

**The Annual Scientific Meeting of College of Pathologists, Academy of Medicine of Malaysia: Opportunities and Challenges in Laboratory Medicine, was held at Riverside Majestic Hotel, Kuching, Sarawak on 27-28 June 2019. Abstracts of K. Prathap Memorial Lecture, plenary, symposium and paper (poster) presented are as follows:**

***K Prathap Memorial Lecture:***

**Opportunities and challenges for laboratory professional in patient safety**

Yasmin Ayob

*National Blood Centre & National Heart Institute, Kuala Lumpur, Malaysia*

Pathology has been the engine of healthcare system in understanding diseases and in the last few decades in monitoring therapy. However, the approach and technique we use remain very much the same. As we move into the future of the digital age and artificial intelligence, the challenge is should we continue doing the same or do we need to change and reinvent the discipline and the service we provide. To remain relevant, we have to embrace the change and move with the times. The digitization of pathology laboratories makes the specialty more efficient, specimen more reproducible and the work of pathologists less cumbersome. New technologies that produce biomedical “big data” (next generation sequencing, multiparameter / multiplex flow cytometry, high-throughput proteomics and metabolomics, systems biology analysis) have also caused us to rethink the best approach to diagnostics. While these opportunities and challenges seem daunting, we still have to grapple with old challenges of funding and leadership.

***Plenary 1:***

**Challenges in diagnosis of monoclonal gammopathy**

Pavai Sthaneshwar

*University of Malaya (UM), Kuala Lumpur, Malaysia*

The monoclonal gammopathies (MG) are a group of disorders characterised by the proliferation of clonal plasma cells to produce resulting in a detectable abnormality called monoclonal component or M-protein or paraprotein. Direct measurement of the M-protein spike by electrophoresis and immunochemical measurements of specific isotypes or free light chains pairs has provided useful information about the quantity of M-protein. Nonetheless, quantitation of M-protein by electrophoretic method gives suboptimal measurements on small M-proteins. In addition, measurements by electrophoresis of M-proteins migrating in the  $\beta$ - and  $\alpha$ -regions are difficult due to the presence of normal serum proteins in those regions. The nephelometric quantitation of immunoglobulins (Igs) is a simple automated method that uses anti-human Ig antigen binding fragments (Fabs) that target the constant region of Ig. The method measures both monoclonal and polyclonal immunoglobulins, and therefore, its diagnostic use for identification of monoclonal proteins is not recommended and is also of no value for biclonal and triclinal gammopathies. Use of the serum free light chain (FLC) immunoassay, has led to improvements in the diagnosis and monitoring of patients with plasma cell dyscrasia and other monoclonal gammopathies. Not all MG secrete excess FLC. Abnormal serum FLC ratios have only been detected in 90–95% of intact Ig multiple myeloma and 40% of MGUS. Since these two patient groups can be easily diagnosed by serum M-proteins by protein electrophoresis, a combination of tests is needed to detect all MGs. Nephelometric methods using antisera specific for Ig heavy and light chain epitopes separately quantitate IgG kappa and IgG lambda, IgA kappa and IgA lambda, and IgM kappa and IgM lambda and may be useful for monitoring monoclonal proteins migrating in the beta fraction. The heavy-light, isotype-specific kappa to lambda ratio has been proposed as a potential monitoring method for IgA or IgM M-proteins migrating in the beta fraction. Although the assay is not sensitive enough to use as a routine screening method for MM, a 97% sensitivity observed in IgA MM and IgA MGUS indicates that almost all IgA MM patients can be monitored by HLC for both detection of the disease clone and quantitation using the IgA HLC assay. A 24-hour urine collection allows the quantitation of both the albumin and M-protein that has been rapidly cleared by the kidneys. The potential broad use of mass spectrometry for MG has been recently demonstrated by the application of matrix assisted laser desorption ionization – time of flight instruments (MALDI-TOF) for detecting monoclonal proteins. The Mayo Clinic group performed a large retrospective study in which patients with an assortment of plasma cell proliferative diseases had SPE, IFE, and FLC as well as urine protein electrophoresis and IFE performed at the time of diagnosis. The study shows patients would have had M-proteins detected by the various tests singly or in combination and if urine assays are removed from the diagnostic panel, there is no decrease in sensitivity. This and other studies have led the IMWG to recommend a panel of serum protein electrophoresis, immunofixation electrophoresis and FLC to screen for a MG; the inclusion of diagnostic urine testing is only recommended if amyloidosis is suspected, which simplifies collection for the patient and workflow for the laboratory and reduces costs as well.

**Plenary 2:**  
**Challenges in rabies diagnosis: The Sarawak experience**

Chua Hock Hin  
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Sarawak is facing an unprecedented outbreak of rabies, which was declared on 1<sup>st</sup> July 2017. The initial outbreak was unveiled through human rabies cases and not through animal surveillance which was non-existence in 2016 and 2017 till the outbreak was declared in Sarawak. As of date, Sarawak reported 17 human rabies cases with 16 deaths. Clinical specimens were sent to Institute for Medical Research (IMR) laboratory for confirmation. Among the clinical specimens sent were cerebrospinal fluid (CSF), saliva, urine and nuchal skin biopsy. These specimens were triple packed and hand-carried to IMR. Real time polymerase chain reaction (RT-PCR) was performed on the clinical specimens. Clinically, the human rabies patients presented with clinical features of either acute meningo-encephalitis or Gullain Barre Syndrome, whereby virus infection is the usual cause. Therefore, timely laboratory results which confirmed the aetiology helped clinicians in the case management of these patients.

**Symposium:**  
**1A: Approach to soft tissue tumours with myxoid stroma**

Noraini Mohd Dusa  
*Hospital Kuala Lumpur, Kuala Lumpur, Malaysia*

Soft tissue tumours with myxoid stroma (myxoid tumours of soft tissue) are characterised by their abundant extracellular matrix material. This heterogenous group comprised of benign tumours, tumours with potential for local recurrence (intermediate), and sarcomas. It is important to emphasize on several features including depth of tumour, the extent of myxoid stroma, the presence of nuclear pleomorphism and the presence of distinctive vasculature when dealing with myxoid tumours of soft tissue. This talk will focus on some myxoid tumours encountered in surgical pathology practice.

**1A: Pitfalls in diagnosis of soft tissue tumours**

Noraini Mohd Dusa  
*Hospital Kuala Lumpur, Kuala Lumpur, Malaysia*

An unexpected or unforeseen danger may be encountered by a surgical pathologist in interpreting soft tissue tumours resulting in incorrect diagnosis. Among the problems are over interpretation (benign lesion mistaken as malignant), under interpretation (malignant lesions mistaken as benign), misinterpretation of immunohistochemistry profile or non-soft tissue tumours misdiagnosed as soft tissue sarcomas.

**1A: Elusive causes of death: Pinning our hopes on laboratory examination**

Razuin Rahimi  
*Universiti Teknologi MARA (UiTM), Sungai Buloh, Selangor, Malaysia*

Some forensic autopsy cases may be more perplexing than another, such as sudden natural death of a child, a healthy adolescent or a pregnant mother. From histopathology examination, toxicology analysis to genetic testing, from local laboratories to reference laboratories abroad, one of the biggest problems with forensic specimens is getting the suitable sample for the intended laboratory testing. The fact that we only have one shot at obtaining the samples, laboratory restraints on analysing the post-mortem samples further exacerbate the matter. Thus, effective communication with the respective Pathologist such as Microbiologist, Haematologist, Histopathologist, Geneticist or Toxicologists plays an important role in order to assist us in getting the appropriate samples for a laboratory testing uncommonly requested from the mortuary. Careful pre-autopsy planning includes making the necessary preparations for the samples by identifying the type of specimens to be obtained, storage, transport and ultimately the laboratory to which it should be sent. Positive results from the laboratory examinations confirming our suspicion on the elusive and atypical presentations of disease, not only concludes the cause of death, also gives closure to the next-of-kin.

**1B: Opportunities and challenges in haemostatic tests**

Wan Zaidah Abdullah  
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The practice of haemostasis investigation is evolving under new paradigms of efficiency. Screening and specialized tests to diagnose bleeding and thrombotic disorders are important and critical in the patient management. However, the driving forces of haemostasis laboratory operation are mainly dependent on economic resources. In reality, it is undergoing a substantial reorganization, with emergence of new tests under various settings such as bedside testing, instrument automation and other on

demand investigations. The paradigms under which these changes are being developed include a variety of clinical needs, pre-analytical issues, technological advances and increasing knowledge in the haemostatic aspects including understanding of the tests and related diseases. The maintenance of continued quality is indeed the major challenge to be faced ongoingly. However, challenges also emerge in a variety of test processes, which basically involve laboratory results (unmet expectation), preanalytical variables, inadequate facilities/skills, as well as lack of standardization in the analytical methods. This presentation is aimed to provide an overview of the current haemostatic diagnostic opportunities and challenges and to discuss the changing face of hemostasis testing in modern laboratories. These hopefully provide a synthetic analysis for future planning and solutions. The issues induced by the complexity of diagnostic tool in haemostatic disorders and problems in international standardization of reagent materials are acknowledged by many parties. Finally, the opportunities where laboratory could provide the best diagnostic activity are discussed and hopefully would allow significant improvement in the related services.

### **1B: Red cell membrane disorder: Challenges in diagnosis**

Norazah Mohd Yusoff

*Advanced Medical and Dental Institute (AMDI), Universiti Science Malaysia (USM), Bertam, Penang, Malaysia*

Red blood cell (RBC) membrane disorders are inherited conditions arising from mutations in genes encoding the cytoskeletal proteins of RBC and the transmembrane transporters. There is decreased RBC deformability and permeability resulting in reduced half-life of RBC with premature removal. RBC membrane disorders represent a heterogeneous group of haemolytic defects with overlapping phenotypes, thus the clinical definition of patients is often difficult. For some conditions, the great phenotypic variability is partially explained by the high genetic heterogeneity thus, it is sometimes complicated to distinguish one form from the others since the signs can be masked in symptom-free carriers or in mildly affected patients. Moreover, some subtypes of RBC membrane disorders can be easily confused with other clinically related hereditary haemolytic conditions. Specialized tests provide additional evidence in supporting the diagnosis to facilitate the management of the patient. In the case of a patient's clinical phenotype being more severe than the affected members within the immediate family, molecular testing of all family members is useful for confirming the diagnosis and allows an insight into the molecular basis of the abnormality.

### **1B: Approach in managing thalassaemia from transfusion service perspective**

Nor Hafizah Ahmad

*National Blood Centre, Kuala Lumpur, Malaysia*

Thalassaemia is the most common hemoglobinopathies in Malaysia. It is estimated 120-350 babies are born with thalassaemia each year (National Screening Program, 2016). It is indeed a health public issue which has numerous psychological, social and economical impacts to the patients, family and nation. Transfusion remains the mainstay of the treatment for this population of patients. The two main aims for transfusion are to suppress extramedullary haemopoiesis and to improve anemia or quality of life of the patients. Decision to start blood transfusion requires proper assessment and it must be initiated promptly when there is clinical evidence of severe anaemia with symptoms or signs of cardiac failure, failure to thrive, and/or bone deformity. Alloimmunization in thalassaemia patients presents a major challenge for the transfusion service similarly like other group of transfusion dependent patients. Risk of alloimmunization to minor red blood cell (RBC) antigen will increase with repeat transfusion. Alloantibodies development can complicate transfusion management and lead to delay in blood supply. It is of clinical importance as it can lead to hemolytic transfusion reaction. Patients who received regular transfusion also have higher risk to develop febrile non-hemolytic transfusion reaction hence leucofiltered blood would be the best option. Transfusion service must ensure that we are able to supply safe and appropriate blood to the patients. Policy and guideline are used to guide transfusion support and critical strategies must be outlined. Among the strategies that have been recommended are Baseline RBC phenotyping, extended RBC phenotyping, leucofiltered blood and enhancing donor recruitment. National Blood Centre has instituted extensive measures to ensure safe and adequate blood supply for the thalassaemia patients for years. These are done by ensuring adequate blood collection, improved safety of blood supply by using Nucleic Acid Testing, supplying filtered/leucodepleted and phenotype matched blood to prevent adverse reactions and also building a good database of blood donors to match our patients' need. Currently our team is embarking on genotyping for thalassaemia as the way forward.

### **1C: Standardised reporting of serum protein electrophoresis**

Pavai Sthaneshwar

*University of Malaya (UM), Kuala Lumpur, Malaysia*

Protein electrophoresis (PE) is commonly used as an aid in the diagnosis of monoclonal gammopathies. Contrary to high volume automated chemistry results, serum (SPE) and urine (UPE) protein electrophoresis and immunotyping are the few results that require interpretation by laboratory staff to be included in the report. Laboratorians are trained to review and interpret electrophoretic patterns and must convey accurate written interpretation of the results to the clinicians. Clinicians are primarily interested in whether a paraprotein is present or not, and if present, what its characteristics are and how great its concentration is. Along with a pattern interpretation, laboratories also report quantitative values for the normal protein fractions (*e.g.* albumin, alpha-1, alpha-2, beta, and gamma) identified by electrophoresis, as well as monoclonal fractions when present. The international

multiple myeloma working group has published guidelines in relation to the diagnosis, monitoring and treatment of plasma cell dyscrasias, it only gives passing attention to laboratory aspects of protein electrophoresis. There is very little in the published literature to guide reporting of SPE and UPE and systematic reporting standards are not available. There are few agreed upon criteria for reporting of fractions, use of nomenclature for fractions nor standardised nomenclature or structure for the interpretive report associated with the electrophoretic pattern. The Canadian Society of Clinical Chemists (CSCC), Australasian association of Clinical Biochemists (AACB) and the International Federation of Clinical Chemistry (IFCC) have published recommendations for protein electrophoresis reporting. There need to be consensus in reporting of protein electrophoresis by Malaysian laboratories.

### **1C: Updates in biochemical lipid testing**

Subashini C Thambiah

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Coronary heart disease (CHD) is a leading cause of morbidity and mortality in developed countries. Although the conventional lipid profile [total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL) and triglyceride (TG)] is a well-established platform for cardiovascular disease (CVD) risk prediction and management, a significant burden of CVD events remains unaddressed. The role of lipids in atherogenesis has been established but the methods for evaluating CVD risk continue to be a debatable topic. HDL is low, TG is raised and LDL levels are typically normal in atherogenic dyslipidaemia but there is a higher fraction of small dense LDL (sdLDL) particles, which are not detected on conventional lipid profile measurement. While international and national lipid guidelines do not currently recommend measurement of LDL subfractions as a screening tool, they do acknowledge that sdLDL is a useful indicator of atherogenic dyslipidaemia and the metabolic syndrome (MetS) and its presence supports intensified therapeutic lifestyle changes. The preliminary data of a local study done on LDL subfractions in asymptomatic multiethnic Malaysian adults using the FDA-approved LipoPrint system from Quantimetrix is presented here. This polyacrylamide tube gel electrophoresis system separates LDL into seven subfractions. LDL phenotype is reported as Pattern A [large, buoyant LDL (LDL-1, LDL-2)] and Pattern B [sdLDL (LDL-3 – LDL-7)], indicating low and high risk for CHD, respectively. As dyslipidaemia is a component of both MetS and Framingham Risk Score (FRS), the association of LDL subfractions with MetS and FRS were also determined in this study. While routine measurement is not recommended, it should be recognised that LDL subfraction testing conveys a level of CVD risk not possible with conventional lipid profile.

### **1C: *Candida auris* infection: Emerging fungal disease**

Tzar Mohd Nizam Khaithir

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In 2009, a novel *Candida* species was isolated from the ear discharge from the external ear canal of a 70-year-old Japanese woman. It has since been reported globally, including in Malaysia, from various body sites. This particular *Candida* species has attracted increased clinical attention because of its ability to cause various candidiasis in humans and its multiple antifungal drug resistance. Treatment is further complicated because this new species is frequently misidentified as other *Candida* species by conventional identification methods. Subsequent molecular studies identified the isolate as a novel fungal pathogen closely related to *Candida haemulonii* species complex. This new *Candida* species was later named after the source of its first isolation, the ear, hence, *Candida auris*.

### **2A: Approach to inflammatory skin disorder**

Ikmal Hisyam Bakrin

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The accurate diagnosis of inflammatory dermatoses in dermatopathology requires integrating the histological findings with the clinical features (clinico-pathological correlation). As a reporting pathologist, patient's age, relevant clinical history, and the site from which the skin biopsy was obtained should be provided to you. Having said that, even with adequate information this can still be challenging especially when skin biopsies are infrequently seen and the terminologies are unfamiliar, in a general surgical pathology practice. The "Approach of Inflammatory Skin Disorder" presents a pattern-based approach to the diagnosis as well as reviews of the salient clinical and histologic features of inflammatory dermatoses. Spongiotic, psoriasiform, interface/lichenoid, granulomatous, vasculitis/vasculopathy, superficial and/or deep inflammation and bullous skin reaction patterns will be discussed in this topic.

**2A: Forensic entomology in Malaysia: Opportunities for service expansion**

Heo Chong Chin

*Universiti Teknologi MARA (UiTM), Sungai Buloh, Selangor, Malaysia*

Since Reid (1953) published the first record of forensic entomology in Malaysia, researches have been carried out extensively and the number of publications in the last decade increased significantly. Typically, forensic entomological specimens collected by police and hospital staff are sent to the Institute of Medical Research (IMR) or National University of Malaysia (UKM), and a smaller number of specimens to other institutions. The main purpose of forensic entomology is to obtain the minimum post-mortem interval (mPMI), as entomological evidence is very useful for outdoor death cases which took place >72 hours. In order to provide more accurate estimation of mPMI, standard protocol has been developed internationally. Besides that, there are also developmental studies on individual fly species of forensic importance according to temperatures. In countries with seasons or areas with contrasting day-night temperatures, statistical models using accumulated degree hour (ADH) has been useful. When interpreting results from entomological evidence, basic ecological studies on insect succession suggest that chance factors in the environment should not be overlooked. Additionally, the effects of population genetics, gene expression and phenotypic plasticity on mPMI are currently being investigated. Researches on how necrobiome, nematodes, mites, and soil chemistry may assist in forensic investigations are also opportunities to expand the service of forensic biology in Malaysia.

**2B: Genomic profiling in acute leukaemias**

Zubaidah Zakaria

*Institute for Medical Research (IMR), Kuala Lumpur, Malaysia*

Molecular profiling of DNA and RNA has provided valuable new insights into the genetic basis of haemato-oncology. In the last decade, our understanding of the somatic cancer genome has been greatly advanced through gene discovery studies. These studies delineated the genomic complexity and have identified recurrent somatic alterations particularly in acute leukaemias. It has significant clinical impact in the diagnosis of acute leukaemias defined by recurrent somatic alterations and in the development of more precise prognostic schema. Most importantly, these studies have identified disease alleles that have guided the use of molecularly targeted therapy. Historically, these genetic alterations have been identified by low-resolution or limited-scope genetic tests, such as karyotyping or single gene assays. Cytogenetic studies identified recurrent chromosomal translocations in a spectrum of hematologic malignancies especially acute leukaemias, which impact clinical outcome and can guide therapeutic decisions. More recent studies have identified recurrent mutations and, creating a pressing need to develop comprehensive genomic assays to identify somatic alterations in hematologic malignancies. Recent technological advances have enabled the analyses of genomic and epigenomic variation in a comprehensive, high-throughput fashion using next generation sequencing. Moreover, there is growing interest in new areas of research, such as the epi-transcriptome and its relevance to health and disease. These advances have important implications for future research and clinical practice in such areas as molecular diagnostics, the implementation of gene or pathway-directed targeted therapies, and the use of such information to inform drug discovery. Latest update on molecular classification and recent advances used for genomic profiling in acute leukaemias will be discussed.

**2B: Immunophenotyping in acute leukaemias: Challenges and issues**

Lee Shir Yin

*National University Hospital (NUH), Singapore*

This talk explains how the process of immunophenotyping can be used to maximum benefit in diagnosis of acute leukaemia. The talk will be of an interactive format with case discussions and will seek to highlight how in-depth immunophenotypic analysis can provide personalised medicine.

**2B: Multiple myeloma diagnosis: Challenges and issues**

Lau Lee Gong

*Borneo Medical Centre, Kuching, Sarawak*

Multiple myeloma (MM) is a neoplastic plasma-cell disorder characterized by clonal proliferation of malignant plasma cells in the bone marrow microenvironment, monoclonal protein in the blood and/or the urine, and associated organ dysfunction. It accounts for approximately 1% of all cancers and 10% of all haematologic malignancies. The median age of patients at diagnosis is about 65-70 years. The diagnosis is made according to the International Myeloma Working Group (IMWG) updated criteria as published in 2014. It requires the presence of one or more myeloma defining events in addition to evidence of either 10% or more clonal plasma cells on bone marrow examination or a biopsy-proven plasmacytoma. Data from randomized controlled trials using modern therapy show that the median survival in MM has improved over the last 2 decades. In younger patients eligible for autologous stem cell transplantation, the median overall survival is approximately 8 years. Among elderly patients (age >75 years), median overall survival is lower, about 5 years. As in other cancers, survival in MM is affected by host characteristics, tumour burden (stage), biology (genetic abnormalities), and response to therapy. Tumour burden in MM has traditionally

been assessed using the Durie-Salmon Staging and the International Staging System (ISS). The recently published Revised International Staging System (R-ISS) combines elements of tumour burden (ISS) and disease biology (high risk cytogenetics or elevated lactate dehydrogenase level) to create a unified prognostic index. The R-ISS is a powerful and useful prognostic tool that can stratify MM patients effectively. All these (diagnostic criteria and staging system), however, present management challenges to pathologists and clinicians, especially those practising in resource-limited setting in the developing countries. The non-availability and high cost of medications are other problems plaguing clinicians seeing MM patients. These and other issues will be presented and discussed in this lecture.

## 2C: Tumour markers: Applications and abuses

Leslie Charles Lai Chin Loy  
Gleneagles Hospital, Kuala Lumpur, Malaysia

Tumour markers are substances related to the presence or progress of a tumour and may be present in higher than normal concentrations in the tissue and body fluids of cancer patients. Serum tumour markers may aid cancer diagnosis and the assessment of prognosis, guide choice of treatment, monitor response to treatment and to detect recurrence early and/or be used as screening tests. When tumour markers are requested appropriately and interpreted correctly, they contribute significantly to clinical management. Inappropriately used tumour marker results can cause patients anxiety and distress and lead to unnecessary investigations that may be associated with significant side-effects and potentially delay the correct diagnosis and treatment, in addition to increasing healthcare costs.  $\alpha$ -Fetoprotein (AFP) may be used in conjunction with abdominal ultrasound for the early detection of hepatocellular carcinoma (HCC) in patients with chronic hepatitis or cirrhosis associated with hepatitis B or C virus infection. After a diagnosis of HCC, post-treatment monitoring with AFP is recommended as an adjunct to imaging. For testicular cancer, AFP, human chorionic gonadotropin, and lactate dehydrogenase are recommended for diagnosis, staging, prognosis determination, recurrence detection, and therapy monitoring. Prostate-specific antigen (PSA) is not recommended for prostate cancer screening but may be used to detect cancer recurrence and to monitor therapy. Free PSA is useful in differentiating malignant from benign prostatic disease when total PSA is between 4 and 10  $\mu\text{g/L}$  and when digital rectal examination is negative. In colorectal cancer, carcinoembryonic antigen is recommended for prognosis determination, post-operative surveillance, and therapy monitoring in advanced disease. CA125 is recommended with transvaginal ultrasound for early detection of ovarian cancer in women at high risk for this disease. CA125 is also recommended for differential diagnosis of suspicious pelvic masses in postmenopausal women, as well as for detection of recurrence, monitoring of therapy, and determination of prognosis in women with ovarian cancer.

## 2C: Designing and evaluating auto-verification rules for chemical pathology tests

Mohd Jamsani Mat Salleh  
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Auto-verification is a process where computer-based algorithms automatically perform actions on a defined subset of laboratory results without the need for manual intervention by a laboratorian. Following the analytical phase, the current practice of many hospital laboratories involves manual verification of all test results followed by the production of report. However, manual verification is a time-consuming and tedious process. In an era of diminishing labour and reimbursement, auto-verification in clinical laboratory is a generally accepted mechanism to reduce turnaround times and increase staff productivity. Auto-verification algorithm should be properly designed with clearly defined criteria and any data that do not meet the criteria, must be reviewed and manually validated. Auto-verification has numerous benefits, including shortening of the TAT; reduction in the number of results for manual revision and, consequently, a greater focus on potentially problematic patient specimens; and uniform test reporting that is less subject to subjective variations. It also allows laboratory staff to devote more time and effort to the handling of problematic test results and contributing to improved patient care. However, auto-verification is still only a computerized tool that works according to defined rules, which surely enhances laboratory efficiency but cannot completely replace laboratory personnel work in the process of reporting laboratory results and decision-making.

## 2C: Epidemiology of *Plasmodium knowlesi*: Need for a new rapid diagnostic tool?

Balbir Singh  
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For a considerable period, malaria in humans was thought to be caused by four species of *Plasmodium*: *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. Naturally acquired simian malaria infections were considered extremely rare until the use of molecular tools led to the discovery of a large focus of human *P. knowlesi* infections in 2004 in the Kapit Division of Sarawak, Malaysian Borneo. Human knowlesi malaria cases have since been described throughout Southeast Asia, with Malaysia reporting the highest incidence to date (7,745 cases in 2017 and 2018). The molecular, entomological and epidemiological data, indicate that knowlesi malaria is primarily a zoonosis. Forest-dwelling Anopheline mosquitoes are the vectors and long-tailed and pig-tailed macaques (*Macaca fascicularis* and *M. nemestrina* respectively) are the main reservoir hosts. Humans get infected when they encroach the habitat of the mosquito vectors and macaques. Human *P. knowlesi* infections had been previously diagnosed

by microscopy mainly as *P. malariae*, since these two species are morphologically identical. Molecular detection methods, which are more sensitive and specific than microscopy, are necessary for correct identification of *P. knowlesi*. However, these molecular methods are expensive and not in routine use in rural health settings where most knowlesi malaria cases occur. A sensitive and cheap rapid diagnostic test (RDT) that does not require electricity would be ideal for the diagnosis of knowlesi malaria. However, the RDTs that have been evaluated to date for detection of *P. knowlesi* have low sensitivity, particularly for samples with low parasitaemia, underscoring the need for a more sensitive test.

## 2C: Introduction to transplant immunology

Masitah Arip  
*Institute for Medical Research (IMR), Kuala Lumpur, Malaysia*

Solid organ and tissue transplantation have progressed dramatically over the last 50 years. In addition to the medical and surgical challenges in transplantation, the major biological barrier is immunological. This barrier may lead to graft rejection and loss. An understanding of transplant immunology is essential in order to care for transplant recipients. The roles of the different components of the immune system involved in the tolerance or rejection of grafts and in graft-versus-host disease (GVHD) have been clarified. These components include antibodies, antigen-presenting cells, helper and cytotoxic T-cell subsets, immune cell-surface molecules, signalling mechanisms and cytokines. In order for an allograft to be rejected, the immune system of the recipient must be able to recognize the transplanted tissue as foreign, and then have effector mechanisms by which the graft can be destroyed. In clinical transplantation the recognition process is known as allorecognition, and the entire immune response is known as the alloresponse. There are essentially three types of tissue antigens that can be recognized by the immune system and subsequently provoke an alloimmune response: ABO blood group antigens, human leukocyte antigen (HLA) antigens, and non-HLA antigens (minor histocompatibility antigens). Advances in transplantation immunology have allowed newer immunosuppressive agents controlling solid-organ and tissue rejection and GVHD. Future developments in the field of transplantation immunology will hopefully include novel immunosuppressive with less toxicity and more specificity to control graft rejection while sparing overall immunity and thereby enabling better infection control.

## 3A: Pitfalls in inflammatory dermatopathology

Lee Bang Rom  
*Universiti Putra Malaysia (UPM), Serdang, Selangor, Malaysia*

The practical diagnostic guide for inflammatory skin disorders relies on focusing the practicalities of correlating the histopathologic and clinical features, and highlighting useful diagnostic tips and potential pitfalls. Cases include spongiotic Dermatitis, Psoriasiform Dermatitis, Interface Dermatitis, Granulomatous lesion, Vasculitis and panniculitis are discussed in this lecture. The differential of the pitfalls depends on the clinical and microscopic features, including histopathologic variations. The limitations of a skin biopsy are highlighted. Correlation of the clinicopathologic attributes allows for a more meaningful and accurate diagnosis.

## 3A: Myeloproliferative neoplasm diagnosis: Challenges and issues

Lee Shir Yin  
*National University Hospital (NUH), Singapore*

The classification of haematological malignancies incorporates multifaceted information from a variety of sources and technologies. This talk uses several classic and challenging cases to illustrate issues in myeloproliferative disease diagnosis. It will also discuss the role and impact on the pathologist of new molecular discoveries and treatments of myeloproliferative disease.

## 3B: Updates in laboratory testing for diabetes

Leslie Charles Lai Chin Loy  
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Type 2 diabetes is increasing in prevalence worldwide at an alarming rate. People with diabetes have a two to four-fold risk of acute myocardial infarction and stroke: 50% of people with diabetes die of acute myocardial infarction and 25% die of stroke. Diabetes is the commonest cause of blindness, end stage kidney disease (chronic kidney disease Stage 5) and leg amputations in the world. It is, therefore, crucial for people with diabetes to have not only good glucose control but also optimal control of other cardiovascular risk factors, for example, hypertension, dyslipidaemia, obesity and smoking. The laboratory plays a crucial role in the diagnosis of diabetes as well as in monitoring glycaemic control. HbA1c is now used for both the diagnosis of diabetes and in the assessment of diabetes control. However, since HbA1c reflects the glucose control over the past two to three months it should not be used to diagnose type 1 diabetes or gestational diabetes where the diabetes can develop rapidly over a short period of time. It is important to ensure that lipid levels are optimised to reduce cardiovascular risk and to monitor

patients' renal function (serum creatinine and eGFR using CKD-EPI formula as well as urine albumin/creatinine ratio on a first void urine sample). Insulin and/or C-peptide measurement may be useful in ascertaining the body's ability to produce insulin and help differentiate type 1 from type 2 diabetes although insulin and C-peptide levels can be low in the presence of glucose toxicity even in patients with type 2 diabetes and should be measured when glucose control has been good for several weeks. Islet Cell Cytoplasmic Autoantibodies (ICA); Insulin Autoantibodies (IAA); Glutamic Acid Decarboxylase-65 Autoantibodies (GAD65); Insulinoma-Associated-2 Autoantibodies (IA-2A); Zinc Transporter-8 Autoantibodies (ZnT8A) may be present in type 1 diabetes. GAD65 autoantibodies can accurately predict T1D development in combination with other surrogate humoral biomarkers and they are considered the most sensitive and specific biomarker which identifies a subset of clinically diagnosed type 2 diabetes termed Latent Autoimmune Diabetes in Adults (LADA). Type 1 diabetes may be part of a pluriglandular autoimmune syndrome and the patient with type 1 diabetes may also develop hypothyroidism or hyperthyroidism, and/or Addison's disease. It is important to measure thyroid hormones at least annually in patients with type 1 diabetes or sooner if symptoms of hyperthyroidism or hypothyroidism develop. The homeostasis model assessment 2 (HOMA<sub>2</sub>) is a method used to estimate beta cell function (HOMA-%B), insulin sensitivity (HOMA-%S) and insulin resistance (HOMA-IR) from fasting glucose and insulin or C-peptide levels.

### **3B: Challenges in ensuring quality performance in microbiological laboratory in the context of ISO 15189**

Alex Francis

*Standards Malaysia, Kuala Lumpur, Malaysia*

The technical requirements of Medical Microbiology testing in the context of ISO 15189 Accreditation standards is exhaustive and sometimes can be intimidating because in addition to the above standards, the accreditation body in Malaysia *i.e.* Standards Malaysia, requires addressing its Specific Criteria and Specific Technical requirements in Microbiology (SC 2 and STR 2.5) which are a prescriptive and acclimatized interpretation to the above international standards. However, this perceived feeling of anxiety can be reduced if we see laboratory testing in 3 phases, Pre-analytical, Analytical and Post-Analytical. There are many elements involved all these processes but I would like to highlight some key challenges which affect quality performances based on my extensive assessment of these laboratories for the past 16 years. Starting In the pre-analytical phase, reagent acceptance testing is vaguely understood by staff as an essential early performance indicator. Instructions for pre-collection and collection are almost always incomplete. Sample transportation to referral laboratories often times does not meet the requirements. Verification of freezer temperatures is frequently not carried out. The in-house media preparation has several stringent requirements that not all laboratories are able to show. It is disheartening to observe that almost all laboratories do not seem to have the correct procedure for the management of quality control culture collection. Understanding lineage history and preservation of fastidious organisms is blurred in most laboratories. In the examination phase, verification and validation of examination procedures are often the least understood requirements, even among senior scientist. Alternative approaches when EQA is not available such as inter-laboratory comparison is rarely developed as an alternative but effective solution. Sensitivity testing of fastidious organisms and methods of detection of resistance mechanism are not clearly demonstrated in most laboratories. In the post examination processes, the report content requirement is comprehensive and often times overlooked. This stringent requirement of ISO 15189 accreditation standards should not be disheartening but must become a clarion call to uplift medical microbiology testing to world standards.

#### **Lunch Symposium:**

##### **Opportunities and challenges in high sensitive troponin (hsTn)**

Robert Charles William Hawkins

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Troponin is a complex of three regulatory proteins (troponin C, troponin I, and troponin T) that is integral to muscle contraction in skeletal muscle and cardiac muscle, but not smooth muscle. Cardiac specific troponin I isoform has amino acid sequences that are found only in cardiac tissue, making it highly specific for detecting cardiac damage. After injury to heart cells, the rate of appearance of cardiac markers in the circulation is determined by both the size and the intracellular localization of these proteins or enzymes. In the mid 90s, it was becoming apparent that troponins were superior to CKMB, and clinical guidelines started to recommend troponin as the preferred biomarker for detecting myocardial injury. The latest 4th universal definition of acute myocardial infarction (AMI) recommends troponin as the preferred biomarker to rule in and rule out myocardial injury. It endorses the IFCC analytical criteria for hsTn assays: An imprecision of  $\leq 10\%$  CV at the 99th percentile URL is mandatory for hs-cTn assays; hsTn assays should be able to measure cTn values in  $\geq 50\%$  of healthy individuals above the assay's LoD. However, many of the point-of-care testing (POCT) Tn assays do not meet these criteria, creating challenges for clinicians and laboratories offering high sensitive lab-based Tn assays. This talk will discuss how to balance handle Tn testing from both the lab and POCT perspective.



**Poster Abstracts:****AP-01. A retrospective study of neonatal and infant oral lesions diagnosed through microscopic examination in Stomatology Unit, Institute for Medical Research (2000-2017)**

Nadia Najwa Shuhairi, Lau Shin Hin, Ajura Abdul Jalil  
*Stomatology Unit, Cancer Research Centre, Institute for Medical Research, Malaysia*

*Introduction:* A large number of retrospective studies on oral and maxillofacial lesions in paediatric population have been documented including the Asian countries. However, there is still paucity of oral lesion status in the newborn particularly in Malaysia. This study mainly investigates Malaysia's neonate and infant oral lesions diagnosed by the main Oral Pathology Diagnostic and Referral Centre in Malaysia, Stomatology Unit. *Materials & Methods:* Biopsy records from year 2000-2017 of patient aged 2 years old and below were extracted from Oral Pathology Information System (OPIS) and confirmed through patient's biopsy request form archived in Stomatology Unit. Oral lesions were divided into four main categories; inflammatory/reactive, cystic/pseudocystic, tumour/tumour-like lesion and miscellaneous lesion based on two age groups; neonate (0-30 days old) and infant (>1 month to 2 years old). *Results & Discussion:* A total number of 115 samples were gathered from patient of age 2 years and below from a total number of 29,940 biopsy specimens received. Only 10 patients were neonate with youngest aged 2 days old. The most common lesion was from Inflammatory/Reactive category (mucous extravasation cyst; n=25, fibroepithelial hyperplasia; n=6 and fibrous epulis; n=5) followed by tumour/tumour-like category (Langerhan's cell histiocytosis; n=6 and congenital epulis; n=5) and cystic/pseudocystic-like lesion (dermoid cyst was the most frequent; n=3). Maxilla was found to be the most common site for both lesions mentioned in tumour/tumour-like lesion. 12 patients were diagnosed with malignant lesions. *Conclusions:* The vast majority of oral lesion found in newborn was inflammatory/reactive or benign, with 10.43% were malignant lesions. The data provides an impression of oral lesions that can occur in a very young age, thus this is helpful for both of the surgeon and pathologist as investigations can be tailored accordingly to diagnose the oral lesion.

**AP-02. An Analysis of salivary gland tumour: A 10-year, single institution review in Malaysia**

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*Introduction:* Salivary gland tumour constitutes a group of disease with variants in histopathologic and clinical behaviour hence the demographic and clinicopathological features of this tumour have been reported differently with lack of published reports among Malaysian. Therefore, the aim of the present study is to describe the demographic and clinicopathologic characteristics of salivary gland tumour in Stomatology Unit, Institute for Medical Research, the national referral centre for oral pathology cases in Malaysia in the hope of gaining better understanding about the tumour. *Materials & Methods:* A cohort, retrospective study was carried out on the period spanning from January 2005 to December 2015 (10 years) in Oral Pathology Service, Stomatology Unit, Institute for Medical Research, Kuala Lumpur. Information on demographics, clinical and histopathology profile of salivary gland tumour cases were retrieved from Oral Pathology Information System (OPIS) and laboratory request form. *Results & Discussion:* Among 231 cases recruited, 119 (52.8%) were benign and 112 (47.2%) were malignant, which occurred in 110 males and 121 females. Pleomorphic adenoma was the most frequent benign neoplasm (92.6%) while mucoepidermoid carcinoma represented the most prevalent malignant neoplasm (26.8%). Benign salivary gland tumour occurred mainly between 5<sup>th</sup> to 6<sup>th</sup> decade of life with female preponderance whereas the malignant counterpart was diagnosed between 3<sup>rd</sup> to 4<sup>th</sup> decade of life, predominantly in male patients. Majority of the cases involving intraoral minor salivary gland with palate (37.2%) as the commonest site of occurrence followed by buccal mucosa (11.7%). Clinically, the patients' complaint was essentially slow growing painless swelling with duration of more than 1 year (44.6%). *Conclusions:* The data demonstrated about an equal incidence of benign and malignant salivary gland tumours, contrary to most of the studied literatures. However, other epidemiologic and clinicopathologic profiles corroborated most of the other published studies.

**AP-03. Glomus tumour of the lower lip: A case report**

Zarina A Karim<sup>1</sup>, Farveen Marican Abu Bakar<sup>2</sup>, Geetha Siva Sankaran<sup>3</sup>, Norita Abdul Rahim<sup>3</sup>, Sumairi Ismail<sup>4</sup>  
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*Introduction:* Glomus tumours are rare, mesenchymal neoplasms (<2%) that majority occur in the distal extremities i.e. subungual regions as most glomus bodies found there. These tumors are rarely seen in the oral cavity, with scarce reported cases available. Here, we report a case of glomus tumor of the lower lip in a 15-year-old girl. *Case Report:* The patient presented with a painless pedunculated swelling over left lower lip and was completely excised. Histopathological features of the lesion were found to be numerous hemangioma-like vessels, surrounded by cohesive sheets of round to spindle-shaped cells with well-defined basal lamina. Immunohistochemistry examination of the neoplastic cells was positive for smooth muscle actin, with CD31 and CD34 stains highlighting the blood vessels. Clinical differential diagnoses of mucocele, hemangioma or salivary gland neoplasm may be considered. Excision is the mainstay management for this lesion with no established recurrence rate in the

oral cavity region. On regular review, the biopsy site appeared healed with no sign of recurrence. *Discussion:* Although pain is the most characteristic symptoms at the other sites, majority of the lesions in the oral cavity are painless. Among the etiology for these lesions are inactivating mutations in the glomulin gene in chromosome arm 1p, with reported cases associated with neurofibromatosis type 1 (NF1) and autosomal dominant inheritance in multiple familial glomus tumours. *Learning Points:* Since these tumors are rarely encountered in the oral cavity, high index of suspicion and awareness among the clinician are crucial for the diagnosis. Therefore, it is warrant for consideration in differential diagnoses of a small, painless swelling in the oral cavity.

#### AP-04. A case report of metastasizing ameloblastoma in lymph node

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*Introduction:* Ameloblastoma is a benign intraosseous odontogenic tumor characterized by expansion and a tendency for local recurrence. Rarely, ameloblastoma may metastasize in lung, followed by lymph nodes and bone. We report a case of metastasizing ameloblastoma in cervical lymph node, 6 years after the right hemimandibulectomy in a 48-year-old man. *Case Report:* The patient presented with a painless swelling over the right mandible for 2 years in duration. He was then undergone right hemimandibulectomy with uneventful recovery and regular follow-up. After 6 years, he presented with a painless, slow growing swelling over right neck and undergone FNAC of right cervical lymph node (level III). He was then again undergone wide surgical excision and recover uneventful. The radiographic findings show extensive, corticated multilocular (soap-bubble) radiolucency over right mandible with root resorption of tooth 47 and 48. The histopathological and FNAC studies demonstrate identical benign ameloblastoma features. Borderline between histopathological features of ameloblastic carcinoma and ameloblastoma is difficult to define. Surgery is the most acceptable modality of treatment. *Discussion:* Recent studies revealed that human ameloblastoma are potentially responsive to molecular targeted therapies, like those that have already been in clinical use against BRAFV600E mutation. Up to date, patient was still on a regular follow-up with no sign of recurrence or metastases. Recent updates of genetic studies concluded that despite of its local aggressiveness and propensity to recur, ameloblastoma remained benign in nature. Metastasizing ameloblastoma is defined by its clinical behavior (retrospectively) rather than its histology features which appeared identical in both the primary and metastases lesions. *Learning Points:* Therefore, a regular and long-term follow-up is warrant in every ameloblastoma cases since there is no specific feature predicting metastases and may occur after a long latent period.

#### AP-05. Primary Non-Hodgkin's lymphoma of the breast: A rare case report

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*Introduction:* Primary breast lymphoma (PBL) is an unusual clinical entity accounting for <0.5% of all malignant breast tumours and <2.2% of all patients with extranodal lymphoma. Based on the histopathological examination, diffuse large B-cell lymphoma (DLBCL) is the most common identifiable type of primary breast lymphoma. *Case Report:* A 29-year-old nulliparous, Bidayuh lady presented with a month history of a progressive, painless left breast swelling associated with redness. Breast examination revealed left breast lump at 8 o'clock region measuring 5x5 cm with erythematous skin. There was no axillary lymphadenopathy bilaterally. Ultrasound showed a large, ill-defined heterogenous, hyperechoic lesion occupying the inner quadrant of the left breast, measuring 4.6x5.3 cm, suspicious of malignancy. The right breast showed normal breast parenchyma pattern with no mass lesion or ductal dilatation seen. There is no axillary lymphadenopathy. A biopsy was taken and microscopic examination revealed sheets of dyscohesive atypical medium to large sized cells, displaying hyperchromatic nuclei with multiple nucleoli and scanty amphophilic cytoplasm. The Ki67 proliferative index is about 60%. The atypical cells are immuno-positive for CD45, CD20, Bcl6 and MUM1 and immuno-negative for CD3, CK WSS, ER, PR, HER2 and CD10. A diagnosis of high-grade B-cell lymphoma, favoured diffuse large B-cell lymphoma (DLBCL), non-germinal centre B phenotype was made. *Discussion:* PBL is defined as the presence of both mammary tissue and lymphoid infiltrates in close association with no evidence of widespread lymphoma or preceding extra-mammary lymphoma. As in this case of young lady, early and accurate diagnosis of PBL is crucial for selecting an appropriate treatment strategy to avoid unnecessary surgical interventions. *Learning Points:* Since the incidence of PBL is rare and their radiological features may mimic carcinoma, histological and immunophenotypical studies are definitely required for confirmation of lymphoma.

#### AP-06. Synchronous occurrence of malignant steroid cell tumour and diffuse large B-cell lymphoma: The rare entity

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*Introduction:* Malignant steroid cell tumour of ovary is a rare entity, and synchronous occurrence of lymphoma make it extremely unusual. Here we report a case of a 48-year-old lady with underlying hypertension and secondary amenorrhea. *Case Report:* She presented to casualty with dyspnea and low GCS. Physical examination revealed an ulcerated umbilical mass measuring 10x8 cm. Features of hirsutism is also noted. Emergency laparotomy done and revealed a huge paraumbilical mass measuring 15x15

cm and a huge left ovarian mass measuring 15x15 cm. Multiple tumour nodules are seen over liver surface and left infundibular pelvic ligaments. Grossly, the paraumbilical mass is composed of a solid-cystic mass with variegated surface occupying the entire subcutaneous area measuring 170x145x50 mm. The left ovarian mass shows a large lobulated mass measuring 210x135x90 mm exhibiting solid cystic tumour occupying the entire specimen. Microscopically, the paraumbilical mass and left ovarian mass show similar tumour morphology. Both show multiple lobules of tumour cells with interlobular fibrosis. The tumour cells are composed of sheets, nests and strands of round to polygonal cells with centrally placed nuclei, mild nuclear atypia and well-demarcated cytoplasmic margin. Mitotic activity is marked especially in extensive areas of tumour necrosis. These cells are immunoreactive for calretinin, Inhibin and Melan-A. In addition, sections from paraumbilical mass also show a few areas exhibiting sheets of neoplastic cells of different morphology and immunohistochemical pattern as the tumour cells described earlier. These neoplastic cells display severely pleomorphic and vesicular nuclei with coarse chromatin pattern, prominent nucleoli and moderate amount of cytoplasm. Mitosis is easily seen (38/10 hpf). These cells are immunoreactive for LCA, CD20, PAX-5, BCL-2, BCL-6 and MUM-1. There is no kappa or lambda light chain restriction. *Learning Points:* Overall histomorphology and ancillary studies support the diagnosis of synchronous malignant steroid cell tumour and diffuse large B-cell lymphoma.

#### **AP-07. Endocrine mucin-producing sweat gland carcinoma - newly described skin appendageal tumours: The first case reported in Malaysia**

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*Introduction:* Endocrine mucin-producing sweat gland carcinoma (EMPSGC) is a recently described adnexal tumour with predilection for the face particularly the eyelids. Considered a precursor lesion of mucinous adenocarcinoma, it may represent part of a morphological spectrum. We describe a case of this entity, which we believe to be the first case reported in Malaysia. *Case Report:* A 59-year-old Chinese male presented with a slow-growing cystic lesion over the left lower lateral canthal region. The lesion became progressively larger and nodular with occasional itchiness within the last 6 months. Histologically, the lesion is a well-circumscribed intradermal tumour with pushing borders, extending into the subcutaneous tissue. The tumour cells are arranged in lobules of solid, papillary and cribriform architecture. The cells display uniform, medium-sized, round to oval nuclei with stippled chromatin pattern and ample eosinophilic granular cytoplasm. Intracellular mucin (highlighted by mucicarmine stain) is observed in areas with focal extracellular mucin seen. Mitotic figures are not particularly impressive. By immunohistochemistry study, the tumour cells diffusely expressed ER, PR, CK7, GCDFP-15, mammaglobin and EMA. Chromogranin A and Synaptophysin highlighted significant number of tumour cells. The patient underwent a second excision a month later as the deep margin was involved. Subsequent report showed no residual malignancy. He is now on a three-monthly follow up under surgical team. *Discussion:* The morphology and immunohistochemical profile showed similarities between EMPSGC and solid papillary carcinoma of the breast (SPCOTB), thus considered to be a cutaneous analogue of the latter. Both tumours produce mucin, exhibit endocrine differentiation and are positive for ER and PR. In fact, one should rule the possibility of metastatic SPCOTB before considering the diagnosis of EMPSGC. *Learning Points:* This tumour, in the absence of mucinous adenocarcinoma shows excellent prognosis after excision with clear margins. Distant metastases have not been documented to date.

#### **AP-08. Squamous cell carcinoma arising from choledochal cyst: A rare entity**

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*Introduction:* Choledochal cysts (CDC) are rare congenital or acquired pathologic dilatations of the biliary tract that have been associated with an increased risk of malignancy in both the gallbladder and bile ducts. They are predominantly present in children before 10 years old, with only 20% to 30% of the patients being older than 20 years and male-to-female ratio of 1:4. Malignancy in CDC is a rare condition. The incidence of malignancy increases with age, 0.7% in the first decade of life to 14.3% after 20 years of age. It is widely known that cholangiocarcinoma is the most common malignant tumour associated with CDC and squamous cell carcinoma arising from CDC is a rare entity. Malignancy occurs as a result of chronic inflammation, cell regeneration, and DNA breaks leading to dysplasia. *Case Report:* We present a case of a 21-year-old female with no comorbidities who presented with abdominal discomfort for a duration of 1 month. Imaging modalities included contrast-enhanced computed tomography (CECT) of the abdomen and magnetic resonance cholangiopancreatography (MRCP) which showed gross dilatation of the upper 2/3<sup>rd</sup> of the common bile duct extending to the proximal intrahepatic ducts. Histopathological examinations demonstrated a large CDC with thickened wall and irregular, whitish intraluminal lesion composed of well-differentiated squamous cell carcinoma arising from the lining columnar cells showing squamous metaplasia. *Learning Points:* Associated biliary malignant tumour should always be considered in patients with CDC especially in aged patients. Lifelong follow-up is needed even after complete cyst excisions because of the risk of developing a metachronous biliary malignancy. Randomized controlled trials are still needed to ascertain the combined benefit of chemotherapy and radiotherapy. Therefore, surgical resection remains the best treatment option in the aim to cure.

**AP-09. Classical Hodgkin's lymphoma mimicking necrotizing granulomatous lymphadenitis: The conundrum**

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*Introduction:* Granulomas may sometimes occur in patients with malignant tumours and lymphomas. Such reaction is reported in 4.4% of malignancies, 7.3% of non-Hodgkin's lymphomas (NHL) and 13.8% of Hodgkin's lymphoma (HL). The coexistence of HL and granulomas can be tricky and are very rare. However, atypical presentation of HL with formation of epithelioid cell granuloma along with tumour cells has been known in literature. HL mostly affects the age group of 20-34 years with median age of 39 years. *Case Report:* We present a case of a 60-year-old female with multiple comorbidities who presented with history of fever, loss of weight and loss of appetite for 2 weeks duration. Imaging modalities included contrast-enhanced computed tomography (CECT) of the abdomen and pelvis which showed persistent liver and splenic hypodense lesions with multiple abdominal lymphadenopathies. Pathology demonstrated mixed cellularity HL mimicking a necrotizing chronic granulomatous lymphadenitis. *Learning Points:* Presence of granuloma in HL is a common finding which is often a source of diagnostic confusion. The morphology of Reed-Sternberg (RS) cells and immunohistochemical (IHC) stains are most helpful in differential diagnosis. Pathologists should always recommend further diagnostic investigations to be performed in cases of negative acid-fast staining granulomas.

**AP-10. Clear cell hidradenoma of the breast: A case report**

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*Introduction:* Clear cell hidradenoma is a benign skin adnexal tumour which arises from the excretory ducts of eccrine glands. This tumour is commonly seen on the face and upper extremities. Clear cell hidradenoma of the breast is rare with less than 20 reported cases in the literature. *Case Report:* A 59-year-old female presented with a painless right breast lump for the past 5 years. The lump was painless but slowly growing in size. A biopsy of the lesion was done which showed a breast tumour with clear cell change. She subsequently underwent a wide local excision of the lesion. Intraoperative findings showed a solid tumour located at the retroareolar region of the right breast. Macroscopically, there was a tumour beneath the overlying skin measuring 30x20x15 mm with greyish cut surface and lobulated margins. Histology examination showed a circumscribed tumour within the dermis with extension into the subcutaneous adipose tissue. The tumour cells were composed of a mixture of polygonal cells exhibiting small hyperchromatic nuclei with abundant clear cytoplasm and cells with eosinophilic cytoplasm. No significant nuclear atypia was seen. In view of the location of the lesion and histomorphological features, other tumours such as primary breast ductal carcinoma, adenomyoepithelioma, sebaceous carcinoma and metastatic clear cell carcinoma are possible differential diagnoses. Immunohistochemical studies showed the cells were positive for Cytokeratin 7, Cytokeratin AE1/AE3 and p63 and negative for Estrogen receptor, PAX8, CD10, S100, SMA, Mammaglobin and GCDFP-15. Ki67 proliferative index was less than 1%. Patient was well post-procedure. *Learning Points:* Clear cell hidradenoma of the breast is thought to arise from the eccrine and apocrine glands of the nipple and subareolar tissue. Skin adnexal tumours may be rare in the breast but are important to consider in the differential diagnosis of breast neoplasms.

**AP-11. Giant cell rich osteosarcoma: A case report**

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*Introduction:* Many osteosarcomas contain benign osteoclast-like giant cells. One of the subtypes of conventional osteosarcoma is giant cell-rich osteosarcoma which is characterized by proliferation of atypical stromal cells with abundant osteoclast-like giant cells. It is a rare tumour that is difficult to distinguish from other bone lesions, such as giant cell tumours of the bone. The location and radiographic features of these tumours may be similar and the histologic differentiation between a giant cell rich osteosarcoma and giant cell tumour can be difficult. *Case Report:* We report a case of a 45-year-old lady with a left knee swelling for four years. The swelling was increasing in size and painful for the last six months associated with limited range of movement and limping gait. Radiographic investigation showed a left proximal tibial meta-epiphysis lesion with aggressive features. Radiological diagnosis of telangiectatic osteosarcoma with differential diagnosis of giant cell tumour was made. Initial biopsy showed features consistent with giant cell tumour of the bone. She was started on pamidronate infusion and subsequently had curettage with bone cement and proximal tibial plating. A few months later, she developed pain and swelling over the left leg. CT scan during this visit showed aggressive lesion at left knee region with left proximal tibia destruction and multiple lung metastasis. Above knee amputation was performed and diagnosis consistent with giant cell rich osteosarcoma was made. The patient underwent further treatment in the oncology department. However, she defaulted after one year of follow-up. *Learning Points:* The major challenge is differentiating malignancy in giant cell tumour with giant cell rich osteosarcoma. Giant cell rich osteosarcoma has certain characteristics although lacking in specificity; thus, integration of clinical, radiological and pathological features are important for the final diagnosis. When a giant cell rich osteosarcoma occurs in a common location for giant cell tumour, adequate sampling is mandatory as histology becomes the most important factor in differentiating the two.

**AP-12. Pseudomyogenic haemangioendothelioma of the lower extremity**

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*Introduction:* Pseudomyogenic haemangioendothelioma is a rare vascular tumour of intermediate malignant potential with propensity for local recurrence. It typically affects young adult male with a predilection the lower extremity, characterized by multifocality in different tissue planes. Despite of its multifocality presentation, this tumour has a relatively favourable long term prognosis. *Case Report:* We present a case of pseudomyogenic haemangioendothelioma in a young adult male, who has suffered from a local recurrence in the thigh four months after the primary tumour excision. The excised left thigh specimen showed two solid, circumscribed subcutaneous nodules with ill-defined margins. Histologically, the nodules are composed of plump spindled cells with abundant bright eosinophilic cytoplasm arranged in sheets and loose fascicles. They display ovoid-spindled mildly pleomorphic vesicular nuclei with small nucleoli resembling rhabdomyoblasts in areas. Prominent stromal neutrophil, lymphocyte and eosinophil infiltration is present. Mitotic activity is low with no area of necrosis observed. Most of the lesional cells showed positivity for CKAE1/AE3, FLI-1, ERG and CD31, and they are negative for EMA, CD34, D240, Myogenin, Desmin, S100 and CD117. The most important differential diagnosis is epithelioid sarcoma as both share several features - affects young adults, predilection for soft tissue in the distal extremities and showed spindled and epithelioid morphology. *Learning Points:* In summary, pseudomyogenic haemangioendothelioma is a distinctive locally recurrent, rarely metastasizing vascular tumour which occurs in young adult with a striking male predominance. Although sharing some features with epithelioid sarcoma, it differs by having predominant myoid appearing spindled cell morphology with the expression of FLI1 and CD31, and lack of EMA and CD34 expression. In the absence of morphological evidence of a vascular neoplasm, this tumour can be challenging and broad immunohistochemical panel with clinico-radiological correlation is rendered the correct diagnosis. Treatment options include surgery, chemotherapy and radiotherapy. Long-term follow up is recommended.

**AP-13. Squamous cell carcinoma arising from an epidermal cyst: A case report**

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*Introduction:* Epidermal cysts and squamous cell carcinoma are two common entities encountered in practice. Malignant transformation of this benign lesion is a rare occurrence. There are few case reports concerning malignant transformation of an epidermal cyst into squamous cell carcinoma. *Case Report:* We report a case of squamous cell carcinoma arising from a 30-year epidermal cyst in the left thigh of a 76-year-old man. The epidermal cyst had progressively increased in size for the past three months prior to presentation. The enlarging mass subsequently affected his daily activities. He was planned for elective surgery. Initial investigations of full blood count, coagulation test and chest X-ray were unremarkable. Intra-operatively, a large cystic mass containing thick whitish fluid were drained, compatible with an epidermal cyst. Gross examination of the cystic mass showed focal solid area. A diagnosis of squamous cell carcinoma arising from an epidermal cyst was confirmed histologically. He was referred to oncology unit for chemotherapy. Staging CT thorax revealed multiple lung nodules suggestive of metastasis. However, due to his weakened condition and lung progression, palliative care was opted. He expired nine months after his diagnosis. *Discussion:* Epidermal cyst is the commonest cutaneous cyst of the skin. Malignant transformation arising from this cyst is extremely rare. The commonest location of malignant transformation is the head and neck followed by the trunk and limb. There is male preponderance. The commonest malignant transformation is squamous cell carcinoma followed by basal cell carcinoma. The aetiology of this malignant transformation remains uncertain. Chronic irritation is suggested as a possible factor. *Learning Points:* Despite the rarity of malignant transformation of epidermal cysts, malignant change should be suspected in cases with rapid growth, ulceration or frequent recurrence. Hence, we suggest that all cutaneous cystic lesion to be completely excised and subjected for detailed histopathological evaluation.

**AP-14. Renal presentation of Boeck's disease: The great imitator**

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*Introduction:* Sarcoidosis, known previously as Mortimer's Malady or Boeck's disease is a chronic multisystem inflammatory disease of unknown etiology. It is characterized by non-caseating epithelioid granuloma in multiple organs, mainly involving the lungs and lymph nodes. Renal involvement of sarcoidosis is rare. *Case Report:* We report a case of a 38-year-old gentleman who presented with vague symptoms of abdominal pain and acute kidney injury. Examination on him revealed that he had multiple generalized lymphadenopathy with unexplained hypercalcemia. During his 2 years of follow up, his creatinine level steadily increased from 1.6 mg/dL to 4.9 mg/dL and subsequently he developed proteinuria. His serum angiotensin converting enzyme was raised. The patient was finally diagnosed as systemic sarcoidosis with renal involvement after exclusion of all other causes. Interestingly, his renal biopsy showed chronic granulomatous interstitial nephritis (GIN) with non-caseating naked epithelioid cells granuloma, similarly seen in his previous lymph nodes biopsy. Patient responded well to treatment with prednisolone. His serum creatinine level normalized to baseline within 1 year of commencement of therapy. Repeat renal biopsy showed mark

improvement exhibiting features of minimal chronic changes, with no evidence of granuloma. *Discussion:* This case describes how early initiation of treatment can help in complete resolution of the kidney function. Most patients with renal sarcoidosis can have increased creatinine value or renal impairment without evidence of involvement in renal tissue. Although GIN is a widely and well-known manifestation of sarcoidosis, histologically apparent sarcoid granuloma is very rare, accounting to 13-22% of kidneys surveyed. In this patient, the co-existence of sarcoid infiltration in the lymph nodes and kidney aided in establishing the diagnosis. *Learning Points:* Even though, renal failure is uncommon, few studies showed that late treatment can result in irreversible renal disease. Therefore, diagnostic delay should be avoided.

#### CP-15. Heart fatty acid binding protein (H-FABP) versus high sensitivity troponin I as a marker for acute coronary syndrome

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*Introduction:* Heart fatty acid-binding protein (H-FABP) is an abundant cytoplasmic protein of heart muscle which has an emerging role as an early cardiac injury marker. The aim of this study is to compare the efficacy of H-FABP with high sensitivity Troponin I (Hs-Troponin I) as diagnostic markers for acute coronary syndrome (ACS). *Materials & Methods:* This is a cross-sectional prospective study by looking into 97 patients who presented to Emergency Department with suspected ACS. Patients were classified into 3 groups according to window periods of chest pain onset (<3h, 3-6h and >6h). Cardiac Hs-Troponin I, Troponin I and H-FABP concentrations were measured in all patients at the time of admission. Levels of H-FABP and Troponin I were measured using combo kit test analyzed by Hubi-Quan Pro point-of-care testing (POCT) while Hs-Troponin I were measured using Abbott Architect immunoassay. Diagnostic sensitivity, specificity and receiver operating characteristic (ROC) curve were evaluated. *Results & Discussion:* From 97 patients, 30 (30.9%) patients were diagnosed to have acute myocardial infarction (MI), 28 (28.9%) patients with unstable angina, 16 (16.5%) patients with decompensated congestive heart failure and another 23 (23.7%) were having other medical illness. The sensitivity and specificity of H-FABP was 66.7% and 79.1%, for Troponin I it was 63.3% and 95.5%, and for Hs-Troponin I it was 96.7% and 74.6%. Area under ROC curve at 95% CI for H-FABP, Troponin I and Hs-Troponin I were 0.75, 0.86 and 0.95 respectively. *Conclusions:* Hs-Troponin I is still the most superior cardiac biomarker for the diagnosis of myocardial infarction because of its high sensitivity. However, in view of Hs-troponin I POCT is yet to be available, measurement of H-FABP in combination with Troponin I in one POCT combo kit test provides additional diagnostic value in suspected ACS patients in Emergency Department.

#### CP-16. Determination of glycated haemoglobin (HbA<sub>1c</sub>) peak in capillary electrophoresis in comparison with high performance liquid chromatography method

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*Introduction:* Certain biomarkers manifested in common test methods used by different sections in pathology may cause interpretation dilemma. These issues were recently encountered in haemoglobin (Hb) analysis screening. In Hospital Melaka, it was observed some patients' samples who were sent for Hb analysis expressed abnormal peak at zone 10 of capillary electrophoresis (CE). It is postulated that this peak is of glycated haemoglobin (HbA<sub>1c</sub>) peak. Objective of this study is to determine HbA<sub>1c</sub> peak in CE for Hb analysis in comparison with high performance liquid chromatography (HPLC) in blood samples from patients with Type 2 diabetes mellitus (DM). *Materials & Methods:* This cross-sectional study was carried out in Hospital Melaka, for 24 months. Samples of HbA<sub>1c</sub> from Type 2 DM patients with level of >6.5% were selected from Biochemistry laboratory, subsequently sent to Haematology Laboratory for Hb analysis using CE and HPLC method. Presence of zone 10 in CE and P2 peak in HPLC were correlated and analysed. *Results & Discussion:* A total of 131 samples were analysed. Overall incidence of Type 2 DM with HbA<sub>1c</sub> ≥6.5% detected at zone 10 of CE is n=50 (38.2%). The mean (SD) of HbA<sub>1c</sub> level in this study was observed to be 10.2% (2.0). Out of 50 samples, 47 (94%) were from patients with HbA<sub>1c</sub> level of >10%, whilst 3 (6%) were from samples with HbA<sub>1c</sub> level of 6.5% to 10%. It is 18 times more likely for the abnormal peak (95%CI: 5.9-54.9) to appear in zone 10 of CE in patients with HbA<sub>1c</sub> level of >10%. The best cut-off level of HbA<sub>1c</sub> level in predicting the presence of zone 10 in CE is 10.5%. HbA<sub>1c</sub> level of ≥10.5% showed 92% sensitivity and 86.4% specificity with presence abnormal peak in zone 10 CE from blood samples with Type 2 DM patients. The observed percentage of zone 10 ranges from 0.5% to 1.6% as seen in our study. *Conclusions:* Identification of HbA<sub>1c</sub> peak in CE for Type 2 DM cases help to reduce cost in Hb analysis screening whereby secondary method like HPLC is unnecessary for further workout for thalassaemia in patients with Type 2 DM with high HbA<sub>1c</sub> level.

### CP-17. Mid-pregnancy HbA<sub>1c</sub> as a screening marker for gestational diabetes mellitus and its relationship with adverse pregnancy outcomes

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**Introduction:** Pregnancies affected by gestational diabetes mellitus (GDM) impose risk of various obstetrical complications and adverse pregnancy outcomes. Hence, screening and early diagnosis of GDM is important to prevent clinical complications. The gold standard diagnosis for GDM is oral glucose tolerance test (OGTT), however, the procedure is time consuming and often poorly tolerated by pregnant women. The clinical utility of glycosylated haemoglobin (HbA<sub>1c</sub>) in GDM is not yet established despite its role as a marker for chronic hyperglycaemia outside the pregnancy population. Therefore, we prospectively evaluated the mid-pregnancy HbA<sub>1c</sub> as a screening biomarker for GDM and prognostic indicator for the adverse pregnancy outcome. **Materials & Methods:** This study enrolled 150 Malaysian with singleton pregnancy, at weeks 24 to 30 who fulfilled the inclusion criteria. The mid-pregnancy HbA<sub>1c</sub> was measured at the time the OGTT was performed. The diagnosis of GDM was based on OGTT result. The patient was then followed up until the delivery. A receiver operating characteristic (ROC) curve was used to determine the relationship between the mid-pregnancy HbA<sub>1c</sub> level and GDM. Youden index was calculated to determine the optimal cut-off value and kappa reliability was used to assess the degree of agreement between HbA<sub>1c</sub> and OGTT. Chi square test and odd ratio (OR) was used to evaluate the pregnancy outcome and the cut-off A<sub>1c</sub>. **Results & Discussion:** Among the 150 women, 20 were diagnosed with GDM with OGTT. HbA<sub>1c</sub> cut-off value <5.05% (31.7 mmol/mol) gives high Youden Index (28), but unsatisfactory sensitivity (65%) and specificity (63%). While HbA<sub>1c</sub> cut-off value <4.95% (30.6 mmol/mol) presented adequate sensitivity (75%) and specificity (46%) for screening GDM and could eliminate the need for OGTT in 42% women in our study, but with 8% wrongly diagnosed as no GDM. There was only slight agreement between HbA<sub>1c</sub> and OGTT (kappa value=0). A<sub>1c</sub> >4.95% (30.6 mmol/mol) associated with increased risk of caesarian section ( $p < 0.05$ , OR 1.46) and no effect on the prematurity. **Conclusion:** The mid-pregnancy HbA<sub>1c</sub> can be considered as a screening biomarker for GDM and can be utilized as a prognostic indicator for the adverse pregnancy outcome.

### CP-18. Study on screening of serum ferritin request in Hospital Teluk Intan

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**Introduction:** Serum ferritin levels commonly used to demonstrate body iron store. Serum ferritin was developed as clinical test in 1970s. This test widely used in diagnosing and monitoring diseases associated with iron deficiency and iron overload. Ferritin is an acute phase reactant. Serum ferritin level is measured by using immunoassays. The level will increase with recent infection/inflammation, liver damage, alcoholic liver disease and malignancies. These clinical conditions may increase serum ferritin level to a degree disproportionate to that iron stores and can mask the actual body iron store causing incorrect result interpretation with exclusion of clinical suspicious of haemophagocytic syndrome. This misleading diagnosis ultimately may compromise patient management. This might cause significant or adverse clinical consequences to patient and financial consequences on laboratory expenses. Therefore, starting January 2018 we have taken measurement to screen all ferritin requests although facing few limitations. **Materials & Methods:** A retrospective study was done in Pathology Department, Hospital Teluk Intan. Serum ferritin requests from January till October 2018 were analysed to evaluate the root cause. **Results & Discussion:** There were a total of 907 samples of serum ferritin requested in 2018. From this total samples, 29.65% (235) were rejected. 87.7% (206) of the samples rejected were due to low serum iron level. 7.7% (18) samples were rejected due to recent infection/inflammation. 4.7% (11) were rejected due to others cause (*i.e.* duplicate request). **Conclusions:** Screening on serum ferritin request can help in minimizing inappropriate and unnecessary testing on serum ferritin. This does not only ensure a positive impact on patient outcome, but can ensure significant financial saving on laboratory expenses from unnecessary/inappropriate testing. In this study, rejection criteria were not based on scientific journal/studies and variable pre-analytical conditions on serum iron level as a rejection criterion were the limitations of this study.

### CP-19. Pre-analytical challenges of CSF neurotransmitters analysis for diagnosis of inherited neurotransmitter metabolism disorders

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**Introduction:** The quantification of neurotransmitter metabolites; biogenic amines and pterins in cerebrospinal fluid (CSF) can provide valuable clues for the detection of treatable neurotransmitter disorders. These analyses are technically challenging since the concentration is evaluated in nanomolar. To date, we are the only laboratory working on these analyses in Malaysia. Since the metabolites are unstable at room temperature and very sensitive to heat and light, proper sample collection is very crucial. This paper will describe our laboratory experiences on pre-analytical issues associated with the analysis of neurotransmitter metabolites. **Materials & Methods:** We received a total of 421 CSF samples requesting for neurotransmitter analysis within year 2016 to 2018. 0.5ml of CSF collected in sterile microtube, frozen and wrapped to protect sample from light is required for

both biogenic amines and pterins analyses. Dithioerythritol (DTE) and diethylenetriaminepentaacetic acid (DETAPAC) were needed as preservatives in CSF sample for pterins analysis to prevent the degradation of tetrahydrobiopterin (BH<sub>4</sub>). Sampling errors were assessed based on unsuitable container, insufficient sample volume, empty/leaking container and unprotected sample or unfrozen sample. The rejection and inappropriate condition of samples were recorded in percentages. **Results & Discussion:** Pre-analytical errors were observed in 66 samples, encompassing 15.68% of the total number of samples received. The most common error was unfrozen and unprotected sample (40.9%) followed by unsuitable container (27.3%). Rejection rate was 9.26%. Samples were rejected due to unsuitable container (27.3%), no specimen received (18.2%) and insufficient volume of sample (10.6%). The non-diagnostic profiles were observed in 27 results of unfrozen and unprotected samples which may be due to deterioration of metabolites. These inconclusive results caused wastage of precious CSF samples. **Conclusions:** It is important to understand the pre-analytical requirements for neurotransmitter analysis with special emphasis on sample collection. A close communication between laboratory experts and clinicians is necessary to ensure accurate interpretation of CSF neurotransmitters.

#### **CP-20. Diagnostic challenges for detection of amino acids disorder using reversed phase high performance liquid chromatography (RP-HPLC): What benefits us?**

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**Introduction:** Improvement for amino acids (AA) analysis for inborn error of metabolism using reversed phase high performance liquid chromatography (RP-HPLC) comes with advantages and few challenges with technical needs in terms of experimental optimization and problems encountered during sample analysis, in order to produce reliable diagnosis in our laboratory setting. **Results & Discussion:** RP-HPLC takes advantage of automated derivatisation, thereby limiting manual manipulation of samples which improved our turn-around time. Two derivatisation reagents were manipulated to produce important AA. Cystine, a dibasic (AA) could not be detected using this protocol which required ion exchanged chromatography (IEC) for further investigation if indicated for cystine related disease such as cystinuria, lysinuric protein intolerance (LPI) or hyperornithinemia-hyperammonemia-homocitrullinuria (HHH). Co-elution of methionine during the actual application with unknown AA due to column degradation can lead to false positive for CBS deficiency or methionine adenosyltransferase I/III. This can be resolved immediately by changing to a new column when methionine peak started to co elute. **Conclusions:** RP-HPLC is rapid, accurate, sensitive, reproducible and cost effective for diagnosis of AA disorder but comes with limitations that need to be coupled with technical needs and IEC to provide better, faster and reliable diagnosis for AA disorder.

#### **CP-21. Cases of alkaptonuria in Institute for Medical Research from 2009 to 2018: A descriptive study**

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**Introduction:** Alkaptonuria is a rare genetic metabolic disorder characterized by accumulation of homogentisic acid in the body. It is due to mutations in the HGD gene. The affected individuals will have lack of functional enzyme required to breakdown homogentisic acid. They usually present with dark urine from infancy. However, affected individuals generally are asymptomatic and often remain unaware of their condition until adulthood. Ochronosis, a buildup of dark pigment in connective tissues such as cartilage and skin, is also characteristic of the disorder. We described here cases of alkaptonuria diagnosed from our laboratory from year 2009 to 2018. **Materials & Methods:** This is a 10-year retrospective study involving urine samples sent for urine organic acid to Biochemistry laboratory, Institute for Medical Research (IMR). Organic acids in the urine were subjected to liquid-liquid extraction followed by derivatization prior to analysis. The samples were injected into gas chromatography-mass spectrometry (GC-MS) and homogentisic acid peak was identified semi-quantitatively using Mass Hunter software. **Results & Discussion:** We identified 8 patients (7 males, 1 female) with metabolic profile characteristic of alkaptonuria. Mild to marked excretion of homogentisic acid was identified in all urine samples on chromatogram. Patients aged from 1 year to 16 years old. 4 patients were of Malay ethnicity, 3 of Indian ethnicity and 1 sample was received from overseas. 3 patients had a positive family history of metabolic disease with 2 of the diagnosed cases being siblings. 4 patients presented with abnormal discoloration of urine. 1 patient had normal clinical presentation and was referred to us for diagnosis through a positive family history of metabolic disease. **Conclusions:** Urine organic acid is a reliable diagnostic tool for alkaptonuria disorder. We were able to diagnose 8 patients from urine organic acid analysis during a 10-year period of study.



**CP-22. Oximetry measuring error in a patient with Hb M Hyde Park**

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*Introduction:* Assessment of oxygenation status can be determined by using approaches such as pulse oximetry and CO-oximetry. Pulse oximetry measures the absorbance ratio from lights emitted at two different wavelengths for oxyhaemoglobin and deoxyhaemoglobin, whereas CO-oximetry measures the total absorbance of four haemoglobin forms at multiple wavelengths. *Case Report:* We report a case of a 55-year-old gentleman with underlying Hb M Hyde Park and concomitant heterozygous alpha<sup>+</sup> thalassaemia trait, who presented with acute on chronic lower limb ischaemia. He was found to have very low transcutaneous oxygen saturation readings on pulse oximetry, without exhibiting signs of respiratory distress. Arterial blood gas analysis performed on Radiometer ABL800 blood gas analyser gave “oximetry measuring error” warning message. Repeat analyses on different Radiometer blood gas analysers gave similar warning, excluding analyser problem. Oxygen supplementation in this patient did not improve his pulse oximetry readings. As per manufacturer’s manual, oximetry measuring error indicates deviation of spectrum from expected blood or quality control (QC) due to possible interfering substances or calibration problem which may cause unreliable measurement. QC and calibration at the time of analyses were acceptable. *Discussion:* Hb M is a group of rare abnormal haemoglobin variants formed due to substitutions of amino acids in the globin chains, forming methaemoglobin. Pulse oximetry is unreliable in Hb M disease as it does not measure absorbance of methaemoglobins. Methaemoglobins originating from Hb M variants differ structurally from physiological methaemoglobins, thus giving a different absorbance spectrum that cannot be reliably assessed by CO-oximetry in blood gas analysers. *Learning Points:* Methaemoglobin-forming haemoglobin variants are rare. Low pulse oximetry readings and unreliable oxygen saturation by CO-oximetry can be seen with these haemoglobin variants. We highlighted the issue of assessing oxygenation status in a patient with Hb M disease, that can pose a challenge in patient’s management.

**CP-23. Case series of free light chain paraproteinaemia in plasma cell dyscrasias**

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*Introduction:* Serum free light chains (sFLC) is an established tool for diagnosing and prognostication of plasma cell dyscrasias. These diseases may lead to disproportionate increment of the involved to the uninvolved sFLC. We report three cases of sFLC paraproteinaemia and the role of sFLC assay in disease management. *Case Reports:* *Case 1:* A 71-year-old lady presented with lower back pain and multiple lumbar fractures. Protein electrophoresis showed kappa light chain (LC) in between beta and gamma region and 22% plasmacytosis on bone marrow examination (BME), confirming the diagnosis of kappa LC disease. *Case 2:* A 42-year-old gentleman with clavicular fracture and incidental finding of clavicular solitary plasmacytoma. Further workup revealed kappa LC paraproteinaemia in between alpha-2 and beta zone with 5% plasmacytosis in BME leading to the diagnosis of kappa LC disease. *Case 3:* A 57-year-old lady presented with multiple lymphadenopathy associated with night sweats. Investigations revealed findings consistent with chronic lymphocytic leukaemia (CLL). Immunofixation electrophoresis detected faint kappa LC. Blood samples were sent to an external laboratory for sFLC measurement. Raised sFLC ratio was seen in case 1 and 2, whereas case 3 had normal sFLC ratio. *Discussion:* sFLC ratio of 100 or more is one of the three myeloma defining events in diagnosis of multiple myeloma. It has a role in monitoring of disease progression and treatment response, and as an emerging prognostic tool in CLL. However, assays for sFLC have several limitations including inter-assay variability and absence of traceability. *Learning Points:* sFLC has undeniable role in plasma cell dyscrasias. However, sFLC assay limitation prevents it from being a definitive marker for disease burden. Further studies are needed to improve the current assay and reporting of sFLC.

**CP-24. Laboratory profiling of alcoholic liver disease**

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*Introduction:* Alcoholic liver disease (ALD) comprises a spectrum of liver injury ranging from hepatic steatosis to frank liver cirrhosis. It is often an indolent disease and presents with complications such as ascites, hepatocellular carcinoma (HCC) and hepatic encephalopathy. *Case Report:* A 74-year-old chronic alcoholic Indian man presented to the emergency department with abdominal pain, fever, poor oral intake associated with tea-coloured urine and pale stools. On examination, he was jaundiced, with hepatomegaly and mild ascites. His laboratory investigations revealed hyperbilirubinaemia, predominantly direct bilirubin and increased alkaline phosphatase, consistent with cholestasis. Aspartate (AST) and alanine (ALT) transaminases were also raised with the AST/ALT ratio >2, characteristic of alcoholic hepatitis. Hypoalbuminaemia noted was due to decreased liver synthetic function, as well as malnutrition associated with excessive alcohol consumption. Urea was disproportionately increased compared to creatinine with eGFR 19mL/min/1.73m<sup>2</sup>, suggesting hepatorenal syndrome. On admission, abdominal ultrasonography revealed a liver lesion with mesenteric lymph nodes and cirrhotic liver changes. Serum alpha-fetoprotein (AFP) was markedly raised. Based on the Maddrey discriminant function (DF) that includes total bilirubin and prothrombin time values

to evaluate the severity in alcoholic hepatitis, his prognosis was poor. His renal, liver and coagulation profiles were increasingly deranged. His condition deteriorated in the ward as he developed septic shock with disseminated intravascular coagulation. Despite intravenous antibiotics, he succumbed to his illness on day 9 admission. *Discussion:* In Malaysia, alcohol is the main aetiology for liver cirrhosis in Indians, as evident in this patient whereas hepatitis B is a more common cause in Malays and Chinese. This patient presented with clinical features of cholestasis supported by biochemical findings. Raised AST/ALT ratio narrowed the liver pathology to ALD. Liver ultrasound findings with raised AFP pointed to HCC. *Learning Points:* This case illustrates the importance of laboratory investigations in the diagnosis, management and prognosis of ALD.

#### CP-25. Parathyroid hormone method comparability in the management of chronic kidney disease

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*Introduction:* Chronic kidney disease-mineral bone disorder (CKD-MBD) consists of alterations in the bone turnover rate, which may be increased (osteitis fibrosa) or severely decreased (adynamic bone), abnormal mineralisation (osteomalacia) and bone loss. Secondary hyperparathyroidism is related to early phosphate accumulation, which is responsible for FGF-23 overproduction by bone tissues, decreased calcitriol production by the kidneys and hypocalcaemia. Kidney Disease Improving Global Outcomes (KDIGO) 2017 guidelines emphasises the importance of monitoring parathyroid hormone (PTH) levels in the management of CKD. *Case Report:* A 31-year-old lady with end-stage renal disease (ESRD) on dialysis secondary to lupus nephritis presented 10 years later with CKD-MBD, supported by biochemical (worsening hypocalcaemia, hyperphosphataemia, increased alkaline phosphatase, hyperparathyroidism) and clinical findings (abnormalities of the facial bone with cervical and upper thoracic spine kyphoscoliosis). She had refused surgery and was on conservative medical therapy but the bony changes rapidly worsened compromising her airway. She was referred to another specialised centre for parathyroidectomy. The serum PTH measured at two tertiary diagnostic laboratories within similar time frame revealed markedly different values with one centre reporting a PTH value 40 times the upper reference limit (URL) whereas the PTH value at another centre was only three times URL. *Discussion:* A third generation PTH assay is analytically specific for whole (bioactive) PTH (1-84) whereas the second generation PTH assay (intact PTH) quantifies both whole PTH (1-84) and other truncated PTH fragments including PTH (7-84), which tends to increase in CKD. *Learning Points:* This case highlights the issues of lack of standardisation of PTH assays in the management of CKD due to inter-method assay variation. Clinicians should be aware of the poor PTH method comparability between hospitals and as such monitor CKD patients using the same assay.

#### CP-26. Plasmapheresis: Is there a role in thyroid storm?

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*Introduction:* Thyroid storm commonly associated with Graves Disease is an endocrine emergency. There is no specific laboratory test to confirm thyroid storm hence diagnosis is primarily clinical. Early diagnosis for prompt treatment is essential as it has a high mortality rate. *Case Report:* A 31-year-old Indonesian lady with underlying hyperthyroidism and dilated cardiomyopathy with severe mitral regurgitation, presented to the emergency department with low Glasgow Coma Scale (GCS). She had history of upper respiratory tract infection for a week prior to developing shortness of breath. She was on fluid restriction of 1 L/day; however non-compliant. Upon arrival at ED, her GCS dropped further and she was intubated. She was in atrial fibrillation. Her SPO<sub>2</sub> was 78% under high flow mask. Wartschky score was 90, suggesting thyroid storm. Her blood investigations revealed increased white cell count, raised free thyroxine (fT4) with suppressed thyroid stimulating hormone, deranged liver enzymes, renal and coagulation profiles. She was admitted and parenteral treatment was commenced. On day 2 admission she was started on continuous veno-venous haemofiltration. As the initial treatment did not improve her condition, plasmapheresis was commenced on day 4. Biochemically her thyroid function test (TFT) showed improvement; however because of multi organ failure, she succumbed to her illness on day 5. *Discussion:* Plasmapheresis is considered in thyroid storm if there is no clinical improvement within 24-48 hours of initial treatment. Plasmapheresis removes 5'-monodesiodase that converts T4 to triiodothyronine (T3), thus reducing serum T3. Improvement in patient's TFT post plasmapheresis signifies its role in treating her thyroid storm. Unfortunately, there was delay in commencing plasmapheresis due to haemodynamic instability in this patient. *Learning Points:* Plasmapheresis for management of thyroid storm is rarely done in Malaysia and should be considered as an early treatment option.

### HM-27. A randomized control trial comparing peginterferon- $\alpha$ -2a versus observation after stopping tyrosine kinase inhibitor in chronic myeloid leukaemia patients with deep molecular response for at least two years: Interim analysis

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**Introduction:** Treatment free remission (TFR) is a fairly new treatment concept in chronic myeloid leukaemia (CML) that develops after two frontier studies from French and Australia published in 2010. About 40% of CML patients, who have achieved deep molecular response (DMR) with tyrosine kinase inhibitor (TKI), are able to remain in TFR after stopping their TKI. Studies are going to search means to increase TFR rate. Consolidative therapy using interferon (IFN), the standard treatment of CML before era of TKI, is a logical possibility because of data suggesting IFN-induced immunity towards the leukemic clone. We conducted the first randomized controlled trial comparing the use of pegIFN versus observation in CML patients attempting TFR. **Materials & Methods:** Adult CML patients from multi-centre in Malaysia with stable DMR for 2 years or more and at least two readings of MR4.5, were stopped TKI and randomized into two arms: (1) subcutaneous pegIFN- $\alpha$ -2a starting at 180 $\mu$ g weekly for a year, followed by observation, or (2) observation. Outcome is relapse, defined as either (i) one reading of loss of major molecular response ( $>0.1\%$ <sup>IS</sup>), or (ii) positivity of *BCR-ABL1* transcripts, as confirmed by a second analysis point, indicating the increase ( $\geq 1$  log) in relation to the first analysis point at two successive assessments. **Results & Discussion:** A total of 30 patients started intervention from July 2015 to October 2018 (pegIFN n=15, observation n=15). Analysis was taken on 13<sup>th</sup> Mar 2019. A total of 9 patients relapsed (pegIFN n=4, observation n=5). The median time of relapse was 13.1 months (range 9.2 to 25.5) and 1.8 (1.2 to 12.0) after stopping TKI in pegIFN and observation arm, respectively. Dose of tolerable pegIFN was age dependent. Commonest adverse event of pegIFN was transaminitis. Quality of life assessment using EORTC QLQ-C30 showed similar result between the two arms. **Conclusion:** PegIFN is a potential consolidative therapy to increase TFR.

### HM-28. Prevalence of normal population harbouring *BCR-ABL1* fusion gene in Southern Sarawak, Borneo Island

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**Introduction:** Level of *BCR-ABL1* fusion gene, the driver mutation in chronic myeloid leukaemia (CML), is monitored using quantitative polymerase chain reaction (PCR) (qPCR) reported in International Scale (IS) to guide disease treatment. *BCR-ABL1* was also found in asymptomatic normal subject without blood/marrow feature of CML. Previous studies used convenient sampling and qualitative PCR or qPCR but not IS to study normal subjects harbouring *BCR-ABL1*. Hence, the result could neither infer to normal population nor impact treatment of CML. **Materials & Methods:** We conducted the first normal population study to determine population prevalence of normal subject harbouring *BCR-ABL1* using qPCR<sup>IS</sup>. It was a cross sectional community-based study studying southern Sarawak population aged  $\geq 18$  and using two-stage sampling (stratified followed by cluster) based on Malaysia Department of Statistics population survey procedure. The sampling frame was divided into enumeration block (EB) and subdivided into living quarter (LQ). qPCR<sup>IS</sup> *BCR-ABL1* was done using validated commercial kit. **Results & Discussion:** A total of eight EBs, total of 88 LQs and total subject of 190 were studied and analysed. 23 (12.1%) out of 190 samples had poor quality with sum of control gene, *ABL1*, less than 10,000 copy number, while 102 (53.7%) had good quality with sum of *ABL1* more than 100,00. Quality of each run of qPCR<sup>IS</sup> *BCR-ABL1* was satisfactory fulfilling the evaluation criteria. One subject was found positive, i.e. 0.0023%<sup>IS</sup>. Repeat qPCR<sup>IS</sup> was 0.0032%<sup>IS</sup>. Sequencing confirmed e13a2 transcript. **Conclusions:** Prevalence of normal population harbouring *BCR-ABL1* in southern Sarawak was 0.5% to 1%. Sum of control gene *ABL1* copies number in two replicates should be adequate ( $>100,000$ ) to enable efficient screening.

### HM-29. Genomic landscape of *BCR-ABL* kinase domain mutation in chronic myeloid leukemia patients with imatinib resistance

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**Introduction:** Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder involving the pluripotent haemopoietic stem cell compartment. It is caused by a reciprocal translocation between chromosomes 9 and 22, t(9;22) (q34;q11) which encodes for the *BCR-ABL* fusion protein. Discovery of imatinib mesylate (IM) as targeted *BCR-ABL* protein kinase inhibitor

(TKI) has resulted in its use as frontline therapy. However, emergence of mutation in the *BCR-ABL* kinase domain (KD) impairs IM binding capacity thus contribute to IM resistance. Our study aims to determine the genomic landscape of *BCR-ABL* KD mutations, to determine the prevalence of these mutations in our population and to identify novel, pathological mutations. **Materials & Methods:** A cohort of 86 CML patients with IM resistance was enrolled in this study. RNA extraction was performed using QIAamp RNA Blood Mini Kit (QIAGEN, Germany). Multiplex nested reverse transcriptase PCR was performed for *BCR-ABL* gene amplification. All mutations were characterized using Sanger sequencing. **Results & Discussion:** *BCR-ABL* KD mutations were observed in 23 patients (27.6%). Fifteen different types of mutations have been identified: Y253H, E255K, T267A, K285I, A287T, M290R, F311I, T315I, F317L, F359V, F359I, F359C, K357T, A399T and E459K. We also discovered two patients with silent mutation at codon 389 and 401. Amongst all mutations identified, Y253H is the most common mutation found in this study. Interestingly, of all the mutations identified, four appeared to be novel mutations namely M290R, K285I, K357T and A287T. **Conclusions:** Mutation analysis of *BCR-ABL* KD is recommended in CML patients with IM-resistance. Knowing the exact mutations responsible for IM resistance will help to select the most suitable TKIs for CML patients. Furthermore, early detection may allow timely treatment intervention to prevent or overcome resistance. Therefore, this test should be offered as diagnostic platform to guide therapy for precision medicine.

### HM-30. Cytokines and small molecules expression profiles in patient with acute myeloid leukaemia: A multiplexed immunoassay approach

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**Introduction:** Acute myeloid leukaemia (AML) is an aggressive and heterogeneous bone marrow malignancy characterized by the accumulation of somatically acquired genetic changes, altering self-renewal, proliferation, and differentiation of hematopoietic progenitor cells. It has been suggested that substantial cytokines deregulation in AML patients could be associated with pathogenesis, disease progression, and survival in AML. The aim of this study was to evaluate plasma level of multiple cytokines and small molecules (analytes) in patients with newly diagnosed AML. This approach allows multi-analytical determination from a single sample thus providing greater insight as diagnostic and prognostic markers of AML. **Materials & Methods:** We used bead-based multiplex immunoassay to simultaneously quantify 32 analytes expression level in 76 AML patients and 38 matched healthy subjects. These archived plasma samples were analyzed on the Luminex platform. The results were expressed in nanograms per litre (ng/L), micrograms per litre (µg/L) and units per millilitre (U/mL). Statistical analysis was performed using SPSS 16.0. **Results & Discussion:** Our results indicated that 15 analytes were found to be significantly deregulated (Cathepsin D, Galectin-3, Ferritin, FAPa, MIAP, SHBG, IFBP3, FGF-2, HGF, IL-8, Leptin, MIF, TGF-α, CA15-3, IL8; Mann-Whitney U-test,  $p < 0.001$ ) where 5 of them had never been reported before in AML. No significant difference was found in the levels of other evaluated analytes. **Conclusions:** These significantly altered cytokines and small molecules in AML patients reflecting the pathological state of the disease. Whether these alterations could serve as a prognostic marker for AML is not known. The knowledge gained from multiple cytokine and small molecules analysis could allow better diagnosis and disease management, since cytokines or their receptors may also represent a target for specific anticancer therapy at the molecular level.

### HM-31. Correlation of initial blast and minimal residual disease with biological characteristics of acute leukaemia

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**Introduction:** Acute leukaemias (AL) are highly malignant neoplasms and responsible for a large number of haemopoietic cancer-related deaths. Prognosis of AL is dependent upon various biological and clinical factors. There is growing body of evidence that supports minimal residual disease (MRD) values and initial blast count (IBC) at diagnosis in predicting treatment outcome and relapse risk in AL. However, there is scarcity of data on the relationship of IBC and MRD with biological characteristics [gender, age groups, AL types and immunophenotypic aberrancy (IA)]. Therefore, this study was designed to determine the correlation of IBC, MRD (post-induction chemotherapy) and biological characteristics of AL. **Materials & Methods:** This was a retrospective study involving all the 493 AL patients diagnosed at the Flow Cytometry Laboratory of UNIMAS from 2006 to 2014. **Results & Discussion:** The AL patients comprised 44.2% children and 55.8% adults with a male predominance (55.6%). The mean ages for children and adults were 5 and 45 years old, respectively. There were more AML (55.2%) than ALL (44.8%) cases. B-ALL and AML-M2 predominated the AL subtypes in children and adults, respectively. ALL patients showed significantly higher IBC ( $p \leq 0.001$ ) and MRD ( $p \leq 0.001$ ) levels than AML. Significantly higher IBC ( $p \leq 0.001$ ) and lower MRD ( $p = 0.014$ ) levels were observed in children, indicating a better response to treatment, as compared to adults. However, there was no significant difference in IBC and MRD found between genders. In addition, expression of IA was more common in AML than ALL ( $p = 0.037$ ). **Conclusions:** To the best of our knowledge, this was the first report of a significant negative correlation between IBC and MRD ( $r = -0.24, p = 0.001$ ), whereas IBC and MRD did not correlate significantly with IA. As MRD studies were more routinely performed in ALL, these findings reflected the successful management of ALL patients in our local clinical settings. Future studies should be embarked to further assess the value of IBC, MRD and IA in prognosticating the disease outcome among the local AL patients.

**HM-32. Impact of sports on haematological parameters among the university students**

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*Introduction:* Participation in sports is increasingly popular among youths. Athletes are perceived to be healthier than non-athletes. Optimal athletic performance depends on proper function of many organs, including blood. Hence, haematological profile is one of the best biological indicators to differentiate athletes and non-athletes. There is no published haematological data among Malaysian athletes. Therefore, this study was designed to examine the impact of sports on haematological parameters among UNIMAS students, as well as to compare their nutritional (body mass index, body fat) and health status (anaemia, hypertension, haemoglobinuria, haematuria). *Materials & Methods:* This cross-sectional study involved 140 students (45.7% males, 54.3% females) with 64 athletes and 76 non-athletes from various faculties. Nutritional status was determined by a stadiometer, body composition monitor and electronic blood pressure (BP) set. Health status was assessed by full blood count, blood film examination and urinalysis. *Results & Discussion:* Prevalence of anaemia among UNIMAS students was 10%, which was higher in females ( $p=0.021$ ), but not significantly different between athletes and non-athletes ( $p=0.259$ ). Sports anaemia and haematuria were detected in 6.3% and 4.7% of the athletes respectively, who played intermittent sports. Athletes showed significantly lower white blood cell (WBC) and platelet (PLT) counts, but no significant difference was noted in red blood cell (RBC) parameters. Total training hours per week was significantly correlated with mean cell volume ( $r=0.249$ ,  $p=0.048$ ). Despite BP and nutritional status were not significantly different between athletes and non-athletes, athletes had significantly lower pulse rate ( $p<0.001$ ). However, body fat composition among athletes had exceeded the recommended ideal range. *Conclusions:* This study found no significant difference in RBC parameters, however WBC and PLT were significantly lower among athletes. Further investigations are required to confirm the underlying aetiology of anaemia among the students so that proper management can be administered.

**HM-33. Comparison study of qualitative and quantitative tests for G6PD deficiency in Hospital Wanita dan Kanak-Kanak Sabah**

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*Introduction:* Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is a common hereditary abnormality in Malaysia. Neonatal screening programme in Malaysia has stated that all newborn babies must be screened for G6PD deficiency. G6PD deficiency is an X-linked inheritance which explains why most males are affected while females usually become carriers. Fluorescent spot test (FST) has been used widely as a screening method for G6PD deficiency. However, this test is subjective and has limitation in detecting intermediate or moderate enzyme deficiency which is commonly occurs in female heterozygotes. *Materials & Methods:* This study was done to compare the result of a quantitative G6PD test kit, Wellsbio Carestart Biosensor with qualitative method which is currently being used. Reference value used for quantitative test was according to a published study done in 2010 at Hospital Universiti Kebangsaan Malaysia. *Results & Discussion:* 11 adult and 24 newborn samples were used in this study. 81.82% ( $n=9$ ) of adult samples and 29.17% ( $n=7$ ) of newborn samples showed normal result on FST. 1 out of these 9 normal adult samples on FST showed intermediate result by Biosensor. Whereas all deficient samples on FST (adult  $n=2$  and newborn  $n=17$ ) showed intermediate result on biosensor. *Conclusions:* The different interpretation in quantitative method can be caused by either variation of mutation in different ethnics in Sabah, or a new reference range for Sabah population needs to be established as the previous published ranges only include population from Peninsular Malaysia.

**HM-34. Red Blood cell distribution width and Framingham Risk Score: Cardiovascular disease risk**

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*Introduction:* Red cell distribution width (RDW) is routinely reported as part of full blood count (FBC) test. Higher levels of RDW may be associated with high risk of cardiovascular events among healthy adult population. This present study was aimed to assess the potential role of RDW as a marker for cardiovascular disease risk assessment in its relationship with Framingham Risk Score (FRS). *Materials & Methods:* A total of 75 healthy individual in Universiti Putra Malaysia were recruited. Respondents were required to answer a simple research questionnaire. Respondents' clinical data, anthropometrics measurement and 5 mL of collected blood samples were subjected for full blood count, blood sugar and lipid profile. *Results:* There were 19 males and 56 female respondents with the majority (77%) were between 30 to 40 years old. They were divided into four groups based on their RDW levels: Group I,  $<12\%$  ( $n=8$ ); Group II,  $12-13.4\%$  ( $n=42$ ); Group III,  $13.5-14.8\%$  ( $n=22$ ) and Group IV,  $>14.8\%$  ( $n=3$ ). Respondents with higher levels of RDW from this study, tended to be younger, female, non-smoker, normal lipid profile and fasting blood sugar, normal body mass index, and had low FRS. There was no statistically significant correlation between RDW and FRS ( $p>0.05$ ) where most of the respondents were with low FRS. *Discussion & Conclusions:* A novel association was revealed between higher levels of RDW and an elevated FRS in patients with coronary artery disease, which raises the possibility that a simple readily available in FBC parameter, RDW, may be associated with an increased risk of heart events. However, a multicentre with a larger scale of study population is required to further verify the insignificant role of RDW as a potential additional marker to FRS for cardiovascular disease risks assessment of this study.

**HM-35. Diagnostic performance of extended monocyte parameters in the detection of clinically suspected dengue infection**

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*Introduction:* Monocytes have been implicated in both pathogenesis and protection of dengue. Increased monocyte percentage (Mono%) and monocyte anisocytosis were suggested as new markers for dengue fever detection. Extended monocyte parameters in DxH 800 (Beckman Coulter, USA) can serve as diagnostic parameters to discriminate between dengue infection and other febrile illness. *Materials & Methods:* A cross-sectional retrospective study using suspected dengue fever patients was conducted to explore the diagnostic utility of Mono% and monocyte volume standard deviation (MoV-SD) as a dengue predictor. Patients were classified into dengue positive and dengue negative based on dengue IgM and/or NS1 result. The diagnostic performance of monocyte parameters was analyzed by receiver operating characteristic (ROC) curve analysis. The cut-off value of the monocytes parameters was determined and evaluated with the validation group. Chi-square test was used to assess the association between the parameters. *Results & Discussion:* A total number of 182 samples of suspected dengue fever were identified for this study and 88 (48.4%) were confirmed to have dengue infection. ROC curve analysis showed Mono% at cut off value of 10.5 with area under the curve (AUC) of 0.869 with 84.1% sensitivity and 84% specificity (CI: 0.812-0.925) and MoV-SD cut off value at 22.2 (AUC 0.776, 80.7% sensitivity, 61.7% specificity, CI: 0.709-0.843) are an excellent parameters in separating dengue positive and dengue-negative patients. The cut-off value for both Mono% and MoV-SD were applied to the validation group showed 83.1%, 66.4% sensitivity and 84.9%, 77.3% specificity respectively. Chi-square test also showed a significant association ( $p < 0.001$ ) between the Mono% and MoV-SD with dengue serology. *Conclusion:* Extended monocyte parameters have the potential to be used as a screening test in a suspected dengue infection with good sensitivity and specificity.

**HM-36. Molecular characterization of variants with a small peak at S window or zone 1 of haemoglobin analysis**

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*Introduction:* Haemoglobin A<sub>2</sub> (Hb A<sub>2</sub>) variant is haematologically silent and can be detected as a small peak at S window and zone 1 by high-performance liquid chromatography (HPLC) and capillary electrophoresis (CE), respectively. The sole importance lies in the under-estimation of Hb A<sub>2</sub> quantity during the workup of  $\beta$ -thalassaemia. This study aims to describe the significance of detection of Hb A<sub>2</sub> variant by Hb analysis and to confirm the diagnosis at the molecular level. *Materials & Methods:* We carried out a retrospective analysis of 29 cases based on the presence of a small peak at S window/Zone 1 by Hb analysis from 2012 to 2018. They were further analysed accordingly based on the presumptive diagnosis. There are few differential diagnoses of the cases such as  $\delta$ -variant/thalassaemia,  $\beta$ -thalassaemia, and  $\alpha$ -variant. For characterization of the mutation,  $\beta$ ,  $\alpha$ , and  $\delta$  sequencing,  $\alpha$ -GAP and ARMS were performed according to the diagnosis. To exclude the possibility of  $\delta$ -globin (HBD) variant,  $\delta$ -globin gene sequencing was performed in all cases. The data were recorded and tabulated and analysed using IBM SPSS Statistic version 23. *Results & Discussion:* Based on Hb analysis, majority of the cases were diagnosed with  $\delta$ -thalassaemia (n=14, 48.3%) followed by  $\beta$ -thalassaemia (n=8, 27.6%), when the quantity of S-window/Zone 1 peaks were taken into account. Those cases suspected with  $\delta$ -thalassaemia have lower MCV, MCH, Hb A<sub>2</sub> and Hb A<sub>2</sub>' with mean $\pm$ SD of (78.36 $\pm$ 6.23), (25.9 $\pm$ 1.9), (1.65 $\pm$ 0.21) and (0.92 $\pm$ 0.3) respectively as compared to cases with co-inheritance  $\beta$ -thalassaemia, mean $\pm$ SD of (65.28 $\pm$ 9.86), (21.16 $\pm$ 3.57), (2.67 $\pm$ 0.57) and (1.96 $\pm$ 0.75), respectively. We found that majority of the cases suspected with  $\beta$ -thalassaemia (n=26, 89.5%) have a significant abnormality in  $\delta$ -sequencing. Three cases (10.5%) that presumed to have  $\delta$ -variant were negative by  $\delta$ -sequencing. *Conclusions:* In order to make a diagnosis of  $\beta$ -thalassaemia trait, Hb A<sub>2</sub>' and any other variant A<sub>2</sub> must be added to normal Hb A<sub>2</sub> and the total used to determine whether Hb A<sub>2</sub> is elevated. The presumptive diagnosis should be confirmed at the molecular level.

**HM-37. Establishing reference intervals for prothrombin time and activated thromboplastin time at two different laboratories in Universiti Teknologi MARA (UiTM) campuses**

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*Introduction:* Establishing reference intervals (RI) for coagulation tests such as prothrombin time (PT) and activated partial thromboplastin time (aPTT), with each new reagent lot is recommended by the US Clinical and Laboratory Improvement Amendments (CLIA) legislation and the Malaysian Ministry of Health for the pathology services. The Faculty of Medicine UiTM has two diagnostic laboratories at Sungai Buloh and Selayang campuses. We use the same samples when establishing the RI at these sites. We decided to test whether freezing and thawing will give a different PT and aPTT results from fresh samples. *Materials & Methods:* Plasma samples from 60 eligible blood donors were evenly divided into secondary tubes labelled as *fresh* or *thawed*. All samples were duplicated to be run in either Sungai Buloh (SBC) or Selayang (SLC) campuses. PT and aPTT were immediately performed on all *fresh* samples at both campuses using mechanical clot detection coagulation analyser

(Stago Diagnostica, France). *Thawed* samples were stored frozen at  $-30^{\circ}\text{C}$  and PT and APTT were performed after thawing. Paired-samples t-test was conducted to evaluate the impact of freezing and thawing on PT and aPTT at both campuses. *Results & Discussion:* The mean PT and aPTT of *fresh* SBC and SLC were found to be statistically different, whereas, no significant difference was found in PT and aPTT in *thawed* samples at SBC and SLC ( $p>0.05$ ). The mean difference between thawed PT and aPTT in SBC and SLC were 0.071s and 0.2s, respectively. This experiment showed that by freezing, the samples were more stable, and determination of RI can be carried out at a more convenient time. *Conclusions:* Although the samples were not exactly treated the same as the patient's sample, it can serve as an alternative in a centre where the satellite laboratories are far apart but share the same RI samples.

#### HM-38. Digital mobile applications as alternatives to tabletop counters for manual white blood cell differential count

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*Introduction:* Traditionally, manual white blood cell (WBC) differential count is done using a microscope to identify up to a hundred white cells in a peripheral blood film and then counting them using a tabletop counter, which could be mechanical or electronic. With the invention of smart phones and tablets, digital applications have been designed for WBC cell counting, as alternatives to manual tabletop counters. These applications could be downloaded to the mobile device, from digital distribution site such as Google Play Store for the android devices, to be used anywhere at any time. *Materials & Methods:* A search was made through the Google Play Store. WBC differential count applications which are free of charge were selected and downloaded into a smart phone. Each application is then tested to determine whether they have a good user interface, efficiency in operation, desired features, user-friendliness and accuracy. *Results & Discussion:* Five applications were downloaded for evaluation. The applications are: *Blood Counter, Haematology Counter, Bloodroid Cell Counter, WBC Counter, and WBC Counter – White Blood Cells Differential Count*. They all have a similar user interface but come with different alert sounds and vibrations. Beside basic WBC differential count, some includes extended differential counting for other cells and even allows bone marrow differential counting. All applications are user-friendly and efficient. *Conclusions:* Digital mobile applications are acceptable alternatives to tabletop counters for manual WBC differential count. They have the potential of replacing their tabletop counterparts since they are free.

#### HM-39. Factors associated with acute transfusion reaction in Hospital Tuanku Ja'afar Seremban: Retrospective data analysis (2015-2016)

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*Introduction:* Blood transfusion is an important life-saving procedure; however, blood transfusion can cause acute or delayed transfusion reaction. Thus, awareness and knowledge among doctors in blood component usage, signs and symptoms of transfusion reaction, and management of transfusion reaction are paramount important. Objective of the study is to identify the types of transfusion reaction, signs and symptoms of transfusion reaction and types of blood components associated with development of transfusion reaction. *Materials & Methods:* This is a retrospective, cross-sectional study. Data collection included all transfusion reaction cases from January 2015 till December 2016 in Hospital Tuanku Ja'afar Seremban. SPSS was used to analyse the data. *Results & Discussion:* There were a total 326 cases of transfusion reaction: 202 cases (0.8% of 25,103 transfusion cases in year 2015) and 124 cases (0.5% of 23,085 transfusion cases in year 2016) were recorded. Fever is the commonest sign (159 cases, 48.8%), followed by urticaria (102 cases, 31.3%), chills and rigors (94 cases, 28.8%). Itchiness, rashes, vomiting, nausea and headache are rarely found. Dyspnoea happened in all 10 cases of transfusion associated circulatory overload (TACO) and 1 case of transfusion related acute lung injury (TRALI). Types of transfusion reaction reported include acute febrile non-haemolytic transfusion reaction (159 cases, 48.8%), mild allergic reaction (141 cases, 43.3%), TACO (10 cases, 3.1%), moderate allergic reaction (9 cases, 2.8%), transfusion associated dyspnoea (6 cases, 1.8%) and TRALI (1 case, 0.3%). RBC transfusion was the main associated factor ( $p=0.005$ ), causing acute transfusion reaction (ATR) – 201 cases (61.7%). Leuco-filtered RBC transfusion had the lowest frequency in causing ATR. This study showed that patients' underlying medical illnesses were not the factor associated with ATR ( $p=0.181$ ). *Conclusions:* Types of blood components transfused is the main factor associated with ATR. Prompt recognition of ATR is important so that treatment can be given to the patients in a timely manner to ensure patient safety.

#### HM-40. Prevalence and specificity of red blood cell alloantibodies among patients attending a tertiary care hospital

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*Introduction:* Red blood cell (RBC) alloimmunization results from genetic disparity of RBC antigens between donor and recipients. Antibody identification is important to identify the presence of autoantibody or alloantibody if the antibody screening test is positive. Objective of this study is to identify prevalence and specificity of alloantibody and to identify demographic of patients with positive antibody study among Hospital Tuanku Ja'afar Seremban (HTJS) patients. *Materials & Methods:* This

is a retrospective, cross-sectional study. Data collection included all the cases with positive result of antibody identification from June 2015 till August 2016 in HTJS. SPSS v21.0 was used to analyse the data. *Results & Discussion:* There were total 496 cases of antibody identification: 405 cases (81.7%) was presence of alloantibody, 74 cases (14.9%) was autoantibody, 17 cases (3.4%) was presence of both allo & autoantibodies. 78.4% (359 cases) were female patient & 21.6% (99 cases) were male patient. Patient aged between 31 & 50 years old were the highest (172 cases) among those positive with antibody. According to blood group, 34.9% (173 cases) were Group O, 31.7% (157 cases) were Group B, 24.8% (123 cases) were Group A, 8.6% (43 cases) were Group AB. Majority of the patients were RhD Positive (422 cases, 85.1%). The highest incidence of RBC alloimmunization was observed in obstetrics and gynaecology patients: 165 cases (33.3%). Types of antibody identified were anti-Mia antibody (20.2%), anti-E antibody (14.5%), anti-D antibody (13.5%), anti-Lea & anti-Leb antibodies (9.3%), anti-Lea antibody only (9.1%). Anti-Fyb antibody was the least common alloantibody detected (0.2% only). Anti-Mia antibody has been reported as common antibody present among Southeast Asian patient especially Taiwan and Malaysia. The female population with high incidence of antibody development could be due to pregnancy-induced alloimmunization or due to previous blood transfusion. *Conclusions:* The frequency of RBC alloantibodies varies considerably depending on numerous factors i.e. demographics, pregnancy, genetic constitution, immune competence and disease factors. As alloimmunization complicates the transfusion outcome, pre-transfusion antibody screening and issue of antigen negative blood is paramount important to prevent transfusion related haemolysis.

#### HM-41. Prevalence of Mi<sup>a</sup> antigen: A pilot study among patients in Universiti Kebangsaan Malaysia Medical Centre

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*Introduction:* Mi<sup>a</sup> is a low frequency red cell antigen that belongs to the MNS glycoprotein (GP) variants or Miltenberger phenotypes; it is associated with the MNS blood group system. Expression of Mi<sup>a</sup> antigen is usually seen in individuals with GP.Mur (also known as Miltenberger subtype III or Mi.III) phenotype in Southeast Asia. Its alloantibody, anti-Mi<sup>a</sup> has been shown to cause transfusion reactions and haemolytic disease of foetus and newborn. This study was aimed to determine the prevalence of Mi<sup>a</sup> antigen expression among patients in Universiti Kebangsaan Malaysia Medical Centre (UKMMC). *Materials & Methods:* The study was conducted at the Blood Bank, UKMMC from April to July 2018 on patients' blood samples received for pre-transfusion test. The blood samples were tested with monoclonal anti-Mi<sup>a</sup> antibody. *Results & Discussion:* A total of 533 patients have been recruited. The prevalence of Mi<sup>a</sup> antigen among the UKMMC patients was 3% (16/533). Chinese patients showed the highest frequency (5.58%), followed by Malay patients (1.68%). None of the Indian patients expressed Mi<sup>a</sup> antigen in this study. *Conclusions:* Malaysia is a multiethnic country and it is important to determine the frequency of Mi<sup>a</sup> antigen expression in the three major ethnic groups. Prevalence of various significant red cell antigens with corresponding alloantibodies have been established in Malaysia. Anti- Mi<sup>a</sup> is one of the commonest alloantibody identified, however the frequency of corresponding Mi<sup>a</sup> antigen is not known. This study shows a low incidence of Mi<sup>a</sup> antigen, probably due to the small number of recruited subjects from a limited setting. A study with a larger population to reflect the true picture of the prevalence of Mi<sup>a</sup> antigen in Malaysia is needed.

#### HM-42. A qualitative study among non-donors: Awareness and hindering factors in blood donation

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*Introduction:* Blood donation is crucial and indispensable in medical process of saving lives. The likelihood for a person to become a blood donor is influenced by many factors including personal experience, family influences, fear and self-awareness. Although blood donation campaigns have been widely organised throughout the country, a low participant has been recorded. To explore the blood donation awareness amongst non-donors and to study the factors that hinder them from voluntarily donating blood. *Materials & Methods:* This is a qualitative study involving semi-structured interviews. It was a convenience sample of 11 non-donor who were a healthy caregiver in ICU of a public hospital in Sabah. Four focus group discussions (FGD) were conducted. The studies were held in separate closed rooms. All the sessions were recorded with the participants' permission. The discussions were carried out in a local language, and the verbatim was later translated into English. Data were analysed using Atlas T.I. It was analysed in three phases: data filtering, index in full transcript and identify the themes and sub-themes. *Results & Discussion:* Majority of the participants professed the importance of donating blood are to save a life and as charity work. The three hindering factors themes that preventing them from becoming a voluntary blood donor are fears and concern, lack of awareness and lack of accessibility. Fear is a common factor stated by the participants including fear of the needle/blood, fear of own blood inadequate, fear own health affected or a general fear of the whole blood donation process. *Conclusions:* Blood donation awareness is very crucial in the effort to increase the number of voluntary blood donors. The use of advertisements that could increase the knowledge and awareness among the community is a must to overcome the fears and concern and give a significant impact to increase a donation rate in this country.



**HM-43. Effect of using social media as promotional medium for blood donation campaigns in Hospital Langkawi**

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*Introduction:* Langkawi island is a very popular tourist attraction with a local population of 94,777 peoples. And the number increases during holidays. Over the years, Langkawi Hospital has shown increment in the number of donated blood collection but still inadequate for usage in the Hospital which is the only hospital in the island. In March 2017, we have decided to make an improvement by using social media as a promotion medium to educate and advertise all the blood donation campaigns to the populations. *Materials & Methods:* Data of total blood collection for Hospital Langkawi in 2015, 2016, 2017 and 2018 are collected. We compare the increment of blood collection the year before and after the project was started. Facebook page was created in March 2017 for the educational purposes and a means to reach out to the public. *Results & Discussion:* The total blood collected are 2148, 2264, 2877 and 3180 bags in 2015, 2016, 2017 and 2018, respectively. There is a sudden increment in total blood collection in 2017 following the Facebook project showing an increment of 613 bags (27%) compared to 2016 collection. Only a small yearly increment was seen in 2016 (116 bags (5.4 %) before the project was started. And thanks to Facebook project, a further increment of 303 bags (10.53%) is seen in 2018. *Conclusions:* Using social media as a medium for promotion of blood donation campaign has a huge impact on collection of blood for Hospital Langkawi. Its continuation as a main medium of promotion will bring more positive impact for many years to come; not just as a promotional medium but also to develop a closer bond with donors and locals.

**HM-44. Retrospective review of molecular and clinical presentation of adult Hb H disease in Kuching**

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*Introduction:* Alpha thalassaemia is the commonest inherited disorder of the haemoglobin and we believe that many are not diagnosed until clinical complications occur. Haemoglobin H disease (Hb H) is the result of either deletion or non-deletional of  $\alpha$ -globin gene, resulting in a spectrum of non-transfusional dependant thalassaemia (NTDT). Objective of this study is to identify the molecular characteristics and clinical presentation of Adult patients with Hb H disease treated in Sarawak General Hospital (SGH), Kuching. *Materials & Methods:* Review of clinic notes of all adult alpha thalassaemia patients treated in SGH and retrieved from Sarawak thalassaemia registry since year 2000. *Results & Discussion:* There were 34 patients diagnosed with Hb H, with mean age of 38.4 years, majority females (n=22). Adults Hb H patients in SGH are mainly of Chinese (50%) ethnicity, followed by Malays (35.3%) and local Dayaks (14.7%). All Hb H were NTDT, only needing transfusion during pregnancy or at times of infections. There were 3 reported deaths among the Hb H patients. Of all these Hb H patients, only 24 molecular results that were available for review, 80% were deletional Hb H disease, while 20% were non-deletional type. Molecular analysis of 24 patients revealed  $-\alpha3.7$  deletion is the commonest (79.1%), followed by  $\alpha$ -thalassaemia-Southeast Asian deletion ( $-\text{SEA}$ ).  $-\alpha3.7$  deletion is observed the highest among the Malays (50%) followed by local Dayaks (27.8%), while mutation  $-\text{SEA}$  is found almost equally in the Chinese (53.3%) than Malay ethnicity (46.7%).  $-\alpha3.7/_/_\text{Fil}$  is found exclusively among the local Dayaks. Among the non-deletional mutation, with Hb Adana was the commonest, exclusively among the Malays. *Conclusions:* Genetic epidemiology studies of Hb H are important due to diverse ethnicity in Sarawak. We hope to understand the genotype-phenotype associations of this disease based on the clinical parameters and outcome of this disease.

**HM-45. Secondary haemophagocytic lymphohistiocytosis following invasive fungal infection in a setting of immunosuppression**

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*Introduction:* Haemophagocytic lymphohistiocytosis (HLH) is a potentially fatal disorder resulting from uncontrolled immune activation. It can be categorised into primary and secondary HLH. Primary HLH is due to genetic mutations whereas secondary HLH is due to causes infection, autoimmune, malignancy and metabolic causes. Here, we highlight a case report of secondary HLH secondary to disseminated fungal infection in the setting of immunocompromised patient. *Case Report:* A 41-year-old Chinese lady with IgA nephropathy since 2002, presented with fever associated with right elbow swelling and pain for one-week duration. She denied any connective tissue signs and symptoms. She is on prednisolone, mycophenolate mofetil and azathioprine for IgA nephropathy. Physical examination demonstrated warm erythematous swollen forearm. She had no hepatosplenomegaly. Full blood count showed pancytopenia. Peripheral blood film showed severe normochromic normocytic anemia, leucopenia and occasional reactive lymphocytes. She had renal impairment, hypoalbuminemia and mild transaminitis. C-reactive protein was positive. She was treated as right elbow cellulitis and Azathioprine was withheld, thought to be a cause for the pancytopenia. However, she had persistent high-grade fever despite antibiotics and negative blood cultures. Her cellulitis did not improve. Bone marrow examination was performed two weeks later in view of persistent pancytopenia which revealed haemophagocytosis and increased macrophages with intracytoplasmic organisms. Gomori Methenamine-Silver stains confirmed the presence of fungal bodies in the trephine biopsy. Skin biopsy showed numerous fungal yeasts within papillary dermis extending to subcutis. She

was diagnosed to have secondary HLH secondary to histoplasmosis. She passed away despite on antifungal due to multiorgan failure. *Learning Points:* This case illustrated a case of secondary HLH that was triggered by invasive fungal was always under-recognised due to its non-specific symptoms of infections in the setting of chronic immunosuppression. The diagnosis of HLH was difficult and challenging due to non-specific signs and symptoms.

#### HM-46. Rare cases of hemoglobin variant: Masked amongst patients with isolated erythrocytosis

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*Introduction:* Erythrocytosis could be a presentation of various diseases, which may pose as a diagnostic challenge leading to extensive futile investigations. High oxygen-affinity hemoglobinopathies are very rare. We described two cases of haemoglobin (Hb) variant; Hb Johnstown and Hb Bethesda that were detected following various unremarkable results of investigations for persistent erythrocytosis. *Case Reports: Case 1:* A 49-year-old diabetic lady was incidentally noted to have persistent erythrocytosis with family history of erythrocytosis. She was otherwise asymptomatic. Her JAK2 mutation analysis revealed a wild type, while bone marrow aspiration showed only erythroid hyperplasia with normal cytogenetics. Subsequently Hb analysis (chromatography method) showed a variant Hb peak eluted after Hb A<sub>2</sub>, and DNA analysis confirmed the presence of a Hb variant: Hb Bethesda ( $\beta$ 145 histidine). *Case 2:* An asymptomatic 67-year-old lady who was noted polycythaemic with normal serum erythropoietin level during an admission for dengue fever. The bone marrow aspiration and trephine showed mainly erythroid hyperplasia. JAK2 mutation testing was negative. Subsequently Hb analysis (electrophoresis method) showed raised Hb A<sub>2</sub> of 5.1% suggestive of beta thalassaemia trait which did not correspond with the erythrocytosis picture. The DNA analysis confirmed a Hb variant: Hb Johnstown [ $\beta$ 109(G11)Val $\rightarrow$ Leu]. Both cases underwent venesection to control the Hb level and continued to be monitored on an outpatient basis. *Learning Points:* An isolated erythrocytosis with the absence of secondary causes and hepatosplenomegaly raises the suspicion of high affinity haemoglobinopathy. Both Hb Johnstown and Hb Bethesda are the Hb variants with high oxygen affinity causing erythrocytosis detected using HPLC and CE respectively. In the evaluation of a patient with erythrocytosis, the identification of high-affinity haemoglobinopathies can prevent unnecessary testing and treatment. Thus, a high index of suspicion especially in cases with positive family history allows proper diagnostic strategy which is less invasive and more cost effective.

#### HM-47. Secondary haemophagocytic lymphohistiocytosis due to *Penicillium Marneffe* in a HIV patient with pancytopenia: A case report

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*Introduction:* Haemophagocytic lymphohistiocytosis (HLH) in an immunocompromised patient is a severe condition with high mortality rate caused by infections or immunodeficiency. Due to overactivation of the immune system, HLH requires early diagnosis and treatment to prevent multiorgan failure and eventually death. Here, we report a case of a HIV positive patient with pancytopenia and incidentally detected to have haemophagocytic activity and intracellular organisms within the histiocytes in his bone marrow aspirate and biopsy. *Case Report:* A 23-year-old homosexual man presented with one-week history of fever, chills, rigors and loose stool. He was recently diagnosed to have retroviral disease with CD4+ count of 5/uL. On examination, he was noted to have oral candidiasis and hepatomegaly. Full blood picture revealed pancytopenia, with white blood cell count of  $2.2 \times 10^9/L$  (neutrophil count:  $1.76 \times 10^9/L$ ), hemoglobin of 58.0 g/L, and platelet counts of  $74 \times 10^9/L$ . Full blood picture showed pancytopenia with leucoerythroblastic picture. No blast or abnormal lymphoid cells seen. There was no intracellular organism noted in his blood smear. Other biochemical investigations revealed hyperferritinaemia with ferritin level of 39530  $\mu$ g/L and LDH was 2674 U/L. A bone marrow aspirate was proceeded and showed increase in histiocytes with haemophagocytic activity, with presence of fungal bodies within these histiocytes which resembles either *Histoplasma capsulatum* or *Penicillium marneffe*. The trephine biopsy showed similar findings. Bone marrow culture results grew *Penicillium marneffe*. The patient responded well to specific antifungal with good blood count recovery. *Discussion:* Early detection and treatment of secondary HLH is crucial to prevent mortality. Studies has shown that the prognosis is worse in patients with CD4 counts less than 200 cells/ $\mu$ L. *Learning Points:* HLH secondary to intracellular organisms, should be suspected in immunodeficient patients with pancytopenia, as they usually have nonspecific symptoms which leads to a vast range of differential diagnosis. Thus, appropriate diagnostic tests allow a timely and effective clinical approach.

**HM-48. Is cryosupernatant more superior for therapeutic plasma exchange in thrombotic thrombocytopenic purpura management?**

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*Introduction:* Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disorder characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, neurological symptoms, renal injury and fever. It is a result of deficiency of a metalloprotease protein, ADAMTS13. Therapeutic plasma exchange is the main treatment for TTP and if left untreated, the mortality is about 90%. The role of cryosupernatant and fresh frozen plasma (FFP) in the management of TTP will be elaborated in this case study. *Case Report:* A 69-year-old lady presented with chest pain and suprapubic pain for 3 days, associated with headache and vomiting. On admission, her hemoglobin was 9.3 g/dL and platelet was  $20 \times 10^9/L$ . Peripheral blood smear revealed features of MAHA. She also had acute kidney injury. Few days later, she became confused and fitter. Her GCS dropped to E4, V3, M5. CT brain showed multifocal old infarcts. She was then diagnosed to have TTP. She was subsequently intubated and plasma exchange was initiated. A total of 4 units FFP and 8L cryosupernatant was given to her over 5 days and her platelet increased to  $125 \times 10^9/L$ . However, she deteriorated again few days later, with further decrement in platelet count to  $9 \times 10^9/L$ . ADAMTS13 activity was within normal limits and ADAMTS13 inhibitor was not detected. A total of 21 units of cryosupernatant was then transfused during plasma exchange procedure over next 12 days. She was discharged well 2 weeks later. *Learning Points:* Therapeutic plasma exchange is the principle treatment for TTP which has significantly reduced the mortality rate. Patients who develop neurological or cardiac events require twice daily plasma exchange. Daily transfusion should be continued for at least 2 days after complete remission. Study by Brunskill *et al.* stated that cryosupernatant was as favourable as FFP. Cryosupernatant with steroids as method of treatment is more cost effective compared to FFP, and in a study done by Palaniappan *et al.* in 2013, remission is attained within 2 weeks.

**HM-49. Persistence of host-type haematopoiesis after allogeneic haematopoietic stem cell transplantation without disease relapse: A case report**

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*Introduction:* Successful allogeneic haematopoietic-stem-cell-transplant (HSCT) occurs when there is complete replacement of host by donor lympho-haematopoiesis (complete chimerism). When both donor and recipient haematopoietic cells are present (mix chimerism, MC), it is a strong indicator of relapse. This is commonly seen if the recipient cells are in increasing trend. Here, we report a patient who had no disease relapse. *Case Report:* The patient was a 45-year-old Malay man. He was in the first complete remission from acute myeloid leukaemia (AML). The chromosomal translocation (8;21)/RUNX1-RUNX1T1 and FLT3 gene mutation were detected at the initial diagnosis of AML. At transplantation, he was in molecular remission (RUNX1-RUNX1T1 negative). He underwent an allogeneic HSCT from a match sibling. Myeloablative conditioning consisting of busulfan and cyclophosphamide was given prior to transplantation. Methotrexate and cyclosporine were administered for graft-versus-host-disease (GVHD) prophylaxis. No GVHD develop. Chimerism analysis using qRT-PCR on biallelic insertion/deletion markers was performed. This test revealed that the informative recipient marker was not reducing after 30 days (96.8%) transplantation. Subsequent chimerism status were still at high side at day 60 (60.1%) and 107 (84.9%). Though, the patient was clinically healthy and his serial blood counts were also improving. No intervention was undertaken for these results. *Discussion:* This condition maybe explained by complete eradication of the malignant clone with selective survival of residual normal host hematopoietic stem cells. This may have resulted either from the myeloablative conditioning and/or from alloreactive donor lymphocytes directed toward leukemia associated antigens. The residual myeloid and erythroid cells were reserved, thus creating split hematopoiesis without relapse of the original disease. The recipient-derived chimerism pattern might be reduced if we run the analysis on sorted lymphocytes. *Learning Points:* In our case, the chimerism analysis was done on whole white blood cells without sorting into myeloid, B and T cells. We proposed subset-specific analyses of chimerism for patients with persisting increased recipient MC.

**HM-50. A rare hemoglobin variant, hemoglobin Singapore, [ $\alpha 141$ , Arg @ Pro], in a Malay family**

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*Introduction:* Hemoglobin (Hb) Singapore [ $\alpha 141$ , Arg @ Pro] is a very rare alpha globin chain variant. It was first discovered in a Malay family living in Singapore by Clegg *et al.* in 1969. This is a second case report with similar findings of fast-moving variant containing an amino acid substitution arginine to proline at position  $\alpha 141$ . *Case Report:* A 3-year-old Malay boy from Kelantan was investigated for hemoglobinopathy in view of slightly hypochromic microcytic red cell indices and morphology. He was otherwise asymptomatic with normal haemoglobin level. The Hb analysis was performed using high performance

liquid chromatography (HPLC). The results showed levels of Hb A, Hb A<sub>2</sub> and Hb F were 62.3%, 1.9% and 1.4% respectively. Additionally, an abnormal Hb peak, X, with a value of 29.4% was observed at the retention time of 1.43 minutes. This abnormal Hb was also seen at zone 12 capillary electrophoresis (CE), which was similar to Hb J variant (*i.e.* Hb J-Singapore, Hb J- Meerut). Further molecular study using amplification refractory mutation system (ARMS) and Gap-Polymerase Chain Reaction (Gap-PCR) to detect known deletions and point mutations were negative. The direct DNA sequencing revealed the CGT>CCT mutation at codon 141 of  $\alpha 2$ -globin gene identified as heterozygous Hb Singapore. Three other family members (mother, a brother and a sister) also had the variant. However, both siblings had co-inheritance of heterozygous  $\alpha 3.7$  deletion with higher presentation of Hb variant fraction, X>35%. **Learning Points:** Hb Singapore has similar HPLC pattern and CE migration time with Hb J variants which is a potential pitfall for misinterpretation. The confirmatory diagnosis can only be made by DNA sequencing. Therefore, the knowledge of this Hb variant is important to be used in diagnosis, management and counselling of patients.

#### HM-51. Bone marrow histoplasmosis in a renal transplant patient

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**Introduction:** Fungal infections remain an important cause of mortality and morbidity in post solid organ transplant patients due to chronic immunosuppression. **Case Report:** A 58-year-old renal transplant recipient presented to the hospital with a four-day history of fever with chills. A full blood count revealed pancytopenia (haemoglobin 8.9 g/dL, white cell count  $2.7 \times 10^3/\mu\text{L}$ , platelet count  $51,000/\mu\text{L}$ ). Blood films for malarial parasite, serological studies for dengue and cytomegalovirus were negative. Peripheral blood film showed presence of intracellular organisms within the monocytes and neutrophils. Many intracellular organisms were seen in the bone marrow aspirate, which were positive for Periodic Acid-Schiff. Intracellular fungal bodies in the trephine sections stained positive for Gomori Methenamine-Silver stain. Fungal culture of the bone marrow aspirate was positive for *Histoplasma capsulatum*. **Discussion:** In solid organ transplant recipient, disseminated histoplasmosis can occur either as a primary infection, as a reactivation of latent infection or as a donor-transmitted infection. The incidence of histoplasmosis in solid organ transplant recipients is low and there have only been a few case series involving renal and liver transplant recipients. Prolonged fever is the main clinical feature of histoplasmosis among organ transplant recipients. Splenomegaly, hepatomegaly and mucocutaneous lesions which are associated with features of disseminated histoplasmosis have also been reported to be quite common in renal transplant recipients. Majority of cases occur within the first 18 months of surgery. Post-transplant histoplasmosis can be established by performing culture or histopathological examination. However, *Histoplasma* urine antigen test or the *Histoplasma* serological test may provide rapid results. Detection of the antigen in the urine is currently the most sensitive serological test available for disseminated histoplasmosis. **Learning Points:** This case illustrated the importance of having a strong clinical suspicion of a disseminated fungal infection in an organ transplant patient, presenting with non-specific symptoms of infection.

#### HM-52. A child with pancytopenia: Is this childhood myelodysplastic syndrome?

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**Introduction:** Pancytopenia is not uncommon in children. The cause for pancytopenia in children varies, it can either be benign as in infections or malignant as in acute leukaemias and myelodysplastic syndrome (MDS). MDS is very uncommon in childhood and accounts for only less than 5% of all hematopoietic neoplasms in children below the age of 14 years old. Here, we describe a child who presented with pancytopenia and suspected to have MDS. **Case Report:** An 8-year-old girl was referred to our centre for pancytopenia, with haemoglobin of 9.4 g/dL, neutrophil count of  $0.85 \times 10^9/\text{L}$  and platelet of  $12 \times 10^9/\text{L}$ . She has been having this problem for the past 2 years. On clinical examination, she had multiple small cervical lymph nodes and hepatomegaly. There was no other significant finding. Peripheral blood film showed pancytopenia with no blast cells. Bone marrow (BM) aspirate showed hypocellular marrow with presence of significant dyserythropoiesis and dysmegakaryopoiesis. Trephine biopsy findings favoured MDS with excess blasts. However, marrow cytogenetic was unable to proceed due to low count. This patient is currently managed supportively, by giving blood transfusion whenever necessary. Being the only child, finding a matched donor for haematopoietic stem cell transplant (HSCT) is not easy. **Learning Points:** This case highlights MDS as a cause for pancytopenia in children. Even though uncommon, a diagnosis of MDS should be considered in a child presenting with pancytopenia. Due to its rarity, diagnosing MDS in childhood is a challenge to clinicians as well as pathologists. Comprehensive and intensive work-up is required to confirm the condition. Cytogenetic testing in MDS not only aids the diagnosis but also useful for prognosis.

### HM-53. A novel translocation t(7;11)(p22;q14) with t(8;21)(q22;q22) in acute myeloid leukaemia: Its clinical significance and benefits of conventional cytogenetic over molecular identification

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**Introduction:** Chromosome analysis and molecular characterization in acute myeloid leukaemia (AML) are the two crucial modalities used in WHO AML classification and for prognostic indicator. In this report, we described the benefit of conventional cytogenetic in detecting novel translocation t(7;11)(p22;q14) with t(8;21)(q22;q22) over molecular identification and clinical significance of this novel translocation. **Case Report:** A 5-year-old boy presented with 5 days history of low-grade fever, lethargy and right lower limb bruise. His physical examination revealed pallor and 1x1cm bruises over his lumbar region and right knee. Full blood count (FBC) revealed white cell count (WCC) of  $38.5 \times 10^9/\text{mL}$ , haemoglobin and platelet count of 4.2 g/dL and  $11 \times 10^9/\text{mL}$  respectively. Peripheral blood film showed features consistent with acute leukaemia with 64% of blasts. Both bone marrow aspiration and trephine showed 84% of blast cells with some Auer rods present (AML-M2: FAB classification) and majority of the cells were expressing CD34+, CD117+ and MPO+. RUNX1/RUNX1T1 transcript t(8;21)(q22;q22) was detected in both reverse transcriptase polymerase chain reaction (RT-PCR) and conventional cytogenetic analysis. However, additional translocation of t(7;11)(p22;q14) was only identified in the latter. AML mutation study was positive for FLT3 D835 and negative for internal tandem duplication ITD. Patient was started on chemotherapy using AML-UK (17) protocol and successfully completed the treatment with no complication. Fortunately, he achieved a complete remission as reassessment of his bone marrow showed normocellular with 4-5% blasts and patient remained asymptomatic till date. He also had a haematological remission achieved evidenced by normal FBC (WCC of  $4.6 \times 10^9/\mu\text{L}$ , haemoglobin and platelet count of 11.5 g/dL and  $313 \times 10^9/\mu\text{L}$  respectively). **Discussion:** This remarkable discovery is outstanding as chromosome 11 abnormalities or D835 FLT3 mutation in AML usually possesses a poor prognosis. We correlated the results of concurrent molecular and cytogenetic analysis of AML patient to determine the presence of prognostically relevant t(7;11)(p22;q14). The fusion gene was missed by RT-PCR as this method only had primer-specific to the common molecular abnormalities for AML; hence, unable to detect novel translocation. **Learning Points:** This concludes conventional cytogenetic may remain as the gold standard modality for identification of recurrent and novel chromosome abnormalities in AML.

### HM-54. A case of acute promyelocytic leukemia with monosomal karyotypes

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**Introduction:** Acute promyelocytic leukemia (APL) is a type of acute leukaemia that has a good prognosis and almost every patient will achieve complete remission with the current chemotherapy regime. However, the presents of monosomal karyotypes may turn the table around and catastrophe will ensue and can change the prognosis drastically. **Case Report:** Here, we present a case of APL with monosomal karyotype that usually characterize myelodysplastic syndrome, in which the patient died during treatment due to inevitable septic shock. Bone marrow aspirates of the patient shows abnormal promyelocytes with abundant and intense azurophilic granulation. However, there were no faggot cells, blasts cells or bilobed promyelocyte. Her karyotyping result showed a complex karyotype of 39-47 chromosomes with monosomy X, 5, 7, 8, 13, 17, 18, 19, 20 as well as the translocation chromosome 15 and 17. There were also three copies of chromosome 21 and other additional chromosomal markers seen. This are also evident by Fish analysis. We strongly emphasise the need of a large multi-center collaborative trials to establish a prognostic significance of additional cytogenetic abnormalities (ACA) especially monosomal karyotypes in APL patients both generally and specifically. **Learning Points:** Although APL confers a good prognosis and that increased in karyotype complexity in this particular haematological malignancy does not adversely affect their clinical outcomes, the prognostic significance of monosomal karyotypes in APL still remained a matter of debate.

### HM-55. Trephine biopsy findings in marginal zone lymphoma

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**Introduction:** Marginal zone lymphoma (MZL) is an indolent Non-Hodgkin lymphoma (NHL) that arise from memory B cells in the marginal zone of lymphoid tissue. In adults, MZL accounts for 5-17 % of all NHL. Based on WHO classification, MZL is divided into nodal MZL (NMZL), splenic MZL (SMZL) and extranodal MZL of mucosa-associated lymphoid tissue (MALT lymphoma). **Case Report:** We present four cases of MZL diagnosed in Hospital Sultanah Nur Zahirah, Kuala Terengganu in 2018. At diagnosis, all patients had bone marrow involvement hence diagnosis were established from trephine biopsy. All patients had different clinical presentation depending on stages of disease and type of MZL. The lymphoid cells are small to moderate in size with irregular nuclei and fine to dispersed chromatin pattern. The lymphoid cells were distributed in the intertrabecular and paratrabecular region. The overall cells were positive for CD20 and IgM and negative for CD3, CD5, CD10, CD23, Cyclin

D1 and Ig D. Two patients were started on chemotherapy and recuperating well. One patient is under palliative therapy and another one patient refused chemotherapy and succumbed to the disease. The 5-year overall survival rate for MZL is more than 50 %. Advanced patient age, B symptoms and advanced disease stage associated with worse prognosis. *Discussion:* MZL is characterized by presence of mature B cells expressing surface immunoglobulin, CD20 and pan-B-cell markers and typically negative for CD5 and CD10. The morphologic and immunophenotypic findings of the MZL can overlap with other indolent B-cell lymphoma. *Learning Points:* Trephine biopsy plays a role in diagnosing MZL with bone marrow involvement especially in cases with no lymphadenopathy where the lymph nodes biopsy cannot be performed.

#### HM-56. Hb H hydrops fetalis caused by haemoglobin Adana

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*Introduction:* Hydrops fetalis is an ominous condition in fetus and is generally incompatible with extrauterine life. The most common cause of hydrops fetalis is Hb Barts hydrops fetalis due to 4 alpha genes deletion. Rarely compound heterozygosity for  $\alpha^0$  thalassaemia and severe non-deletional  $\alpha^+$  thalassaemia can result in hydrops fetalis. Haemoglobin (Hb) Adana is an example of a severe non-deletional  $\alpha^+$  thalassaemia. *Case Report:* We present a case of hydrops fetalis due to compound heterozygous  $\alpha^0$  thalassaemia (--<sup>SEA</sup>) and non-deletional  $\alpha^+$  thalassaemia (Hb Adana). The mother had 1 previous pregnancy which also resulted in hydrops fetalis. She was diagnosed to have Hb H disease and her husband had beta thalassaemia trait. The father's DNA analysis showed heterozygous state of  $\alpha 2$  Codon 59 (GGC>GAC) Hb Adana mutation and heterozygous state of  $\beta^0$  thalassaemia, Filipino. The presence of Hb Adana in the husband explained the recurrent fetal demise due to hydrops fetalis. During pregnancy, this fetus was monitored closely with ultrasound and Middle Cerebral Artery peak systolic volume. Two occasions of pregnancies in 2016 and 2018 ended with fetal demise due to hydrops fetalis. *Discussion:* As highlighted in this case, the presence of beta thalassaemia trait do not exclude concurrent presence of alpha thalassaemia. According to a study in Hong Kong and China, around 10 % of beta thalassaemia subjects concurrently carry the alpha thalassaemia 1 gene. In our case, there will be 25 % possibility of hydrops fetalis in each pregnancy since presence of single Hb Adana mutation in combination with 2 alpha gene deletions manifest as hydrops fetalis. *Learning Points:* Rarely, hydrops fetalis can also be caused by compound heterozygosity for  $\alpha^0$  thalassaemia and non-deletional alpha thalassaemia. Thus, exclusion of alpha thalassaemia among beta thalassaemia carriers can reduce the incidence of hydrops fetalis.

#### HM-57. A child with pancytopenia and recurrent infection

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*Introduction:* Pancytopenia in paediatric population may cause diagnostic and management dilemma to pathologists & paediatrician respectively. At extreme of ages, one has to act fast to ensure patients are well managed. *Case Report:* MAF, a 16- month-old boy who presented with recurrent infections since 13 months of age. His developmental and immunization history were up to date. There was no similar family history and he is product on non-consanguineous marriage. Examination revealed active child with no dysmorphism other than mild pallor with generalized petechial rashes. Mild hepatosplenomegaly and multiple shotty lymph nodes were noted. Initial investigations revealed pancytopenia with absolute neutrophil count (ANC) of 0. Infective screening was non-reactive. Bone marrow examination revealed erythroid hyperplasia with increased megakaryopoiesis. Granulopoieses showed arrested maturation at promyelocytes stage. Bone marrow immunophenotyping showed no increase in blast cells. Further investigation revealed normal phagocytic, B and T cell functions. An acquired cause either infection or immune related abnormality is entertained. However, congenital causes need to be considered if acquired causes have been exhausted. He was covered for neutropenic sepsis with multiple intravenous antibiotics. Due to his unresolving fever, he was prophylactically covered for fungal infection. He was transfused with multiple platelet & packed cell transfusion. Subsequently, he was treated with monthly intravenous immunoglobulin (IvIg). His fever and peripheral count improved after IvIg treatment and did not require further blood product support. *Discussion:* Bone marrow examination is one of the essential investigations to elucidate the cause of pancytopenia. An arrested promyelocytes findings in the bone marrow is usually associated with congenital neutropenic causes like Kostmann syndrome. However, it can also be seen in immune related abnormalities as in autoimmune neutropenia. As in this case, gradual recovery is seen following use of IvIg. *Learning Points:* Bone marrow examination is essential in investigating pancytopenia. Correlating its findings with clinical presentation and other investigations help in optimal management of patient to achieve desired outcome.

**HM-58. Anti-c antibody: A silent killer**

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*Introduction:* Hemolytic Disease of the Newborn (HDN) most frequently occurs due to an incompatibility of the Rhesus (Rh) blood group between mother and the fetus. Commonly triggered by the D antigen follow by anti-c. *Case Report:* We present a fatal case of HDN secondary to Rh anti-c of Rh positive mother. The mother blood group was O positive, delivered a baby girl at 36 weeks and 5 days period of amenorrhoea via Emergency Lower Segment Caesarean Section (EMLSCS) due to fetal distress. The baby was born vigorous at birth then rapidly developed pallor and succumbed within nine hours of life due to refractory hypotension. The initial baby's haemoglobin level of 2.8 g/dL. Coombs test for both mother and baby were positive. Further history revealed that she had two other children who died; one intrauterine and another at the age of four years old due to complications of choreoathetoid cerebral palsy, who required exchange transfusion at birth due to severe jaundice secondary to minor group antibodies. Antibody screening, identification and red cell phenotyping proceed for the mother and baby revealed, Mother; Group O positive, Rh phenotype R1R1 (CDe/CDe) and with anti-c while the Baby; group O positive with Rh phenotype R1r (CDe/cde). Further workup for the father showed similarity with baby's blood group. *Learning Points:* Over the last few decades the spectrum of HDN has changed. The most concerned fact is that, some of these occurred in Rh D positive women. Antenatal screening in all pregnant women needs to be initiated, since Rh D positive women are just as likely as D negative women to form alloantibodies.

**HM-59. Carry-over effect of high performance liquid chromatography method**

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*Introduction:* Carry-over, defined as sample left over from a previous injection that may co-elute with analytes of interest and often interfering with accurate quantitation, is one of the known limitations in high performance liquid chromatography (HPLC) which needs troubleshooting. In this study, we report 2 cases of hemoglobin A<sub>2</sub> (Hb A<sub>2</sub>) level discrepancy between HPLC and capillary electrophoresis (CE). *Case Report:* Both cases were asymptomatic female in reproductive age who were screened for thalassemia. The full blood count for the first and second case were: Hb 11.7 g/dL and 9.4 g/dL, red blood cell 4.52x10<sup>6</sup>/μL and 4.10x10<sup>6</sup>/μL, mean corpuscular volume 81.6 fL and 77.6 fL, mean corpuscular hemoglobin 25.9 pg and 22.9 pg, respectively. Iron profile was normal for the first case but not done for the second case. Both cases showed hypochromia picture in peripheral blood film. HPLC done in Selayang Hospital showed raised Hb A<sub>2</sub> level of 4.1% and 4.0%. Second method was done at Institute for Medical Research using CE method and showed normal Hb A<sub>2</sub> level of 2.5% and 2.3%. Upon further investigation, these 2 samples were analyzed immediately after a sample of homozygous Hb E, which carries Hb A<sub>2</sub> level of 75.5%. CE method showed Hb A<sub>2</sub> level were within normal range. Following this incident, we will rerun the subsequent samples with borderline Hb A<sub>2</sub> level whenever there is preceding high Hb A<sub>2</sub> level (>13%). *Learning Points:* Hb A<sub>2</sub> determination plays a key role in thalassemia screening. However, as the normal Hb A<sub>2</sub> window is very narrow (2.0-3.3%), it is critical to conduct a detailed technical work and clinical interpretation to avoid misdiagnosis. As in our case, we managed to escape from misdiagnosing both patients as Beta-thalassemia trait. This proves that HPLC and CE are complementary techniques especially in cases which renders HPLC unable to separate Hb A<sub>2</sub> sufficiently from other Hb variants.

**HM-60. Haemolytic crisis in haemoglobin H patient**

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*Introduction:* Haemoglobin H (Hb H) disease is a form of alpha-thalassemia with wide spectrum of phenotype and genotype presentations ranging from mild to severe clinical manifestations. As it has high prevalence in South East Asia, prospective and systematic studies of the natural history of Hb H disease should be implemented so that potential risk factors associated with severe disease could be identified and hence would navigate course of treatment in future. *Case Report:* We present a moderate to severe haemolytic disease in a 44-year-old non-transfusion dependent Hb H patient. Her blood group is A positive R1R1 Jka+b- Fya+b-, and she had been receiving filtered phenotyped blood product due to multiple times of blood transfusion received in 2013. She was transfused in daycare but developed haematuria at home and thus further work up done suggesting of haemolytic crisis. Pre-transfusion Hb is 6.9 g/dL while post-transfusion Hb is 6.2 g/dL and further drop to 5.2 g/dL. Other laboratory indices are raised, reticulocyte count is 10.15%, LDH is 1199 U/mol, total bilirubin is 84 μmol/L, urine FEME shows blood (3+). Full blood picture report shows anisocytosis, polychromasia, microspherocytes and dimorphic picture. Direct Coomb's test reveal negative result and no antibody detected in antibody identification result. Few fragmented and target cell seen. Similar trend seen in transfusion 3 weeks earlier where the Hb is 6.7 g/dL (pre-transfusion) and 6.9 (post-transfusion), reticulocyte count is 11%, LDH is 1204 U/L and total bilirubin is 45 μmol/L. There is increasing pattern of blood transfusion

in recent years where she had been transfused 3 times in 2017, 1 time in 2018, but she already received 3 times transfusion in the first quarter of 2019, with no increment of Hb. Clinically, she has splenomegaly about 10 cm on palpation. She was diagnosed with hyper-haemolysing syndrome secondary to haemolytic transfusion reaction and treated with immunoglobulin and corticosteroid regime.

#### MM-61. Susceptibility pattern of *Burkholderia pseudomallei* isolates in Negeri Sembilan, Malaysia

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**Introduction:** Antibiotics resistance of *Burkholderia pseudomallei* has been reported in few studies. The aim of this study was to determine the *in vitro* antibiotic susceptibility patterns of *B. pseudomallei* isolated in Negeri Sembilan. **Materials & Methods:** A total of forty-six *B. pseudomallei* non-repeat clinical isolates were isolated from October 2017 until June 2018 in Negeri Sembilan. All isolates were subjected to Minimum inhibitory concentration (MIC) determination using E-test method (bioMérieux) to five antibiotics namely, ceftazidime, imipenem, amoxicillin/clavulanic acid, co-trimoxazole and tetracycline. The MIC ( $\mu\text{g/mL}$ ) interpretation was carried out following the CLSI guideline M45-A2. In addition, 27 from total of *B. pseudomallei* isolates had additional MIC tested for meropenem and interpretative criteria outlined by the E-test manufacturer for aerobes were followed as no breakpoint interpretation in EUCAST and CLSI. **Results & Discussion:** This study demonstrates all *B. pseudomallei* isolates were 100% susceptible to ceftazidime while 97.8% were susceptible to imipenem, amoxicillin-clavulanic acid, tetracycline and co-trimoxazole. One isolate that was intermediately resistant to imipenem, also had co-resistance to amoxicillin/clavulanic acid and tetracycline. From our study, one isolate was found to be resistant to co-trimoxazole alone. There were no resistant documented from all 27 isolates tested for meropenem. These findings were comparable with a study from IMR which has shown that *B. pseudomallei* isolates from Malaysia were also highly susceptible. Meropenem has been used for patient with severe melioidosis which associated with good outcome. However, EUCAST and CLSI do not provide a standard for assessing of susceptibility and breakpoint interpretation of *B. pseudomallei* to meropenem. It is important to have clinical breakpoints for meropenem as we might wrongly interpret the susceptibility as treatment failure with meropenem is possible. **Conclusions:** *B. pseudomallei* isolates in Negeri Sembilan were still susceptible to all recommended antimicrobial agents used for the treatment of melioidosis. However, regular monitoring is needed to detect any emergence of resistance.

#### MM-62. Distribution of Group B *Streptococcus* and its antibiotic sensitivity pattern among isolates in Kelantan: A 5-year review

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**Introduction:** Group B *Streptococcus* (GBS; *Streptococcus agalactiae*) is a well-known causative agent for invasive disease in pregnant mother and newborns. Currently, the organism has emerged as an important cause of morbidity and mortality among non-pregnant adults with underlying medical conditions. The study on the epidemiology and characterization of GBS infections in Malaysia remain limited. The aim of this study is to review the distribution of GBS isolates in Kelantan population. **Materials & Methods:** A retrospective laboratory based on analysis of GBS isolates from two general hospital in Kelantan (Hospital Raja Perempuan Zainab II and Hospital Universiti Sains Malaysia) from January 2014 to December 2018 were done. Antimicrobial susceptibility was determine using a disc diffusion method and interpreted according to the Clinical and Laboratory Standards Institute (CLSI). **Results & Discussion:** A total of 7649 of GBS were isolated in 2014 till 2018. GBS isolates mainly from adults 91.4% (n=6597) which include pregnant and non-pregnant mother, 4.3% (n=306) elderly age and remaining 2.3% (n=165) and 2.0% (n=147) were from pediatric and neonate groups respectively. Majority of the GBS organism 68.17% (n=5005) were isolated from vaginal swab samples. The remaining 31.83% (n=2337) were from various samples such as blood 13.13% (n=329), swab and pus 42.06% (n=1054), tissue 20.2% (n=506) and urine 16.65% (n=417). Susceptibility rates to penicillin and erythromycin were 95.3% and 89.33% respectively, while susceptibility rate for clindamycin was 87% but it was tested in one center only. **Conclusions:** GBS isolates are common in adult especially among pregnant women. However, the isolation of GBS isolates in soft tissue sample are increasing. The organism showed good sensitivity among commonly used antibiotics. Additional data is needed for determination of prevalence among pregnant and non-pregnant adults.

#### MM-63. Isolation and characterization of lytic bacteriophages infecting *Klebsiella pneumoniae* from sewage samples

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**Introduction:** *Klebsiella pneumoniae* is a Gram-negative bacterium that can cause different types of infections such as pneumonia, septicemia, wound infections and meningitis. *Klebsiella pneumoniae* is one of the top aetiological agents for nosocomial infection, and it has gained its notoriety with the emergence of multidrug resistance to beta lactam and carbapenem antibiotics. The emergence of multidrug resistant *Klebsiella pneumoniae* is reverting mankind to the pre-antibiotics era. In this study, we explored the possibility to isolate and characterize bacteriolytic bacteriophages from our local sewage as potential antimicrobial



candidates against *Klebsiella pneumoniae*. **Materials & Methods:** Five lytic *Klebsiella* bacteriophages namely  $\phi$ KPaV03,  $\phi$ KPaV04,  $\phi$ KPaV08,  $\phi$ KPaV10 and  $\phi$ KPaV12 were isolated from the raw sewage at Universiti Malaysia Sarawak (UNIMAS) sewage runoff and characterized based on their biological properties, such as their plaque and structural morphologies, host range, growth curve, bacteriophage multiplicity of infection (MOI) and structural protein composition. **Results & Discussion:** These bacteriophages have large burst size with high titer assay between  $10^8$ - $10^{12}$  pfu/mL and were predominantly stable at 4°C. Two among the five bacteriophages were capable of efficiently lysing more than five *Klebsiella pneumoniae* strains out of 18 clinical and community-acquired isolates from Borneo Medical Centre (BMC) and students of UNIMAS, respectively. These bacteriophages also exhibit several properties indicative of potential utility in phage cocktails and phage-antibiotic synergy (PAS) approaches in reducing antibiotic-resistant *Klebsiella pneumoniae* strains. **Conclusions:** The use of bacteriolytic bacteriophages as an alternative to antibiotics treatment is not new and numerous clinical trials have been carried out with excellent safety records and are considered as risk group 1 agents. This study confirms that potent bacteriolytic bacteriophages can be easily isolated from local raw sewage and be potentially developed into in-house anti-*Klebsiella pneumoniae* therapeutic agents.

#### **MM-64. Prevalence, clinical manifestations and predictors of immune reconstitution inflammatory syndrome in HIV-infected patients started on HAART in 2017 in Hospital Sungai Buloh: A retrospective study**

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**Introduction:** Highly active antiretroviral therapy (HAART) has significantly reduced HIV-associated morbidity and mortality. The access to HAART in the last decade has improved, especially in low- and middle-income countries including Malaysia. However, a subgroup of patients experiences paradoxical clinical deterioration despite satisfactory control of viral replication and improvement in CD4 T-lymphocyte counts. This condition is known as immune reconstitution inflammatory syndrome (IRIS) which occurs due to infectious and non-infectious aetiologies. Incidence of IRIS varies according to population and the clinical manifestations are wide with increasing symptoms and aetiologies being reported. Our objective is to determine the prevalence, clinical manifestations and predictors of IRIS in Hospital Sungai Buloh, a reference centre for infectious diseases in Peninsular Malaysia. **Materials & Methods:** A retrospective study of 256 HIV-infected patients who were started on HAART between 1 January 2017 and 31 December 2017 in Hospital Sungai Buloh. Medical records were reviewed to identify clinical events consistent with IRIS after HAART was initiated. Relevant laboratory parameters were obtained from Laboratory Information System (LIS). **Results & Discussion:** From 256 patients, majority was males (92.2%) of Malay ethnicity (53.5%) and aged between 26-50 years old (88.7%). IRIS was identified in 45 (17.6%) of patients. The most common IRIS cases were *Mycobacterium tuberculosis* infections (53.3%), followed by pneumocystis pneumonia (11.1%) and talaromycosis (6.6%). Two cases of each toxoplasmosis, herpes zoster infection, cytomegalovirus infection and salmonellosis were identified. Only one case of non-infectious IRIS (subacute lupus erythematosus) was observed. Baseline CD4 T-lymphocyte count of less than 100 cells/ $\mu$ L (OR 7.14, 95% CI: 3.28-15.59;  $p < 0.001$ ) and baseline viral load of more than 5.5 log (OR 3.56, 95% CI: 1.39-9.14;  $p = 0.008$ ) are independent predictors for developing IRIS. **Conclusions:** Non-infectious IRIS does occur despite commoner infectious aetiologies. Patients with low CD4 T-lymphocyte count and high viral load at HAART initiation are at higher risk of developing IRIS.

#### **MM-65. Determination of specific antigenic protein for detection of *Burkholderia pseudomallei* infection**

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**Introduction:** *Burkholderia pseudomallei* is the causative agent for melioidosis, a disease endemic in Southeast-Asia and Northern Australia. The disease causes great deal of morbidity and mortality. Culture remains as the current gold standard diagnosis for melioidosis. The method requires lengthy time. Upon successful isolation, identification of the organisms using panels of biochemical testing is non-definitive as reactions produced are similar with other bacteria such as *Pseudomonas* spp., *Burkholderia cepacia*, *Burkholderia vietnamiensis* and *Stenotrophomonas maltophilia*, requiring additional test for confirmation. Serological method is not widely available. The aim of this study is to identify specific protein/s in *B. pseudomallei* that can be used as target antigen/s for development of diagnostic tool. **Materials & Methods:** Purified proteins were obtained from overnight culture of *B. pseudomallei* isolates. The proteins were subjected to 1D and 2D gel electrophoresis to separate them based on molecular weight. Western blotting was performed using reactive human sera against *B. pseudomallei*. The proteins were also tested against sera reactive for Leptospirosis, Q fever and Brucellosis. The potential antigenic proteins were identified and sent for sequencing. **Results & Discussion:** Five protein spots sequenced were identified as groL1 chaperonin (57kDa/pI5.13), NAD dehydratase (22kD/pI6.7), oxoacid CoA transferase A subunit (25kD/pI5.5), oxoacid CoA transferase B subunit (22kD pI4.7), and Phasin granule associated protein (20kD/pI5.9). Among all, groL1 chaperonin protein was the most suitable candidate. The protein did not exhibit cross reactivity with sera reactive for other diseases. **Conclusion:** GroL1 chaperonin protein is a potential antigen to be used in serological test for diagnosis of melioidosis.

**MM-66. Emergence of class D  $\beta$ -lactamase (bla<sub>OXA-23</sub> and bla<sub>OXA-24</sub>) genes among multidrug-resistant *Acinetobacter baumannii* isolated from a tertiary hospital in Malaysia**

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**Introduction:** *Acinetobacter baumannii*, a Gram-negative opportunistic pathogen, commonly associated with nosocomial infections including pneumonia, bloodstream, urinary tract and wound infections. In current practices, carbapenems; a broad-spectrum beta-lactam antibiotic is one of the treatment of choices for these infections. Unfortunately, treatment options are limited as this organism has developed high antibiotic resistance due to production of carbapenemases. Hence, these warrant urgent need for alternative treatment. To facilitate development of drugs, this study focuses on surveillance and genetic characterization of multidrug-resistance *Acinetobacter baumannii*. Preliminarily, the mechanism of carbapenem resistance was investigated. Carbapenem resistance is conferred by carbapenemases, active efflux of drugs and target site modification. **Materials & Methods:** In this prospective study, thus far 60 isolates of *Acinetobacter baumannii*, from a tertiary hospital in Malaysia was collected. The samples were isolated from patients in the intensive care unit (ICU), coronary care unit (CCU), neonatal intensive care unit (NICU), high dependency ward (HDW), and other general wards. The source of the samples includes tracheal aspirate, bronchoalveolar lavage, blood, cerebrospinal fluid and others. Standard biochemical methods were performed to confirm the identity of the isolates and antimicrobial susceptibility test was carried out based on CLSI guidelines. The antibiotics tested include imipenem (IMP), ceftazidime (CAZ), amikacin (AN), gentamicin (GN) and ciprofloxacin (CIP). The isolates were tested for presence of bla<sub>OXA-23</sub>, bla<sub>OXA-24</sub> genes and insertion elements flanking these genes using PCR. **Results & Discussion:** Preliminary results revealed class D  $\beta$ -lactamase (bla<sub>OXA-23</sub>) to be the most prevalent gene amongst the isolates tested. As yet, gene encoding bla<sub>OXA-24</sub> has not been detected among our isolates. **Conclusions:** This finding is in correlation with previous reports from Malaysia suggesting that bla<sub>OXA-23</sub> plays an important role in carbapenem resistance amongst isolates circulating in Malaysia. However, other mechanism of resistance needs to be elucidated to conclude the orchestrated genes responsible towards emergence of carbapenem resistance.

**MM-67. Isolation and characterization of bacteriophage T27 infecting *Acinetobacter baumannii***

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**Introduction:** *Acinetobacter baumannii* is a nosocomial pathogen capable of causing hospital-acquired wound, urinary tract and respiratory tract infections. *A. baumannii* has increasing resistance to antibiotics dramatically reducing the number of antibiotics available for the treatment of infection associated with this pathogen. Due to the limited therapeutic options for *A. baumannii* infection, the discovery of alternative therapy is needed to overcome this problem. Thus, the objectives of this study are to screen and characterize specific bacteriophages capable of eliminating a broad host of multidrug-resistant *A. baumannii* isolates from patients of Sarawak General Hospital. **Materials & Methods:** The bacteriophages were screened and isolated from sewage water and screened using double-layer agar method. **Results & Discussion:** Bacteriophage T27 was successfully isolated from sewage water from Kuching centralized sewage plant and found to be lytic against *Acinetobacter baumannii* clinical strains isolated from Sarawak General Hospital. Phage T27 was able to infect and lyse 27% (10/37) multidrug-resistant clinical *A. baumannii* clinical strains forming clear plaques. The phage is classified under the *Myoviridae* family with an icosahedral head of 89 nm in diameter and a contractile tail of 19 nm in diameter by 135 nm in length. Phage T27 exhibited stability at a wide pH range notably between pH 6 to 10 and temperature of up to 40°C for an hour. **Conclusions:** The versatile characteristics of phage T27 make T27 an attractive potential candidate for phage cocktails in therapeutic application to control *A. baumannii*-associated hospital acquired infection in Sarawak.

**MM-68. A rare case of *Corynebacterium bovis* pulmonary infection in Sibul Hospital**

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**Introduction:** *Corynebacterium bovis*, a Gram-positive rod that is contagious and well-known of causing bovine mastitis. Its infection in humans is rarely reported and has not been described as a part of human microbiota compared to the other *Corynebacterium* species. Therefore, identification of organism by biochemical methods is challenging. **Case Report:** A 45-year-old man, with underlying unknown health status first presented with sudden onset of seizure and non-specific constitutional symptoms. Patient was initially treated as chest infection to rule out pulmonary tuberculosis. However, his condition kept deteriorating despite various types of antibiotics. Thorough investigations carried out were unable to elicit the cause of his deterioration. Case was then referred to Rheumatology team whereby broncho-alveolar lavage was suggested. Surprisingly, pure, <10<sup>4</sup> CFU/mL *Corynebacterium bovis* was identified by BBL Crystal™ Gram-Positive Identification System from both of his broncho-alveolar lavage specimens which yielded 0.82 level of confidence. Patient's antibiotic was changed to intravenous vancomycin after culture report was released. Even so, his condition did not improve and eventually he passed away due to sepsis secondary to severe pneumonia. **Discussion:** Cases reported *Corynebacterium bovis* associated with human disease in

the past were uncommon, non-specific and unrelated to each other with unknown source of infection. These included bacterial endocarditis, chronic otitis media, persistent leg ulcer, prosthetic joint infection and eye infection. *Learning Points:* This is a rare case of *Corynebacterium bovis* pulmonary infection that had never been reported. It is worrying that this organism portrays lethal potential in causing human lung infection with unknown source. This organism should not be underestimated and should be tackled before it starts to spread among humans. Both the microbiological diagnosis and appropriate antimicrobial susceptibility tests should be carried out promptly before it is too late to save the patient.

#### MM-69. An outbreak of *Ralstonia pickettii* bloodstream infection associated with contaminated chlorohexidine solution

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*Introduction:* *Ralstonia pickettii* grows in moist environment and is associated with contaminated solutions used in healthcare facilities especially disinfectants such as Chlorhexidine. It is commonly associated with nosocomial infections and it has also been reported causing bloodstream infection. *Case Report:* The authors noted a sudden increase of *Ralstonia pickettii* isolation from blood culture specimens from a tertiary hospital in Sarawak. These specimens were taken from 7 different wards within a month. Thus, we had done contact tracing and tried to identify the source and to intervene the ongoing infections. The cases were identified as patients with positive blood cultures for *Ralstonia pickettii* during the outbreak period. Various samples from suspected sources were then taken and analysed microbiologically. A total of 13 samples taken including environmental samples and showed 9 samples isolated *Ralstonia pickettii* from which the samples were taken from chlorohexidine solution 1:2000 (0.05%) in aqueous, distilled water and utensils which are used to make the chlorohexidine solutions. All culture specimens from 21 case patients isolated *Ralstonia pickettii* and almost all patients related with history of fever prior to blood culture takings procedure. Fourteen clinical isolates were closely related except one clinical isolate. However, strain-relatedness between the probable source and clinical isolate were not able to be demonstrated as the isolates from probable source were not growing to proceed for Pulsed-field gel electrophoresis (PFGE). We report *Ralstonia pickettii* outbreak occurring among patients with probable source was from contaminated chlorhexidine solutions are used for skin disinfection for blood culture procedure. The reported cases were most likely caused by contamination during preparation of the solution in the pharmacy. *Learning Points:* A prompt investigation and adequate preventive measures by the infection control team, clinicians and hospital administration is important to prevent similar occurrence.

#### MM-70. Mix pathogens in diabetic foot ulcer patient who refused surgical intervention: Case report and literature review

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*Introduction:* Diabetic foot ulcer (DFU) is a significant complication of diabetes mellitus and often precedes lower limb amputation. Polymicrobial organisms are common in severe cases of DFU that can lead to fatality without surgical intervention. *Case Report:* A 45-year-old man with DFU developed polymicrobial organisms septicaemia namely, *Arcanobacterium haemolyticum* and *Streptococcus constellatus*. *A. haemolyticum* can cause wound infection in immunocompromised patients and a common causative agent for pharyngitis. Meanwhile *S. constellatus* commonly associated with abscesses and bacteremia. Both organisms were identified with MALDI-TOF MS with excellent identification. Minimum inhibitory concentration (MIC) was done for both isolates. The MIC interpretation was carried out following the CLSI guideline M45 (*A. haemolyticum*) and M100 (*S. constellatus*). *A. haemolyticum* shows susceptibility to penicillin, vancomycin, and meropenem meanwhile *S. constellatus* shows susceptibility to penicillin. During this current admission, wound debridement of the left foot was done. Intraoperatively, noted a pocket of pus discharge tracking into the lateral of the calcaneum with osteomyelitic changes of the midfoot bone. After the procedure, patient was advised for below knee amputation however he strongly refused and only keen for antibiotic treatment. Eventually, the patient agreed for below knee amputation and he managed to fully recover from his sepsis condition. *Learning Points:* Clinicians should use broad spectrum antimicrobial therapy targeting Gram positive cocci, Gram negative bacilli and obligate anaerobic organisms in DFU cases. Early and aggressive surgical interventions may reduce the risk for above-the-ankle amputation and length of hospitalization.

#### MM-71. A case of sepsis secondary to hospital-acquired *Corynebacterium pseudotuberculosis* pneumonia in Hospital Sibul

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*Introduction:* *Corynebacterium pseudotuberculosis* is a facultative anaerobic pleomorphic Gram-positive bacillus. It is a well-recognised pathogen in veterinary medicine infecting ungulates, predominantly sheep and goats but is a relatively rare occurrence in human. We report a case of sepsis secondary to hospital-acquired *Corynebacterium pseudotuberculosis* pneumonia. *Case Report:* A 34-year-old man with no premorbid presented with an alleged road traffic accident in which he sustained an intra-abdominal injury. Patient was initially treated conservatively but after 4 days of admission, an emergency exploratory

laparotomy with small bowel resection and double barrel stoma was performed after his condition deteriorated. Post-operatively, patient developed sepsis secondary to pneumonia. Subsequent left and right bronchoalveolar lavage specimens sent grew pure significant growth ( $>10^5$  CFU/mL by using semi-quantitative method) of *Corynebacterium pseudotuberculosis* identified using BBL Crystal™ Gram-Positive Identification System which yielded 0.99 level of confidence. This organism was presumptive susceptible to gentamicin and vancomycin. Following the release of this culture results, patient's antibiotic was changed from intravenous piperacillin/tazobactam to intravenous vancomycin. Despite started on intravenous vancomycin, patient condition did not improve, and he developed left sided pleural effusion. His condition worsened following chest tube insertion and unfortunately, he later succumbed to his condition. **Discussion:** Previous reported *Corynebacterium pseudotuberculosis* pneumonia cases were described in veterinary students who had worked in veterinary laboratories. Other than pneumonia, *Corynebacterium pseudotuberculosis* has been reported to cause necrotizing granulomatous lymphadenitis in human. **Learning Points:** Since *Corynebacterium pseudotuberculosis* infection may lead to detrimental consequences including laboratory associated infection, awareness amongst laboratory personnel about this organism needs to be created as this isolate may be regarded as non-significant and wrongly dismissed as a 'skin diphtheroid'. In addition, management guidelines for treating this organism also need to be established.

#### MM-72. A case of *Helcococcus kunzii* infected lower limb wound in Hospital Sibul

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**Introduction:** *Helcococcus kunzii* is a non-motile, catalase negative, facultative anaerobic Gram-positive coccus. This avirulent nonpathogenic normal human skin flora can act as a human pathogen, primarily recovered from infected wound of lower limbs or cultured from skin and soft tissue abscesses. We report a case of *Helcococcus kunzii* infected lower limb wound in Hospital Sibul. **Case Report:** A 42-year-old man with underlying right foot fibrosarcoma, done excision of fibrosarcoma, and free flap procedure of the right foot in Sarawak General Hospital in 2005. He presented with painful, erythematous and swollen right foot associated with bullae formation and pus discharge. Multiple wound debridement over the right foot and ankle done during the hospitalization in view of poor wound condition where *Helcococcus kunzii* was isolated and identified by Matrix-assisted laser desorption/ionization-Time of Flight (MALDI-TOF) from different culture samples. This organism was presumptive susceptible to Clindamycin, Erythromycin, Fusidic acid, Gentamicin, Oxacillin, Penicillin, Rifampicin, and Co-trimoxazole. Oral Erythromycin was given following the release of the culture results, for total of one month. Upon completion of antibiotic, patient able to ambulate without crutches, with clean wound over right foot. He was discharged home with analgesic with outpatient orthopaedic clinic appointment. **Learning Points:** *Helcococcus kunzii* is a normal human skin flora which can be pathogenic when patient is immunocompromised or particularly having infected wound of right lower limb, skin and soft tissue abscesses. This organism might be neglected due to its slow growing resulting in an inappropriate choice of antibiotics being used for the patient. A proper method to identify the organism must be implemented and appropriate antimicrobial susceptibility testing need to be established as soon as possible.

#### MM-73. Neurological melioidosis in young lady

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**Introduction:** Melioidosis is an infection caused by *Burkholderia pseudomallei*, an aerobic, non-spore forming gram negative bacillus. The disease is more prevalent in the tropics and leads to significant morbidity and mortality. It characteristically produces widespread caseous lesions and abscesses, and can present with varied clinical manifestations. Pneumonia is the commonest manifestation. Neurological manifestation of melioidosis is uncommon. **Case Report:** This is a case of 25-year-old Malay lady with no comorbid, complaints of fever and lethargy for 2 weeks. Blood gas shows metabolic acidosis with blood glucose 24 and urine ketone 2+. Patient was treated as severe diabetic ketoacidosis with possible melioidosis and started with intravenous ceftazidime 1g 8 hourly. In ward, she was progressively tachypneic with persistent temperature spike. Lung examination revealed crepitation on right side and left middle zone. Patient was intubated in view of impending respiratory collapse and her antibiotic was escalated to intravenous meropenem 1g 8 hourly. She was then transferred to intensive care unit and required inotropic support and hemodialysis. Blood culture revealed *Burkholderia pseudomallei*. Oral trimethoprim-sulfamethoxazole was also started. Patient's condition improved and had self-extubated in intensive care unit. However, she developed 2 episodes of fit in ward. Central nervous system examination was unremarkable and contrast enhanced CT brain revealed features subdural collection. Hence, she was treated as neurological melioidosis. Intravenous meropenem dose was increased to 2g 8 hourly and completed for 33 days and continue her oral trimethoprim-sulfamethoxazole with tablet folic acid. Repeated CT brain after 3 weeks showed resolved subdural collection and clinically improving. **Learning Points:** Neurological melioidosis is an unusual presentation of melioidosis where the diagnosis can be easily missed. Knowledge of the protean manifestations of melioidosis is importance in order to detect and treat this potentially fatal infection appropriately, especially in endemic countries.

**MM-74. A fatal case of *Trichosporon* fungemia in a hematologic malignancy patient during anidulafungin treatment**

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**Introduction:** *Trichosporon* fungemia is increasingly recognized as an opportunistic infection, causing fatality in patients with underlying hematologic malignancies. **Case Report:** A 22-year-old lady, previously healthy, complained of spontaneous bruising for few days and feeling unwell. On admission, she was hemodynamically stable. Multiple bruises noted at both her upper and lower limb and no hepatosplenomegaly appreciated. Her full blood picture showed bicytopenia with leukocytosis, and further diagnosed with acute lymphoblastic leukemia, confirmed by bone marrow study and other diagnostic modalities. She was started on chemotherapy UKALL XII induction phase. After two weeks, she developed febrile neutropenia and started on several antibiotics. She was also covered with oral fluconazole. After a month, she had spiking temperature and acute liver impairment. Chemotherapy and fluconazole were stopped, blood culture taken, grew *Klebsiella pneumoniae* and she was covered with meropenem. Her condition worsened as she was intubated and admitted to ICU with septicemic shock, acute kidney injury and DIVC. Another blood culture was taken. Blood cultures grew yeast cells. On SDA, colonies were white to cream-coloured, powdery, suede-like to farinose with radial furrows. The colonies were then subjected to API 20C AUX test. Anidulafungin was started soon as blood culture grew yeast cells and treated as Candidemia. Two days later she succumbed to death, the culture identified as *Trichosporon asahii* the next day. **Discussion:** Antifungal triazoles have the best activity in disseminated *Trichosporon* infections especially the newer voriconazole. Unfortunately, the patient was put on anidulafungin, a type of echinocandins, which have low activity against *Trichosporon* spp. and not recommended for disseminated trichosporonosis. Early diagnosis of *Trichosporon* infection is important as different antifungal could have been initiated. **Learning Points:** Clinicians should have high index of suspicions of *Trichosporon* infection in haematologic malignancy patients where echinocandins are not an option.

**MM-75. A dangerous threat lurking ahead: A case report**

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**Introduction:** The world is facing the threat of a rapidly emerging multidrug resistant pathogenic yeast, *Candida auris* which causes severe invasive infections associated with high morbidity and mortality. We report a first fatal case of *Candida auris* fungemia in a tertiary hospital in Sarawak. **Case Report:** A 65-year-old local native lady with underlying diabetes mellitus and hypertension, presented to a district hospital with 2 days history of watery diarrhoea, vomiting more than 10 episodes a day as well as epigastric pain. On arrival to our hospital, she became hypotensive and was intubated for impending respiratory collapse. Her care was transferred to intensive care unit (ICU) whereby she received mechanical ventilation and renal dialysis. She was treated for infective acute gastroenteritis and later nosocomial infection on day 5 post admission. Blood and stool culture taken on admission were negative. On day 14 of admission, she turned septic and developed hematochezia, needing blood transfusion. Bedside sigmoidoscopy showed multiple bleeding rectal ulcers. Blood culture grew yeast cells which were identified as *Candida auris*, using Matrix Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry (MALDI-TOF; Biotyper, Bruker Daltonics, Germany) with a score of 2.07. This was later confirmed using polymerase chain reaction method. She was commenced on intravenous micafungin. Her blood cultures also grew *Corynebacterium striatum* and coagulase negative *Staphylococci*. However, she died on day 28 post admission after another bout of hematochezia. **Discussion:** The availability of MALDI-TOF allowed prompt identification of *Candida auris* in our patient and introduction of strict infection control measures. Risk factors present were underlying gastrointestinal pathology, ICU care, urinary and central venous catheter use, renal dialysis as well as prolonged usage of broad-spectrum antibiotics. **Learning Points:** The unexpected isolation of *Candida auris* in our case signalled its presence in healthcare setting in Sarawak.

**MM-76. A rare complication of oropharyngeal infection: A case report of Lemierre's syndrome**

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**Introduction:** Lemierre's syndrome is a serious rare complication of oropharyngeal infection that was first described in early 1900s that initially linked the syndrome with anaerobic sepsis following an oropharyngeal infection. It affects primarily healthy young adults and may also present in school-aged children. We report a case of Lemierre's syndrome caused by typical anaerobic organism, *Fusobacterium necrophorum*. **Case Report:** A 22-year-old gentleman, previously no known medical illness presented to the emergency department in sepsis. He has history of upper respiratory tract symptoms with fever. He was given fluid resuscitation and subsequently required inotropic support as blood pressure was unable to maintain. Initial investigation showed viral picture. However, dengue serology was negative. A cervical radiography was done revealed prevertebral soft tissue thickening. He was then proceed with computer tomography scan of the neck revealed an ill-defined hypodense region suggestive of infection/inflammation at the left parapharyngeal space adjacent to the left palatine tonsil, extension inferiorly to the retropharyngeal soft tissue until the pyriform sinus, with no brain abscess and patent bilateral internal jugular veins. Blood culture was taken and intravenous ceftriaxone was started empirically. Blood culture grew *Fusobacterium necrophorum*

(identified by MALDI-TOF MS, score: 2.29). The diagnosis was revised to Lemièrre's syndrome, antibiotic treatment was changed to intravenous augmentin for 2 weeks. There was no surgical intervention. Subsequently he was discharged home well. *Discussion:* Although our case is not associated with internal jugular vein thrombosis, but based on the literature review, it is found to be present in only less than 50% of cases but higher association of anaerobic organisms especially *Fusobacterium necrophorum* with this condition. *Learning Points:* There is no standard criterion for diagnosis of this rare yet potentially devastating disease, but it is hoped that the physicians are well aware of this condition as prompt diagnosis and management will eventually give a better outcome to the patients.

#### MM-77. A case series on diagnostic dilemma on *Microbacterium* spp. identification

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*Introduction:* *Microbacterium* spp. is yellow-pigmented Gram-positive bacilli that have been isolated from human specimens. However, the difficulty to identify the organism in a laboratory without widely accessible sequencing services creates a diagnostic dilemma to the microbiologists. We describe the difficulties in identifying three cases of *Microbacterium* spp. isolated from our laboratory. *Case Report:* A 6-year-old boy with underlying Wilm's tumour stage IV presented with fever and poor appetite for 2 days. He was started on cefepime and blood culture from central line and peripheral were sent to rule out catheter-related bloodstream infection (CRBSI). Only central blood culture grew *Microbacterium* spp. that was regarded as colonizer. The colonies are yellow-pigmented, catalase positive and identification via Vitek-2 CBC card showed *Microbacterium* spp. with excellent identification. A 9-year-old boy with underlying B-ALL completed chemotherapy presented with fever for 3 days and blood culture from central line and peripheral were sent to rule out CRBSI. Both specimens grew *Microbacterium* spp. in which central grew more than 2 hours earlier than peripheral. The colonies are yellow-pigmented, catalase negative and identification via Vitek-2 ANC card showed *Microbacterium* spp. with excellent identification. A 50-year-old man with underlying diabetes mellitus and hypertension presented with shortness of breath for 2 days and treated as decompensated congestive cardiac failure. Blood culture sent isolated *Microbacterium lacticum* once and regarded as contaminants. The colonies are yellow-pigmented, catalase negative and identification via Vitek-2 CBC card showed *Microbacterium lacticum* with excellent identification. *Learning Points:* *Microbacterium* spp. possess a diagnostic dilemma to the microbiologists for identification. Difficulty in identification leads to misidentification of *Microbacterium* spp. as *Corynebacterium* species. Positive culture from immunocompromised patient especially those with central catheter should alert the microbiologist the possibility of *Microbacterium* spp. as it could lead to severe fatal disseminated human infection. Therefore, sequencing can be one of the alternatives to fasten the process of identifying *Microbacterium* spp.

#### MM-78. Pleural empyema: An atypical presentation of *Salmonella* Typhi infection

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*Introduction:* Typhoid fever remains a life-threatening infection which caused by *Salmonella* Typhi, a gram-negative, facultatively anaerobic bacillus. *S. Typhi* infections often produce gastroenteritis, enteric fever, bacteremia, and chronic carrier state. Localized infection may occur at any site often after bacteremia. Pulmonary involvement due to *S. Typhi* infection is rare. We present a case of pleural empyema, an atypical presentation of *S. Typhi* infection. *Case Report:* A 58-year-old man with underlying diabetes mellitus and superficial malignant fibrous histiocytoma presented with fever for 3 days associated with a sudden onset of shortness of breath. The patient was tachypnoeic, hypotensive and later requiring mechanical ventilation. CT pulmonary angiogram showed bronchopneumonia with severe left pleural effusion and adjacent lung collapsed. Left chest tube was inserted and drained out 800mls of pus. He was admitted to ICU, treated as severe pneumonia with left posterolateral chest wall abscess in septicemic shock. CT thorax showed a large multicystic lesion at posterolateral aspect of the left chest wall. Ultrasound guided drainage of left pleura was done. Both pus culture and cystic pleura fluid grew *Salmonella* Typhi which was sensitive to all other antibiotics tested with intermediate sensitivity to ciprofloxacin. Pleural fluid sent for PCR also positive for *S. Typhi*. No blood cultures positive for any organism. He was started on IV ceftazidime in view of strong suspicion for melioidosis but then escalated to meropenem as his condition worsened. He was discharged with oral trimethoprim-sulfamethoxazole for 2 weeks with an appointment to repeat chest X-ray. *Learning Points:* Pleural empyema is an atypical presentation of *S. Typhi* without evidence of bacteremia. There was no clinical suspicion of typhoid in view of patient did not present with gastrointestinal symptoms to suggest enteric fever. Without proper diagnosis and treatment, death will ensue, or patient can become a carrier with the possibility of recurrence. This is the first case of *S. Typhi* presented with pleural empyema being reported in Malaysia to our knowledge.

**MM-79. A case of ciliate protozoa *Colpoda* spp. (ciliata: Colpododae) detected in paediatric urine**

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**Introduction:** In the urine of a patient initially suspected acute glomerulonephritis (AGN) we have found ciliate protozoa *Colpoda* spp., both in vegetative and cystic form. Until recently, only 5 cases of *Colpoda* spp. found in human urine has been reported. **Case Report:** A 4-year-old girl presented with facial swelling and generalized abdominal pain, vomiting, poor oral intake, low urine output and fever for 2 weeks. Upon presentation patient was afebrile, normotensive, normal heart and respiratory rate, SPO2 100% under room air. Urine investigation noted patient having gross hematuria. Patient was admitted with first impression of AGN. Renal profile was normal. Ultrasound kidney-urinary bladder (KUB) also normal however gross hematuria persisted and urine microscopy showed ciliated protozoa *Colpoda* spp. No urine cast or stool parasite ova or cyst was found. Patient was diagnosed as ciliated protozoa (*Colpoda* spp.) urinary tract infection (UTI). Initial management was based on the diagnosis of AGN which include blood pressure monitoring, IV frusemide 15mg TDS, nephrotic chart, daily urine inspection (urine FEME), fluid restriction 260 mL/day (400 mL/m<sup>2</sup>), and oral penicillin 50 mg per kg QID for 5 days. After 5 days of treatment, patient recovered from facial swelling and abdominal pain. However, hematuria still persisted. Repeated urine microscopy showed no more protozoa seen. Patient was discharged home with oral bactrim. **Discussion:** This is the first ciliated protozoa, *Colpoda* spp. UTI reported in children and in Malaysia. The fact that both cases related to *Colpoda* spp. UTI in 2011 and 1968 was also having uricemia crisis cannot be a mere coincident. **Learning Points:** Many factors can contribute to the finding of this ciliate in the urine namely poor hygiene status or contaminated water. Urine microscopic examination is a must to exclude presence of microorganisms in the urine.

**FM-80. Cadaveric body weight estimation from regression analysis of corpse length and anterior abdominal subcutaneous fat thickness using computed tomography**

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**Introduction:** Forensic pathology has taken an important leap. Due to relatively low maintenance costs, short examination times, and ease of operation make computed tomography (CT) a widely used cross-sectional imaging technique in modern postmortem imaging. This study was to determine the regression formula for cadaveric body weight estimation using spine length, anterior abdominal subcutaneous fat thickness (ASCFT) and body weight (BW) of the Malaysian corpse bodies. **Materials & Methods:** Retrospectively, 107 corpses were analyzed to assess the correlation between the length of each corpse on post-mortem computed tomography (PMCT) by measuring the topogram length (TL), sternal length (SL) and thoracic column length (TCL) and compared them to the autopsy length (AL) using linear regression analysis. Similarly, we measured the anterior subcutaneous fat thickness (ASCFT) on both side at the level of the umbilicus and compared them to the autopsy weight (AW). Subsequently, multiple regression analysis technique was done to assess the correlation and significance between TL, SL, TCL and ASCFT with AW in order to derive regression equations for cadaveric body weight estimation. **Results & Discussion:** The findings of this study confirm and substantially extend earlier observations that PMCT as an accurate method for estimating length and weight of the body, and there is a good linear relationship between TL, SL and TCL compared to the length of the corpse and its weight. In our study, TL has the best correlation with coefficient of determination. ASCFT measurements showed a good correlation for both side with no significant different but poor correlation with AW. Multiple regression analysis showed a significant linear relationship using TL, SL, TCL and ASCFT with AW. **Conclusions:** PMCT can be used in the estimation of cadaveric height and weight. This is particularly important when dealing with incomplete corpses or mass disaster. The regression equation could also be applied for patients in emergency circumstances.

**FM-81. Get hold of the placenta. It is not too late!**

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**Introduction:** Examination of placenta provides an insight into the aetiology of stillbirth. Obstetricians and general pathologists have tendency to underestimate the significance of placental examination. We report a case of a perinatal death, where the placenta was retrieved from the burial site and was in fact the cause of death in the stillborn. **Case Report:** A 26-year-old lady, G2P1 at 28 weeks gestation, was investigated for persistent sudden left upper limb pain and numbness associated with bluish discoloration of the fingers. Further investigations revealed a left ulnar artery stenosis and she was suspected to have microvascular/connective tissue disease. During her admission, a fetal assessment performed showed absence of fetal heart activity. Her first child was born 2 years ago at 35 weeks with low birth weight of 1.28 kg. She subsequently underwent induction of labour and delivered a macerated stillborn. After a small focal sampling of the placenta in the labour room for

histopathological examination, it was handed over to the parents for burial purposes. A consent for autopsy was obtained afterwards. Upon request by the pathologists and with the consent of the parents, the placenta disc was immediately retrieved from the burial site within 24 hours. On thorough examination of the placenta, there was a significant area of infarction within the placental disc. Microscopically, there was decidual spiral arterioles vasculopathy. Both the macroscopic and microscopic changes were not seen in the initial tissue sampling. These underlying uteroplacental insufficiency were supportive evidences to the hypoxic mode of death identified at autopsy. *Learning Points:* Placental examination remains necessary as part of investigations in any stillbirth. In instances where a consent for autopsy cannot be obtained, the placenta may provide the answer to the cause of the perinatal death.

#### FM-82. Sudden unexpected death of infancy: The value of postmortem microbiological sampling

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*Introduction:* Sudden unexpected death of infancy (SUDI) refers to when the occurrence of death is sudden and not expected in previously healthy child. Infection is recognized as one of the leading identifiable causes of SUDI, and a significant proportion of currently unexplained infant deaths may be infection related, possibly mediated by abnormal systemic immune responses. We would like to share some of these cases and highlight the importance of microbiological investigations as part of investigations of SUDI. *Case Reports:* *Case 1:* A 2-month-old female, was found unresponsive on bed by the mother. Autopsy tissue histopathological examination showed acute stress changes in thymus and features of early pneumonic changes. Microbiology investigations isolated pure cultures of *E. coli* from blood, lungs and spleen tissue cultures. *Case 2:* A 2-month-old female, was found unresponsive by the father. There were history of vomiting and shortness of breath post-feeding the day before. Postmortem investigations concluded *Klebsiella pneumoniae* infection as primary cause of death. Additionally, there were features to suggest misalignment of pulmonary vein with pulmonary hypertension, enlarged heart with pleural effusions and chronic stress changes in thymus. *Case 3:* A 3-month-old female, with 2-week history of NICU admission after birth following meconium aspiration syndrome, was found unresponsive by the caretaker. Autopsy findings revealed lung changes in keeping with previous pneumonitis and Group B streptococcal sepsis. *Learning Points:* The postmortem microbiological investigations remain a critical value in investigations of SUDI. Moreover, these microbiological investigations will identify unexpected infections in cases with absence of histologically identifiable focus of infection. Appropriate and correct technique of postmortem microbiology sampling will increase the likelihood in identifying infection-related cause.

#### FM-83. Bird nest in a heart: A case report

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*Introduction:* Myocarditis is an inflammation of the heart muscle (myocardium). Myocarditis can affect heart muscle and heart electrical system, reducing heart ability to pump and causing abnormal heart rhythms. Symptoms include shortness of breath, chest pain, decreased ability to exercise, fatigue, ankle swelling and palpitations. We present a rare case finding in autopsy and clinically was not detected, who died of myocarditis. *Case Report:* A 14-year-old Malay boy brought in dead after 10 days onset of fever with history of tonic-clonic phase like-fitting a day after fever. Family brought to hospital for treatment and did a Computed Tomography (CT) of brain plain and with contrast as suspected meningitis but no evidence of meningitis was found. Other clinical investigation as blood investigation, blood culture and chest x-ray reveal normal. After all investigations done, patient and family demands for discharge after doctor told that CT brain was normal, and they wanted to seek for alternative traditional or conservative treatment. During 10 days of illness at home, family claimed that patient only had symptom of lethargy and loss of appetite despite having on and off fever. On day 10<sup>th</sup> of fever, patient had no appetite at all and more lethargic, parents did bring patient to hospital, but upon arrival, patient had no sign of life and confirmed death. Postmortem findings show yellowish fluid in pericardium around 320 mL fluid, vast of fibrinous attachment around pericardium to its wall. Pericardial fluid and cerebrospinal fluid cultures show *Staphylococcus aureus*. Rapid test HIV, blood for hepatitis B antigen and anti-hepatitis C virus reveal negative. A diagnosis of acute infective endocarditis is made. *Learning Points:* Auscultation must be done thoroughly to detect cardiac problem. As in this case, we doubt that auscultation had been done or had been thoroughly done.

#### FM-84. Asymptomatic hepatic granuloma probably caused by *Bacillus Calmette-Guérin* (BCG) vaccination found incidentally at autopsy: A case report

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*Introduction:* We present an incidental finding of asymptomatic hepatic granuloma probably caused by *Bacillus Calmette-Guérin* (BCG) vaccination in autopsy and clinically was not detected before. *Case Report:* A 48 days of life Malay baby boy brought in dead after founded by parents, baby's face turns pale and had frothy secretion from nostrils. Prior to that, parents told that baby had breastfed before putting to sleep on his father's arm on bed. Both parents slept on same bed and after



woke up; noted baby had changes as mention before. Otherwise, baby was healthy, no history of fever, flu, cough, vomiting, passing loose stool, fitting and others that suggest any illness. Baby was able to feed normally and active as usual. There was no history of suggesting other family members had suffered from active tuberculosis. Postmortem findings showed lividity more on posterior and right side of face and shoulder. No external injury. Internally, both lungs revealed hemorrhagic, liver showed hepatomegaly and other organs were grossly normal. Microscopically revealed proteinaceous or pink material in alveoli and bronchiole with presence of hemosiderin but Perl's iron stain was negative. There is no sign of inflammation nor granuloma in both lungs. H&E stain of liver section showed there is a granuloma in a liver. *Discussion:* In a child with a normal immune system a granulomatous skin reaction develops only at the site of BCG vaccination. If an individual has an underlying immunodeficiency this can lead to dissemination of the bacteria followed by widespread granulomatous inflammation. Cause of hepatic granuloma such as Tuberculosis, Visceral larva migrans, Hepatitis C, Primary biliary cirrhosis, autoimmune hepatitis, drug-induced, neoplasm and disseminated BCGitis. Disseminated BCG infection has an incidence of 1-20 per 10 million doses of vaccine, with a mortality of 50-80%. Tuberculosis could not be the definite cause of death as no suggestive finding during postmortem and microscopic examination. Ziehl-Neelsen stain showed negative for mycobacterium. Finding of hepatic granuloma was incidental. This infant had history of injection of BCG vaccination during birth and hepatitis B, two weeks before for the second dose injection. Therefore, hepatic granuloma that we found was most probably due to BCG vaccination after excluding all other possible cause. *Learning Points:* The cause of asymptomatic granuloma in this case was not identified, but BCG vaccination was considered the most likely.

#### GP-85. A comparison of whole slide imaging (WSI) viewers

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*Introduction:* Pathologists diagnose disease and guide therapeutic decision making through accurate interpretation of microscopic images on glass slides. With the advancement of technology, whole slide imaging (WSI) allows pathologists to view glass slides on computer monitor like navigating Google Maps. WSI consists of two processes. The first process is acquiring high quality images as tiled or stripes using high-resolution camera, combined with one or more high-quality microscope objectives, from glass slides. These individual images were then combined to produce a single whole slide image. The second process is viewing or analysing the scanned images using specialised software, i.e. virtual slide viewer. *Materials & Methods:* We have evaluated several WSI viewers based on the following features: Documentation, Data management, Usability, Visualisation, Flexibility and Segmentation. We also performed a case study using the various viewers. These viewers were downloaded from the website of the respective provider. *Results & Discussion:* Viewers evaluated included *CaseViewer*, *QuPath*, *Pathomation*, *ImageScope*, *Image J*, *Zen Blue* and *NIS-element*. We found that *CaseViewer* and *QuPath* are superior among the evaluated viewers for the prescribed features. However, certain software programs which are equipped with built-in function such as cell counts and interface with other programme languages such Matlab and Phyton could be the choice for the intended purpose. *Conclusions:* Hence, we would recommend the *CaseViewer* or *QuPath* for essential viewing of whole slide imaging.

#### GP-86. Association of body mass index, waist circumference and prevalence of proteinuria among the university students

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*Introduction:* An increasing prevalence of obesity regardless of age is endemic throughout the world. Obesity is associated with several chronic conditions including chronic kidney disease (CKD). However, the association of body mass index (BMI) and waist circumference (WC) with proteinuria has not been studied well. A study was conducted to determine the prevalence of underweight, overweight and obesity among the students from nursing programme, Faculty of Medicine and Health Sciences (Universiti Malaysia Sarawak); and to determine the association between BMI and WC with the prevalence of proteinuria. *Materials & Methods:* A cross-sectional study was held from August 2016 to May 2017 among 163 students using a pre-tested questionnaire and measured their BMI and WC. Participants were also tested for proteinuria by dipstick urinalysis. Participants with proteinuria were referred to the primary health care for further investigation. *Results & Discussion:* The study population included 23 males (14.1%) and 140 females (85.9%), age 19 to 28 years. Among male students, the prevalence of underweight, normal weight, overweight and obesity was 13.0%, 65.3%, 13.0% and 8.7% respectively whereas in female students, the prevalence was 17.2%, 62.1%, 11.4% and 9.3% respectively. Overall, 21.0% were high BMI (overweight/obese) (21.7% of males and 20.7% of females) in our study. The prevalence of normal WC and high WC among males was 73.9% and 26.1% respectively whereas in females, the prevalence was 70.7% and 29.3% respectively. Proteinuria was detected in 5 students (3.6%). Among these students, 3 were underweight and 2 had CKD stage II (eGFR: 60-89 mL/min/1.73m<sup>2</sup>). Prevalence of proteinuria was statistically significant in the underweight female group ( $p < 0.05$ ). *Conclusions:* The prevalence of proteinuria was significantly associated with underweight female students and the participants from the present study were found to be more obese than Malaysian national standard and university students in Malaysia.

**GP-87. The role of Epstein-Barr nuclear antigen 1 (EBNA-1) gene expression in nasopharyngeal carcinoma chromosome rearrangement**Tan Siew Huang<sup>1</sup>, Tay Siow Phing<sup>2</sup>, Sim Sai Peng<sup>1</sup>*Departments of <sup>1</sup>Paraclinical Sciences & <sup>2</sup>Pathology, Faculty of Medicine & Health Sciences, Universiti Malaysia Sarawak, Malaysia*

*Introduction:* Nasopharyngeal carcinoma (NPC) is a cancer of the nasopharynx epithelium. Epstein-Barr virus (EBV) is one of the factors that contributes to NPC. However, its direct role is still unclear. The Epstein-Barr virus nuclear antigen 1 (EBNA-1) is the only latent protein expressed in all EBV-carrying malignancies. Expression of EBNA-1 was found to result in genomic instability, possibly through reactive oxygen species (ROS) production. ROS is known to induce apoptosis-mediated chromosome breaks within the *AF9* gene. Therefore, we hypothesise that, EBNA-1 expression may induce ROS production and subsequently results in chromosome breaks within the *AF9* gene, which eventually contributes to chromosomal rearrangement. This study focused on *AF9* gene situated at 9p22 which is a common deletion region in NPC. Besides, *AF9* gene is also commonly translocated with the *MLL* gene in secondary leukaemia. The main objective is to evaluate the role of EBNA-1 expression in the production of ROS and subsequently the generation of chromosome breaks within the *AF9* gene. *Materials & Methods:* NP69 was transfected with EBNA-1 gene expression plasmid using Lipofectamine 3000. Western blot was performed to ensure the expression of EBNA-1. Oxidative stress assay was performed using 2',7'-dichlorofluorescein diacetate (DCFH-DA) method. Oxidative stress assay data were statistically analysed with t-test. *Results & Discussion:* Oxidative stress level was significantly higher in NP69 cells transfected with EBNA-1 as compared to the control ( $p \leq 0.05$ ). In addition, chromosome breaks within the *AF9* gene were analysed by inverse polymerase chain reaction (IPCR). It was found that, the cleavage frequency in EBNA-1 transfected cells were significantly higher than the control ( $p \leq 0.05$ ). *Conclusion:* EBNA-1 expression induced oxidative stress and resulted in chromosome breaks within the *AF9* gene.