur.

Autoimmune neurological diseases are an expanding group of potentially treatable syndromes. The most common antibody-associated neurological conditions, focusing on autoimmune myasthenic syndromes and neuromyotonia in the peripheral nervous system, and their central nervous system counterparts including neuromyelitis optica and autoimmune encephalitis. Other related conditions, including stiff person syndrome and classical paraneoplastic neurological syndromes. Although individually these conditions are uncommon, they form a significant group of treatable diseases that frequently present to general medicine and are important for all physicians to recognize promptly. There are now established distinctive clinical clues to diagnose the diseases, definitive investigations and increasing experience regarding the beneficial effects of immunotherapies. A number of these conditions are believed to be mediated by autoantibodies and often respond well to immunotherapies including corticosteroids, plasma exchange, intravenous immunoglobulins, cyclophosphamide and/or rituximab.

4B: MARKERS IN REPRODUCTIVE MEDICINE: MYTHS AND REALITY

Farid Abdul Hadi

Regional Medical and Scientific Affairs Manager Asia-Pacific, Women's Health, Roche Diagnostics Asia Pacific, Singapore.

There have been rapid advances in the area of biomarkers in reproductive medicine. Whilst many are conceptually feasible, there is only a small handful that contributes significant role for the success of Assisted Reproductive Technology (ART). Some studies showed proof of concept and initial practice in the pre-implantation genetic test, identification of endometrial receptivity, measurement of ovulatory potential and refinement of individualised stimulation cycles.

The two latter topics have been studied extensively with proven reproductive outcomes. Anti-Mullerian Hormone (AMH) is the marker that has gone through significant progress over the decade. From previously known to create doubts among clinicians due to inconsistent results, AMH has evolved into a reliable reproductive endocrinology marker. It has been identified as a crucial element for the individualised dosing for in-vitro fertilization (IVF) and the utility has been studied to extend beyond IVF, such as for primary ovarian insufficiency and polycystic ovarian syndrome (PCOS).

4B: ANTI-MULLERIAN HORMONE: A CLINICAL PERSPECTIVE

Adibah Ibrahim

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The anti-Mullerian hormone (AMH) is a dimeric glycoprotein and a member of the transforming growth factor (TGF) superfamily. In the male embryo, AMH inhibits the Mullerian duct from developing into fallopian tubes, uterus, cervix and upper part of the vagina. In female embryo, it is produced exclusively by the granulosa cells of the early developing follicles. Its level in female serum is almost undetectable at birth, subtle increase during puberty, but decline with the declining of ovarian function.

Compared with other markers, serum AMH proved to be a good marker for detecting declining ovarian reserve and function in female's reproductive life. The AMH serum level may indicate the quantity of ovarian antral follicles, as it can predict the prognosis of patients receiving assisted reproductive techniques (ART) cycles. AMH is noted to be high in patients with polycystic ovarian syndrome, and thus may be a good surrogate for diagnosis of the disease. Its role in monitoring the progress of ovarian epithelial malignancy is yet to be proven. It can also be used to predict the menopausal transition and serves to be more accurate than serum FSH. Thus, AMH may guide the clinician in a broad range of clinical conditions and management. Despite the emerging advantages of AMH, it is not readily available in many hospitals, most probably due to financial constraint. However, we believe that AMH plays a significant role not only for academic purpose but also in clinical practice.

4C: FORENSIC APPROACH IN DEATH DUE TO CHEMICAL

Mohd Shah Mahmood

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Chemical warfare agents are extremely toxic synthetic chemicals in the form of gas, liquid, aerosol or powder. These agents have either lethal or incapacitating effects on human. During World War I, chlorine and phosgene gases were rampantly utilised. They were released from canisters on the battlefield and dispersed in the wind. Mustard gas was also being utilised during that time resulting in more than 90,000 deaths. Those who survived exposure to chemical warfare agents suffered permanent disability and side effects.

Since then, chemical agents had evolved to newer agents such as VX nerve agent and sarin gas. The means of delivery of chemical agents had also changed over the years. Thus, the detection of chemical agents has become very challenging.

Death due to chemical warfare agents is very rare and Malaysia recently had a fatality case due to Vx nerve agent exposure. Dealing with such case requires proper planning, adequate staff protection, decontamination procedures and detection methodology. The approach and experienced in handling this case will be shared and discussed.

4C: PATHOPHYSIOLOGY OF DRUG ADDICTION

Ravindra Fernando

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Drug addiction is characterized by behavioural and other responses that always include an overpowering desire (compulsion) to take the drug on a continuous or periodic basis and to obtain it by any means, in order to experience its psychic effects (psychic dependence) and sometimes to avoid the discomfort of its absence (physical dependence). Addictive or dependence producing drugs include opiates, amphetamines, hallucinogens, new psychoactive substances, alcohol and tobacco products. Drug addicts suffer from substance use disorders (SUD), a condition in which the use of one or more substances leads to effects that are detrimental to the individual's physical and mental health. Drug addiction leads to impaired performance, confusion, hallucinations, drowsiness, lack of concentration, respiratory depression, and heart muscle disease, coronary artery disease, liver disease, brain hemorrhages and sudden cardiac death.

Drug addicts die prematurely from acute overdose, inhalation of vomit, acute ulcerative endocarditis, tuberculosis, bronchopneumonia, hepatitis and HIV/AIDS. They are more likely meet with accidents and commit suicide. Cellular adaptations in prefrontal glutamatergic innervation of the accumbens promote the compulsive character of drug seeking in addicts by decreasing the value of natural rewards, diminishing cognitive control (choice), and enhancing glutamatergic drive in response to drug-associated stimuli. Δ FosB, a gene transcription factor, has been identified as playing a critical role in the development of an addiction. Over-expression of Δ FosB in the nucleus accumbens is necessary and sufficient for many of the neural adaptations seen in drug addiction and it has been implicated in addictions.

THE ROLE OF SUBSTANCE ABUSE IN INMATES' DEATHS

Drug overdose deaths are an internationally recognized public health concern. Prolonged or repetitive drug administration leads to a variety of adaptive changes throughout the nervous system at the cellular level that result in the development of physiological tolerance and dependence. This tolerance necessitates larger and more frequent administrations of the drug to achieve similar effect and contributes to prison inmate deaths. While any drug user is at risk for overdose, those who have had a recent period of abstinence are at an even greater risk.

The number of deaths of drug dependent inmates is increasing worldwide according to latest reports. Circulatory system disease, suicide, drug overdose, acquired immunodeficiency syndrome, cerebrovascular disease and homicide are the leading cause of inmate deaths. Deaths due to drug overdose or withdrawal are disproportionately higher among female inmates compared with male inmates. Another disturbing feature is that researchers have noted that about six percent of all the prisoners died within the first five years of their release. Among those who died from alcohol and drug-related causes, 42 percent of the male deaths and 70 percent of the female deaths came from preventable causes like accidental overdoses or suicide. Review of mortality rates and causes of deaths of inmates can be a useful tool to better understand health issues and their needs. Surveillance of illnesses and strategic revising of prison health care is a key to quality improvement.

LUNCH SYMPOSIUM: ARTIFICIAL INTELLIGENCE-DRIVEN TELEHEALTH SYSTEM FOR EYE SCREENING.

Tan Geok Leng

AIDA Technologies Pte Ltd

An overview of the rapid progress in the application of AI/Machine Learning to address societal problems especially those related to healthcare. This is followed by a description of a telehealth system that is being deployed in Singapore for the mass screening of eyes for the general public. We describe how the capacity of the system is limited by availability of trained graders and how this limitation may be overcome using an AI-engine.

SAFETY & QUALITY**MEDICAL LABORATORY ACCREDITATION: THE MALAYSIAN JOURNEY**

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The accreditation of medical testing laboratory or pathology laboratory provides a formal recognition that the laboratory is competent to carry out its tasks, thus providing a ready means for customers to identify and select reliable pathology testing services. In Malaysia the activities towards accreditation of pathology laboratories started in the year 2001 when the Ministry of Health (MOH) set a policy that all medical testing laboratories under the pathology and blood transfusion services to be accredited under the ISO /IEC 17025 which was then the applicable standards for laboratory accreditation. Following that a few pathology laboratories of MOH hospitals and Institute of Medical Research were accredited by the National Association of Testing Authorities, Australia (NATA).

Meanwhile in 2002 the need for establishment a medical laboratory accreditation activities to cater for the accreditation of all local medical laboratories of the universities, private sectors and other government laboratories (which have not been accredited yet) was addressed through the collaborative effort of College of Pathologist of the Academy of Medicine Malaysia (CPath AMM) and Department of Standards Malaysia (Standards Malaysia), Ministry of Science Technology and Innovation (MOSTI). On 5th October 2002, a Memorandum of Understanding (MoU) was signed between CPathAMM and Standards Malaysia to co-operate in a project to establish the medical accreditation programme under Skim Akreditasi Makmal Malaysia (SAMM).

The project was funded by a grant from MOSTI and the MOH provided the necessary expertise in the various fields of Pathology. The project team consisted of 6 pathologists under the leadership of Project Director, Professor Dr. Looi Lai Meng with Standards Malaysia as the secretariat. This project involved the development of some guidance documents, supplementary requirement, assessors training services and technical information to support the accreditation programme. Many pathologists, scientists and senior medical laboratory technologists were also engaged in the work which progressed rapidly in the subsequent 2 years. By then the specific international standards for accreditation of medical laboratories ISO 15189 has been introduced. It was adopted to MS ISO 15189 and was used by Standards Malaysia as the basis for accreditation of medical testing laboratories in Malaysia. MS ISO15189 was successfully launched in December 2004. The accreditation activities have increased progressively since then and until March 2018, a total of 48 laboratories from private, universities and government health facilities have achieved accreditation. The presentation will elaborate on the processes and challenges faced during the journey to achieve the accreditation for medical testing laboratories in Malaysia.

QUALITY AND SAFETY IN PATHOLOGY – THE WAY FORWARD

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In the era of quality and safe patient care, quality and safety in Pathology is very much an important component of good patient care and patient safety. Ensuring quality and safety in our laboratory practices do contribute to a desirable outcome whilst failure to ensure appropriate measures may result in incorrect management and adverse outcome in patient care. Even though we have progressed in terms of technology including automation, algorithm software, digital pathology but errors and accidents are still occurring. Attention to quality and safety need to be given in all areas encompassing the pre-analytical, analytical and post-analytical phases.

Obtaining and maintaining laboratory accreditation is a good approach to implement and sustain quality and safety measures. Many laboratories have already put many quality and safety measures in place such as incident reporting, indicator monitoring, critical value / result notification, risk management, root cause analysis but one question that need to be asked is how effective are the measures taken.

Quality and safety measures are a dynamic process where the data collection, analysis, review and action taken must be timely and effective. An effective measure can reflect the standard of the service. Ensuring quality and safety in the laboratory is not an accidental or a natural occurring process. It requires a team effort in planning and systematic implementation. All efforts to enhance quality and safety practices are a good investment as it can bring positive impact to the standard of laboratory services and also to the laboratory personnel.

ABSTRACTS

ANATOMIC PATHOLOGY

AP1 Coexistence Adenocarcinoma and Tuberculosis of Caecum: A Rare Encounter

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Introduction: Coexistence of colonic adenocarcinoma and tuberculosis is rarely encountered. Less than 100 cases were reported thus far. The pathogenesis of this uncommon occurrence is briefly discussed. **Case report:** An 82-year-old man with multiple medical illnesses presented with a-month history of intermittent abdominal discomfort and altered bowel habits. This was associated with significant weight loss. On examination, a vague abdominal mass was palpable at the right iliac fossa region. A CT-scan of the abdomen revealed a heterogenous enhancing mass at the caecum suggestive of malignancy. Exploratory laparotomy was undertaken. A large caecal mass with multiple lymph nodes along the draining vessels were discovered intraoperatively. A right hemicolectomy was followed. Gross examination revealed a 5.0cm fungating caecal mass partially obstructing the lumen. Microscopic examination confirmed the diagnosis of a well-differentiated adenocarcinoma of caecum with subserosal invasion and multiple regional lymph node metastases. Surgical margins were clear. Interestingly, granulomatous inflammation with central caseous necrosis was evident adjacent to infiltrating malignant cells. Similar granulomas were also found in the draining metastatic regional lymph nodes. Ziehl Neelsen stain highlighted the presence of acid fast bacilli highly suggestive of concomitant intestinal tuberculosis infection. The patient was started on anti-tuberculosis treatment and was well hitherto. **Discussion:** The association between colonic adenocarcinoma and tuberculosis is largely debatable. While some suggested that coexistence of the two is merely a coincidence, some may argue chronic inflammatory mucosal damage by undiagnosed tuberculosis infection predisposed to neoplastic change. Further research is needed to shed more light on this unusual occurrence.

AP2 EBV-positive DLBCL: A case report

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Introduction: Diffuse large B cell lymphoma (DLBCL) is a heterogenous entity that comprises 30% of Non-Hodgkin lymphoma (NHL) cases. Epstein Barr Virus (EBV)-positive DLBCL is composed of lymphoid proliferation associated with EBV infection, and no history of immunodeficiency or history of NHL. Given the rarity of this disease, we report a case of EBV-positive DLBCL. **Case Report:** A 65-year-old man with hypertension, diabetes mellitus complicated with chronic kidney disease and history of ischaemic stroke. He presented with multiple painless lymph node swelling at the neck with loss of weight and appetite. He has no history of immunosuppressive state. Peripheral blood film showed lymphocytosis with no abnormal lymphoid cells. Radiological investigation showed predominantly discreet nodes involving the neck, mediastinum, abdominal, pelvic and inguinal lymphadenopathy. No EBV DNA serum done. Inguinal lymph node excision done and showed two whitish firm lymph nodes measuring 15 to 20 mm in maximum dimension. Microscopic examination showed large neoplastic lymphocytes with background of small lymphocytes, histiocytes and plasma cells. Foci of angioinvasion, extensive necrosis, high mitotic index and association with EBV were established by in situ hybridization for EBV. **Conclusion:** In this case, detection relies on clinical suspicion and looking for EBV in especially elderly cases of DLBCL. Prognosis wise, EBV-positive DLBCL have worse prognosis than EBV-negative DLBCL. Therefore, recognition of the disease is vital in the management of the patient.

AP3 A single institution experience in intraoperative frozen section sentinel lymph node assessment in breast cancer.

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Introduction: Intraoperative frozen section lymph node assessment helps to predict axillary lymph node metastasis in breast cancer. However, the accuracy of this frozen section analysis may vary between different institution. **Objective:** This study describes our institution's experience in intraoperative analysis of sentinel lymph node and aim to determine the accuracy, sensitivity and specificity of our assessment. **Methods:** We retrospectively analysed the histopathological material and data from 82 breast cancer patients diagnosed over a period of four years who underwent intraoperative frozen section evaluation of sentinel lymph nodes. **Result:** Frozen section analysis detects metastasis in 13 out of 82 cases and definitive pathology examination on the paraffin section confirm these positive findings. There was no false positive case (specificity of 100%). The true positive cases comprised of seven macrometastases, five micrometastases and one isolated tumour cells. Sampling error was noted in two cases in which the malignant cells were only present in the deeper final paraffin sections (false negative rate of 13.3%). The test sensitivity was 86.7% and the accuracy rate was 97.5%. These findings are comparable to other published data. **Conclusion:** Intraoperative frozen section analysis is a safe and reliable method for assessment of sentinel lymph node. A knowledge on limitation of frozen section analysis with diligent evaluation of frozen section specimen will be beneficial in reducing interpretation error.

AP4 Malignant adenomyoepithelioma of the breast

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Introduction: Adenomyoepithelioma is an uncommon biphasic tumour composed of proliferation of myoepithelial and ductal epithelial cells. It can be found in salivary gland, skin adnexa, and lung but more commonly in the breast. **Case report:** A 58-year-old female presented with a painless left breast swelling. Physical examination revealed a peri-areolar mass measuring 5x4cm. The total mastectomy and axillary resection specimen showed a tumour with an irregular invasive margin. Histology showed biphasic proliferation of spindle-shaped malignant myoepithelial cells surrounding benign epithelium-lined glands in a fibrocollagenous stroma. Arising from these benign glands are a few foci of Grade 2 invasive ductal carcinoma. Both the malignant myoepithelial and ductal epithelial cells exhibit moderate atypia. Foci of malignant squamous differentiation and myxoid change are present within the malignant myoepithelial component. The surrounding breast showed stromal fibrosis, sclerosing adenosis and apocrine metaplasia. The myoepithelial cells were immunopositive for p63 and vimentin, whereas the ductal epithelial cells were immunopositive for CK7. One out of eleven axillary lymph nodes showed nodal metastasis.

Discussion: Adenomyoepithelioma of the breast is a rare neoplasm characterised by lobules of epithelial lined ducts surrounded by a mantle of myoepithelial cells. Malignant transformation may involve either one or both elements. The presence of tumour necrosis, marked cytological atypia and increased mitotic activity is usually associated with malignant transformation. Metastasis may occur with lung, brain, liver and thyroid gland being the common sites. Complete excision with adequate margins is recommended to reduce the potential for local recurrence and metastasis.

AP5 Co-existent multifocal gastrointestinal stromal tumour and adenocarcinoma

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Introduction: Gastrointestinal stromal tumour (GIST) is a rare neoplasm of the gastrointestinal (GI) tract, while extraintestinal GISTs (EGISTs) are even rarer, constituting less than 1% of all GIST. Additionally, GIST can co-exist with either benign or malignant neoplasms. Such co-existent GIST may be an incidental finding and associated with certain syndromes. **Case Report:** A 58 years old lady with no known medical illness, and having multiple skin nodules, had presented with jaundice and fever for 1 week, associated with constitutional symptoms. Imaging showed a distal common bile duct (CBD)/ ampullary mass. Distal CBD brush cytology showed features compatible with cholangiocarcinoma. The patient underwent a pylorus preserving pancreaticoduodenectomy. Macroscopic examination showed an infiltrative tumour at the distal CBD and ampulla of Vater, with nodules noted on the duodenum and posterior pancreatic surface. Microscopic examination showed a moderately differentiated adenocarcinoma of the distal CBD infiltrating into the pancreas, with multifocal GIST present in the duodenum (intestinal) and posterior pancreatic surface (extraintestinal), and was of low risk. **Discussion:** This case illustrates the incidental finding of GIST co-existing with another primary neoplasm, which is seen in up to 20% of cases, in a patient with probably undiagnosed neurofibromatosis. The literature review suggests that asymptomatic, incidentally discovered GIST is usually low risk. Certain syndromic associations may affect tyrosine kinase inhibitor treatment outcomes. Recognition of these factors aid in further management of the patient.

AP6 Angioimmunoblastic T-cell Lymphoma Masquerading As Prominent Cutaneous Granulomatous Reaction: A Rare Clinical Manifestation.

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Introduction: Angioimmunoblastic T-cell Lymphoma (AITL) is a rare and aggressive non-Hodgkin lymphoma, accounting for 1-2% of cases. Cutaneous involvement is seen in 50% of AITL and granulomatous response is observed in 2-7% of non-Hodgkin lymphoma. **Case report:** We report a 70-year-old Chinese gentleman who presented with multiple pruritic skin lesions associated with hepatomegaly, multiple cervical, axillary and inguinal lymphadenopathy with weight loss over the course of one year. Repeated skin biopsies showed intense cutaneous granulomatous inflammation with florid proliferation of epithelioid histiocytes. Excisional biopsy of a cervical lymph node showed dermatopathic lymphadenopathy. In view of high clinical suspicion, careful cytomorphological re-evaluation and immunohistochemical stainings revealed the presence of atypical lymphoid infiltrate and led to the diagnosis of AITL. **Discussion:** AITL presenting with prominent granulomatous cutaneous reaction is rare and such presentation may cause a delay in its diagnosis. Therefore, in instances when clinical suspicion of cutaneous T-cell lymphoma is high but histologically, the granulomatous component of skin biopsy is so intense, immunohistochemical markers such as CXCL13, CD10, PD-1 and CD21 can be used to highlight the subtle underlying lymphomatous counterpart. Demonstration of T-cell clonality via gene-rearrangement studies can also help to confirm the diagnosis of AITL.

AP7 Glomangiopericytoma, a rare tumour of nasal cavity: Case report

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Introduction: Glomangiopericytoma (sinonasal-type hemangiopericytoma), is a rare sinonasal tumour demonstrating perivascular myoid differentiation, and accounts for less than 0.5% of all sinonasal tumours. It tends to behave in a more indolent fashion, thus considered as a distinct entity that differs from conventional soft-tissue haemangiopericytoma in biologic, clinical, and histologic features. WHO has classified glomangiopericytoma as a borderline low malignant tumour that offers excellent prognosis if completely excised. **Case report:** A 61-year-old man presented with a history of traumatic chronic right subdural hematoma. Head CT scan showed an incidental finding of a soft tissue lesion at the left nasal cavity measuring 5x2x5cm, extending into the nasopharynx and obstructing the left sphenoid ostium. Further history revealed that he had left nasal obstruction with rhinorrhoea for more than 20 years. Rhinoscopic examination showed left nasal mass occupying the nasal cavity. The tumour was removed successfully by endoscopic endonasal surgery. Microscopically, the tumour was covered by normal respiratory epithelium. The underlying submucosa was effaced by closely packed spindle cells arranged in diffuse pattern, interspersed with variably sized vascular channels. Perivascular hyalinization was present mainly involving the small vessels. Necrosis, cytologic atypia and mitosis were absent. Immunohistochemically, the tumour was positive for smooth muscle actin, and negative to CD34 and cytokeratin. A diagnosis of glomangiopericytoma was rendered. **Discussion:** There are a few differential diagnoses of sinonasal spindle cells and vascular neoplasm includes lobular capillary hemangioma, solitary fibrous tumour, leiomyoma, and angiofibroma. Hence, morphological and immunohistochemical stains are very helpful to differentiate between them.

AP8 Immunohistochemical analysis of p53 and WT1 in serous and endometrioid carcinoma of the endometrium in Hospital Serdang.

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Introduction: Endometrial carcinoma is one of the most common gynaecological malignancies. Endometrioid carcinoma accounts 80% of endometrial cancer. It is a diagnostic challenge to discriminate a high grade endometrioid carcinoma from serous carcinoma as distinct features are not prominent. Therefore p53 and WT1 staining might play a role in differentiating these two tumours. **Materials and Methods:** 101 cases of endometrial carcinoma comprising endometrioid and serous carcinoma were studied. The histology pattern, grade, lymphovascular invasion, lymph node metastasis and staging were recorded. The formalin-fixed paraffin embedded tissue sections were stained with p53 and WT1. p53 was scored into patchy/rare weakly or diffuse. WT1 staining was scored into 1+ (<10%), 2+(10-50%) or 3+(>50%). **Results:** The proportion of endometrioid carcinoma was 82.2% and 17.8% for serous carcinoma. In endometrioid carcinoma, p53 staining was patchy/ rare weakly in 92.2% of cases and diffuse in only 7.8%. Majority of serous carcinoma (78.6%) showed positivity for p53, only 21.4% showed patchy/rare weakly. As for WT1, only one case of endometrioid carcinoma was positive (1.4%) with a score of 1+ while serous carcinoma showed 55.5% positivity. 30% of serous carcinoma scored 2+ and 70% scored 3+. There was a significant correlation between p53 expression with grade of endometrioid carcinoma (p=0.003). For serous carcinoma, no significant correlation was seen in both p53 and WT1 staining with grade of tumours. **Discussion:** Strong and diffuse p53 staining and strong WT1 staining can be used to support the diagnosis of serous carcinoma instead of a high grade endometrioid carcinoma.

AP9 Multiple epidermal cysts in a benign phyllodes tumour: an uncommon presentation

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Introduction: Phyllodes tumours are uncommon fibroepithelial lesion of the breast that usually present as a rounded or lobulated well circumscribed mass that contain cysts or calcifications on imaging. They are characterized by stromal proliferation and overgrowth. The epithelial component may exhibit hyperplastic and metaplastic changes; however, epithelial squamous metaplastic changes forming epidermal cysts are rare occurrence. **Case report:** We report a case of a 56-year-old woman presented with enlarging right breast mass with suspicious clinical and radiological findings. Clinically, she had a huge mobile mass in the right breast with palpable axillary lymph node. Mammogram revealed a complex mass with BIRADS score 5, which is highly suggestive of malignancy. She underwent wide local excision. Histopathology revealed benign phyllodes tumour with multiple unremarkable epidermal cysts. There are areas displaying squamous metaplasia giving rise to the cysts. **Discussion:** Epidermal cysts arising from squamous metaplasia within a phyllodes tumour are rare. Radiologically, their presence may harbour features mimicking malignancy such as ill-defined border and heterogenous echogenicity. Primary squamous metaplasia is thought to arise from the myoepithelial cell layer within the ducts of fibrocystic disease or fibroepithelial lesion. There has been documented squamous cell carcinoma arising from squamous metaplasia, thus warrants careful examination of this entity. At present, adequate removal of both phyllodes tumour and epidermal cysts is the mainstay of treatment.

AP10 Association between the histopathological subtypes and chest radiograph pattern of lung cancer patients in Hospital Serdang

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Introduction: Lung cancer is the leading cause of cancer deaths in Malaysia. To diagnose lung cancer, chest radiograph is commonly used as screening tool while histopathological examination is the gold standard to confirm the diagnosis. The aim of this study is to determine the association between the histopathological subtypes and chest radiograph pattern of lung cancer patients. **Materials and Methods:** This is a cross sectional study using retrospective data of 111 lung cancer patients, carried out at the Imaging Department of Hospital Serdang. Data was obtained from the hospital information system and analysed using SPSS version 21.0. **Results:** Adenocarcinoma was the most common histological type (78%) followed by squamous cell carcinoma (21.0%), small cell carcinoma (8.6%) and adenosquamous carcinoma (7.4%). Most of small cell carcinoma (57.1%) were located at the periphery of the lung whereas non-small cell carcinoma were located at the centre. Small cell carcinoma tends to show spiculated pattern of lesion (42.9%) while non-small cell carcinoma showed more of consolidation pattern (36.5%), single nodule (31.7%) and speculated pattern (21.2%). However none of the patterns show significant correlation with different histological subtypes. Significant findings observed in terms of tumour location ie. majority of adenocarcinoma (52.6%) were located at the centre of the lung and small cell carcinoma mostly affects the hilar region (57.1%). Squamous cell carcinoma tends to involve the entire lung zone (40%). **Conclusions:** Chest radiograph pattern is not helpful in suggesting the histological types of lung cancer as any radiographic pattern may be present in a single histological type.

AP11 Infectious mononucleosis mimicking malignant lymphoma: A case report

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Introduction: The diagnosis of acute infectious mononucleosis (IM) is made on the basis of clinical presentation and laboratory tests. Atypical presentation will lead to histological assessment in order to exclude malignant lymphoma. We hereby describe a case of acute IM misclassified as malignant lymphoma initially. **Case report:** An 18-year-old male patient had sore throat and fever for two days with rapidly increasing bilateral cervical lymphadenopathy. Biopsy was performed on a huge pus coating mass at nasopharynx. The biopsy showed infiltration of single and sheets of atypical mononuclear cells with prominent nucleoli. Reed-Sternberg (RS) like cells were seen. The atypical cells were CD3-/CD20-/CD79a-/PAX 5+/CD30+/CD15-. Classical Hodgkin lymphoma (CHL) was diagnosed. However, additional immunostains showed OCT 2+ and BOB 1+. EBER ISH was positive. The neck lymph node revealed paracortical hyperplasia. During lymphoma workup, he recovered and the lymph nodes gradually subsided. The final diagnosis was revised as IM. He is well for more than 9 months after first biopsy. **Discussion:** Coupled with clinical information, in the setting of young patient with (1) uncommon location, such as Waldeyer's ring (2) CD30+ RS like cells with CD15- and presence of both OCT 2/BOB 1 expression, (3) reversed CD4/CD8 ratio of background small lymphocytes; one should rise the possibility of IM before diagnosis of CHL is made. When a spontaneous clinical improvement occurs in a patient with diagnosis of lymphoma, atypical presentation of EBV infection has to be considered.

AP12 Lipoma of the ascending colon: A case report

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Introduction: Colonic lipomas are rare non-epithelial neoplasms, and account for 0.035% to 4.4% of all polypoid lesions in the colon. They are often difficult to diagnose because of the asymptomatic or intermittent nature of the patients' symptoms. Colonic lipomas are often found incidentally during colonoscopy, computed tomography (CT) scan, surgery or autopsy. **Case report:** A 64-year-old man presented with four months history of epigastric pain, altered bowel habit, and a palpable epigastric mass. Computed tomography of the thorax, abdomen and pelvis revealed a large mass of fat density within lumen of transverse colon causing colocolic intussusception with no evidence of intestinal obstruction. Colonoscopy showed a huge pedunculated tumour mass almost occluding the lumen located 90-100cm from anal verge. Intraoperatively, a 6.5x3.5x5cm tumour was seen within the ascending colon along with multiple enlarged mesenteric lymph nodes. Microscopic examination showed ascending colon tumour composed of mature adipocytes intersected by fibrovascular septae arising from the submucosal region without involvement of the muscular layer with no evidence of lipoblasts or malignancy seen. A diagnosis of lipoma was made. **Discussion:** Colonic lipomas most commonly involve the ascending colon (45%) and 90% of them are localized to the submucosa. Definitive diagnosis of lipoma is made commonly after surgical resection and subsequently subjected to histopathological staining.

AP13 MYCN fluorescence in-situ hybridization (FISH) to aid prognostication and the association with clinicobiological characteristics in neuroblastoma patients in Hospital Kuala Lumpur

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Introduction: Neuroblastoma (NB) is the commonest extracranial solid tumour in children in which, the prognostic classification and risk group assessment depends on clinical and biological heterogeneity. A total of 132 cases per 100,000 Malaysian population from varied sites were reported from the year 2007 to 2011. The number of cases reported in Hospital Kuala Lumpur (HKL) from 2016 until 2017 is 35. According to literature reviews, prevalence of MYCN gene amplification which correlates with a high-risk disease and poor outcome is approximately 20% of neuroblastoma cases. This study aimed to evaluate MYCN gene status using interphase FISH for prognosis and the association with clinicobiological characteristics (age, primary site, histology and ploidy status) in NB cases reported in HKL. **Materials & Methods:** We performed a retrospective study to evaluate MYCN gene status by advocating interphase FISH in 9 NB cases and one negative control breast tissue from 2014 to 2017. Subsequently, the association of clinicobiological characteristics in NB cases were analysed. **Results:** 3 cases (33%) were MYCN amplified, 1 case (11%) was MYCN gain and the remaining 5 cases (56%) were MYCN non-amplified. Among the MYCN amplified cases, those with diploid DNA content are associated with unfavourable histology of poorly-differentiated and stroma-poor neuroblastoma, intra-abdominal origin and age range from 1 to >5 years. **Discussion:** MYCN gene status assessment using FISH is a highly valuable tool for the prognostication in NB. MYCN gene amplification associated with unfavourable clinicobiological features correlates with high-risk neuroblastic tumours and poor patient prognosis.

AP14 Tumour infiltrating lymphocytes in invasive breast carcinoma: Correlation with tumour grading and staging.

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Introduction: Invasive breast carcinoma is the most common cancer in women accounting for 23% of all cases in women globally. The two main prognostic factors for breast cancer are tumour grading and tumour staging. Tumours are commonly infiltrated by lymphocytes and their number are considered to reflect the host immune response to malignancy. The presence of tumour infiltrating lymphocytes (Tils) has been recognised as a biomarker of anti tumour immune response across wide range of tumours. This study was undertaken with the aim to study the significance of Tils in invasive breast carcinoma in correlation with tumour grading and staging. **Materials & Methods:** We studied 120 mastectomy cases with confirmed diagnosis of invasive breast carcinoma. All the slides of these cases were retrieved. Two slides with the largest tumour area were selected. Tils were quantified and scored according to Rathore et al (low: 1-25 cells, moderate: 25-50 cells and high: >50 cells). **Results:** There is a fair correlation between Tils score and lymph node metastasis ($\rho=0.286$, $p=0.001$). However, there are no significant correlation between Tils score and tumour grade ($p=0.357$), tumour size ($p=0.120$) and distant metastasis ($p=0.098$). **Discussion:** Tils in invasive breast carcinoma reflects immune response directed against lymph node metastasis and may be associated with the outcome of the disease. It may serve as an additional biomarker in the management of patients, especially in the absence of lymph node status such as patients subjected for neoadjuvant chemotherapy or post wide local excision without axillary lymph nodes.

AP15 A case of congenital parvovirus B19 infection diagnosed through placenta

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Introduction: Parvovirus B19 infection is a well-established cause of fetal death in hydrops fetalis. The diagnosis is usually made through histological identification of the characteristic nuclear inclusions in the placenta or fetal organs. However, the search for these inclusions are difficult at times particularly when placental sampling is limited or consent for fetal autopsy is not obtainable. We would like to share a case of congenital parvovirus infection with these characteristic inclusions and highlight the usefulness of immunohistochemistry. **Case report:** A 30-year-old lady, in her fourth pregnancy was referred for hydrops fetalis at 21 weeks gestation. She has three living children whom are currently well. Following induction of labour she delivered a male fetus. There were no dysmorphic features observed. However, the placenta was markedly large for gestational age, pale and friable with low fetoplacental ratio. On histology there were hydropic villi with increased nucleated red blood cells (RBC) within chorionic fetal vessels, many of which contained the characteristic intranuclear inclusions. They stained positively on immunostaining with parvovirus antibody. The parvovirus serology at the time of presentation was equivocal for IgM and positive for IgG. Other relevant microbiological investigations were negative. **Discussion:** Parvovirus infection is one of the commonly occurring intrauterine infections. Recognizing the histopathological features may aid in identifying the cause of intrauterine death as many of these women are asymptomatic. The use of immunostaining is very useful in confirming viral inclusions in the nucleated RBC and usually reveals a larger number of positive cells compared to H&E staining alone.

AP16 Abnormal circulating leukaemia-like megakaryoblasts in the placenta of a stillborn: Congenital Leukaemia (CL) vs Transient Abnormal Myelopoiesis (TAM)

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Introduction: The preleukaemic and leukaemic diseases of infant and early childhood have been described. CL is a rare haematologic disease most often diagnosed at birth or within the first month of life and commonly are of acute myeloid leukaemias (AML). This however need to be differentiated from TAM of the newborn. We present a case and highlight challenges encountered in placental examination. **Case report:** A 35-year-old lady, in her fifth pregnancy presented at 40 weeks of gestation with absence in fetal movement. Further investigation confirmed an intrauterine death. Following induction of labour a male macerated stillborn was delivered. It was observed that the umbilical cord was short and the right testis was undescended. There were no associated syndromic features seen. The parents did not consent to a postmortem examination. The placenta was pale, foul smelling with meconium stains. Microscopically, there were numerous circulating immature precursors and nucleated red blood cells within the fetal vessels in the umbilical cord and chorionic villi. The morphology and immunohistochemistry were suggestive of a megakaryoblastic lineage. **Discussion:** Both AML and TAM are known manifestations in neonates with Down's syndrome, predominantly involving the megakaryoblastic series. Although clinically and haematologically indistinguishable, TAM is transient and usually exhibits a spontaneous regression. However, with heart and liver involvement TAM may cause fetal demise. The underlying genetic contributions were not established in this case. However, both entities along with other neonatal leukaemoid and leucoerythroblastic conditions need to be considered. Hence detailed placental examination with relevant immunohistochemistry analysis is recommended.

AP17 Expression of CXCL 16 in renal cell carcinoma and its correlation with prognostic clinicopathological parameters

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Introduction: Renal cell carcinoma (RCC) is an infrequent cancer in Malaysia and worldwide. It has the propensity to metastasize to unusual sites and late metastasis is not uncommon. We investigated the expression of chemokine CXCL 16 in RCC in particular the clear cell type by immunohistochemistry study and its correlation with clinical parameters. **Materials & Methods:** Immunohistochemistry study was performed on tissue microarrays of 40 cases of RCC diagnosed at Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM). Results: Our study showed that high CXCL16 expression (2+ and 3+) was present in RCC (which was suggested to represent soluble CXCL16). When correlated with clinical parameters, we found that the tumours with higher nuclear grading and at the higher stage of disease at presentation were showing stronger CXCL16 staining intensity ($p=0.048$ and $p=0.049$ respectively). A higher tumour stage was also correlated with higher CXCL16 immunoreactivity score ($p=0.000$). However, no significant correlation was noted between the immunoreactivity score of CXCL 16 and nuclear grading of the tumour ($p=0.050$). **Discussion:** These findings suggested that soluble CXCL16 had a role in progression of RCC. Possible explanation for these findings included the effects of transient signaling by the interaction between the soluble CXCL 16 and its receptor CXCR6 that might stimulate cellular growth as well as promoting tumour cell detachment thereby leading to metastasis.

AP18 Spectrum of IgG4 related diseases of the eye and lung: two case reports

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Introduction: IgG4 related disease is a fibroinflammatory condition of unknown aetiology affecting various organs and tissues. In 2011, Deshpande V. et. al. endorsed 3-tiered diagnostic terminology for pathological diagnosis of IgG4 related disease, with special consideration of some organs including the lacrimal glands and lung. **Case report:** We reported two cases of IgG related disease of different diagnostic terminology. The first case is a 66 years old man with 6 years history of worsening bilateral eye proptosis and blindness. Computed tomography (CT) orbit showed bilateral eye intraconal and extraconal masses involving the optic canal with extension into left extracanal space. Right infratemporal mass biopsy revealed all histopathological features of IgG4 related disease; dense lymphoplasmacytic infiltrate, interstitial fibrosis and obliterative phlebitis. Immunohistochemistry study shows IgG4 positive plasma cells of more than 100 per hpf. Thus reported as 'highly suggestive of IgG4 related disease'. The second case is a 56 years old lady with incidental finding of restrictive lung function test and pulmonary nodules on CT thorax. Patient underwent video-assisted thoracoscopic surgery which revealed adhesions at right lung. This case was diagnosed as having 'probable histological features of IgG4 related disease as the right upper lobe resection showed only two histopathological features with occasional patches of IgG4 positive plasma cells that slightly exceeded 50 per hpf. **Discussion:** Both cases demonstrated the importance of correct diagnostic terminology to aid the clinicians for further investigations and correlation with clinical, radiological and serological evidence to achieve the definitive diagnosis of IgG4 related disease.

AP19 An incidental finding of rare ectopic pleural thymoma: A case report

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Introduction: Thymoma is a neoplasm arising from or exhibiting differentiation towards thymic epithelial cells, regardless of the presence and relative numbers of non-neoplastic lymphocytes. It is usually located in the anterosuperior mediastinum but its occurrence in other mediastinal compartments, neck, thyroid, pericardial cavity, pulmonary parenchyma or pleura has also been reported although it is extremely rare. **Case report:** A 65-year-old gentleman with incidental finding of right lower lung mass on chest radiograph after presented with traumatic lung injury secondary to motor vehicle accident. Computed tomography of the thorax revealed a heterogeneous mass with centre hypodensity at the right lower thorax measuring 13.8 cm x 8.7 cm x 9.7 cm arising from the extraparenchymal and compressing the adjacent segments of right lower lobe likely pleural based. Ultrasound guided biopsy was performed. Histopathological examination showed biphasic tumour comprised of bland looking cells of dual morphology of spindle cells intermixed with ovoid cells. Immunohistochemical studies expressed strong positivity of the tumour cells towards some of the epithelial markers (CK7, CK5/6, CKMNF116 and p63) as well as vimentin. Scattered lymphocytes amongst the tumour cells expressed CD3, CD20 and CD45. Ki-67 showed low proliferative activity of less than 2%. **Discussion:** Although ectopic pleural thymoma is a highly unusual phenomenon, this entity should be considered as one of the possible differential diagnosis of pleural mass. Because of the peculiar location and variability of histologic patterns, it may be confused with other neoplasms and consequently may cause diagnostic problems clinically, radiologically and histologically. This case highlights the importance of awareness for this entity, the characteristic morphological features and immunohistochemical profile that may help prevent a misdiagnosis.

AP20 Primary Giant Cell Tumour of Soft Tissue in Scalp: An Uncommon Tumour at Uncommon Location

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Introduction: Primary giant cell tumour of soft tissue (GCT-ST), also known as soft tissue giant cell tumour of low malignant potential, is a rare soft tissue tumour. Histologically, these lesions bear a close resemblance to their bony counterparts, GCT of bone. Although predominantly a benign condition, its capacity to recur or evolve into malignant lesion is well recognized. The lesions are usually superficial and involve lower extremities and trunk but rarely occur in head and neck. Here we report a rare benign primary GCT-ST at an uncommon location. **Case report:** A 27-year-old Malay gentleman presented with painless right forehead swelling for 3 months. Physical examination revealed a mobile, benign looking superficial skin lesion measuring 3x1cm. Grossly, the lesion showed greyish solid surface enwrapped by thin pseudo capsule. Microscopically, it composed of round to oval polygonal neoplastic cells intermixed with osteoclast-like giant cells. The cells display mildly pleomorphic vesicular nuclei with small nucleoli and moderate amount of cytoplasm. Mitotic figures were frequent, but no atypical form was observed. The neoplastic cells were weak and diffusely expressing SMA. Homogenous and strong expression of CD68 is noted on the osteoclast-like giant cells. **Discussion:** GCT-ST is uncommon but distinct entity. It is important to recognize this pathological entity in order to avoid misdiagnosis with other fibrous tumour associated with giant cells such as GCT of tendon sheath, nodular fasciitis, benign fibrous histiocytoma and undifferentiated pleomorphic sarcoma. Complete excision results in benign clinical course because distant metastasis and tumour associated death seem to be exceedingly rare.

AP21 An arteriovenous malformation of the uterus in a term pregnancy

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Introduction: Uterine arteriovenous malformation (AVM) is a rare, potentially life-threatening condition. Because of the abnormal communication between arteries and vein, the high vascular flow may result in massive haemorrhage. We present an unexpected case of uterine AVM in a term pregnancy. **Case report:** A 35-year-old lady, G2P1 at 39 weeks of gestation, with a previous history of caesarian section, had a vacuum assisted delivery following poor maternal effort. There was light meconium stained liquor seen. However, she had to undergo an exploratory laparotomy due to a sudden worsening abdominal pain with symptomatic anaemia. Intraoperatively, there was a massive intraperitoneal collection of blood with intractable bleeding from a localized source in the left parametrium. Inevitably, a subtotal hysterectomy had to be performed. No tear nor disruption of the myometrial wall was identified. Serial sections of the uterine specimen showed groups of dilated spaces containing blood within the parametrial serosa. Histological sections demonstrated a mixture of vascular structures with walls of variable thickness consistent with an arteriovenous malformation. **Discussion:** Both congenital and acquired forms of uterine AVM have been described, the latter being associated with previous uterine trauma or caesarian section. Hormonal changes in a pregnancy

such as in this case may play a role in endothelial proliferation and hence the increase in vascularity of the existing lesion in the uterus. Although embolization is the initial treatment option in selected patients, there can be emergency situations where hysterectomy remains the only choice.

AP22 Ovarian struma carcinoid: a case report.

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Introduction: Struma carcinoid of the ovary is a type of monodermal germ-cell tumour characterized by an intimate mixture of thyroid tissue and carcinoid. These tumours of the ovary are uncommon and rarer than struma ovarii. It usually occurs as a nodule or mass within a dermoid cyst, struma ovarii or a mucinous cystic tumour. **Case report:** A 56 year old lady, Para 5, post-menopausal for 3 years. She was under surgical outpatient follow up for chronic constipation. The colonoscopy was inconclusive due to poor bowel preparation. Ultrasound examination and CT abdomen and pelvis scan noted bilateral complex adnexal masses and faecal loaded colon. The tumour markers were sent and the CA125 level was slightly raised at 59.2 U/ml and CEA level was normal at 1.5 ng/ml. She underwent uneventful exploratory laparotomy, total abdominal hysterectomy and bilateral salpingoopherectomy, omentectomy and pelvic lymph node dissections. Macroscopic histopathological examination revealed right and left ovarian cysts measuring 60x60mm and 45x30mm respectively. Cut sections show solid and cystic lesions. The solid component show brown, tanned cut surface. Microscopic examination of the right ovarian cyst shows struma carcinoid and the carcinoid component are arranged in trabecular pattern. **Discussion:** Struma carcinoid is a rare tumour in ovary. Many of the tumours are incidental findings, endocrine symptoms occur rarely. This case illustrated the histological findings and its uncommon symptom that can occur in this type of tumour, which in this case presented with constipation due to polypeptide secretion.

AP23 Unilateral primary lung hypoplasia diagnosed at clinical post mortem of a young pregnant mother

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Introduction: Unilateral primary pulmonary hypoplasia is a development abnormality usually diagnosed during childhood. The patients present with different severity from completely asymptomatic, repeated chest infections to severe respiratory distress. Hence, they are often wrongly diagnosed for more common things and diagnosis is even more challenging in adults. **Case report:** We received a request to perform a clinical autopsy to look for the cause of death of a 21 year-old primigravida lady at 29 weeks of gestation. Prior to her death, she was treated as severe respiratory distress secondary to pneumonia with underlying bronchial asthma. She succumbed on table in the radiology department where she was planned for a CT thorax. Post mortem examination revealed a small and underdeveloped left lung which was confirmed by histopathology examination. Cause of death given as severe acute pneumonia of right lung causing respiratory failure with underlying left lung hypoplasia. **Discussion:** This patient was initially misdiagnosed as having bronchial asthma in view of the lung auscultation findings when she was young. Regrettably, no chest x rays were taken. This rendered the diagnosis of left lung hypoplasia impossible to be made and this became even more difficult during her pregnancy. If the lung hypoplasia was diagnosed earlier, perhaps more aggressive and longer duration of antibiotics will be given to this patient. Hence, it is perhaps wise to consider the differential diagnosis of lung hypoplasia, among other common chest pathology, when encountering the lung findings of persistent wheezing, even in an adult patients.

AP24 Gastric schwannoma: a mimicker of gastrointestinal stromal tumour (GIST)

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Introduction: Gastric schwannoma (GS) is a rare mesenchymal tumour as compared to gastric GIST. Clinically, both entities may have similar presentation and microscopically they show proliferation of spindle cells within the submucosa. **Case report:** A 60 year old lady presented with abdominal pain and underwent a subtotal gastrectomy and gastro-jejunostomy with pre-operative impression of GIST. Intra-operatively, there was a large exophytic and circumscribed mass at the greater curvature of the stomach measuring 175x60x52 mm. Cut section showed solid tan surface with vague whorling pattern. Microscopically, the submucosal gastric tumour was composed of spindle shaped cells arranged in interlacing fascicles and palisading pattern with prominent peritumoural lymphocytic cuffing. There were hypo and hypercellular areas, Verocay bodies and microcystic spaces accompanied by hyalinised blood vessels. Immunohistochemical study showed the tumour cells were strong and diffusely immunoreactive for S100 and were negative for CD117, DOG1, CD34, SMA and Desmin. The proliferative index was low (1%). A diagnosis of GS was made. **Discussion:** Gastric schwannomas only account for 0.2% of all gastric tumours and 6.3% of gastric mesenchymal tumours. They arise from the peripheral neural plexus within the gastric wall. Immunohistochemical study is crucial in differentiating GS from GIST as morphologically they may look similar. GIST would be positive for CD117 and DOG1. Clinically and morphologically, both entities may appear similar, but they have different immunophenotypic profiles and carry different prognoses. Gastric schwannomas are benign neoplasms with excellent prognosis after surgical resection, while a small proportion of GIST may have aggressive behaviour.

AP25 Extranodal NK/T-cell lymphoma, nasal type mimicking granulomatous inflammation

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Introduction: Extranodal NK/T-cell lymphoma (ENKL) is a rare aggressive non-Hodgkin's type lymphoma that associated with Epstein Bar Virus (EBV) infection. Patient usually came with symptoms of nasal obstruction, epistaxis or with extensive destructive midline facial lesions. The tumour is characterized by destructive, vascular damage with angiocentricity and prominent necrosis which can sometimes mimics granulomatous inflammation and necrosis. It has an unpromising prognosis but survival seem to be improved in recent years with intensive therapy. **Case report:** A 22-year-old Indonesian man presented with painful left cheek swelling for 4 month and intermittent fever for a month. The swelling is gradually increasing in size associated with nasal obstruction. Otoscopic examination revealed infiltrative mass extending to nasopharynx and oropharynx. Nasal biopsies was done twice, reported as necrotic tissue and chronic granulomatous inflammation **Pathological findings:** As the previous HPE was inconclusive, multiple biopsies was taken from different sites. Microscopically, the tissue is markedly necrotic tissue with dense acute and chronic inflammation. At focal area, atypical neoplastic cells of medium to large cells seen infiltrating the stroma with features of angiocentricity. These cells are positive for CD3, CD7, CD2 and CD4. EBER in situ hybridization study is positive. The proliferative with Ki67 is increased. We conclude the diagnosis as ENKL, nasal type. **Conclusion:** The diagnosis of ENKL can be difficult and requires high index of suspicion as mostly the biopsies finding can be inconclusive. The diagnosis of ENKL can be confused infections, autoimmune or inflammatory disease. Correlation between clinical, radiological with multiple biopsies are required in giving such diagnosis as it is highly aggressive with short survival and poor response to therapy.

AP26 Tumour Lysis Syndrome in Angioimmunoblastic T cell Lymphoma: A Case Report

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Introduction: Angioimmunoblastic T-cell lymphoma (AITL) is a rare neoplasm of mature T follicular helper cells phenotype. It occurs in middle-aged and elderly group with male predilection. It is extremely aggressive and typically presents with advanced-stage disease at diagnosis. AITL is associated with generalised lymphadenopathy, hepatosplenomegaly, systemic symptoms, polyclonal hypergammaglobulinemia and haemolytic anaemia. Most cases were implicated with the presence of EBV infection. **Case report:** An Egyptian man in his early 40s presented to Hospital Selayang with fever, progressive dyspnoea, cough, night sweats and neck swelling for 1 year. He had hypothyroidism with mild obstructive symptoms. He was tachypnoeic and desaturated on room air. Subsequently he developed respiratory failure requiring intubation. There were multiple lymphadenopathies over the neck, axillary and inguinal regions. An excisional biopsy of a right inguinal lymph node was performed and examined histologically. The lymph node measured 30mm by largest dimension. It showed a completely effaced nodal architecture with neoplastic T cell lymphocytes (positive for all pan-T cell markers), arborized high endothelial venules (HEV), EBV positive B-blast cells and numerous abnormal mitotic figures. Other laboratory parameters demonstrated evidence of tumour lysis syndrome, coagulopathy and acute kidney injury. **Discussion:** Being an aggressive neoplasm, AITL is a challenging entity – both to diagnose and to plan treatment strategies. Complicating this is the interference of tumour lysis syndrome which mimics other medical illnesses clinically and biochemically. Therefore, a high index of suspicion, along with histological and immunophenotypical examinations are warranted.

AP27 Neuroendocrine neoplasm in liver: A clinicopathological challenge

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Introduction: Neuroendocrine tumour (NET) arises preferentially in the bronchopulmonary tree or gastrointestinal tract and usually metastasized to the liver. A primary hepatic neuroendocrine tumour (PHNET) is extremely rare. Herein, we report a neuroendocrine neoplasm, suspected to be hepatocellular carcinoma (HCC) before operation with prospect being a liver primary. **Case report:** A 37-year-old pregnant woman at 32 weeks with progressively increasing painless abdominal mass. The palpable mass was located at epigastrium and measured 5x5cm. It had lobulated surface and well-defined border. MRI abdomen showed large liver mass at segment IVb suspicious of HCC. Other imaging studies showed no other mass in the gastrointestinal tract or in the lung. Ca 19.9 and AFP were raised. Exploratory laparotomy was performed postdelivery at 33 weeks showed a huge tumour encompassing both lobes. Tissue biopsy was taken. Histologically, extensive sheet like areas of small blue cells favouring NET with focal necrosis and adjacent regenerative hepatocytes were observed. These cells were moderately pleomorphic, having hyperchromatic nuclei with nuclear moulding, inconspicuous nucleoli and many mitoses. They were positive for Synaptophysin, Chromogranin A, CK7 and focally to TTF1, CD99 and CK19 while negative for HSA, AFP and CK20. Ki 67 index was high. Subsequent serum Chromogranin A was performed and found to be raised. **Discussion:** The diagnosis of PHNET is a medical challenge, requiring differentiation of other type of hepatic malignancy and exclusion of occult primary neuroendocrine tumors. The diagnosis of PHNET can be ascertained after complete work-up to exclude another primary origin.

AP28 Primary angiosarcoma of the breast: a case report.

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Introduction: Primary angiosarcoma is a rare malignancy in the breast with incidence of 0.05% of all primary malignancies of the breast. It carries poor prognosis and mastectomy with or without radiation is the current treatment. **Case report:** A 35 year old with underlying epilepsy presented with huge left breast swelling for 3 months. There was no history of breast lesion or radiation prior to the presentation. Ultrasound shows a large vascularized and heterogenous mass of the left breast which was confirmed by subsequent MRI and CT scan. Initially, ultrasound guided biopsy was performed in which the result was unsatisfactory. Patient developed hematoma post-biopsy and required multiple blood transfusion. Hence, angiogram and embolization was done prior to surgery. She underwent radical mastectomy with lattisimus dorsi flap. The gross examination of the breast showed a large ill-defined tumour with cavity filled with blood measuring 105x100x70mm. A few purplish nodules are also seen on the skin. Microscopically, there are multi-focal, ill-defined vascular tumour consisting of proliferation and anastomosing vascular channels lined by malignant endothelial cells. Immunohistochemical studies show the tumour cells are immunoreactive to CD31 and ERG. CKAE1/AE3 is negative. **Discussion:** The knowledge regarding primary angiosarcoma of the breast is limited as it is a very rare malignant tumour. Unlike secondary angiosarcoma, primary angiosarcoma is not related to history of radiation. Patient is usually young and the presentation is very short as the tumour is very aggressive. Thus, accurate diagnosis is needed for proper management of the patient.

AP29 Tonsillar follicular dendritic cell sarcoma mimicking a spindle cell tumour: a diagnostic challenge

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Introduction: Follicular dendritic cells (FDC) sarcoma is a rare neoplastic entity, and is even rarer extranodally including tonsils. It affects adult age group with no sex predilection. **Case report:** A 51-year-old clerk with background diabetes mellitus and hypertension, presented with right tonsillar hypertrophy for 10 months. It was associated with intermittent fever, throat pain and bleeding. There was no obstructive symptoms. Intraoral examination revealed a grade 3 right tonsillar enlargement which was diagnosed as a fibroma on biopsy. Computed tomography scan of the neck reported as a heterogeneous enhancing lesion of the right palatine tonsil with local mass effect. Patient agreed for bilateral tonsillectomy. Post operatively, the right and left tonsils appeared fibrotic, measuring 30mm and 20mm in largest dimension respectively. Microscopically, the right tonsil showed a partially effaced nodal architecture and was replaced by two populations of neoplastic cells. They were bland-looking epithelioid cells possessing vesicular nuclei and spindle-shaped cells with elongated hyperchromatic nuclei. The former imparted a syncytial pattern and the later assumed a storiform and whorled patterns. The neoplastic cells were strongly positive for vimentin, CD21 and CD23. Meanwhile, the left tonsil exhibited reactive follicular hyperplasia. **Discussion:** FDC sarcoma is typically an indolent tumour with local recurrences. Many cases showed FDC sarcoma behaved as low- to intermediate grade tumour. Despite fairly well characterised histologically, with a distinct immunophenotype, it remains misdiagnosed especially in small biopsies. Therefore, a high index of suspicion and awareness of this entity are required in order to achieve the definite diagnosis.

AP30 Primary renal synovial sarcoma: A rare case report

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Introduction: Primary renal synovial sarcoma (SS) is a rare neoplasm whereby the presenting clinical features are similar to other common renal tumours, making early diagnosis difficult. To date, around 50 cases have been reported in literature review, and this is one of the few diagnosed in Hospital Kuala Lumpur. **Case report:** A 27-year-old man, presented with a short history of painless gross haematuria and a palpable abdominal mass. CT-scan reported a large heterogenous tumour at the upper pole of right kidney measuring 10.0x9.0x10.9 cm. Patient underwent right radical nephrectomy without complications. Microscopic evaluation showed a non-encapsulated tumor composed of monomorphic spindle cells arranged in solid sheets and intersecting fascicles. The tumour cells are plump and elongated with indistinct cell borders, some with conspicuous nucleoli and scanty cytoplasm. Mitoses are high (88 per 10 high power fields). The tumour blends irregularly into the adjacent renal parenchyma. Immunohistochemistry shows diffuse immunoreactivity of tumour cells towards TLE-1, BCL 2 and vimentin with focal positivity towards FLI-1, CKAE1/AE3, and EMA. Synaptophysin, SMA, Desmin, CD34, WT-1, S100 and Chromogranin are negative. **Discussion:** Other than its rarity, primary SS of the kidney is difficult to be differentiated morphologically from other renal spindle cell tumours such as adult Wilms tumour, primary PNET/Ewing sarcoma, sarcomatoid RCC, and undifferentiated carcinoma. Hence, besides IHC findings the necessity for molecular studies becomes helpful for diagnostic and confirmation of SS. Having said that, due to the lack of availability of molecular studies, diagnosis is made best with immunohistochemistry studies in many centers.

AP31 Clinical and pathological features of nasopharyngeal carcinoma in Sabah

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Introduction: In Peninsular Malaysia, nasopharyngeal carcinoma (NPC) is the fifth most common cancer. This research aims to determine the clinicopathological characteristics of NPC cases in Sabah as there is lacking of such data described in the literature. **Materials & Methods:** We studied 258 NPC cases from 2014 to 2016 reported at Hospital Queen Elizabeth Kota Kinabalu, Sabah. **Results:** Almost half (49.2%) of the cases were males ages 40 to 64 years whereas in females, the cases also peaked at ages 40 to 64 years but only accounting for 16.7%. The mean age is 48.7 years with the lowest age is 10 years old and the highest age is 81 years old. Male is more predominant (74.4%) compared to female (26.6%) yielding a 2.8:1 ratio over the years. For indigenous population, Kadazan–Dusun is the highest numbers of NPC (39.5%) and Chinese is the highest from the non-indigenous population (20.2%). Non-keratinizing squamous cell carcinoma is the most frequent subtype (98.8%). The number of cases each year is increasing in trend from 75 to 84 to 96 cases per year, in the years 2014, 2015 and 2016 respectively. Most patients presented late with advanced diseases (77.5%). Most of our patients (69.4%) presented with neck swelling. There is no association between age, gender, and ethnicity on histological subtypes (p values >0.05). **Discussion:** Further investigations are recommended to determine the probable genetic susceptibility related to the pathogenesis of NPC as well as the studying factors causing the increasing trend of NPC cases in Sabah.

AP32 An incident in the groove, a case of groove pancreatitis.

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Introduction: Groove pancreatitis is a rare form of chronic pancreatitis affecting area between superior aspect of pancreatic head, duodenum and common bile duct also called the “grove”. The exact cause is unknown, however it is highly associated with alcohol abuse. **Case report:** A 58 year-old man, ex-alcoholic with a history of gastric ulcer, presented with generalized colicky abdominal pain, associated with vomiting and loss of appetite. He also noticed weight lost over few months period. No jaundice noted. CT-Scan abdomen showed ill-defined heterogenous enhancing head of pancreas lesion, which raised suspicion of pancreatic head tumour associated with extensive surrounding inflammation. Oesophagoduodenogastroscopy showed pangastritis, duodenitis with extraluminal D2 duodenal compression. Biochemical investigation showed raised CA19.9 A diagnosis of duodenal gastrointestinal stromal tumour (GIST) was made based on imaging, scope and biochemical findings. Whipple’s procedure was performed. Histological sections show an ill-defined lesion composed of proliferation of haphazardly arranged smooth muscle bundles arising from duodenal wall with fibrotic and hyalinized stroma, involving the duodenal submucosa and extending into the adjacent soft tissue and pancreas. Many cystic lesions encased by myofibroblastic proliferation with absence of lining epithelium observed. The lesion is composed of bland looking spindle cells with scanty cytoplasm. These spindle cells are positive for SMA, Desmin, Vimentin and negative for CD34, c-kit, DOG1, ALK1, Fac8 and CD31. **Discussion:** Diagnostic imaging of groove pancreatitis can be challenging and misleading in many cases, however it should always be a key differential in a patient with head of pancreatic mass without jaundice.

AP33 Adrenal extramedullary hematopoiesis associated with beta-thalassemia trait in an adult male

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Introduction: Extramedullary hematopoiesis (EMH) is a physiological compensatory phenomenon in response to altered hematopoiesis occurring secondary to inadequate bone marrow function. It often occurs in hemoglobinopathies, hemolytic anemias, leukemias, lymphomas, and myeloproliferative disorders. EMH in the adrenal gland is rarely reported and may be clinically detected as incidental myelolipoma. **Case report:** AL 40 year old male, with underlying intermediate beta thalassaemia was admitted to the Medical ward for symptomatic anemia and persistent vague abdominal pain. An abdominal CT scan revealed a right adrenal incidentaloma, indeterminate in nature. Grossly, it is a well-circumscribed mass with variegated yellow to red-brown cut surface. The histomorphology and immunohistochemical staining profile were compatible with extramedullary hematopoiesis with erythroid and myeloid precursors and megakaryocytes. **Discussion:** Adrenal myelolipomas are rare tumors frequently discovered incidentally during imaging studies or autopsies. Previous study revealed that there is no gender predilection but advanced age is associated with greater susceptibility for mass. Multiple case reports described the defects in hemoglobin production associated with sickle-cell disease, hemoglobin H constant spring disease, thalassemia and impaired red blood cell membrane production linked with hereditary spherocytosis as pathological causes of EMH in the adrenal gland.

AP34 Enteropathy-associated T-cell lymphoma (EATL) Type II: The Case Report of two cases in Selayang Hospital

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Introduction: Enteropathy-associated T-cell lymphoma (EATL) is the most common type of T-cell lymphoma arising in the intestine but it is still an uncommon neoplasm. A common initial presentation of this cancer is a small bowel perforation which necessitates emergency surgery. The diagnosis is rarely made prior to histopathological examination. **Case Report:** We report two cases of elderly women who both presented with non-specific symptoms such as fever, poor oral intake, vomiting and generalized abdominal pain. Radio imaging showed pneumoperitoneum with perforated small bowel which subsequently requiring emergency laparotomy. Gross examination revealed perforation with adjacent flattened mucosal wall having focal thickening and ulceration. Microscopically, there was transmural infiltration of moderate to large mononuclear cell having scanty cytoplasm with high mitotic index. Tumour cells were immunoreactive to CD3, CD8, and CD56 while negative to CD4. Features were suggestive of T cell lymphoma favouring Type II, Enteropathy-Associated T-cell lymphoma (EATL). Both patients sadly had succumbed after a short stay in the ward post operatively. **Discussion and conclusion:** Enteropathy-associated T-cell lymphoma (EATL) is a rare subtype of lymphoma. This disease has no typical presentation which may be masked by other abdominal related disease. Patient usually comes late with bowel perforation which requires emergency exploration. EATL has a grave prognosis due to poor chemo sensitivity, rapid tumour growth and a tendency to disseminate causing death from abdominal complications.

AP35 Immunohistochemical expression of LIM homeobox proteins (ISL1 and LHX5) in urothelial carcinoma of the bladder

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Introduction: LIM homeobox genes encode a series of LIM-homeodomain (LIM-HD) proteins featuring two LIM domains in their amino termini and a centrally located homeodomain that is used to interact with specific DNA elements in target genes. Recent studies reported that LIM homeobox genes (ISL1 and LHX5) played an important role in cancer. This study was carried out to determine the immunohistochemical expression of LIM homeobox proteins (ISL1 and LHX5) in urothelial carcinoma of the bladder. **Materials & Methods:** 100 histological blocks of paraffin-embedded tissues of urothelial carcinoma cases were selected from the Department of Pathology, Hospital Kuala Lumpur and immunohistochemical stainings using ISL1 and LHX5 antibodies were performed to determine their proteins expression. **Results:** Positive expression for ISL1 was detected in 94 (94%) samples and LHX5 was positively expressed in 98 (98%) samples. High expression of ISL1 showed decreasing trend as the grades increased and increasing in trend as the cancer progressed from stage 2 to stage 4. As for LHX5, there was no distinct expression pattern across the grades and stages. There was a significant association between LHX5 expression and grades (low and high grades) of urothelial carcinoma ($p = 0.044$). **Discussion:** An inversely proportional and proportional relationship of ISL1 expression throughout the increasing grades and stages respectively raises its potential as a biomarker for early diagnosis of urothelial carcinoma of the bladder. A significant correlation between LHX5 with the grades suggests that it may play a role in the development of urothelial carcinoma of the bladder.

AP36 Glomus tumour of the stomach

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Introduction: Gastric glomus tumours (GGT) are rare, accounting for less than 2% of all benign gastric tumours. It is composed of cells that closely resemble the modified smooth muscle cells of glomus body. GGT are solitary well-circumscribed submucosal lesions, usually located in the antrum, presenting with variety of symptoms. **Case report:** A 47-year-old female presented with symptomatic anaemia secondary to upper gastrointestinal bleeding. Oesophageal-gastro-duodenal endoscopy revealed an elevated antral mass measuring 30 x 20 mm in diameter. Radiological finding showed an antral hypochoic mass measuring 20 to 60 x 20 to 30 mm in diameter with calcification. Clinical diagnosis was gastrointestinal tumour (GIST). She refused for surgical intervention. Two years later, she presented again for epigastric pain. CT abdomen showed an antral mass and luminal narrowing. The patient underwent distal partial gastrectomy with gastrojejunum anastomosis. Gross examination revealed a well-circumscribed, solid grayish brown tumour measuring 30x20x20mm. Microscopically, the tumour comprised of varying sizes vessels surrounded by cohesive clusters of uniform round cells with scanty cytoplasm. There was no cellular atypia or muscularis propria invasion. Mitotic figures were 2/50 HPF. The tumour cells were immunopositive for SMA. CD34, CKAE1/AE3 and S100 were negative. **Discussion:** GGT are distinct lesions that are rarely occur in stomach. It is difficult to distinguish from GIST by radiography, without biopsy sample and immunohistochemical study. Even though most GGT are

benign, malignant cases have been reported. *Folpe et al* proposed deep tumour location, tumour size more than 2 cm or atypical mitotic figures as criteria for malignancy.

AP37 Gene expression and DNA methylation status of HER3 in primary colorectal adenocarcinoma (CRC)

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Introduction: DNA methylation of CpG islands plays an important role in carcinogenesis through the regulation on gene expression. Aberrant DNA methylation of the ErbB gene family has been implicated in carcinogenesis of CRC. HER3 has been linked with activation of oncogenic PI3K/Akt and Ras/Raf/MAPK pathways, leading to tumour initiation, progression and drug resistance. Our study is aimed to determine DNA methylation and its effects on HER3 gene expression in CRC. **Materials & Methods:** 44 FFPE archived CRC cases with normal adjacent tissues were selected. HER3 gene expression was determined using RT-qPCR method. RNA was transcribed into cDNA by reverse transcriptase followed by qPCR using HER3-specific primer. DNA methylation status was determined using methylation specific PCR. This involved DNA extraction, bisulfite conversion and methylation detection. **Results:** Upregulation of HER3 mRNA was found in CRC compared to normal colon. Of 44 samples, 5 (11.4%) were methylated, 31 (70.5%) were unmethylated and no amplification was found in 8 (18.2%) samples. The corresponding pattern found in normal adjacent tissues were 3 (6.8%), 37 (84.1%) and 4 (9.1%) samples, respectively. DNA methylation was not associated with HER3 mRNA overexpression ($p > 0.05$). **Discussion:** HER3 overexpression may play a key role in carcinogenesis of CRC. Our results show that there is no relationship between DNA methylation and HER3 mRNA overexpression. Hypomethylation of CpG island promoters may result in gene over-expression. It has been reported that hypomethylation of CpG islands occurs at the early step in carcinogenesis. This may occur in the normal-adjacent tissues surrounding the cancer (the field defect). In conclusion, our data suggest that there is no relationship between DNA methylation at CpG islands and HER3 mRNA expression. Further investigation on DNA hypomethylation is required.

AP38 The effects of Gardnerella vaginalis intrauterine infection on rabbit foetal lung.

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Introduction: Gardnerella vaginalis (GV) is the main causative agent for bacterial vaginosis. GV is the second most common cause of intrauterine infection after Ureaplasma and is implicated in intrauterine growth restriction. There is insufficient evidence if antenatal infection with GV also impairs fetal lung development or maturation. The aim of this study was to evaluate the effects of GV infection on fetal lung development. **Materials & Methods:** GV was inoculated into the amniotic cavity of pregnant New Zealand white rabbits on day-21 gestation. At day-28, the foetus was removed and the lung were sent for histological processing. Lung morphometry was assessed by determination of the thickest alveolar septae, number of alveolar spaces and surface area of alveoli. Investigators were blinded to the GV status of the tissue samples. **Results:** The average weight of GV-infected foetal rabbit lung (0.6+0.11 g) was significantly lower than control (0.9+0.08 g) ($p = 0.002$). The GV-infected rabbits ($n = 11$) showed a significant increase in the thickness of alveolar septa compared to control ($n = 9$) (14.75+2.76 μm and 12.40+3.75 μm respectively; $P = 0.007$). However, there were no significant difference between the GV-infected and control groups in the alveoli number (13.93+2.97 and 14.64+3.35 respectively) and alveoli surface area (1806.03+1060.74 μm^2 and 1792.05+1006.20 μm^2 respectively) ($P > 0.05$). **Discussion:** The thicker alveolar septae in the GV-infected group may represent a sign of lung immaturity. Our next step is to determine whether the alveolar septae are infiltrated by mononuclear inflammatory cells.

AP39 Intracystic papillary neoplasm of the gallbladder

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Introduction: Intracystic papillary neoplasm is one of the precursors for carcinoma of the gallbladder. It is being recognized by 2010 World Health Classification of tumours of digestive system as a separate entity from the gallbladder adenomas. It is usually of more than 1cm in size, composed of papillary, tubular or mixed pattern of mainly biliary and to lesser extent gastric phenotype. **Case Report:** We reported a case of 58-year-old Malay man presented with two days history of pricking epigastric pain relieved by bending forward associated vomiting. Computed tomography (CT) abdomen revealed a gallbladder tumour along with common bile duct and intrahepatic duct dilatation. Grossly, the cholecystectomy specimen showed a polypoidal tumour measuring 30x20x10mm at body, which is located 20mm from the neck surgical margin and 5mm from the non-peritonealised margin. The remaining wall of the gallbladder measures 1mm to 5mm thick with the most thickened area adjacent to the tumour. Histopathological examination showed a tumour with tubulopapillary glandular architecture, lined by pyloric and foveolar type epithelium. Foci of cells with high grade dysplasia are also seen. No architectural complexity, lymphovascular invasion or

perineural invasion seen. The adjacent gall bladder mucosa showed pyloric metaplasia and chronic cholecystitis features. Thus, the diagnosis of intracystic papillary neoplasm of gallbladder with high grade dysplasia was concurred. **Discussion:** Intracystic papillary neoplasm is a rare neoplasm of gallbladder. Distinguishing from papillary adenoma may be difficult. However, vast majority have biliary or gastric phenotype compared to intestinal phenotype in the latter.

AP40 Pulmonary large cell neuroendocrine carcinoma in 6-year-old girl: A Case Report

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Introduction: Pulmonary tumours in paediatric age group are extremely rare; most common are metastases from other primary organs. Majority of primary pulmonary tumours (~76%) are malignant with carcinoid tumours being the most common malignant pulmonary neoplasm in paediatrics. **Case report:** A 6-year-old girl presented with prolonged cough for 2 months, intermittent shortness of breath for two weeks with constitutional symptoms. Examination showed decreased breath sounds over the right lung. Chest X-ray showed consolidation of the right lung. Computed tomography scan of the chest showed a total collapse of the right upper lobe and partial collapse of right lower lobe. Flexible bronchoscopy showed vascularized intraluminal mass causing total obstruction of the right main bronchus. Subsequently, open biopsy was done and sent for histopathological examination. The partial lobectomy specimen showed two well circumscribed nodules with yellowish cut surface measuring 30-40mm. Microscopic findings showed large cells arranged in sheets, nests and rosette pattern having round to ovoid nuclei, salt and pepper chromatin pattern. Punctate necrosis and high mitotic index is evident (Ki67: 70-80%). The cells are immunoreactive to Synaptophysin, Chromogranin A, CD56, CK7, FLI-1 and TTF-1, while negative for WT-1, CK20, CD99, S100 and Vimentin. **Discussion:** Large cell neuroendocrine carcinoma is rare and aggressive neoplasms with poor prognosis. A significant delay in diagnosis is common due to their rarity and non-specific presentation. Microscopic features of neuroendocrine morphology, high Ki67 index, high mitosis with presence of necrosis aid in diagnosis. In conjunction to morphology features, immunohistochemistry staining positivity is useful to establish the diagnosis.

AP41 Teratoma with Malignant Transformation (TMT) in a teenage patient: A Case Report

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Introduction: TMT is defined as the transformation of mature teratoma component to morphological malignant and becoming aggressive. It is a rare condition and commonly encountered in adult with germ cell tumour. **Case report:** A 14-year-old teenage boy presented with a previous history of testicular immature teratoma during infancy. He was well until he presented at 13-year-old with symptom of shortness of breath and chest discomfort. CT-scan showed anterior mediastinal growth. Chemotherapy was given prior to surgical intervention in October 2016. The histopathology examination showed mature teratoma, with no immature component. On follow up, he developed similar symptom this time with haemoptysis. CT scan showed multiple lesions in the pleura, liver and bone. Intraoperative findings in January 2018 revealed a tumour adherent to pericardium and surrounding soft tissue which was removed in multiple fragments. Histopathological finding showed extensive tumour necrosis and sheets of malignant spindle cells arranged in interlacing bundles and haphazard whorled pattern. There were also large pleomorphic cells showing ample eosinophilic cytoplasm and rhabdoid features. Pleomorphic multinucleated giant cells and aberrant mitoses were present. The tumour was seen to involve the intervening stroma of mature teratoma which were essentially composed of ectoderm, mesoderm, and endoderm element. **Discussion:** The diagnosis of TMT (rhabdomyosarcoma) was concluded with the microscopic finding of malignant rhabdoid features supported by residual teratomatous element and immunohistochemical studies of desmin and myogenin. Mediastinal TMT or rhabdomyosarcomatous differentiation has a poor prognosis and chemoresistant. It was reported that if complete excision was performed, recurrence rate will decrease.

AP42 Oxidative stress induced nephrotoxicity in chronic low dose organophosphates (OP) exposure

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Introduction: There were significant epidemiological evidences that suggested the association of end-stage renal diseases of unknown aetiology with chronic pesticide exposure. Our previous assessment of renal tissues from Sprague-Dawley rats exposed to chronic low dose OP had found significant microscopic features consistent with renal tubular damage. This study postulated that the renal damage is the consequences of oxidative stress which may lead to cell death through apoptosis. The aims of the current study is to determine the pathways involved in the above microscopic changes. **Materials & Methods:** Two groups of males Sprague-Dawley rats of 6 rats each: control group and exposed group (received an alternate day of subcutaneous 18.0 mg/kg BW chlorpyrifos) were sacrificed at 150 days. A small tissue section from the renal cortex was preserved in RNAlater

whilst the other half of the renal was preserved in formalin for tissue processing. RNA was purified from the tissue preserved in RNAlater and subsequently subjected to qPCR array on real-time platform. The relative expression of selected markers representing the oxidative stress and apoptosis pathways was normalized to two reference genes and quantitatively measured using $\Delta\Delta C_q$ method. Immunohistochemistry for MDA and p53 were performed in formalin fixed paraffin embedded renal tissue. **Results:** There were significant downregulation of GR ($p=0.04$), NOS2 ($p=0.03$) and Ripk3 ($p=0.01$) and significant upregulation of p53 ($p=0.02$). Subsequently IHC test showed significant MDA and p53 expression. **Discussion:** The OP exposure to the kidney results in tubular injury through oxidative pathways and subsequent cell arrest by activation of p53.

AP43 Primary cutaneous extrarenal malignant rhabdoid tumour in infants: A report of two case series

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Introduction: Malignant rhabdoid tumour (MRT) is a distinctive paediatric neoplasm which classically develops in the kidney. Primary cutaneous extrarenal MRT is extremely rare with less than 10 cases being reported to date. Most cases presented with multiple skin nodules. Both renal and cutaneous extrarenal MRT show highly aggressive clinical course with a survival rate of one year in most patients. **Case reports:** Two infants, aged one-week and five-months old presented with rapidly growing cutaneous nodules and a solitary mass at right palm respectively. Clinically, the lesions appeared bluish mimicking haemangioma. Renal imaging of both patients showed no concurrent tumour, excluding the possibility of metastatic MRT. Histologically the lesions were intradermal and arranged in solid sheets with intervening fibrous septae. The cutaneous nodule showed large epithelioid cells with eccentrically located nuclei and abundant eosinophilic cytoplasm, resembling rhabdoid cells. The lesion from right palm showed small round blue cells with occasional rhabdoid cells. Both cases showed loss of INI-1 protein expressions. Based on these findings, a diagnosis of primary cutaneous MRT was made. The first infant deteriorated rapidly and succumbed to pulmonary and liver metastases within a week of diagnosis. The second infant was in stage III disease and received chemoradiotherapy. **Discussion:** MRTs are highly aggressive neoplasms regardless of their location. Histologic diagnosis depends on the characteristic rhabdoid cells. INI-1 immunohistochemistry is an important biomarker which should be employed in suspicious cases. Definitive diagnosis of MRT is important for clinical implications although there is no effective treatment for this tumour.

AP44 Immunohistochemical analysis of a rare case of melanotic neuroectodermal tumour of infancy

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Introduction: Melanotic neuroectodermal tumour of infancy (MNTI) is a rare benign neoplasm that usually occurs during the first year of life. MNTI is a locally aggressive tumour with a high recurrence rate. The tumour is generally accepted to be of neural crest origin. MNTI shows striking trend for the maxilla (68-80%) and less occurrence sites reported such as skull, testis, mandible and brain. **Case Report:** We report a case of MNTI in a 3-month-old Malay infant presented with a swelling at the upper anterior ridge causing upper sulcus obliterate and labial fullness on upper lip. MRI and ultrasound findings were suggestive of a well-defined soft tissue tumour. A complete surgical excision was performed by an intraoral approach. **Result:** Histological findings of a well circumscribed lesion with characteristic biphasic population of large pigmented epithelioid cells and small round blue cells was observed. The immunohistochemical (IHC) findings showed both small and epithelioid cells were diffusely positive for Vimentin, Synaptophysin and NSE. CK AE1/AE3 and HMB45 immunostaining show positivity to the epithelioid cells while CD56 and GFAP highlighted the small round blue cells population. A diagnosis of MNTI was rendered. **Discussion:** IHC studies are rarely applied on the MNTI due to its very characteristic features, classical clinical presentation and very distinctive histopathological features of a dual population of small neuroblastic cells and larger melanin-containing epithelial cells. In cases whereby the diagnosis is difficult to make by morphology alone, IHC markers can be very helpful especially in differentiating MNTI from other round blue cell tumours.

HAEMATOLOGY

HM1 Evaluation of pre-donation deferral reasons among prospective blood donors attending blood donation drives in Faculty of Medicine, UiTM Sg Buloh Campus.

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Introduction: Malaysia is facing shortage of blood supply despite continuous blood donation campaigns especially during local festive seasons. Thus, Centre for Pathology Diagnostic and Research Laboratory (CPDRL) UiTM Sg Buloh Campus had

initiated blood donation drives in collaboration with National Blood Centre (Pusat Darah Negara) since 2015. However, the pre-donation deferral rate was relatively high leading to loss of valuable blood units. The aim of this study is to evaluate the pattern and reasons of pre-donation deferral among prospective blood donors in our centre. **Materials & Methods:** This is a retrospective study over a 2-year period from January 2016 to December 2017. The data was retrieved from official reports of each drives and was analyzed using SPSS software version 23. **Results:** A total of 613 prospective blood donors had attended blood donation drives during the study period. The overall pre-donation deferral rate is 25.1%. The main causes of deferral are low haemoglobin (Hb) level (20.1%) followed by sleep less than 5 hours (13.0%), upper respiratory tract infection (12.3%) and low blood pressure (4%). **Discussion:** The deferral rate among our prospective blood donors is relatively high compared to internationally reported rates. In our study sleep less than 5 hours is one of the common reason for deferral whereby this could be prevented if the prospective donors aware of the donor selection criteria. We recommend efficient tools for disseminating information on donor selection information such as handy flyers, keepsake notes and catchy posters prior to blood donation drives aiming to reduce the number of deferrals.

HM2 Evaluation of blood utilization for elective surgeries in a small tertiary medical centre: A retrospective analysis

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Introduction: Preoperative over ordering of blood for elective surgery is common. Over ordering of blood can create an artificial shortage in the blood reserves, increase cost and cause wastage of time and effort. It has been shown that implementation of maximum surgical blood ordering schedule (MSBOS) can reduce unnecessary blood cross-matching and improve blood stock management. The objective of this study is to evaluate preoperative blood ordering and transfusion practices in UiTM Medical Specialist Centre (UiTMMS). **Materials and Methods:** We analyzed blood ordering practices for elective surgeries performed in 2017 at UiTMMS. The cross-match-to-transfusion-ratio (CT ratio) and transfusion index (TI) were calculated for each type of elective surgery. **Results:** There were 111 surgical patients in this study. 588 of blood units were cross-matched, 393 were transfused (CT ratio 1.50). Ten elective surgeries had CT ratio >2.5 and 11 elective surgeries had TI <0.5. These include minimal invasive coronary surgery (CT ratio 6, TI 0.17) and hysteroscopy (CT ratio 5, TI 0.2). **Discussion:** Overall CT ratio was <2.5, however 10 (52.6%) of elective procedures showed CT ratio >2.5 and 57.8% showed low TI. These indicate poor compliance towards transfusion policies and over-ordering of blood units. To overcome these, a local MSBOS should be reviewed and updated. Further reduction in units cross-matched or a conversion to group, screen and hold (GSH) are recommended. Informal discussions between the clinicians and transfusion unit should be made on regular basis. Regular monitoring on blood traffic is necessary to ensure compliance towards blood transfusion practices.

HM3 Three years Evaluation of Specimen Rejection Rate in Haematology Unit, Pusat Perubatan Pakar UiTM (PPUiTM) Sungai Buloh

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Introduction: The Haematology Unit, Centre for Pathology Diagnostic and Research Laboratories (CPDRL) receives haematology specimens from various wards and clinics in PPUiTM Sungai Buloh. The samples are accepted according to the rejection criteria of the laboratory. The aims of this study are to evaluate the rejection rate for haematology samples from 2014 to 2016 and to determine the cause of its rejection. **Materials & Methods:** A retrospective study was conducted at the Haematology Unit, PPUiTM from January 2014 to December 2016. The data were retrieved from the laboratory records. **Results:** Rejection rate was 4.0% in 2014, 3.5% in 2015 and 2.4% in 2016 respectively. The most common reasons for specimen rejection for all three consecutive years were due to clotted specimens; followed by haemolysed and insufficient specimens. **Discussion:** Rejection rate of specimens is one of the performance indicators for quality improvement activities in the laboratory. Thus, the evaluation of specimen rejection rate allows the laboratory to identify problem areas where improvement is necessary. One of the contributing factors for the reducing trend was due to an ongoing exercise of customer education series which is biannually held in our centre.

HM4 Beneficial Effects of Dates (Phoenix Dactylifera) and Goat Milk in Iron Deficiency Anaemia

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Introduction: Iron deficiency anaemia (IDA) is a global health problem. It is common in poverty areas and indicates poor nutrition and health. According to Islamic beliefs, dates and goat milk are considered as superfood for preservation of health. Therefore, this study aimed to determine the beneficial effects of dates and goat milk on IDA. **Materials & Methods:** A cross-sectional study was conducted among 57 female adults with IDA. They were assigned to 5 groups with different feeding protocol (normal diet, dates, goat milk, both dates and goat milk and ferrous fumarate). Full blood count and iron profile were assessed at the beginning of the study and repeated at weeks 4, 8 and 12. **Results:** There was significant improvement in reticulocyte count and

haemoglobin level in all three groups supplemented with dates and goat milk. The group supplemented with dates also showed increased in packed cell volume ($p < 0.005$) while group supplemented with goat milk showed raised red cell count ($p < 0.005$). The iron profile (ferritin and transferrin level) improved in all three groups supplemented with dates and goat milk ($p < 0.005$). **Discussion:** Dates and goat milk improved the haematopoietic and iron profile in IDA subjects in accordance with previous reports on animal model. This may be contributed by the high iron content in dates and presence of biochemical components in dates and goat milk that enhanced iron bioavailability. Therefore, inclusion of dates and goat milk may be considered as a supplementary diet in IDA subjects.

HM5 Frequency of possible cases of undiagnosed heterozygous Hb variants from HbA1c results in PPUiTM Sg Buloh

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Introduction: Haemoglobin (Hb) A1c measurement is used as a long-term monitoring tool in diabetes patients. Haemoglobin is chosen because of its long, life span (120 days), and therefore blood sampling can be feasibly done over two to three months. However, there are limitations related to the HbA1c measurement, such as haemoglobinopathies, thalassaemias and hemolysis. The objective of our study is to report the number of possible Hb variants, incidentally detected from HbA1c samples. **Materials & Methods:** We collected all HbA1c results showing 'presence of possible heterozygous Hb variant', over 6 months, together with a full blood count (FBC). HbA1c was measured using the BioRad D10. **Results:** We found 80 HbA1c results showing 'presence of possible Hb variant', of which 52 had FBC done. The mean Hb was 12.7g/dl with 15 (28.8%) patients having anaemia with Hb less than 12g/dl. The mean MCV and MCH were 77.5fl and 25.3pg, respectively. The mean HbA1c was 8.4%, and the highest was 18.9%. **Discussion:** Patients with hypochromic microcytic anaemia are most likely to have underlying haemoglobinopathy. However, it is known that anaemia does not have to be present in all cases of haemoglobinopathies. Of interest, one of those patients was later diagnosed as having heterozygous Hb E. It would be ideal to do Hb analysis in all new patients with 'possible heterozygous Hb variant', to identify the actual Hb variant present. HbA1c measurement could serve as an indirect detector or trigger for clinicians to proceed to Hb analysis to diagnose haemoglobinopathies, in heterozygous.

HM6 A study of overnight transfusion practice in Universiti Kebangsaan Malaysia Medical Centre

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Introduction: Overnight transfusion (OT) is blood transfusion taking place from 9pm to 8am. During this period, patients are exposed to higher risk of errors. This cross-sectional study aims to determine the incidence and practice of OT in UKMMC. **Materials & Methods:** All OTs in June and July 2017 were collected from recipient-cards, transfusion request forms and patient's case-notes regarding ward involved, indication, time interval from GXM completed to OT commencement, time completion, monitoring of OT and adverse reaction. **Results:** A total of 216 (11.3%) OTs were identified out of 1897 total transfusions with surgery discipline being the highest (30.1%). The indication for OT were acute clinical need: 82.9%, less acute clinical need: 13.9% and no clinical need: 3.2%. A huge delay (average: 5 hours 40 minutes) in starting transfusion after GXM completed was noted. Besides, 25.9% of cases took >4 hours to complete OT; 83.4% cases did not have proper transfusion monitoring and three transfusion reactions were reported. **Discussion:** Most of the OT were clinically indicated, but the huge delay in starting transfusion after GXM completed probably is the main culprit for the transfusion to occur overnight. Besides, the poor monitoring of patient during OT at night may posed higher risks to patients' life if an adverse transfusion reaction ever happened. Cases without absolute indication should avoid OT. The contravention of 4-hour infusion rule increases the patients risk to develop bacterial sepsis or receiving suboptimal blood products. In conclusion, the practice of OT should be discouraged wherever possible except for clinically indicated cases.

HM7 Concurrent JAK2 Positive Myeloproliferative Neoplasm and Plasma Cell Dyscrasia: A Case Report

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Introduction: JAK2 positive myeloproliferative neoplasms (MPN) include polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF). There are cases reported in the literature on simultaneous occurrence of MPN and plasma cell dyscrasia. **Case report:** 56 year old gentleman incidentally found to have polycythemia and leucocytosis on routine blood screening. Examination revealed mild splenomegaly. Peripheral blood film showed polycythaemia, marked neutrophilic leucocytosis, eosinophilia and basophilia. The platelets were plentiful. Marrow aspirate was haemodiluted. Trepheine biopsy was hypercellular for age with increase in erythroid and granulocytic series. There was no significant increase in the megakaryocytes. However, there was an increased in plasma cells (20-30%) associated with scattered Russel bodies. These plasma cells are held in clusters, aggregate and scattered individually. They are restricted to lambda light chain. As JAK2 mutation was detected, this patient was diagnosed as MPN with concurrent monoclonal gammopathy of undetermined significance (MGUS). **Discussion:**

As seen in this case, incidental findings of plasmacytosis in the marrow has led to a diagnosis of simultaneous occurrence of JAK2 positive MPN and plasma cell dyscrasia. In such occurrence, accurate diagnosis requires proper evaluation of marrow findings, molecular testing and relevant investigations to demonstrate the monoclonal paraproteinaemia.

HM8 Severe α -thalassaemia intermedia due to compound heterozygosity of Hb Adana and Hb Constant Spring in an infant requiring multiple red cells transfusions.

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Introduction: Hb Adana is highly unstable and rare haemoglobin (Hb) variant due to a mutation at codon 59 of the $\alpha 2$ - or $\alpha 1$ -globin gene resulting in a glycine to aspartic acid substitution. It is known that co-inheritance of Hb Adana and other non-deletional α -thalassaemia can give rise to more severe spectrum of Hb H disease. **Case report:** An 8-months old Malay baby presented to our casualty with upper respiratory tract infection symptoms and diarrhea. Examination showed a feverish child with bibasal crepitations and hepatosplenomegaly. Haemoglobin on admission was 4.6 g/dL. He was treated for severe lobar pneumonia, hyperactive airway disease and acute gastroenteritis. Laboratory investigations revealed presence of Hb variants: Hb Barts, Hb H and Hb Constant Spring (CS). DNA analysis showed presence of mutations with Codon 59 (GGC→GAC) (Hb Adana) and termination codon (TAA→CAA) (Hb Constant Spring). Family screening showed inheritance of Hb CS from maternal side and Hb Adana from paternal side. Subsequently, patient was transfused with 3 unit packed red cells and able to be discharged. He came for follow-up and required red cells transfusions about 3 monthly apart. **Discussion:** The involvement of two non-deletional α gene mutations; Hb Adana and Hb Constant Spring resulted in more severe phenotype of Hb H disease requiring red cell transfusions from young age. Genetic counseling including screening for prenatal diagnosis should be given to both parents as to aid family planning in future pregnancy.

HM9 Visceral Leishmaniasis (Kala Azar) in the state of Selangor, Malaysia-A Case Report

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Introduction: Visceral leishmaniasis is a protozoan infection. We report a case of visceral leishmaniasis in a 25-year-old Nepalese man whom had stayed in Malaysia for more than two years and presented with six months history of abdominal pain associated with loss of weight and loss of appetite. Upon clinical examination, there was massive splenomegaly and enlarged right inguinal lymph nodes. **Results:** Bone marrow trephine biopsy showed presence of Leishman-Donovan complex and confirmed the diagnosis of visceral leishmaniasis. He was successfully treated with prolonged courses of amphotericin B. **Discussions:** The case highlights the importance of awareness among the treating physicians of this disease occurring in an immigrant from endemic region especially among the patients who presented with prolonged febrile illness and hepatosplenomegaly.

MEDICAL MICROBIOLOGY & IMMUNOLOGY

MM11 A fatal case of *Elizabethkingia meningosepticum* meningitis in infant with septicemia

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Introduction: *Elizabethkingia meningosepticum* is a Gram-negative aerobic rod that is ubiquitous in the environment, found in freshwater, saltwater and soil. *E. meningosepticum* is associated with neonatal meningitis and occasionally bacteremia particularly in premature infants in first 2 weeks of life. **Case report:** We report a case of a 7-month-old boy with history of prolonged hospitalization due to prematurity who presented with 3-day history of fever, runny nose, reduced oral intake and 2-month history of cough. He was noted to be less active and had bulging fontanelle in the ward. Blood culture persistently grew *E. meningosepticum*. Despite treatment with IV vancomycin, he succumbed to death after 21 days of admission. **Discussion:** Prompt and appropriate antibiotic should be given in treating infantile meningitis with risk who is not responding to the general empirical antibiotic. Currently, there is no established guideline for treating *E. meningosepticum* infection which leads to difficulties in determining the best antibiotic of choice for treatment. Previously, vancomycin has been shown to be an effective treatment agent, but some reports produced contradictory results. Combination therapy for infections not responding on single agent should also be explored as a treatment option.

MMI2 A symptomatic *Hymenolepis diminuta* infection in adult migrant worker in Kuala Lumpur, Malaysia

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Introduction: In humans, infection with *Hymenolepis diminuta* is uncommon with prevalence between 0.001% and 5.5% but has been reported from various areas of the world. It is primarily a rodent parasite but sometimes human especially children can act as accidental hosts. Usually the cases were asymptomatic and the diagnosis was accidental. **Case report:** We report a symptomatic case of *H. diminuta* infection in a 29-year old man from Myanmar who works in Malaysia for the last two years. The patient presented to UKMMC with the chief complaints of abdominal pain and discomfort with increasing severity for two weeks. He has history of mild diarrhoea and passing segments of worms in his stool intermittently for the past two years. Direct faecal smear showed multiple eggs with characteristics of *H. diminuta* morphology. **Discussion:** This case is presented to emphasize that there is a lack of awareness about this infection by physicians and there is limited data regarding their true prevalence and clinical presentations. Furthermore, benzimidazole broad-spectrum anti-helminthic which is the drug of choice for deworming helminthic infections in Malaysia is not effective at all for this infection.

MMI3 The distribution of *Candida albicans* genotypes in pathogenic and carrier strains

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Introduction: Although *Candida albicans* is often a coloniser in the oral cavity, it can cause serious disease especially in immunocompromised individuals. Genotyping has been used to study the epidemiology of infections by this fungus, and the propensity of different strains for pathogenicity. **Materials & Methods:** In this study, *C. albicans* genotyping was performed on clinical isolates from hospitalised patients as well as carrier strains from the oral cavity of community residents. *C. albicans* was confirmed by its typical morphology on CHROMagar, germ-tube production, and PCR-sequencing of the ITS (internal transcribed spacer) gene. PCR-based genotyping and subtyping were performed with specific PCR primers of the 25S rDNA and RPS (repetitive sequence) genes respectively. A dendrogram was constructed to demonstrate the phylogenetic relationship of all isolates and reference strains. **Results:** Preliminary results showed 54.5%, 27.3% and 18.2% of 22 community carrier strains to be genotypes A, B and C respectively, with 70% of genotype A strains further classified as subtype 3. In contrast, 14 of 15 (93.3%) clinical isolates were classified as genotype A, of which, 8 (57.1%) were designated as subtype 3/4. **Discussion:** The 25S rDNA and RPS-based tiered genotyping method appears to be a potentially useful tool for the study of *C. albicans* epidemiology. The apparent association between genotype A subtype 3/4 with clinical infection needs to be confirmed with future studies on a much larger sample size and more detailed clinical and epidemiological information.

MMI4 Evaluation of the Dynamiker Cryptococcal Antigen Lateral Flow Assay in detecting the capsular polysaccharide antigen of *Cryptococcus* species

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Introduction: Cryptococci have gained notoriety with the onset of the AIDS pandemic in the 1980s, when fungal infections became AIDS-indicator illnesses. A common method to diagnose cryptococcosis is by detecting the capsular glucuronoxylomannan (GXM) antigen of cryptococci. The aim of this study was to evaluate the performance of a new commercial GXM detection kit (Dynamiker Cryptococcal Antigen Lateral Flow Assay, Dynamiker Biotechnology [Tianjin] Co., Ltd., China). **Materials & Methods:** This study was done on archived serum (stored at -80°C) and CSF samples (stored between 2 - 8°C) from patients admitted to our centre from June 2016 to July 2017. Specimens from the Royal College of Pathologists of Australasia's Quality Assurance Programme and specimens from the inter-laboratory comparison exercise with the Institute of Medical Research, Malaysia were also included. These samples had already been tested using an established commercial GXM kit (IMMY Cryptococcal Antigen Lateral Flow Assay, Immuno-Mycologics, Inc., USA) and were re-tested using the Dynamiker kit, as per the manufacturers' instructions. **Results:** A total of 34 specimens were re-tested using the Dynamiker kit. Using the IMMY kit's results as reference, all 15/15 positive samples were also positive with the Dynamiker kit and 17/19 negative specimens also tested negative using the Dynamiker kit. Thus, the specificity of the Dynamiker kit was 100% and its sensitivity was 89.5%. The kappa statistic was 0.882 (strong agreement). **Discussion:** The Dynamiker Cryptococcal Antigen Lateral Flow Assay performed satisfactorily and may be considered for routine diagnostic use by medical mycology laboratories.

MMI5 Microbead-based spoligotyping of *Mycobacterium tuberculosis* complex isolates from Sabah, East MalaysiaDawn Carmel Paul^{1,3}, Richard Avoi², Jiloris F. Dony², Sook-Fan Yap¹, Yun-Fong Ngeow¹¹Faculty of Medicine and Health Science, Department of Pre-Clinical Sciences, Universiti Tunku Abdul Rahman, Kajang, Selangor, Malaysia; ²Sabah State Health Department, Sabah, Malaysia; ³Kota Kinabalu Public Health Laboratory, Sabah, Malaysia.

Introduction: Sabah, with approximately 3.6 million people (25% migrants), contributes to ~19% of the national TB burden (5106 new cases in 2017). Local epidemiological features, population experiences, risk factors among healthcare workers and individuals with HIV co-infection have been described, but little data is available on TB molecular epidemiology. This study aims to gain insight into the circulating MTBC strains, their evolutionary development and interaction with the population. **Materials & Methods:** 327 MTBC clinical isolates with corresponding socio-demographic data were obtained from MKAKK and the MyTB database. They were subjected to microbead-based spoligotyping and subsequent studies with GIS and phylogenetic analyses. **Results:** 69 spoligotype patterns were identified (39 orphans, 30 SIT patterns), the top 5 being SIT19/EAI2-Manila (55.1%); SIT287/EAI2-Manila (5.5%); SIT1365/EAI5 (5.2%); SIT897/EAI2-Manila (4.9%) and SIT1/Beijing (3.1%). SIT19/EAI2-Manila is seen in all districts except for Kudat which also has a large migrant population. Kota Kinabalu, Tawau and Sandakan, the three most densely populated cities show the largest spread of spoligo and orphan types. Further analyses are on-going to correlate spoligopatterns with gender, age group, ethnicity, occupation and co-morbidities. **Discussion:** The distribution of MTBC spoligotypes in Sabah appears to be markedly different from that in Peninsular Malaysia. Bigger populations harbour more reservoirs, rendering more possibilities for TB transmission and the emergence of more diverse genotypes. DNA sequencing of orphan strains and subtyping of spoligotype clusters will provide more phylogenetic inferences.

MMI6 The effects of chemotherapeutic agents on epidermal keratinocytes modified with human papillomavirus (HPV) genes

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Introduction: Human Papillomavirus type-16 (HPV16) has been associated with various epithelial cancers. Previous studies of HPV16-positive head-and-neck cancers revealed enhanced radio- and chemosensitivity compared to those that are HPV16-negative. An *in-vitro* model based on epidermal keratinocytes was established to investigate the influence of the HPV16 oncogenes, E6 and E7, on chemosensitivity. NIKS cell lines were modified to contain the HPV genome and the E6, E7 oncogenes to represent the precancerous and cancerous stage in the evolution of the oncogenic process respectively. Susceptibility of the models towards cisplatin and topotecan was tested as a proof of concept. Cytotoxicity effects of eupatorin, sinensetin, and tribenzyltin carboxylates 1 & 4 (TC1 & TC4) on the established model was investigated. **Materials & Methods:** Normal immortalised epidermal keratinocytes (NIKS) were modified to harbour episomal HPV16 genome ("pre-cancerous" model) using lipid-based transfection and HPV16 E6 and/or E7 ("cancerous" model) were introduced into NIKS cells by retrovirus transduction. **Results:** HPV16 episomes were maintained up to passage 21 in the HPV16 "precancerous" model. Western blot analysis showed stable expression of the E6/E7 protein in the "cancerous" models. Both models demonstrated higher susceptibility to cisplatin and topotecan than the parental cells. Cells that express E6/E7 were more sensitive to eupatorin and sinensetin. All the models were insensitive to TC4. **Discussion:** The relative enhanced susceptibility of HPV16-associated cancers to chemotherapeutic agents has been recapitulated in our *in-vitro* models and demonstrated for selected natural compounds. The established models could provide a platform for the screening of potentially effective agents/ natural products against HPV-associated cancers.

MMI7 Co-expression of human papillomavirus (HPV) associated oncogenes E6 and E7 increases chemosensitivity of primary cervical keratinocytes to cisplatin treatment

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Introduction: HPV-16 is a major aetiologic factor in the development of cervical cancer. However, HPV-associated cancers are also more responsive to both radiotherapy and chemotherapy, an observation that is quite intriguing. We established a cervical cell-based model modified with HPV-16 oncogenes to determine whether this observation can be reproduced *in-vitro*, and to provide a platform for further studies. Normal cervical epithelial cells were specifically used as they much more closely resemble the natural state in the evolution of neoplasia compared to commercial cancer cell lines. **Materials & Methods:** Normal primary cervical keratinocytes were modified to harbour episomal HPV16 genome using lipid-based transfection and HPV16 E6 and/or E7 by retrovirus transduction. The genetically modified cervical cells were subjected to treatment by cisplatin and the cytotoxic effect of the agent determined by the MTT assay. **Results:** Primary cervical keratinocytes that express both the E6 and E7 oncogenes show significantly higher sensitivity to cisplatin ($0.33 \pm 0.002 \mu\text{g/mL}$; $p = 0.02$) compared to unmodified parental cells ($3.20 \pm 1.193 \mu\text{g/mL}$). Increased sensitivity was also seen in cells that express E6 ($0.47 \pm 0.08 \mu\text{g/mL}$; $p = 0.05$) or E7 alone ($2.45 \pm 0.353 \mu\text{g/mL}$; $p = 0.08$) alone, as well as cells that carry the episomal HPV16 genome ($1.85 \pm 0.353 \mu\text{g/mL}$; $p = 0.18$). **Discussion:** The enhanced susceptibility of HPV16-associated cancers to the cisplatin, a platinum-based chemotherapeutic agent *in-vivo* has been demonstrated in our cervical cell-based model. This model provides a platform for future investigations on the mechanisms of HPV16-associated chemosensitivity.

MM18 Invasive listeriosis in a pregnant lady with non-Hodgkin lymphoma

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Introduction: *Listeria monocytogenes* is a ubiquitous bacterium that may cause severe disease in the immunocompromised. Occurring more commonly in pregnant women, it can result in fetal death. We report a case of a pregnant lady with non-Hodgkin lymphoma with invasive listeriosis resulting in a second trimester miscarriage. **Case report:** A 34-year-old pregnant lady at 19 weeks of gestation with underlying non-Hodgkin lymphoma presented with fever, myalgia and arthralgia for 1 week. Recently, she had completed 6th cycles of chemotherapy. She also had diarrhoea for 3 weeks but resolved 1 week prior to admission. Upon presentation, she was tachypneic and had left lower zone crepitations. She was initially diagnosed with pneumonia and treated with intravenous ceftriaxone. Whilst in ward, she had a miscarriage and underwent suction and curettage. Cultures from her blood, high vaginal swab and placenta isolated pure growth of beta-haemolytic, gram-positive rods with positive catalase and methyl red. The organism showed characteristic tumbling motility and CAMP test was positive with narrow zone of beta-hemolysis. *Listeria monocytogenes* was confirmed with API CORYNE (99.3%). The organism was sensitive to penicillin and co-trimoxazole. She was treated with ceftriaxone and azithromycin. **Discussion:** Taking into account the site of positive cultures, it is likely that an ascending infection of the genital tract has led to invasive listeriosis and fetal loss. High clinical suspicion and relevant clinical history remains important for early diagnosis and treatment whilst preventing related fetal deaths especially in immunocompromised pregnancies, as this organism can be mistakenly dismissed as commensal diphtheroids.

MM19 Detection of islet cell autoantibodies and anti-insulin antibodies among newly diagnosed diabetes mellitus patients in Malaysia

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Introduction: Anti-islet cell and anti-insulin antibodies are useful markers in confirming diagnosis of type 1 diabetes mellitus (T1DM). Recently, anti-glutamic acid decarboxylase (GAD) and anti-protein tyrosine phosphatase (IA2) antibodies have been identified as major part of anti-islet cell antibodies that contribute to the disease development. This study aimed to determine the frequency of anti-islet cell and anti-insulin antibodies among newly diagnosed diabetes patients in Malaysia. **Materials & Methods:** This is a cross sectional study involving 140 newly diagnosed diabetic patients whose blood samples were sent for diabetic associated antibodies tests from October 2017 until December 2017. The antibodies measured include anti-islet cell, anti-insulin, anti-GAD and anti-IA2 antibodies by using ELISA method. **Results:** Fifty nine patients (42.14%) with age ranging from 3 to 56 years old were positive for at least 1 antibody. Approximately half of these patients (30/59) were 18 years old and below. Out of 59 patients, 76.27% have anti-islet cell antibodies, followed by anti-GAD (69.49%), anti-insulin (38.98%) and anti-IA2 (30.51%). Majority of these patients have multiple antibodies, only 14 patients were positive for single antibody. **Discussion:** Diabetes associated antibodies serve as important biomarkers in the diagnosis of T1DM. In this study, majority of the patients are below 18 years old and the anti-islet cell antibody is the most prevalent autoantibodies among T1DM patients.

MM110 Congenital cytomegalovirus infection, common but under-recognised

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Introduction: Cytomegalovirus (CMV) infection is the most common congenital viral infection and the subsequent sequelae are a major medical problem. Despite that, congenital CMV is less known to the general population. **Case report:** A baby girl was born at 39 weeks' gestation via vacuum-assisted delivery secondary to prolonged second stage. Examination showed symmetrical small for gestational age, generalized petechiae, bilateral subconjunctival haemorrhage and hepatosplenomegaly. Blood investigations showed persistent thrombocytopenia. Her mother is a 30-year-old lady, para 2 with no history of fever or antenatal hospital admission. Congenital CMV infection was suspected in view of the clinical findings and persistent thrombocytopenia as well as failed otoacoustic emission hearing screening test and presence of calcification at thalamus, periventricular and right intracerebral region on ultrasound of the cranium. Empirical IV ganciclovir was started at day 12 of life. Blood culture, TORCHES serology, urine for DEAFF, blood HPA-1a were negative. Mother's blood was positive for CMV, rubella, herpes simplex and toxoplasma IgG, however Ig M was negative. CMV viraemia was confirmed using CMV PCR which detected 5,000 IU/mL in the blood. The ganciclovir was completed for 78 days, and successive oral valganciclovir was continued for 6 months. Subsequent review at 7 month showed that she had mild right-sided hearing loss with normal milestone development and no other neurological deficit. **Discussion:** Increased awareness of this common and disabling disease is important in reducing the impact of this virus on the health and well-being of children.

MM111 Performance of rapid immunochromatography test (ICT) against fourth generation enzyme immunoassay for hepatitis B virus infection screening in haemodialysis patient

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Introduction: The use of fourth generation immunoassay analyzer, the electro-chemiluminescence immune-assay (ECLIA) has greatly improved detection of hepatitis B virus (HBV) infection. However, the testing for certain high-risk patients, such as those undergoing haemodialysis warrants a testing method with a better turnaround time (TAT). This is because haemodialysis may sometimes be required in emergency situations. In this study, we aimed to compare the performance of rapid immunochromatography (ICT) kits against ECLIA, for screening HBV infection in high risk patients. **Materials & Methods:** Between the period of May to October of 2017, 30 haemodialysis patients presented to the faculty were recruited. Their blood were collected and centrifuged. The serum were then tested with both Ecotest® immunochromatography test (ICT) rapid kit from Assure Tech and Cobas E411 Automatic Electro-Chemiluminescence Immuno-assay (ECLIA) analyzer from Roche for the presence of Hepatitis B surface antigen (HbsAg). **Results:** Compared with ECLIA, sensitivity and specificity of ICT was 100%. The ICT's positive predictive value (PPV) and negative predictive value (NPV) were both 100%. The mean TATs for ICT method was 15 minutes, whereas that for ECLIA method was close to 2 hours. **Discussion:** Other than offering comparable analysis performance to ECLIA, ICT were superior in terms of its TAT. Furthermore, although not demonstrated in this study, this particular ICT, Ecotest®, is able to test not only serum but also whole blood specimen. Thus, in cases of emergency or unexpected unavailability of ECLIA analyzer, rapid ICT could be considered as an acceptable alternative test to detect HbsAg.

MM112 Morphological alterations of *Streptococcus pyogenes* after in vitro treatment with Malaysian tualang honey and *Citrus aurantifolia* juice

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Introduction: Natural products such as honey and citrus fruits have been highly valued by generations for thousands of years. Previous studies showed that these natural resources able to inhibit the growth of wide range of bacterial. Osmotic effects were assumed to be responsible for antimicrobial effects of the bacterial cells. Although the inhibition by honey and citrus fruits have been established, the effects of these natural resources on bacterial structure have not been studied. The purpose of this study was to investigate the effects of Malaysian tualang honey and *Citrus aurantifolia* juices on structural integrity of *Streptococcus pyogenes* in order to gain insight into its action as an inhibitory agent. **Materials & methods:** The inhibition of tualang and *C. aurantifolia* against *S. pyogenes* was investigated by determining the minimum inhibitory concentration (MIC). Structural changes were observed using scanning electron microscope (SEM) by treating bacterial cells to the MIC of tualang honey and *C. aurantifolia* (3.13 and 0.02 % v/v respectively) and were compared to the untreated bacterial cells. **Results:** There were marked structural changes on the honey and citrus-treated bacterial cell walls. They were found to have distorted shape, rough, convoluted surface and collapsed cells as compared to the untreated bacterial cells which shows well defined shape. **Discussion:** The results provide the evidence of antimicrobial potential that would enhance the effectiveness of therapeutic alternatives of Malaysian tualang honey and *C. aurantifolia* against *S. pyogenes*.

MM113 Development of hand hygiene module and acceptance among pre-school children

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Introduction: Children in pre-schools are at high risk of getting infections due to overcrowding, lack of understanding of basic hygiene and lack of immunity against viruses and bacteria. To the best of our knowledge, study on the effectiveness of current curriculum on hand hygiene (if any) in pre-schools is lacking. Therefore, this study aimed to develop a module on hand hygiene practice in pre-schools. This paper presents the developmental aspects of the module and the results of its evaluation process in a selected pre-school. **Materials & Methods:** Stages of development involved preparation of module and its teaching materials. The module was prepared by subject expert consisted of microbiologists, an infection control specialist and a public health physician. Teaching materials included songs, lyric, video clip, infographic and tablet application. The module was introduced during an intervention day. The acceptance of the module was evaluated before and after the intervention day. Evaluation was done by assessing pre-school children by face to face interview about knowledge on hand hygiene techniques and moments, such as before or after certain activities. **Results:** We managed to provide a module, compose a song in 3 languages (Malay, English & Arabic), produce a video clip, an infographic and tablet application regarding hand hygiene. A total of 227 children participated. Evaluation showed an increase of knowledge in both hand hygiene techniques and moments. **Discussion:** The outcome of this study will help us to recommend the program and module to be integrated into pre-school curriculum.

MMI14 Detection of autoantibodies from sera of patients with unexplained infertility against reproductive tissues and its diagnostic value in Malaysia

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Introduction: In 2016, the total fertility rate (live births per woman aged 15-49) in Malaysia was a record low of 1.9, which is below the replacement level of 2.1. The replacement level is the average number of babies born per woman throughout her reproductive life being insufficient to replace herself and her partner. The aim of this study is to determine the diagnostic value of autoantibodies against various reproductive tissues among patients with unexplained infertility. **Materials & Methods:** This is a retrospective study looking at the frequency of autoantibodies (IgG) measured by indirect immunofluorescence against ovarian, placental, uterine and spermatozoa autoantigens among patients diagnosed with unexplained infertility between 2016 and 2017. **Results:** A total of 33 patients were analysed of which 23 were females (mean age 34±3.86 years) and 10 were males (mean age 31±5.59 years). Fifteen of the 33 patients (45.5%) had presence of autoantibodies, which were only detected against spermatozoa. However, no autoantibodies were detected against the remaining autoantigens. Ten out of these 15 patients were female aged between 29-35 years old whilst the remaining 5 male patients were between the ages 28-37 years old. **Discussion:** Among the panel of infertility autoantibodies, only anti-sperm antibodies were found in this study. This may be beneficial in managing infertility cases which include the IVF procedures. Yet these results still warrant the need for a bigger sample size to further investigate the sperm-antibody interaction in unexplained infertility in child-seeking couples in Malaysia.

MMI15 Polymyxin-Resistant Enterobacteriaceae (PRE): Emerging antibiotic resistance in Malaysia

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Introduction: Multidrug resistance (MDR) infection causes high morbidity and mortality and polymyxin is the last option for MDR infections. Widespread use of polymyxin has caused increased polymyxin resistance leaving clinicians out of options in managing patients. This study aimed to assess this problem in a tertiary centre in Melaka. **Materials & Methods:** A retrospective study between 2014 to 2017. Patients with Carbapenem Resistant Enterobacteriaceae (CRE) were randomly selected and evaluated for PRE. Confirmatory PCR assays for molecular identification was done in IMR and MIC results of polymyxin were interpreted according to the EUCAST breakpoints for Enterobacteriaceae. Demographic data, clinical and pathogen characteristics were compared and analysed using SPSS version 22.0. **Results:** A total of 100 patients were enrolled. The prevalence of PRE among CRE is 31% (n= 31). *Klebsiella pneumoniae* is the most common organism among PRE isolated (n=30, 96.8%) and *Enterobacter cloacae* is 3.2% (n=1). Among PRE isolates, 96.8% have NDM-1 gene, 71.0% have OXA-48 gene and 9.7% have OXA-181 gene. Factors that are positively associated with PRE-infections are: male gender (p=0.020), NDM-1 gene (p=0.033) OXA-48 gene (p<0.001), acute care admission (p=0.004), mechanical ventilation (p=0.027) and central venous catheterization (p=0.040). **Discussion:** Identification of risk factors are important for early recognition of those who are susceptible to get PRE. This is important to contain the spread and to predict potential new cases so that treatment and control measures can be taken.

MMI16 Higher suspicion of Extended Spectrum Beta-Lactamases (ESBL) producers by using Clinical Laboratory Standard Interpretation (CLSI) breakpoint interpretations among clinical isolates in a clinical training centre.

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Introduction: Extended Spectrum Beta-Lactamase (ESBL) infection is a hospital acquired infection occurring worldwide with significant impact in morbidity and mortality. In our centre, Clinical Laboratory Standard Institute (CLSI) is used as a guideline to identify ESBL-positive isolates. Here we compare the performance of screening followed by phenotypic confirmatory method (CDT) between CLSI and EUCAST guidelines. **Materials & Methods:** A retrospective study was performed using data from 2014-2017 of all *E. coli* and *K. pneumoniae* isolated from clinical samples. They were isolated by using standard microbiological method. The antibiotic susceptibility testing (AST) were determined by Kirby Bauer method. The AST for ESBL screening is based on breakpoints used in CLSI compared to EUCAST guideline. Similar sets of antibiotics were used for screening in both guidelines which are ceftazidime (CAZ), cefotaxime (CTX) and ceftriaxone (CRO). The positive isolates were subjected for confirmation by CDT. **Results:** A total of 142 isolates were analysed. Out of 142 isolates, there were 59 (41.5%) isolates and 47 (33.1%) isolates were suspicious of ESBL by using CLSI and EUCAST guidelines respectively. 18 out of 59 suspicious of ESBL isolates by CLSI breakpoint are confirmed positive by CDT method and 18 out of 47 suspicious of ESBL by EUCAST breakpoint were also confirmed positive. All 18 isolates confirmed ESBL were of the same isolates. **Discussion:** Higher index of suspicion of ESBL isolates are observed by using CLSI guideline therefore the chances of failure to detect cases are lower as compared to EUCAST guideline.

MMI17 Assessment of peripheral arterial catheter in critically ill patients as a cause of hospital acquired infection

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Introduction: Arterial catheter bloodstream infection (ACRBSI) is often under-recognised as a significant complication, as it is often thought as uncommon. This study aimed to assess the incidence of arterial catheter colonisation and ACRBSI in intensive care unit (ICU) patients. **Materials & Methods:** This was a prospective observational study done from February to December 2017. Our institution is a teaching hospital and the general ICU receives maximum of 18 patients at a time under the care of intensivist with nurse to patient ratio of 1:1 or 1:2. We included ICU patients that had arterial catheter inserted for more than 3 days. All patients received the standard treatment and care according to ICU management. Simultaneous blood samples were taken from arterial and central intravascular catheters present at catheter insertion day 3 to 5, and day 7 to 9, and percutaneous peripheral venous puncture. The samples were sent to microbiology laboratory for culture and identification. Diagnosis of colonisation and ACRBSI were made based on laboratory and clinical findings. **Results:** In 121 ICU patients with arterial catheters of more than 3 days, the total catheter-days was 706 and mean catheter-days was 5.8±2.1. Only 16 catheters were used beyond 7 days. Fourteen (11.6%, 19.8 per 1000 catheter days) of the arterial catheters were colonised at day 3 to 5. This study did not record any ACRBSI or central venous catheter-related bloodstream infection. **Discussion:** Arterial catheters were colonised at day 3 to 5 and did not show any incidence of ACRBSI.

MMI18 HIV and hepatitis B co-infection in UiTM specialist centre

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Introduction: HIV prevalence in Malaysia remains above 5% among the high risk populations such as person who inject drug, female sex worker, transgender and men who have sex with men. Because of their shared mode of transmission, there are HIV patients that were co-infected with Hepatitis B. The risk of progression to chronic liver disease are significantly higher among those co-infected with HIV and Hepatitis B than those with hepatitis B only. This study aimed to investigate HIV and hepatitis B co-infection prevalence among the attendees in UiTM Specialist Centre. **Materials & Methods:** This retrospective study investigated data of 6963 patients screened for HIV antibody/antigen by chemiluminescence immunoassay (CLIA) during the year 2013 until 2016. These patients underwent HIV screening as a routine either before cardiac procedure or as part of antenatal checkup. Those reactive by CLIA were then confirmed by particle agglutination test. **Results:** There were 22 (0.3%) new cases detected during the screening. Ninety six percent of them were male. Majority of them (90%) in the age range of 35-60 years. Out of these 22, one (4.5%) was also positive for HBsAg. **Discussion:** This preliminary data showed that prevalence of HIV and Hepatitis B co-infection in our centre is comparable with other Asia based studies, which showed prevalence of coinfection between 5% to 10%. As the therapeutic option, follow-up management and prognosis differ from those with HIV only, these patients should be identified as early as possible to enable early intervention and management.

MMI19 Juvenile onset systemic lupus erythematosus: A diagnostic challenge

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Introduction: Juvenile onset systemic lupus erythematosus (JSLE) is rare, with incidence between 0.5 and 6 per 100,000 population worldwide. The symptoms and signs can mimic many other diseases which make diagnosis of SLE in children and adolescents challenging. These frequently cause delays in attaining specialist care. **Case report:** A 15-year-old boy presented with persistent fever and productive cough for 1 month despite completing two courses of antibiotics. He had bilateral joint pain of upper limbs, oral ulcer and erythematous rashes over pinnae and face, loss of appetite and loss of weight. On examination, the patient was febrile (38.9oC) with hepatosplenomegaly and lymphadenopathy over cervical and inguinal region. Laboratory investigations revealed white cell count of 4,900/L, platelet of 116,000/L and haemoglobin of 10,400 dL/g. Erythrocyte sediment rate (ESR) was high at 100mm/hr. The initial diagnosis was pyrexia of unknown origin with bicytopenia with a differential of lymphoma. Lymph node excision biopsy revealed reactive lymphoid hyperplasia. CT-scan showed multiple lymphadenopathies over cervical, mediastinal, abdominal, pelvic and inguinal region. Antinuclear antibody (ANA) and anti-double stranded DNA (dsDNA) were positive. The immunofluorescence study of ANA showed speckled pattern with the titre of 1:640. SLE was diagnosed and he was treated with sunscreen lotion, emollients, oral prednisolone 25mg daily, oral azathioprine 50mg daily and oral hydroxychloroquine 200 mg daily. **Discussion:** The diagnostic criteria used in JSLE are the same as in adult; however they must be used with caution to avoid over- or under-diagnosis.

MMI20 Detection of dengue and chikungunya virus infection among patients with dengue-like illness with negative NS1 antigen

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Introduction: Laboratory diagnosis of dengue infection routinely involve dengue IgM and NS1 antigen. This study sought to determine the prevalence of dengue virus (DENV) and chikungunya virus (CHIKV) infection among patients with dengue-like illness with negative NS1 antigen, in UKM Medical Centre. **Materials & Methods:** A cross-sectional study, where 162 patients with dengue-like illness who presented within 7 days of fever and negative for NS1 antigen were included. Serum samples were tested for NS1 antigen and dengue serology (IgM and IgG) according to standard procedures. Simultaneous detection of DENV and CHIKV was done by real-time polymerase chain reaction (PCR) using Multiplex LightMix® Modular Assay (Roche Diagnostics). **Results:** Among 162 patients, 34 (21.0%) had positive DENV PCR, 2 (1.2%) had positive CHIKV, 2 (1.2%) had co-infections of DENV and CHIKV while 124 (76.5%) were negative PCR. For serology, dengue IgM was positive in 27/162 samples (16.7%), in which 21 (13.0%) were negative PCR. In serology-negative patients, DENV PCR was positive in 26/162 patients (16.0%). Majority of patients (76.5%) presented within 3-5 days of fever. Mean days of fever for PCR-positive patients was 3.91 vs 4.71 days for IgM-positive patients ($p=0.0275$). **Discussion:** Among patients with negative NS1 antigen, dengue IgM was positive in 16.7% while 16.0% of infections were detected only by DENV PCR. Altogether, DENV infection were detected in 35.2%, and CHIKV has low prevalence of 2.4%, including 2 cases (1.2%) of co-infections.

MMI 21 Multidrug-resistant organisms (MDROs): A five-year surveillance

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Introduction: Multidrug-resistant organisms (MDROs) are epidemiologically defined as microorganisms, mainly bacteria, that are resistant to one or more classes of antimicrobial agents. Common MDROs includes Methicillin-Resistant *Staphylococcus aureus* (MRSA), Vancomycin-Resistant Enterococci (VRE), Extended-spectrum β -lactamase (ESBLs) producing Gram-negative bacteria, and MDR gram negative rods. Surveillance is an essential element that allows MDROs detection and monitoring of epidemiologic trend. This study aimed to determine the occurrence of MDROs in the clinical training centre, Faculty of Medicine, UITM. **Materials & Methods:** A total of 14866 cultures and sensitivity data were gathered and analysed from January 2014 to January 2018, including types of specimens and MDROs detected with results of antimicrobial susceptibility testing. **Results:** There were 179 (1.24%) isolates confirmed as MDROs isolated both from sterile and non-sterile specimens. The MDROs includes MRSA: 115 (64.3%), VRE: 1 (0.55%), MDR *Acinetobacter baumannii*: 11 (6.15%), ESBL: 51 (28.5%) of *Escherichia coli* and *Klebsiella pneumoniae*, and carbapenem-resistant enterobacteriaceae (CRE): 1 (0.55%). MRSA was the most commonly isolated MDRO from both sterile and non-sterile specimens, followed by ESBL and MDR *Acinetobacter baumannii*. The detected numbers of MDRO were in parallel with the number of specimen received, and increasing trend of MDRO was observed from one year to another. **Discussion:** There were increasing numbers of MDROs in our institution with MRSA the most predominant. Surveillance demonstrates its importance as significant means in MDROs detection, and epidemiologic trends were evident in this study. Effective interventions can be strategized to reduce the occurrence of MDROs in our institution.

MMI22 Seroprevalence of syphilis in a tertiary teaching hospital in Malaysia

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Introduction: Syphilis is an infectious disease transmitted mainly via sexual route, caused by *Treponema pallidum*. Several sociodemographic groups are associated with increasing prevalence of getting the infection that include MSM, young adult men and sex workers. The annual incidence rate of syphilis in Southeast Asia region is classified as intermediate-high with 4.1 cases per 1000 population. **Materials & Methods:** We studied all samples that were sent to our laboratory for syphilis screening throughout 2017. We excluded the duplicate samples from the same patient and samples from newborns. Rapid plasma reagin (RPR) was the first test performed for syphilis screening. Those with reactive RPR results were confirmed by ELISA test (Syphilis IgG). The demographic data particularly those with reactive RPR were recorded accordingly. **Results:** Total of 3131 non-duplicate RPR samples were included. 75 samples (2.4%) were RPR reactive. From these samples, 25 samples were from the patients that already diagnosed with syphilis and the RPR was for monitoring purpose. 50 out of 75 samples were new reactive RPR cases. Thirty out of 50 new cases were confirmed syphilis by positive Syphilis IgG and 17 of them (56.7%) were HIV positive. The prevalence and incidence of syphilis were 18 in 1000 population and 9.6 in 1000 population respectively. **Discussion:** The incidence rate in our setting is higher in comparison to the published annual incidence rate of 4.1 cases per 1000 population. Screening for both syphilis and HIV is highly recommended as syphilis and HIV co-infection is common.

MMI23 A rare case of *Haemophilus influenzae* intrauterine infection causing early neonatal death

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Introduction: *Haemophilus influenzae* is an uncommon aetiology of obstetric and neonatal infection. We report an early neonatal death due to intrauterine infection with *H. influenzae* in a woman with no signs of infection at the time of or shortly after her preterm delivery. **Case report:** A 31-year-old lady, gravida 2 with an uneventful antenatal history, presented in labour with reduced fetal movements at 31 weeks' gestation. Upon presentation, she was well with normal vital signs. Her cervix was fully dilated with intact membranes. Cardiotocography revealed a fetal heart rate of 180 beats per minute with poor beat-to-beat variability. The membranes ruptured spontaneously with clear liquor followed by immediate spontaneous vaginal birth. A baby girl was born limp, apnoeic, cyanosed, and hypotonic. Resuscitation commenced for 45 minutes before the baby was pronounced dead. Post-mortem findings revealed a structurally normal baby. Placental histopathology examination revealed features of severe acute chorioamnionitis with fetal vasculitis and funisitis. Fetal intracardiac blood culture isolated pure growth of *H. influenzae* after 1 day of incubation; its identification was confirmed based on growth requirements of X and V factors and Analytical Profile Index NH. *H. influenzae* was not isolated from the placental and high vaginal swabs, and the mother remained well with no signs of infection. **Discussion:** Despite the lack of evidence to confirm the route of transmission from mother to fetus in this case, genital tract colonization remains a possible predisposing factor for fetal infection with this organism and can lead to premature birth and fetal death.

MMI24 Does the carriage of virulence genes in methicillin-resistant *Staphylococcus aureus* necessarily indicate a poor outcome?

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Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) harbour various genes that can potentially enhance its ability to cause disease. This study aimed to determine if there is any association between MRSA virulence genes and clinical outcomes of patients infected with MRSA. **Materials & Methods:** In this retrospective study, case notes of MRSA-positive patients whose isolates were previously investigated for virulence genes (*cna*, *seh* and *pvl*) in 2009 were reviewed. Only clinically significant cases were analysed. Information on three clinical outcomes (i.e. "days until afebrile", "days until white cell count normalised" and "days until culture became negative") were recorded. A good clinical outcome was defined as ≥ 2 outcome criteria with a result of ≤ 10 days, whereas a poor outcome was defined as ≥ 2 criteria with a result of > 10 days or death irrespective of the numbers of days. **Results:** Among 87 clinically significant MRSA isolates, 86 (98.9%) harboured *cna*, 19 (21.8%) had *seh* and 2 (4.6%) had *pvl*. Clinical outcomes could be determined for 38/87 eligible cases. Twenty three (60.5%) had good clinical outcome and 15 (39.5%) had poor clinical outcome. The presence of *seh* ($p = 0.273$) and *pvl* ($p = 1.0$) were not significantly related to the clinical outcomes. We could not determine the *p*-value for *cna* due to lack of *cna*-negative cases. **Discussion:** The mere presence of *cna*, *seh* and *pvl* in MRSA isolates do not appear to influence clinical outcomes. It is likely that other (or additional) factors play a role in MRSA pathogenicity.

MMI25 A rare case of primary tuberculosis of the female genital tract

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Introduction: Female genital tract tuberculosis (FGTB) is a rare form of extrapulmonary tuberculosis, known to have a major causal relationship with infertility. Its diagnosis at presentation remains a challenge due to nonspecific clinical manifestations that may even mimic other gynaecological conditions. **Case report:** A 36-year-old lady with previous history of recurrent miscarriages presented with lower abdominal pain and foul smelling vaginal discharge for 1-month duration. Initial pelvic ultrasound assessment revealed a complex left-tubo ovarian mass, leading to a provisional diagnosis of left tubo-ovarian abscess. She was treated with a week course of parenteral ceftriaxone and metronidazole. However, on follow-up ultrasound the lesion showed little improvement and a diagnostic laparotomy had to be performed. Left ovary, uterine wall and cystic fimbrial end biopsy showed numerous caseating granuloma formation composed of epithelioid histiocytes surrounded by lymphocytes with central caseation necrosis. Langhans-type multinucleated giant cells are also present with acid fast bacilli demonstrated upon Ziehl-Neelsen staining of the tissue. Tissue and respiratory samples sent were AFB-negative and no growth on Lowenstein-Jensen media. *Mycobacterium tuberculosis* complex DNA was detected in the tissue biopsy by polymerase chain reaction. The patient was discharged home well following laparotomy and further follow up was scheduled to discuss the findings as well as to decide on treatment options available. **Discussion:** Due to its nonspecific presentation, the diagnosis of FGTB requires a high degree of suspicion especially in endemic regions. Since clinical diagnosis is uncertain, we highlight the role of histological and molecular detection methods in diagnosis of extra-pulmonary tuberculosis.

MMI26 Community-acquired vancomycin-resistant enterococcus: A case of infective endocarditis

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Introduction: Vancomycin-resistant enterococcus (VRE) is gaining reputation as a significant nosocomial pathogen and becoming a major cause of public health concern. Community-acquired case of VRE infections is uncommon though reports are emerging. **Case report:** A 52-year-old man with history of hospitalization almost a year ago for complicated acute coronary syndrome and known to be non-compliant to follow up, currently presented with difficulty in breathing and fever. He was febrile (39.2°C) with a new cardiac murmur detected upon examination. Urgent transthoracic echocardiography demonstrated presence of an aortic valve vegetation. Vancomycin-resistant *Enterococcus faecium* was consistently isolated from his blood. On the basis of clinical, microbiological and imaging evaluation, diagnosis of VRE infective endocarditis was made. The patient was subjected to a six-week course of parenteral linezolid. Repeatedly negative blood culture was first achieved within second week of therapy. Although initially responded well, the patient started to develop progressive pancytopenia, a complication known to be associated with prolonged use of linezolid. Halfway through the course of therapy, severe thrombocytopenia had precipitated development of spontaneous intracranial hemorrhage, discovered following imaging assessment. Since then, the patient progressively deteriorated and eventually succumbed at day 23 of hospitalisation. The cause of death was ascribed to massive intracranial hemorrhage and was not directly related to any underlying infectious cause. **Discussion:** Severe VRE infection is no longer confined to healthcare settings and emergence of community-acquired infection is imminent. Being a multidrug-resistant pathogen, we are left with very limited antibiotic options in treating such infections.

MMI27 Comparative Study between Line Immunoassay (LIA) Test & Fluoroenzyme Immunoassay (FEIA) Test in Measuring Specific Extractable Nuclear Antigen (ENA) Antibodies among the Suspected Systemic Lupus Erythematosus (SLE) Patients

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the presence of autoantibodies directed against nuclear antigens such as single strand (ss) and double strand (ds) DNA (deoxyribonucleic acid), histone proteins, nucleosome (histone-DNA complex), centromere proteins and extractable nuclear antigens/ ENA (Smith antigen/ Sm, Ro, La, ribonucleoprotein/ RNP, etc.). The objective of this study is to determine the results agreement between line immunoassay (LIA) test and fluoroenzyme immunoassay (FEIA) test in measuring specific ENA antibodies among patients with suspected SLE. **Materials & Methods:** A total of 48 serum samples from suspected SLE patients sent from hospitals all over Malaysia were tested for specific ENA antibodies using line immunoassay (LIA) test and fluoroenzyme immunoassay (FEIA) test. **Results:** From overall results, a strong agreement was observed between line immunoassay (LIA) and fluoroenzyme immunoassay (FEIA) technique in the detection of anti-U1RNP (85.4%) and anti-SSA/Ro (87.5%). On the other hand, reasonable agreement was shown between both methods when measuring the presence of anti-Sm (68.8%) and anti-SSB/La (79.2%). **Discussion:** Both line immunoassay (LIA) and fluoroenzyme immunoassay (FEIA) techniques were able to detect specific ENA antibodies which are useful in assisting the diagnosis of SLE among the suspected patients.

CHEMICAL PATHOLOGY

CP1 Evaluation of quality assurance by way of Six Sigma strategy in a high volume clinical chemistry laboratory

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Introduction: Six Sigma strategy measures the degree to which any process deviates from its goal and is used to ensure the quality of laboratory testing. This study aimed to determine the Six Sigma performance in Quantum Diagnostics laboratory. **Materials & Method:** Internal quality control (IQC) data was analysed retrospectively over six months (June-October 2017) for 26 biochemistry tests analysed on COBAS 8000 (Roche Diagnostics, USA). Sigma was calculated using the equation TEA-bias/CV where TEA was obtained from the Westgard's website (2014). **Results:** 'World-class' sigma values (>6) were obtained for 15 (57.7%) analytes for Level 1 QC and 17 (65.4%) analytes for Level 2 QC, signifying less stringent QC rules application whereas satisfactory sigma of >3 were observed in nine (34.6%) analytes for Level 1 QC and seven (26.9%) analytes for Level 2 QC signifying more QC rules implementation. Poor sigma of <3 were seen in only two (7.7%) analytes in Level 1 QC (sodium and magnesium) and Level 2 QC (sodium and chloride) which highlights the need for evaluation and improvement of these methods. However, it should be noted that the biological variability targets for these analytes are very stringent and despite having poor sigma levels, their CV was <2%. **Discussion:** Six Sigma strategy is a useful quality assurance tool that incorporates IQC and EQA data to derive an allowable deviation from established targets. Furthermore, application of the Six Sigma allows the laboratory to streamline the Westgard multirule which improves the efficiency and cost effectiveness of IQC programs.

CP2 Improving turnaround time of urgent tests by improving integration processes between laboratory sections in a high throughput laboratory, Quantum Diagnostics

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Introduction: One measure of efficiency in a diagnostic laboratory is promptness in producing results. Turnaround time (TAT) has become a conspicuous indicator reflecting a lab's efficiency. Delays in TAT in a high throughput laboratory such as Quantum occurs during the handing over of samples from serology to biochemistry section. This study aimed to determine the difference in TAT prior to- and after the implementation of improved work processes in sample handling between these two sections. **Materials & Method:** Urgent tests TAT, which includes H. pylori and EBV tests alongside routine biochemistry tests, were collected from July 2017 till January 2018. Prior to August 2017, priority was given to the biochemistry tests on Cobas 8000 (Roche Diagnostics, Germany) before handing over samples to serology to run H. pylori (Immulite 2000, Siemens) and EBV (Snibe, BMS) tests. Delayed TAT was identified to originate from holdup at the biochemistry section. Work processes were then reorganised to prioritise serology tests first, where samples were loaded on respective analysers and transferred to the biochemistry analyser immediately upon aspiration of sample. In addition, activation of similar biochemistry tests on two analysers was done to ensure no analytical disruption that would affect TAT. **Results:** Percentage TAT achieved was 40.4% in July of 2017. Subsequent TAT achieved in the following months of September, October, November, December 2017 and January 2018 were 78.4%, 77.5%, 86.2%, 85.2% and 88.2%, respectively. **Discussion:** Laboratory indicators are important to identify poor work processes and formulating plans to overcome them improves the TAT.

CP3 A comparison of three modified equations for estimation of low density lipoprotein cholesterol with the traditional Friedewald formula

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Introduction: Low density lipoprotein cholesterol (LDL-c) is the primary target of therapy in the management of dyslipidaemia and cardiovascular risk reduction. The Friedewald formula (FF), which is the most widely used method for estimation of LDL-c, has limited validity at elevated triglyceride (TG) and low LDL-c concentrations. This study aimed to compare LDL-c values estimated by four different equations. **Materials & Methods:** We extracted 5,198 fasting lipid profile results analysed between January-December 2017 from our laboratory database and compared FF-derived LDL-c values with three modified LDL-c equations (Chen, de Cordova and Martin). **Results:** At TG <4.5mmol/L, LDL-c values estimated by all four equations revealed excellent correlation with each other. The strongest correlation was between Friedewald and Martin equations ($r=0.9902$, $p<0.001$). Bland-Altman analysis indicated that Chen equation had the best agreement with FF (mean bias+SD -0.006+0.160), and the highest proportion of LDL-c values within the 95% limits of agreement (95.34%). However, at TG >4.5mmol/L, although correlated, there was a significant difference in the mean LDL-c values estimated by the three modified equations ($p<0.001$). At low LDL-c concentration (<1.8mmol/L), Chen equation showed the highest concordance with FF at 78.88%. **Discussion:** Among the three modified LDL-c formulas, Chen equation which was generated in an Asian population like ours, has the closest agreement with FF. Further studies using direct LDL-c measurements and validation in various populations are needed to determine the exact performance of each equation and their clinical applicability.

CP4 Chylous ascites in a neonate: A case report

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Introduction: Neonatal chylous ascites is due to leakage of lipid-rich lymph into the peritoneal cavity and the primary cause is due to congenital maldevelopment of intra-abdominal lymphatic system. **Case report:** A term baby girl was born with distended abdomen, detected by routine ultrasound at 27 weeks of pregnancy. On examination, she was active and not in respiratory distress. Ultrasound abdomen revealed gross ascites with debris. The mother was IgG positive for toxoplasma and herpes simplex virus. However, the neonate was negative for congenital infections. On day nine of life, she became tachypnoeic with increasing abdominal girth. Peritoneal tapping revealed milky ascitic fluid with markedly raised triglyceride (21.31 mmol/L), protein (46 g/L) and white cell count (>1000 lymphocytes), diagnostic of chylous ascites. She was treated conservatively with total parenteral nutrition. **Discussion:** Intrauterine infection could lead to congenital defect of lymphatic system in utero. However, although the mother was positive, the neonate was negative for these infections. In half the cases, aetiology is unknown and ascites is thought to be due to delayed maturation of the lacteals such that chyle may leak into the peritoneal cavity. This case highlights the importance of recognition of neonatal chylous ascites by the attending clinician despite its rare occurrence, and delivery of reliable results by laboratory personnel to provide a correct diagnosis and appropriate treatment to patient in order to reduce morbidity and mortality. Currently there is no universal guidelines on the laboratory investigations for workup of chylous ascites.

CP5 Repeat testing of carcinoembryonic antigen (CEA) and its significance in Kuala Lumpur Hospital

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Introduction: Carcinoembryonic antigen (CEA) tests are used for cancer patient monitoring, but some repeated tests are performed unnecessarily. Our study aimed to determine the number of repeated CEA tests (RT) and the percentage of unnecessarily repeated CEA tests (URT) among patients admitted to or seen in the various specialist clinics in Kuala Lumpur Hospital. We also aimed to evaluate the clinical significance of changes in consecutive URT test results using reference change value (RCV). **Materials & Methods:** Total CEA tests between November 2017 and February 2018 were evaluated (N=2024). Tests performed more than once per patient were determined as RT. RT with an interval shorter than two months were determined as URT, according to the minimum re-testing interval as stated by the Association for Clinical Biochemistry and Laboratory Medicine. The RCV for CEA test was calculated based on analytical and biological variation. **Results:** 40.5% of CEA tests were RT (n=819). RT were performed for oncology, medical, surgical as well as gynaecology inpatients and outpatients. 76.8% of RT were unnecessary (URT) (n=629). The majority of URT were ordered from oncology wards and clinics. Calculated RCV was 40%. 82.8% of URT showed percentage changes between consecutive results less than RCV, thus were not clinically significant. **Discussion:** A significant number of URT were performed in our laboratory. This data should be shared with clinicians and specific guidelines for serial-monitoring of CEA should be implemented to avoid further unnecessary testing. Calculated RCV can also be reported with test results to aid clinicians in decision-making.

CP6 T-cadherin status among Negrito aborigines and its association with biomarkers of coronary risk

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Introduction: T-cadherin is hypothesised to provide cardioprotection by mediating the anti-atherogenic effects of adiponectin. Previous studies have shown strong expression of the *CDH13* gene which encodes for T-cadherin, among the Negrito aborigines. This study aimed to determine the status of T-cadherin in this population and its association with biomarkers of coronary risk. **Materials & Methods:** This cross-sectional study recruited 150 Negritos (the minimum sample size was established at 120 based on the OpenEpi Sample Size Calculator, with a confidence level of 80% and prevalence of high Framingham risk score among inland aborigines at 25%). The limited sample size is attributable to the small total population of the Negrito aborigines (estimated at 4500), as well as their remote living areas which made access to them a challenge. Serum samples were collected for analysis of hsCRP and Lp(a) concentrations on an automated Cobas 400 PLUS analyser (Roche Diagnostics, Germany), while T-cadherin and sICAM-1 were analysed by ELISA (Wuhan Fine Biological Technology Co., Ltd., Hubei, China and eBioscience Bender MedSystems, Vienna, Austria, respectively). **Results:** There was no correlation between T-cadherin and Lp(a) or hsCRP concentrations. However, an inverse correlation was observed between T-cadherin and sICAM-1 concentrations ($r=-0.28$, $p=0.001$). **Discussion:** This observation (although weak) suggests that T-cadherin could possibly have some influence in ameliorating endothelial activation. However, future studies involving larger sample size would further strengthen these observations and help to identify the specific anti-atherogenic mechanism to which T-cadherin contributes, as well as its potential role in risk stratification strategies for coronary artery disease.

CP8 Free thyroxine positive bias due to a matrix effect of external quality assurance sample

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Introduction: External Quality Assurance (EQA) programs often encounter sample matrix issues because of the need to produce a stable lyophilised material composed of a complex mix of analytes with a wide range of concentrations. We report a case of non-commutable EQA material which resulted in a positive bias for free thyroxine (FT4) results. **Case report:** The chemical pathology laboratory at our institution participates in the Condensed General Chemistry and Endocrine programs from The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) Pty Limited. We noted a persistent positive bias with FT4 throughout Cycle 47 2017 of the Endocrine program where eleven out of twelve results showed higher than target medians and exceeded the allowable limit of performance. Serum FT4 is measured on Siemens ADVIA Centaur® XP analyser with luminescent immunoassay method. We investigated thoroughly to identify the cause of the deviation from target value. Analyser breakdown, faulty parts, poor water quality and unsatisfactory maintenance were ruled out. Calibrator and reagent pack-to-pack variation were excluded after comparison with a different lab using a similar Centaur platform. Internal quality control results using third party control materials were acceptable. A suspicion of matrix effect led us to monitor our FT4 EQA performance using Condensed General Chemistry material which gave satisfactory FT4 performance. **Discussion:** After thorough discussion with RCPA to rule out possible reasons for the unsatisfactory EQA performance, the likely cause for the persistent positive bias was a non-commutable endocrine sample matrix which resulted in variable recoveries across Centaur platforms.

CP9 A rare cause of hypokalaemia

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Introduction: Gitelman Syndrome (GS) is an autosomal recessive inherited disorder of salt-losing renal tubulopathy characterised by hypokalaemic metabolic alkalosis with hypomagnesaemia and hypocalciuria. **Case report:** A 19-year-old male with history of recurrent hypokalaemia presented with generalised body weakness, polydipsia and polyuria. There was no history of laxative or diuretics abuse. Two of his siblings had similar history of recurrent hypokalaemia under nephrology follow up. Biochemical investigations showed severe hypokalaemia (1.4 mmol/L) with compensated metabolic alkalosis (pH 7.438; bicarbonate 29.7 mmol/L), low normal magnesium (0.80 mmol/L), increased urinary potassium excretion (255 mmol/24hr) and low normal urinary calcium excretion (2.5 mmol/24hr). All other biochemical investigations and renal ultrasound were normal. Treatment with potassium, magnesium supplement and potassium-sparing diuretic normalised hypokalaemia, with resolved symptoms.

Discussion: GS is a rare cause of hypokalaemia but it is an important diagnosis to consider. A positive family history with discerning biochemical results made the diagnosis of GS likely. Clinically, GS may be indistinguishable from Type III (classic) Bartter syndrome (cBS) except for normal level of magnesium and absence of hypocalciuria in cBS. Genetic analysis is required to differentiate these two.

CP10 Prothrombin induced by vitamin K absence-II (PIVKA-II) as a diagnostic biomarker of hepatocellular carcinoma. Is it worthwhile?Hana Hadi¹, Raja Affendi Raja Ali², Syed Zulkifli Syed Zakaria³, Hanita Othman¹*¹Department of Pathology, ²Gastroenterology Unit, Department of Medicine, ³Clinical Epidemiology Unit, Universiti Kebangsaan Malaysia Medical Centre, Hospital Canselor Tunku Muhriz, Kuala Lumpur, Malaysia.*

Introduction: Protein induced by vitamin K absence-II (PIVKA-II) has been proposed as an emerging biomarker for hepatocellular carcinoma (HCC). We aimed to compare the diagnostic performance of PIVKA-II and alpha-fetoprotein (AFP) in differentiating HCC and non-malignant high-risk (NMHR) group and to determine their cutoff values. **Materials & Methods:** A total of 163 patients were divided into two groups: HCC (40 patients) and NMHR (100 liver cirrhosis and 23 non-cirrhotic high-risk patients). The level of AFP and PIVKA-II were measured and their cut-off values were determined. **Results:** PIVKA-II and AFP levels were found to be significantly higher in the HCC compared to NMHR patients ($p < 0.0001$). The optimal cutoff values for PIVKA-II and AFP were 36.7 mAU/mL (90% sensitivity; 82.1% specificity) and 14.2 ng/mL (75% sensitivity; 93.5% specificity), respectively, for the differentiation of HCC from NMHR. The areas under the receiver operating characteristic (AUROC) curve of PIVKA-II (0.905, $p < 0.0001$) was higher compared to AFP (0.869, $p < 0.0001$) but the combination of PIVKA-II and AFP gave the highest AUROC value (0.911, $p < 0.0001$). However, their differences were not statistically significant (AFP vs PIVKA-II; $p = 0.4775$, AFP vs Combination; $p = 0.3808$, PIVKA-II vs Combination; $p = 0.2268$). **Discussion:** PIVKA-II and AFP showed similar performance in detecting HCC in high risk patients. The utilisation of AFP as a screening marker for HCC may be adequate and adding PIVKA-II test in current clinical practice could be of little value.

CP11 The deadly haemophagocytic lymphohistiocytosisTengku Zaharah Tengku Ibrahim¹, Intan Nureslyna Samsudin², Subashini C. Thambiah², Alia Nasriana Nasuruddin¹*¹Department of Pathology, Hospital Tuanku Ampuan Afzan, Kuantan Malaysia; ²Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia*

Introduction: Haemophagocytic lymphohistiocytosis (HLH) is a rare condition characterised by overwhelming activation of normal T-lymphocytes and macrophages associated with high mortality and morbidity. HLH can be divided into primary (genetic or inherited) and secondary (acquired) causes. HLH may be triggered by infection, autoimmune disease, malignancy and immunosuppression. **Case report:** A 16-month-old Malay boy, the first of monozygotic twins, was born preterm at 34 weeks with a birth weight of 1.79 kg, presented with six days history of fever, vomiting and abdominal distention. He was noted to be jaundiced with hepatomegaly and multiple lymphadenopathies. On admission, he developed multiple episodes of tonic-clonic seizures. His urgent full blood picture revealed pancytopenia suggestive of severe infection or sepsis, with differential diagnosis of HLH secondary to infection. Other blood investigations showed hyperferritinaemia (221,700 ng/ml), hypertriglyceridaemia (5.49 mmol/L), deranged liver enzymes (ALT 484 U/L, AST 2076 U/L) and low fibrinogen (134 mg/dL). He succumbed to death after four days of admission as his condition deteriorated rapidly with multiorgan failure despite the medical support given. His final blood culture was reported as positive growth for *E. coli* ESBL. **Discussion:** This case highlights the importance of having HLH as one of the differentials especially in a patient who presents with unexplained sudden onset of systemic inflammatory response syndrome. The diagnosis of HLH may be difficult, as it mimics other commoner conditions and no specific test is available. The HLH-2004: Diagnostic and Therapeutic Guidelines for Hemophagocytic Lymphohistiocytosis highlights the biochemical investigations that may assist in the diagnosis which includes hyperferritinaemia, hypertriglyceridaemia, cytopenias and hypofibrinaemia.

CP12 High-sensitivity C-reactive protein (hsCRP) as an additional cardiovascular risk marker among UPM Serdang staff

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Introduction: Identification of individuals who are at high risk of cardiovascular disease (CVD) but asymptomatic is a serious issue in primary prevention. However, using traditional risk factors to predict CVD event might miss some cases. Abundant data confirmed the ability of high sensitivity C-reactive protein (hsCRP) to add prognostic information to the Framingham Risk Score (FRS) and link the latter to metabolic syndrome (MetS). Validation of correlation between hsCRP and other predictors of CVD is thus important in Malaysian population. **Materials & Methods:** We studied 83 adults (aged 30-60 years old) who attended health screening at Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Body weight, height, waist circumference (WC) and blood pressure were measured. hsCRP level, fasting blood sugar, fasting serum lipid and HbA1c were analysed. Body mass index (BMI), FRS, non- high-density lipoprotein (non-HDL-C), total cholesterol:HDL-C ratio and low density lipoprotein:HDL ratio were calculated. **Results:** The study consisted of 22% male and 78% female subjects encompassing all three major ethnicities. Univariate and multivariate analyses revealed that hsCRP was significantly increased in patients with MetS (p=0.009), at-risk WC (p=0.001) and high BMI (p=0.001). Spearman's correlation coefficient showed significant modest positive correlation between hsCRP level and total FRS (r=0.264, p<0.05) and HDL-C score (r=0.255, p<0.05). **Discussion:** hsCRP was able to capture different aspects of cardiovascular (CV) risk in addition to the traditional CV risk markers demonstrated in the FRS and supports the assumption that hsCRP may have an additional role in the overall CV risk determination. Therefore, incorporating hsCRP into MetS criteria and FRS component may improve CVD risk assessment and estimation of 10-year CVD risk.

CP13 Lipaemic serum in a type 1 diabetes mellitus teenager presenting with diabetic ketoacidosis

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Introduction: Ketoacidosis seldom causes diagnostic or therapeutic problems. However milky serum samples resulting from the presence of severe hyperlipidaemia may pose diagnostic challenge for routine sample processing and accurate result generation. This will lead to delayed diagnosis and treatment. **Case report:** We report a case of an 18-year-old girl with underlying type 1 diabetes mellitus who developed diabetic ketoacidosis with severe hyperlipidaemia secondary to upper respiratory tract infection and non-compliance to insulin. The patient's serum sample was grossly lipaemic and hence, not suitable for most blood analysis. Serum electrolytes, liver function test, lipid and renal profiles were unobtainable until day-6 of her hospitalisation. The patient's management was somewhat challenging due to unavailability of blood results. She was initially treated based on clinical evaluation and venous blood gas, urine ketone and glucose results to support the clinical management. **Discussion:** Lipaemia interference mechanism is due either to light scatter causing measurement errors in photometric methods or volume displacement by lipids causing a decreased aqueous phase e.g. with indirect ion-selective electrode (ISE) method. Ideally, ultracentrifugation or high-speed centrifugation should be done to remove or minimise the lipid concentration prior to analysis. However, in our setting, only a benchtop centrifuge with maximum speed of 3000 rpm is available. As such, triglyceride result was not released. Arterial blood gas analyser using direct ISE method was used to analyse sodium, potassium and chloride in venous blood. Laboratory personnel should be aware of lipaemia interference and methods available to remove these interferences to optimise patient management.

CP14 Growth hormone secreting pituitary macroadenoma with thyroid carcinoma

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Introduction: Acromegaly is a clinical syndrome resulting from growth hormone (GH) hypersecretion associated with risk of diabetes mellitus, cardiovascular disease and carcinoma, all of which leads to higher morbidity and mortality. **Case report:** A 55-year-old gentleman consulted a physician for unresolved generalised urticarial lesions who noted acromegalic features in the patient. On further questioning, the patient admitted noticing a change in his facial features and increasingly enlarged hands and feet for the past 3 to 4 years. The patient also complained of difficulty in swallowing and snoring. Physical examination revealed increased arm span and spade-like hands with prognathism and macroglossia. A large multinodular goiter was also noted. An increased serum IGF-1 and failure of GH suppression following an oral glucose tolerance test (OGTT) confirmed the diagnosis of acromegaly. A magnetic resonance imaging revealed a pituitary macroadenoma and the CT-scan of the neck showed multinodular goitre with retrosternal extension. A total thyroidectomy was performed in view of progressive compressive symptoms and histopathological examination confirmed papillary thyroid carcinoma. **Discussion:** Acromegaly increases the risk of malignancy. Although colon carcinoma is the most common cancer in acromegaly, thyroid carcinoma should also be considered as its prevalence in acromegaly is higher than expected.

CP15 HbA1c and fructosamine: Indirect markers for dyslipidaemia and atherogenicity in type 2 diabetes mellitus patientsNur Suraya J¹, Norlaila M², Nurshafini CR³, Dian NN¹¹Department of Pathology, ²Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Hospital Canselor Tuanku Muhriz; ³Department of Pathology, Hospital Kuala Lumpur, Malaysia

Introduction: A high prevalence of dyslipidaemia in type 2 diabetes mellitus (T2DM) contributes to the increased risk of cardiovascular diseases. This study was carried out to evaluate the correlation between glycaemic markers [HbA1c, fructosamine and fasting plasma glucose (FPG)] with dyslipidaemia and atherogenic indices which is reflected by the atherogenic index of plasma (AIP) and atherogenic coefficient (AC) in T2DM. **Materials & Methods:** A total of 395 T2DM patients attending the outpatient endocrine clinic were recruited. Blood samples were measured for HbA1c, fructosamine, FPG, total cholesterol (TC), triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C). Low-density lipoprotein cholesterol (LDL-C), TC/HDL-C and LDL-C/HDL-C ratio, AIP (log TG/HDL-C) and AC (TC-HDL-C/HDL-C) values were calculated. **Results:** HbA1c weakly correlated with all lipid parameters and atherogenic indices, TG ($r=0.262$, $p<0.01$), TC ($r=0.236$, $p<0.01$), LDL-C ($r=0.177$, $p<0.01$), HDL-C ($r=-0.145$, $p<0.01$), TC/HDL-C ($r=0.282$, $p<0.01$), LDL-C/HDL-C ($r=0.213$, $p<0.01$), AIP ($r=0.252$, $p<0.01$) and AC ($r=0.282$, $p<0.01$). Similar weak correlations were also observed for fructosamine; TG ($r=0.157$, $p<0.01$), TC ($r=0.220$, $p<0.01$), LDL-C ($r=0.153$, $p<0.01$), TC/HDL-C ($r=0.220$, $p<0.01$), LDL-C/HDL-C ($r=0.189$, $p<0.01$), AIP ($r=0.140$, $p<0.01$), and AC ($r=0.220$, $p<0.01$), but no significant correlation with HDL-C. FPG demonstrated weak correlation with TG ($r=0.230$, $p<0.01$), TC ($r=0.12$, $p<0.05$), TC/HDL-C ($r=0.142$, $p<0.01$), AIP ($r=0.192$, $p<0.01$) and AC ($r=0.142$, $p<0.01$) but not with HDL-C and LDL-C. **Discussion:** There were weak correlations seen between the glycaemic markers with lipid parameters and atherogenic indices. These findings imply that these glycaemic markers show potential as indirect markers for dyslipidaemia and atherogenicity.

CP16 Modification of Diet in Renal Disease (MDRD) Study equation versus Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine-based equation to estimate glomerular filtration rateFathimah Mohamad^{1,2}, Nadzimah Mohd Nasir^{1,2}, Arjoanna Farra Azizi^{1,2}, Sarina Ali¹¹Centre for Pathology Diagnostic and Research Laboratories (CPDRL), Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia; ²Health and Wellbeing CoRe, Universiti Teknologi MARA, Selangor, Malaysia

Introduction: CKD-EPI creatinine-based equation was developed to address the systematic underestimation of the glomerular filtration rate (GFR) by the MDRD Study equation in patients with a relatively well-preserved kidney function. The objectives of this study were to evaluate eGFR by CKD-EPI versus MDRD equations and to stratify kidney function according to Kidney Disease Improving Global Outcomes (KDIGO) guidelines. **Materials & Methods:** Serum creatinine from 16,333 patients were extracted from our laboratory database from January to December 2017. eGFR were calculated using the CKD-EPI and MDRD equations. CKD stages based on two different eGFRs were compared. **Results:** Sample consisted of 5823 women (36%) and 10510 men (64%). Median age of patient was 59 years and median baseline of creatinine was 96.56 $\mu\text{mol/L}$. Baseline median eGFR was 65.18 and 69.30 mL/min/1.73 m^2 for MDRD and CKD-EPI equations respectively ($p < 0.005$). Of the 16,333 measurements, MDRD classified 3290 (20%) patients as “normal function GFR” (eGFR $> 90\%$) while CKD-EPI classified 4617 (28%) patients as “normal function GFR”. Therefore 8% patients who were classified as “normal eGFR” with CKD-EPI were classified as “reduced GFR” (GFR $< 90 \text{ mL/min/1.73 m}^2$) using MDRD. Besides that, MDRD revealed higher percentage of patients (44%) with eGFR $< 60 \text{ mL/min/1.73 m}^2$ as compared to CKD-EPI (only 41%). **Discussion:** The CKD-EPI equation classified fewer individuals as having reduced kidney function than did the MDRD Study equation. This will lead to decreased classification of CKD among patients which may affect referral patterns and treatment. Further research is needed to determine whether widespread use of CKD-EPI with current guidelines could lead to delayed specialist care among patients with CKD.

CP17 Acute pancreatitis with persistent in vivo haemolysisIntan Nureslyna Samsudin¹, Jin Earn Choo¹, Mohd Jamsani Mat Salleh², Subashini C. Thambiah¹¹Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia; ²Chemical Pathology Unit, Department of Pathology, Penang General Hospital, Malaysia

Introduction: Acute pancreatitis is characterised by reversible pancreatic parenchymal injury associated with inflammation and has diverse aetiologies. Biochemically, it is characterised by elevated serum amylase more than 10 times the upper limit of normal. **Case Report:** A 33-year-old Chinese gentleman with hypertension, dyslipidaemia and established kidney failure on regular haemodialysis presented with severe epigastric pain radiating to the back. The epigastric pain was associated with nausea, vomiting and dyspnoea. He was afebrile but tenderness and guarding were noted over the epigastric region on abdominal examination. Acute pancreatitis was suspected and blood samples were sent for measurement of amylase. Unfortunately, his first two samples were grossly haemolysed with haemolytic index (HI) of 1011 and 924 mg/dL , respectively. A third sample with a HI of 809 mg/dL showed an elevated serum amylase. His random urinary amylase was also raised. Contrast-enhanced computed tomography scan of the abdomen and pelvis revealed features suggestive of acute pancreatitis. **Discussion:** *In vivo* haemolysis can both cause and be caused by acute pancreatitis. *In vivo* haemolysis can result from systemic inflammatory response caused by acute pancreatitis and approximately 25% of cases of massive haemolysis are complicated by acute pancreatitis. It is an undesirable condition that may influence the accuracy and reliability of laboratory testing.

CP18 Untangle the mystery of discordant thyroid function test

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Introduction: Resistance to thyroid hormone (RTH) is an autosomal dominant syndrome characterised by reduced end-organ responsiveness to thyroid hormone and is accompanied by normal or slightly high serum thyroid stimulating hormone (TSH) with raised free thyroxine or triiodothyronine. **Case report:** An asymptomatic 62-year-old lady investigated for bilateral pedal oedema in Hospital Kuala Lumpur (HKL) was found to have discordant thyroid function test (TFT) [free T4: 37.5 pmol/L [12.0-22.0], TSH: 2.36 mU/L [0.27-4.20]. TFT analysis at HKL uses one-step Roche-Elecsys assay. Therefore, samples were sent to Hospital Putrajaya for reanalysis on the two-step Beckman platform. Similar discordant TFT results were obtained ruling out immunoassay interference. Subsequently, the patient developed thyrotoxicosis and was commenced on carbimazole but remained symptomatic. Normal pituitary hormones and oestradiol, absence of elevated sex-hormone binding globulin and a negative magnetic resonance imaging of the pituitary ruled out TSHoma. Clinical assessment and galium uptake positron emission tomography-computerised tomography were unremarkable ruling out ectopic lesion for TSHoma. Thyroid releasing hormone (TRH) stimulation test done showed an exaggerated TSH response (Baseline: 4.18 mU/L; post TRH 30 mins and 60 mins: 44 mU/L and 29 mU/L, respectively) supporting a diagnosis of RTH. **Discussion:** Discordant TFT results require a structured approach and further assessment is essential to avoid unnecessary/inappropriate investigation and treatment. Once confounding influences have been excluded, close liaison with the laboratory is required to systematically exclude TFT assay interference. Only then should further investigation for rare acquired and genetic causes be considered.

CP19 Thyrotoxic periodic paralysis - the diagnostic challenges

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Introduction: Thyrotoxic periodic paralysis (TPP) is a rare complication of hyperthyroidism, more common in Asian men between the second and fourth decades of life with incidence of 1.8% and 1.9% in thyrotoxic Chinese and Japanese, respectively. **Case report:** A 24-year-old Burmese male presented with sudden onset paralysis of his lower extremities and diarrhoea. Neurological assessment of bilateral lower limbs showed hypotonia, with a power of 2/5. Laboratory evaluation revealed a marked hypokalaemia (1.8 mmol/L) with normal electrolytes, acid base and creatinine kinase. The paralysis resolved upon repletion of potassium and he was discharged home. Within days he presented with a similar presentation. Further history revealed that he was losing weight progressively. Additional laboratory tests showed low urinary potassium and suppressed TSH with elevated fT4 which confirmed a thyrotoxic state. The paralytic episodes resolved following treatment with antithyroid medication. **Discussion:** Most TPP cases have subtle symptoms of thyrotoxicosis. The primary defect is an intracellular sequestration of potassium with normal body potassium stores. Thyroid hormone increases potassium permeability and the numbers of β adrenergic receptors in skeletal muscles which result in increased Na/K ATPase activity. The clues to the diagnosis in this patient are extremely low urinary potassium excretion with normal acid base status.

CP20 Hypocalcaemia in a neonate with cardiac anomaly

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Introduction: DiGeorge syndrome is the most common microdeletion syndrome with multisystemic clinical presentation. It should be considered when a neonate presents with hypocalcaemia. **Case report:** A 25-day-old Indian boy presented with rapid breathing and choking post-bottle feeding. He was diagnosed with aspiration pneumonia and started on antibiotics. During admission, he developed multiple episodes of seizures which were initially focal before becoming generalised in nature lasting up to one minute. On examination, he was afebrile with unremarkable neurological findings. Laboratory investigations showed hypocalcaemia with hyperphosphataemia. Serum parathyroid hormone was noted to be inappropriately normal with low vitamin D. Cerebrospinal fluid and blood culture revealed no growth. An incidental finding of a systolic murmur led to a detection of a perimembranous ventricular septal defect in failure. Thoracic ultrasonography confirmed presence of a thymus. Subsequent chromosomal study revealed a deletion in the DiGeorge critical region on chromosome 22, confirming the diagnosis of DiGeorge Syndrome. **Discussion:** Hypocalcaemia secondary to hypoparathyroidism, with a cardiac anomaly in a paediatric patient leads to suspicion of a genetic aetiology as illustrated in this case.

CP21 Role of inferior petrosal sinus sampling in Cushing Disease

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Introduction: Cushing Disease is a condition of excess endogenous glucocorticoid hormone production caused by a pituitary tumour secreting adrenocorticotrophic hormone (ACTH). Non-pituitary or ectopic production of ACTH or rarely corticotropin releasing hormone (CRH) can also cause ACTH-dependent Cushing Syndrome. Laboratory and imaging investigations play important roles in differentiating and localising the site of ACTH production. **Case report:** A 36-year-old lady with underlying diabetes mellitus and hypertension was referred to Hospital Kuala Lumpur for inferior petrosal sinus sampling (IPSS) procedure. She had two years history of weight gain, proximal muscle weakness, irregular menses, and facial puffiness. Elevated morning serum cortisol, 24-hour urinary free cortisol excretion, and plasma ACTH with failure of low dose dexamethasone suppression test suggested an ACTH-dependent hypercortisolaemia. Subsequent pituitary magnetic resonance imaging revealed a pituitary microadenoma. The IPSS findings were strongly suggestive of ACTH-producing pituitary tumour. These findings fulfilled the criteria established by Oldfield et. al. for a valid IPSS procedure. **Conclusion:** IPSS remains the best test to differentiate pituitary from ectopic ACTH-dependent Cushing syndrome.

FORENSIC MEDICINE**FM1 Geometric morphometric study of sexual dimorphism of Malaysian mandibles.**

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Introduction: Geometric morphometric is the statistical analysis of form based on Cartesian landmark coordinates. In this study, geometric morphometric techniques were used to study sexual dimorphism of mandible. The objectives were to determine mandible variation in size and shape, determine the relationship between size and shape in males and females, and visualize allometry patterns of mandible. **Materials & Methods:** About 113 samples human adult mandibles (65 males, 48 females) were sampled. Approximately 12 landmarks were placed on the 2-D image by landmarking software, and were analysed with MorphoJ. **Results:** The first five principal components were taken to represent the morphological variance with 83.64% cumulative variance. The mandible shape was used to determine sex. The variance visualization showed significant variation between male and female. The classification accuracy was 91.96%. **Discussion:** Geometric morphometric is a good method to study sexual dimorphism of mandible. Its potential may be developed in forensic anthropology to determine ancestry and age groups. MorphoJ and other softwares may be used in the application of geometric morphometric study of other bones.

FM2 A case series of autopsy findings in patients with seropositive Human Immunodeficiency Virus in Universiti Kebangsaan Malaysia Medical Centre.

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Introduction: HIV infection is relatively frequent in urban areas, where it develops a wide variety of opportunistic infections involving various organs and becomes fatal. However, the history of HIV status and high risk behaviour life style was not frequently disclosed to the pathologist before the autopsy. It harbours potential transmission of HIV and other pathogens such as hepatitis B, C virus during autopsy and endangers the mortuary staff. **Case report:** We reported 11 cases of postmortem examination of HIV seropositive patient with illustrating variety of histopathological changes of Cryptococcal infection (2), generalised histoplasmosis (2), Pneumocystis carinii pneumonia (1), myocarditis, liver and lung abscesses (1), systemic infection with Proteus mirabilis (1), Pseudomonas aeruginosa (1) and three cases of deaths, which were not directly caused by HIV infection. **Discussion:** Histopathological examination of different opportunistic infections, provide important diagnostic and epidemiological data. The pathologist should be aware of the potential risk of acquiring HIV infection during autopsy, strictly practice the safe autopsy technique and mortuary management. Extensive external examination to acquire the clinical suspicion of HIV infection and serum rapid HIV testing will raise the attention of the mortuary staff towards the potential risk of acquiring HIV infection during autopsy.

FM3 Medico-legal autopsies of homicidal death: A five-year retrospective study in Hospital Sungai Buloh

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Introduction: Homicide is the act of killing one human being by another, encompassing death as a result of criminal act including justifiable homicide such as of judicial killing and self-defense. This study aimed to ascertain the epidemiology and patterns of injury of homicide victims. **Materials & Methods:** We reviewed records of medico-legal autopsy cases performed at the Department of Forensic Medicine, Hospital Sungai Buloh, for a period of five years, from January 2012 until December 2016. Subjects' demographic data such as age, gender, nationality, ethnicity and cause of death were recorded. **Results:** A total of 122 homicide cases were documented. 90% of the victims were 18 to 65 years old. Males contributed 80% of the subjects. An alarming 42% of the subjects comprised of non-Malaysians. Indonesian subjects contributed one third of the non-citizen category, followed by Bangladeshis at 20.4%. Other nationalities were Burmese, Nepalese, Pakistani, Vietnamese and unspecified. Among Malaysians, 50% of the subjects were Indians, followed by Malay (31.5%) and Chinese (17.8%). Sharp and blunt force traumas were the most common injuries found, contributing 33% and 32% respectively. Asphyxiation and firearm injuries recorded an almost similar frequency, contributing 25% in combination. Other patterns included combined sharp and blunt objects (4.9%) and burns (3%). **Discussion:** A large number of immigrants in the country have significantly increased the forensic casework. Sharp and blunt objects continue to be the weapon of choice due to its easy accessibility. As domestic violence including fatal spousal and child abuse continue to rise, in-depth study in the area is warranted.

FM4 A case of fatal septicaemia by acute pyonephrosis due to chronic pyelonephritis secondary to obstructive nephropathy.

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Introduction: Pyonephrosis is collection of pus in collecting system. It is uncommon in adults and rare in children. The risk of pyonephrosis is increased in patients with upper urinary tract obstruction secondary to various causes (eg, stones, tumours). Prompt treatment is crucial and often curable. Here, we report a case of complicated acute pyonephrosis that ensue in death. **Case report:** A 42-year-old woman presented with 2 days of colicky pain and lumpy feel at right side of abdomen. She was later found dead while resting on sofa. Autopsy revealed adhesion at right retroperitoneum with enlarged right kidney. It ruptured and released copious amount of pus on examination. Cross section showed gross dilatation of right renal pelvis and calyceal system with a thinning of the renal cortex. There were multiple brown colour calculi ranging from 5-7cm at renal pelvis. The cortico-medullary junction was obliterated. Pus was collected in right renal pelvis, renal parenchyma, subcapsule, right ureter and bladder. Histopathological examination demonstrated both renals' interstitium have abscesses with neutrophils, fibrin, cell debris and central bacteria colonies. Tubules were damaged and replaced by exudate, inflammatory infiltrates and reactive fibrosis. Glomeruli was scarce. Right renal pus, blood and urine cultures isolated *Escherichia coli*. **Discussion:** Obstruction of urinary tract by renal calculi can cause hydronephrosis. It increased the risk of ascending urinary tract infection that lead to pyelonephritis. Acute pyelonephritis that is not treated can advance to chronic pyelonephritis and acute pyonephrosis. This resulted in septicaemia and patient can deteriorate rapidly without emergency treatment.

FM5 Fatal gastroenteritis in young adult due to Salmonella septicaemia

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Introduction: Salmonella septicemia are serious complications that may not be suspected in mild primary infection. Host risk factors for Salmonella bacteremia include extremes of age and chronic or immunosuppressing conditions. We report a case of fatal gastroenteritis in a young adult due to Salmonella septicemia. **Case report:** A 36 years old man that was previously well complaint of fever, diarrhoea, vomit, and stomach-ache for 2 days. He was hypotensive, dehydrated and collapsed on the way to hospital. Post-mortem examination revealed hepatomegaly, friable spleen but normal gastrointestinal tract. The heart didn't show atherosclerosis changes. There was mild pulmonary edema and other gross examination did not show significant findings. Blood culture isolated non-typhoidal Salmonella species while microscopic examination showed mild aggregates of lymphocytes, plasma cells, and occasional neutrophils at myocardial fibers. HIV antibody was negative. **Discussion:** Salmonella bacteremia has been shown to be a relatively common event but the mortality has been underestimated. They usually presented with gastroenteritis 12 to 48 hours post exposure. Septicemia often results from uncomplicated enterocolitis. The microscopic findings in this patient showed pathology characteristic for salmonella infection however no erythrophagocytosis was noted. Cardiac arrest was secondary to myocarditis due to salmonella septicemia. Death with nonspecific symptoms vomit, diarrhoea and abdominal pain should raise our concern of Salmonella septicemia.

FM6 Melioidosis: A Miliary Tuberculosis Mimicker in Autopsy

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Introduction: Melioidosis is an infectious disease caused by a gram-negative intracellular bacillus *Burkholderia pseudomallei*. Tuberculosis is an infectious disease caused by an acid-fast bacillus *Mycobacterium tuberculosis*. Patients of these two diseases may present with fever and respiratory symptoms leading to respiratory failure and/or sepsis and sudden death, if left untreated. In cases, where unusual clinical presentation of melioidosis and postmortem findings mimicking tuberculosis, it can be quite difficult to differentiate one from another. **Case Report:** A 49-year-old Nepalese man was found dead in a hostel early in the morning. The deceased had fever for one week prior to his death. Postmortem examination was requested by the police to determine the cause of death. External examination showed no evidence of trauma. Internal examination revealed multiple microabscesses in bilateral lungs, liver and spleen, which were similar to miliary tuberculosis. However, microbiological culture of cerebrospinal fluid (CSF), blood, lungs, liver and spleen grew *Burkholderia pseudomallei*. **Discussion:** Differentiation between melioidosis and miliary tuberculosis based on gross examination in autopsy can be quite difficult. In such cases, it is always a good practice to collect all specimens for microbiological culture with full laboratory report before determining the cause of death.

FM7 A collateral damage of a successful programme: A case report of methadone intoxication in an infant

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Introduction: Methadone has been successfully used as a replacement therapy for opiate (such as heroin and morphine) addiction in Malaysia as well as to avoid blood borne infection, due to needle sharing. Patient is usually prescribed with syrup methadone and monitored by medical officer. Ingestion of a small amount may be fatal or even death in children whether incidental or intentional. **Case report:** A 16-month-old boy was brought to hospital by the parent after he was found having difficulty in breathing and subsequently non responsive. He was apparently well until the day of his demise. In hospital, resuscitation was initiated but to no avail. Post mortem examination showed bilateral haemorrhagic congested lungs, dilated bowels, distended bladder and enlarged thymus, spleen with multiple lymph nodes. No fracture seen in skeletal survey. Microbiological cultures from blood, CSF, trachea, peritoneum and lung were unremarkable. Histopathologically, the lungs were oedematous and congested. Dystrophic calcification of thymus with sinus histiocytosis and inflammation in lymph nodes were suggestive of chronic reactive changes. The toxicology report revealed presence of methadone and its metabolite, EDDP (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine) in both the blood and urine. **Discussion:** Findings in post mortem for death due to methadone toxicity can be non-specific at times. The presence of EDDP showed that methadone was metabolized by the deceased, hence indicating that methadone was introduced to the deceased, leading to the demise.

FM8 Pattern of burn injury in delayed burn: An autopsy case report

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Introduction: Homicide by burn is inevitably rare. Homicidal burn seemed to be mainly used as means of covering up homicide or to hamper identification. We, herein report a delayed death in a homicidal burn. This case emphasized on complications following burn injury, which may lead to a fatal outcome. **Case report:** A 32-year-old lady had an argument with her boyfriend before being splashed with an accelerant, and was ignited. She was brought to the hospital and managed for 90% burn with 2nd to 3rd degree burns. She died on the 5th day of admission. Autopsy showed areas of burnt skin that appeared red and leathery, which involved mainly the anterior aspect. The top of head, back and sole were spared. Internal examination showed presence of emboli in the main pulmonary trunk, which originated from thrombus in the deep vein of left calf. No soot particles were seen in the airways. Ancillary investigations showed no evidence of infection. **Discussion:** There are no specific methods in helping forensic pathologist to determine manner of death in burn cases. In suspected homicidal burn, toxicologic analysis should be done as it is usually associated with accelerants. Reconstruction pattern of injuries would help in determining manner of death in combination with detail history and scene investigations. As burn injury lead to high mortality, delayed deaths in burn victims were mostly caused by its complications that developed following burn injury.

GENERAL PATHOLOGY**GEN1 A review of a XYY boy with familial translocation on chromosomes 17 and 20**

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Introduction: The main features of Silver-Russel syndrome (SRS) are pre and postnatal growth restriction and a characteristic small, triangular face. SRS is recognized as a clinically and genetically heterogeneous congenital disorder. Half of the patients have methylation defects on chromosome 11p15, 10% resulted from chromosome 7 maternal uniparental disomy (UPD) and 40% are due to other genetic mechanisms. **Case report:** A 4-year-old dysmorphic boy with cleft palate, global developmental delay karyotyped 47,XYY,t(17;20)(q25;q13.3) has two phenotypically abnormal sisters both with unbalanced karyotype 46,XX,der(20)t(17;20)(q25;q13.3); one of them also has cleft palate. The mother had 6 previous pregnancy losses is a carrier of a balanced translocation; her karyotype is 46, XX,t(17;20)(q25;q13.3). The father karyotype is 46XY. Both parents are phenotypically normal. His baby sister was born with dysmorphic features without cleft palate. Her karyotype was similar to her sisters. **Discussion:** The sisters' phenotypes were resulted from unbalanced translocation. Despite having an apparently balanced translocation, he expressed dymorphic features most probably produced by gene disruption. Two previous reports showed patients with SRS features have reciprocal translocations involving distal chromosome 17q; one of the cases has similar breakpoint as in this case; leads to the putative candidate gene in this region is CSH1. His extra Y chromosome resulted from meiosis non disjunction. This report would highlight the importance of genetic testing in making diagnosis and the role of genetic counselling with regards to fertility issue, conceiving offspring with abnormalities and increased incidence of associated comorbidities.

GEN2 Patients with Milky Blood! Management of Series of Lipaemic Samples in A Medical Laboratory in a Major Specialist Hospital

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Introduction: Lipemia cause significant problem in laboratories due to its interference with test methodology. While most common cause of pre-analytical lipemia is, not-fasting prior to blood collection, other cause is due to hypertriglyceridaemia. We described 3 cases of lipemia with different clinical scenarios presented to our hospital. **Case reports:** A 42-days old male baby, born full-term was noticed to be markedly pale during routine immunization check-up in clinic. His haemoglobin was not readable by the analyzer thus he was referred to our hospital for further management. The sample was lipaemic with no haemoglobin level given. His sample was centrifuged and saline replacement procedure for lipaemia performed. Hb was 3 g/dL. For second case, patient was a 33 year-old lady, G2P1 at 31 weeks period of gestation, presented with bouts of vomiting and abdominal pain. Her sample was markedly lipaemic and triglyceride level was 151 mmol/L. The sample was processed and ultracentrifuged. The patient's condition deteriorated and she had to be intubated. She was treated as having acute pancreatitis secondary to hypertriglycerimia in pregnancy. Plasma exchange was performed and lipid lowering agent was given. Miraculously, she responded to treatment and able to be extubated with triglyceride level came down to 2.4 mmol/L. Last case involved a 5-year-old boy presented with cough and fever. His initial blood sample was lipaemic but it was clear the next morning after fasting overnight. **Discussion:** Although not frequently encountered, lipaemic samples continue to provide challenges to laboratories. Good practices for processing lipaemic samples should be established as to provide accurate results for best patient outcomes.