ICPaLM 2021: International Congress of Pathology and Laboratory Medicine 2021 and 18th Annual Scientific Meeting, College of Pathologists: Exploring the Advances and Potential of Disruptive Technologies in Pathology and Laboratory Medicine, organised by the College of Pathologists, Academy of Medicine of Malaysia and held virtually on 3rd-5th March 2021. Abstracts of K. Prathap memorial lecture, plenary, symposium and paper (poster) presented are as follows:

K. Prathap Memorial Lecture: Exploring Advances and The Potential of Disruptive Technologies in Pathology and Laboratory Medicine

Jo Martin
Queen Mary University of London, Barts Health NHS Trust

Rapid advances in technology are impacting all areas of pathology. Over the next few years we can expect to see even more amazing things come into our world and into our practice. Both the technology that we use and the ways in which we deploy it will change the way we work. We have glimpses of advances that will change the way we assess histological slides, and the data science tools are being developed that will allow us to provide personalised reports of therapeutic options for tumours.

Integrative pathology, with the use of genetic and protein data alongside morphological interpretation, will come into every area of our practice, both benign and malignant. This presentation will highlight some of the new methods that are under development, some of the new tools becoming available and some of the changes that we can expect both in coming years and the longer term.

Plenary 2: Role of Molecular Genetic and Immunohistochemistry in Renal Neoplasms

Brett Delahunt
Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand

There have been major advances in the classification of renal cell neoplasia since the publication of the first classification by the World Health Organization (WHO) in 1981 and while the diagnostic emphasis has been on morphological features, the role of molecular genetics (MG) and immunohistochemistry (IH) is increasing. The Mainz Classification in 1986 established clear cell renal cell carcinoma (RCC), papillary RCC, chromophobe RCC and collecting duct carcinoma as distinctive tumor morphotypes, with renal medullary carcinoma later being added as a separate subtype of collecting duct carcinoma. It was also concluded that sarcomatoid RCC represented an extreme form of tumor dedifferentiation rather than a separate morphotype. Mucinous tubular and spindle RCC and translocation carcinomas were added to the classification in 2004 and here the role of IH and MG took on a new prominence. The Vancouver Classification of 2012 added tubulocystic RCC, acquired cystic disease-associated RCC, clear cell (tubulo) papillary RCC and hereditary leiomyomatosis RCC syndrome-associated RCC to the spectrum of RCC. Two further entities were also recognized. Hybrid oncocytic chromophobe tumor was classified as a variant of chromophobe RCC, while t(6;11) translocation carcinoma was added to the group of translocation carcinomas. In addition to these, three newly recognized morphotypes of RCC (thyroid-like follicular RCC, succinate dehydrogenase B deficiency-associated RCC and ALK-translocation RCC) were classified as emerging entities, emphasizing the increasing diagnostic role of IH. More recently eosinophilic solid and cystic RCC and biphasic papillary RCC have also been recognized as novel tumors with characteristic IH features.

Plenary 3: Using Autopsy Data – More Can Be Done

Philip Beh
Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Despite declining trends and numbers of autopsies throughout the world, large numbers of autopsies are still being performed annually. Findings from such autopsies are compiled in reports and frequently filed away with little attention given to the rich amount of information that can be obtained from such a large database of information. This presentation is a humble description of my personal journey and I hope an encouragement to the audience to think about the possibilities available to them and the opportunities to enrich knowledge and to prevent injuries and death.
Plenary 4: The Uberisation of Laboratory Services: The Impact of Mobile Health Technology on Laboratory Services

Tony Badrick
*Royal College of Pathologists of Australasia Quality Assurance Programs*

Uberisation is the act or process of changing the market for a service by introducing a different way of buying or using it, especially using mobile technology. Common examples are Uber, Waze and Airbnb. Could we see this same concept applied in laboratories?

Uberization of Healthcare is a situation where the healthcare professional is able to reach out to the patient as and when required, using the power of technology and the internet. The concept of Uberization of Healthcare is very straightforward; with the use of smartphones, the internet, mobile apps and GPS, patients will be able to contact medical professionals as per their convenience.

The medical professionals can provide remote treatment or emergency services, if the need arises, without the patients having to step out of their homes. The promise of platform systems is that they will improve aspects of healthcare such as waiting time, logistics support, referrals and times for treatment decisions. In general health care these promises are happening in the form of Retail Clinics in the USA where immediate demand is matched to slack supply.

But there are practical problems. Traditional health care organizations fear patients’ Tweets and Yelp reviews because they are often a consequence of poor care or a bad experience. Funding is an obstacle to this form of disruption and healthcare generally lags decades behind consumer technology.

There have been examples of the Uber concept in pathology. Delivery of specimens in cities by ‘Uber’ cyclists and the recent pandemic with its popup collection centres has shown what could be achieved. There is scope for more mobile PoCT testing for chronic disease markers.

Perhaps looking at the Uber concept of developing universal platforms that improve efficiency, optimize access, and reduce cost of use is a likely development in Pathology. Digital image analysis supported by AI could be an example.

Plenary 5: Lessons from COVID-19 Pandemic: Laboratory Perspective

Ravindran Thayan
*Institute for Medical Research, Kuala Lumpur*

China had reported an outbreak of a respiratory infections in Wuhan province in late 2019. The outbreak was later defined as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), caused by a type of coronavirus similar to SARS-CoV-1 which also occurred in China in 2002-2003. COVID-19 is another name given to SARS-CoV-2 and the virus is zoonotic in nature and full genome sequencing revealed its close homology to pangolin and bat coronaviruses.

Over the past 25 years there have been a number of outbreaks, mostly being zoonotic in nature. Past infections include Nipah, SARS-CoV-2, Pandemic Influenza 09, MERS-CoV, Ebola, Zika and Rabies. Because of the novelty of the infecting pathogen as well as the risk the pathogen, it is very important for laboratories to have the capacity to diagnose these infections, as this is the first step to isolate, contain and manage the infections.

COVID-19 has served to remind us of several important things. First, outbreaks of infectious and transmissible pathogens occur more frequently due to increase in human and animal interface. Second, international travel and globalization are components for the global dissemination of emerging pathogens. Third, limitations of supply chain when a sharp increase in demand for products or substituents of products needs to be addressed. Fourth, clinical microbiology laboratories need to be fully operational and well equipped with the infrastructure and manpower to provide critical care testing for optimal patient care. A robust and well-funded public health system, including microbiology laboratory support, is critical to be able to respond to emerging infectious diseases challenges. Fifth, encourage national and international collaboration for urgent development of necessary interventions (i.e., diagnostic tests, drugs or vaccines).
Central to anatomical pathology practice is the visualization of alterations to tissue structure and cellular details, and the interpretation of what these alterations mean. Thus, the capture of high-quality images is crucial. In principle, there are three essential components of image handling: (1) processing of tissues and cells to allow microscopic viewing, (2) tools to capture microscopic images for study, and (3) a trained histopathologist who can interpret the images and make a clinically relevant diagnosis. Automation for processing and staining of tissues has been the major advancement for the first component. However, it was the development of the virtual microscope, conversion of light microscopy images into electronic images (digital pathology), addressing the second essential component, that has been the major enabler of artificial intelligence (AI) in anatomical pathology. Computing power today can support scanning of complete tissue sections - Whole Slide Imaging (WSI) - to convert the image information to digital format. Using appropriate software, WSI can be navigated on a computer monitor through various magnifications, just like a glass slide. Most of us are now familiar with the application of digital pathology in conferencing and education, multidisciplinary team discussions, remote consultations, online learning and EQA. E-slides also enable digital workflow, digital archives and integration into the e-health record, with impact on patient care. Because digital data is highly amenable to analysis, automated image analysis has been addressing the third essential component of anatomical pathology - image interpretation and diagnosis. Initial challenges include the considerable input by anatomical pathologists to annotate cells and tissue components to train machines (machine learning), ambiguity in ground-truth definition, textural variability and dimensionality. However, the expectation is being realized, that machines can establish their own patterns to interpret and act on new data, such as through deep learning which leverages artificial neural networks. There is immediate potential for AI to "value-add" to anatomical pathology practice by taking over time-consuming and tedious counting/scoring tasks such as grading of tumours and scoring of biomarkers for personalized medicine (companion diagnostics), hence improving timeliness, accuracy and reproducibility of such assessments. Nevertheless, for AI to achieve clinical utility, the pathologist has important roles in quality control, machine training, algorithm development, review of generated data and clinical decision making.

Accelerating Digital Pathology Image Analysis Powered by NVIDIA Clara

Eddie Huang
APAC, NVIDIA, Singapore

Pathologists traditionally interpret dozens of slides per cancer case, searching for clues pointing to a cancer diagnosis, which works on a very manual, challenging and time-consuming process. Artificial intelligence (AI) can help pathologists become more productive by accelerating and enhancing workflow through examining massive amounts of data. AI coming with advanced process and deep learning models gives the pathologists the tools to analyze images and provide insight based on previous cases and diagnose faster by pinpointing anomalies. In NVIDIA Clara computing platform, we provide several pipelines aids on automatic pathology nuclei segmentation and digital pathology image process operator to improves data loading with 15% ~ 22% for loading 2GB/10GB file into GPU memory by cuFile as compared with POSIX. In Clara 4 releasing, we will have the new pre-trained pathology segmentation model that can detect metastases and cuClaraImage to optimize deep learning training pipeline for building similar models by increases of GPU utilization. NVIDIA Clara is the promising GPU-accelerated solutions to AI development in digital pathology.

The Utility of Artificial Intelligence in Diagnostic Pathology

Shahnorbanun Sahran
Center for Artificial Intelligence Technology (CAIT), Faculty of Information Science and Technology, UKM

In the digital world of transformation, the utility of artificial intelligence (AI) is a computer program used to do a particular task. The program includes a set of utilities such as diagnostics tools and can satisfy a specific need, especially in a practical way. In general, research for AI in medicine already started more than 30 years and focus more on Expert Systems. However, AI in digital pathology just started a few years back. The utility of AI in digital pathology has dramatically proven in many case studies and research collections. Pathology is the study and diagnosis of disease by examining body tissue, which is typically fixed on glass slides and viewed under a microscope. Pathology relies almost solely on glass slides to render a diagnosis. This dependency created a delay for initial diagnoses and subsequent second opinions. Therefore, physical delivery of the glass slide or specimen to the appropriate pathologist consumes time, and patient care quality is an issue. Today, the advent of whole slide imaging (WSI) allowed the pathologist to scan glass slides to produce digital images in a vast number of samples. It has the utilization of automated and, high-speed image capture systems. Glass slides can now be scanned in less than a minute and
produce high-resolution digital images. As a result, AI is increasingly to assist digital pathology, enable them to process larger data sets, and perform more detailed and accurate analyses. Here, the utility will concentrate on patient-centric treatments, improve efficiency, positive changes to workflows, more accessible technology, and more time devoted to cases.

Symposium 2A

An Update on Endometrial Neoplasia

Teck Yee Khong
Women’s and Children’s Hospital, Adelaide, Australia

Endometrial cancer is the 6th most commonly occurring cancer in women and 15th most commonly occurring cancer overall. There were an estimated >380,000 new cases in 2018. It is mainly a disease of high-income countries, but age-adjusted rates of endometrial cancer are increasing in countries transitioning from low- to high-income economies. Endometrial cancers have been classified as being endometrioid (or Type I) or non-endometrioid (or Type 2) based on the histology. Type I cancers usually had good prognosis while Type II cancers were more aggressive. There are, however, frequent exceptions. A molecular study (The Cancer Genome Atlas) has identified 4 clusters of endometrial cancers which promise to offer better prognostic value than the dualistic model. Prognostic markers have been proposed but the mainstay of gynaecological pathology remains morphology and use of immunohistochemistry biomarkers. Issues of tumour typing, grading and staging are highlighted.

Current Issues in Gynaecological Pathology

Razmin Ghazali
Department of Pathology, Hospital Kuala Lumpur, Malaysia

The classification of female genital tract tumours has evolved in leap and bounds over the last 10 years. Application of molecular testing for tumour categorisation, have proven to be more reliable and helpful. Integrated morphological and molecular classification that will have an impact on the diagnosis and management of patient is definitely the way forward. However, in laboratories with limited resources, application of molecular testing may not be feasible. Therefore, utilization of immunohistochemistry markers as a surrogate to the more expensive molecular studies can be done to stratify these tumours. The role of HPV as the precursors of lower genital tract tumours have resulted into a re-producible morphological classification of adenocarcinoma of the cervix, with or without HPV analysis. New tumour entities and changes in the terminologies of tumour used by the pathologists may resulted in confusion to the treating clinicians. Therefore, the terminologies should be consistent and universally acceptable for optimal patient’s treatment and care.

Endometrial cancer - Getting Younger and Younger

Nor Hayati Othman
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Endometrial carcinoma is typically a disease of post menopausal women. The occurrences of endometrial carcinomas in younger patients are uncommon, however of late we are seeing increasing number of cases in young women. The possible reasons are due to increasing trend of obesity in our population and due to exposure to xeno-estrogens, artificial estrogens found in processed foods and cosmetics. Obesity is predominantly associated with type 1 endometrial cancers as compared to type 2 endometrial cancers. The risk of endometrial cancer is increased in women with a body mass index (BMI) greater than 30 kg/m² and the risk increases linearly with increasing BMI. Endometrial carcinoma in women less than 40 pose challenges in fertility preservation especially in nulliparous women. Diabetes, obesity, excessive exposure to xenooestrogen are among the potential causes of excessive oestrogen stimulation.

Symposium 3A

Not Just the Mucosa...New Challenges and Pitfalls in the Neuromuscular Structures of the Bowel Wall

Jo Martin
Queen Mary University of London, Hon. Consultant Barts Health NHS Trust

Dysmotility of the intestine ranges from mild and temporary, to severe, disabling and potentially fatal. Many pathologists are unfamiliar with the range of pathology that can be present in the neuromuscular structures of the bowel wall in conditions such as pseudoobstruction, constipation and megarectum. We have previously shown, in a multinational study, that 70% of diagnoses may be missed due to the limited histopathological assessment of cases.

This talk will cover the approach to examination of biopsy samples and resection specimens from patients with these conditions, the special and immunohistochemical stains that are key in examination, and the range of developmental, myopathic and neuropathic features that may be present, and will include key studies and illustrative case examples.
Molecular Update on Astrocytoma

Wong Kum Thong
Department of Pathology, Faculty of Medicine, University Malaya, Malaysia

With the publication of the latest revision of the WHO classification in 2016, brain tumour genetics in gliomas and other tumours, have been given much greater importance and role in definitions of tumour entities. In addition, molecular signatures have impacted on prognosis and response to certain therapies. Important advances include the IDH mutations, 1p/19q co-deletion and the changing role of MGMT. In this seminar, the recent discoveries and advances in genetics in the various types and grades of astrocytomas shall be highlighted and their relevance discussed.

Frontiers in Molecular Diagnostics: Solid Tumour and Cancer Genetics

Roziana Ariffin
Pathology Department, Hospital Tunku Azizah, Kuala Lumpur

Focus mainly on application of NGS (Next Generation Sequencing) for oncology specifically solid tumour. Brief review on cancer genomic targets, NGS, assay design consideration and limitations. Basic workflow of NGS is outlined. NGS based assay includes Targeted Gene Panel testing, WES (Whole Exome Sequencing), WGS (Whole Genome Sequencing), RNA sequencing, Methylome sequencing and Chromatin Immunoprecipitation & sequencing. A quick review of comparison between amplicon-based platform versus hybrid capture. Brief concept of depth and coverage in various assay targets of NGS will be discussed. Variant interpretation explained with understanding that it is not easy to differentiate between germline and somatic mutation as sometimes they can be somatic and germline at the same time. Applicability of WES reviewed and ESMO (European Society of Medical Oncology) recommendation on use of NGS in the diagnosis of solid tumor and future trends/challenges in personalised tumour management is addressed.

Symposium 4A

Intraductal Carcinoma of the Prostate: Facts and Controversies

Brett Delahunt
Department of Pathology and Molecular Medicine, Wellington School of Medicine and Health Sciences, University of Otago, Wellington, New Zealand

High-grade prostatic adenocarcinoma involving duct/acinar structures is labelled intraductal carcinoma of the prostate (IDCP) and was first recognized as spread of cancer into ducts in 1909. More recently the concept has arisen that some IDCP may represent an in situ lesion which has given rise to differing recommendations regarding the reporting of IDCP in prostate biopsies and radical prostatectomy specimens. The current recommendations from the International Society of Urological Pathology are that, when associated with invasive cancer, the grade of IDCP should be incorporated into the Gleason Score, although this is challenged by some groups. The ISUP also recommends that IDCP seen in the absence of invasive carcinoma be not graded. The definition of IDCP, as endorsed by the 2016 WHO Bluebook, is a further source of controversy as it is stated that cases of IDCP with papillary or loose cribriform architecture without comedonecrosis should have cells with ≥6x nuclear enlargement. It is unclear how this size criterion was derived and which of the parameters of nuclear size (nuclear diameter, nuclear surface area or nuclear perimeter) it relates to. Recent studies have raised doubts regarding the validity of this diagnostic feature. As numerous studies have shown that IDCP is associated with high stage disease with a significant negative impact on cancer-specific survival, accurate diagnosis is crucial to ensure appropriate patient management. Failure to recognize IDCP, particularly in needle biopsies, could lead to delays in the treatment of aggressive high grade prostate cancer, resulting in cancer progression and sub-optimal patient outcomes.

Prognostification of Low-Grade Lymphoma by Molecular Subtyping

Noraidah Masir
Department of Pathology, Prince Court Medical Centre, Kuala Lumpur, Malaysia

Low grade lymphomas represent more than half of malignant lymphomas and include small lymphocytic lymphomas, lymphoplasmacytic lymphoma, follicular lymphomas and marginal zone lymphomas. Advancements in the molecular genetics of these tumours has led to better understanding of pathogenesis. This in turn allows more refined tumour classification and stratification based on the molecular subtypes found. This development has significant implications in the management, prediction of the biological behaviour and response of tumour to treatment.
Molecular Characterisation of High-Grade B Cell Lymphoma for Diagnosis and Prognosis

Noraidah Masir
Department of Pathology, Prince Court Medical Centre, Kuala Lumpur, Malaysia

Diffuse large B-cell lymphoma (DLBCL), the most common subtype of non-Hodgkin lymphoma, is characterized by both clinical and molecular heterogeneity. The past decade has witnessed a dramatic expansion of our understanding of the genomic underpinnings of this disease, especially with the application of next-generation sequencing. Current genomic landscape of DLBCL and how this information provides a potential molecular framework for precision medicine-based strategies in this disease.

Symposium 5A

Update in the Pathology of Fatty Liver

Huang Shiu Feng
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The pathology of fatty liver disease is mainly divided into 3 categories, which includes: a. Fatty liver (simple steatosis): mainly macrovesicular fatty change, b. Steatohepatitis, c. cirrhosis. The classic histologic features of steatohepatitis include fatty changes, lobular inflammation and hepatocyte necrosis, which are most prominent in the centrilobular region of the hepatic lobules and perivenular fibrosis. Hepatocytes usually have ballooning change. The inflammatory cell infiltrate, located primarily in the sinusoids and around the necrotic hepatocytes, consists of mononuclear cells and polymorphonuclear cells. In addition to inflammation and necrosis, Mallory body formations is another characteristic feature. Patients with NASH can progress to cirrhosis has been confirmed by series of biopsies, which demonstrated that the diagnostic features of NASH may no longer exist by the time with cirrhosis. Thus, cryptogenic cirrhosis was used interchangeably with NASH-related cirrhosis by some authors. For patients with fatty liver, the only means of proving a diagnosis of NASH and separating it from simple fatty liver is a liver biopsy. If the tissue shows fat without inflammation and damage, simple fatty liver or NAFLD is diagnosed. An important piece of information learned from the biopsy is whether scar tissue has developed in the liver (pericellular and perisinusoidal fibrosis). Currently, no blood tests or scans can reliably provide this information, either for alcoholic or non-alcoholic fatty liver.

Early Pregnancy Loss and Pregnancy of Unknown Location

Teck Yee Khong
Women’s and Children’s Hospital, Adelaide, Australia

An approach to histopathology of early pregnancy is presented. The clinical contexts are induced abortion or termination of pregnancy, spontaneous abortion or miscarriage, pregnancy of unknown location and ectopic pregnancy. Hydatidiform molar pregnancies, while being also a form of early pregnancy loss, will not be discussed. The rate of miscarriage varies according to the gestational age. The loss of a pregnancy needs a structured investigation including history, examination, testing of uterine anomalies, endocrine, immunological disorders and also genetic tests as well as histological examination of the products. The pathologist’s role in examining the products of conception after such a loss is to try to identify a cause and especially those cases with a recurrent cause. For induced or voluntary terminations of pregnancy, a prudent policy is to identify any gestational tissue obtained to verify an intrauterine pregnancy and successful termination. Whether tissue from all cases need to be examined is discussed. Tissue is often sent with a request for an urgent diagnosis for a pregnancy of unknown location. How such tissues should be managed is discussed. The pathology of ectopic pregnancy is presented also to highlight its similarity to placenta accreta.

The National Biobank Consortium: Relevance, Needs and Strategies

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Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

A biobank stores biological samples, usually human, for use in research. High quality research requires high quality biospecimens. In the past decades many biobanks have emerged in most countries including Malaysia. There are large consortiums of biobanks that brings together the main players from the biobanking field and focusing on research collaboration. In Malaysia, there are many small, medium and large scale biobanks located in the universities, research institutions and also hospitals. For Malaysia to be competitive in research, we need to bring together these biobanks under one platform. As a nation, we also need to contribute data from a large number of samples to be part of international research consortiums. For rare diseases and rare cancers, the need to bring together these biobanks become even more crucial. An ideal approach is to have a national biobank which will provide biobanking services to all, with minimum fees. This will be more cost effective than having many biobanks. Governance and policies on access and data sharing will need to be put in place. The other approach is to set up a consortium of biobanks that will link all existing biobanks. A steering or membership committee will be setup to manage and govern this consortium. Harmonisation of protocols and also the sharing of databases from each biobank will be a good start. The National Biobank Consortium will be a good base to start for consolidating our medical research and link our Malaysian researchers to many research consortiums and collaboration.
CONFERENCE ABSTRACTS

Chemical Pathology

Symposium 1B

Cardiac Biomarkers of Acute Coronary Syndrome: A Historical Perspective

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The need for rapid and accurate diagnostic algorithms to diagnose patients with acute coronary syndrome (ACS) is vital to initiate a more effective evidence-based medical management. Clinical assessment, 12-lead ECG and cardiac markers such as troponin (cTn) have become the diagnostic foundations of patients presenting with acute onset chest pain. The role of cardiac markers as a diagnostic tool of ACS has evolved over the years where technological advancements have made contemporary sensitive and high-sensitivity cardiac troponin (hsTn) assays into a highly accurate diagnostic tool in patients with acute chest pain in comparison with conventional cardiac biomarkers. From the time of non-specific cardiac markers such as aspartate transaminase, lactate dehydrogenase in the 1960s and 1970s to the initial 1st-generation assays and now 5th-generation high-sensitivity cardiac troponin (hs-cTn) assays, this presentation will embark on the history and evolution of cardiac biomarkers with particular emphasis on hs-cTn. This talk will further discuss on the current evidence and guidelines of using hs-cTn in clinical practice.

Biochemical Markers for Non-alcoholic Fatty Liver Disease

Pavai Sthaneshwar
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Fatty liver is a common histologic finding in human liver biopsy specimens. Nonalcoholic fatty liver disease (NAFLD) is estimated to affect approximately 1 billion individuals worldwide. NAFLD represents a spectrum of diseases, ranging from simple fatty liver (steatosis) to steatosis with inflammation and necrosis to cirrhosis that occurs in people who drink little or no alcohol. Nonalcoholic steatohepatitis (NASH) represents the more severe end of this spectrum and is associated with progressive liver disease, fibrosis, cirrhosis and liver-related morbidity and mortality. The major risk factors are obesity and insulin resistance, and the prevalence of these risk factors has increased rapidly throughout the world. Until now, liver biopsy has been the gold standard for identifying these disorders, but has well-known limitations, including invasiveness; rare but potentially life-threatening complications; poor acceptability; sampling variability; and cost. Furthermore, due to the epidemic proportion of individuals with NAFLD worldwide, liver biopsy evaluation is impractical, and non-invasive assessment for the diagnosis of NASH and fibrosis is needed. The inability of liver biopsy to meet this challenge makes the development of non-invasive, readily available, and easy-to-perform serum markers a high priority. Recently adipocytokines markers have gained considerable attention. However, no single marker is helpful for diagnosis and staging of the disease, but applying a panel including different types of tests may be more useful.

New Biomarkers in Diabetes Mellitus

Wong Moh Sim
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Diabetes mellitus is a group of metabolic diseases characterised by hyperglycaemia caused by defects in insulin secretion, insulin action or both. The global prevalence of diabetes mellitus, especially Type 2 diabetes, is increasing rapidly. Diabetes is associated with macrovascular complications such as cardiovascular disease and stroke as well as microvascular complications such as retinopathy and nephropathy. Diagnosis and monitoring of diabetes is currently achieved by using the traditional markers of glucose and HbA1c. Biomarkers have been proposed to facilitate early and precise diagnosis of diabetes and prediction of diabetes complications. A biomarker is a biomolecule/biological state that can be used for the prognosis, diagnosis, and follow-up of the pathological state or the severity of a disease. Emerging biomarkers include microRNAs, proteins and metabolites. These new biomarkers have the potential to improve individual risk assessment in diabetes mellitus and ultimately the management of the patient.
Symposium 2B

Experience Sharing in Establishing POCT

Wong Moh Sim
Department of Laboratory Medicine, Khoo Teck Puat Hospital, Singapore

Yishun Health comprises both Khoo Teck Puat Hospital (KTPH), a 690-bed acute care general hospital, and Yishun Community Hospital located in the northern part of Singapore. The Point of Care Testing (POCT) programme was implemented in 2002 in our previous hospital, Alexandra Hospital, prior to our move to KTPH in 2010. There are currently 13 POC tests in Yishun Health. The POCT Committee oversees the use of POCT devices and ensures user competency to meet licensing and accreditation requirements, provides a forum for discussion of ideas and approaches from stakeholders, and facilitates implementation of universally acceptable solutions and project activities. Devices with connectivity capability, where available, are interfaced to the Laboratory Information System (LIS) and the Electronic Medical Records (EMR) to facilitate the timely dissemination of results to users. Regular training and engagement sessions ensure competency and commitment from the staff performing the tests. We will share our POCT experience in this talk.

Point of Care Testing and Clinical Governance in Malaysia

Baizurah Mohd Hussain
Consultant Chemical Pathologist, Malaysia

Point of Care Testing (POCT)/Near Patient testing/Bedside testing is defined as a laboratory testing done by a non-medical laboratory technician, for example physicians, nurses or medical assistants outside a dedicated laboratory. We are all familiar with the Clinical Governance system through which healthcare organisations are accountable for continuously improving the quality of their services and safeguarding high standards of care and the framework pillars. In Pathology, governance has been our stronghold as to bread and butter. POCT, on the other hand, is directly part of the clinical pathway. Clinicians utilise the results for immediate treatment and management of patients. This presentation shows how we try to apply Clinical Governance using the same tools in the pathology laboratory in Malaysia.

Impact of POCT in Clinical Decision Making

Wong Moh Sim
Department of Laboratory Medicine, Khoo Teck Puat Hospital, Singapore

Point-of-care testing (POCT) is defined as ‘testing that is performed near or at the site of a patient with the result leading to a possible change in the care of the patient’ [College of American Pathologists (CAP)]. POCT tests include tests for the measurement of glucose, HbA1c, arterial blood gases and coagulation markers. POCT is an integral part of patient-centred care today. The tests are typically performed by non-laboratory personnel and as such, POCT guidelines from various international bodies, including ISO and CAP, are readily available. The standards define governance structure, roles and responsibilities of POC testing personnel, analytical quality (including selection of appropriate test methods and validation protocols), quality management, data management, and training and competency. Clinical laboratories overseeing POCT in their respective organisations should comply to these standards, to mitigate the risk of patient harm which may result from suboptimal POCT practices.

Symposium 3B

Laboratory Testing in Thyroid Conditions - Pitfalls and Clinical Utility

Mafauzy Mohamed
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Laboratory tests for thyroid conditions includes thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), thyroglobulin (Tg), thyroglobulin antibodies (Tg-Ab), thyroid peroxidase antibodies (TPO-Ab), TSH receptor antibodies (TRAb) and calcitonin. TSH, fT4 and fT3 tests are used to determine functional status of the thyroid gland. TPO-Ab and Tg-Ab are used in diagnosing Hashimoto’s thyroiditis. TRAb tests are used to diagnose Graves’ disease. Tg and calcitonin are important tumor markers used in assessing activity of differentiated thyroid carcinoma (DTC) and medullary thyroid carcinoma (MTC), respectively. It is important to be familiar with the possible pitfalls in the use of these tests so that they can be interpreted properly and accurately. Many factors can interfere with laboratory tests such as human anti-animal antibodies. Certain medications can also interfere with thyroid function tests (TFT) e.g., salicylates, lithium, amiodarone. In pregnancy, normal changes in thyroid physiology and the postpartum period can make TFT interpretation challenging. In non-thyroidal illnesses e.g., critically ill patients, TFT is also affected. Hence when results are discordant, it is important to consider the clinical context when interpreting results.
Bone Health and Cardiovascular Risk Factors

Subashini C. Thambiah
Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia

Both cardiovascular disease (CVD) and osteoporosis are associated with increased morbidity and mortality with significant economic burden, particularly in an ageing population. Several epidemiological studies have demonstrated that these two conditions are closely related, suggesting a possible link in their pathogenesis. Both share similar risk factors such as smoking, alcohol, menopause status and physical inactivity. The potential association between CVD and osteoporosis has important health implications for individuals with (or at risk for) these conditions. This presentation will discuss the possible associations between these chronic conditions. Understanding these is significant for the prevention and management of CVD and osteoporosis.

Data Interpretation of Endocrine Cases

Leslie C Lai
Gleneagles Hospital Kuala Lumpur, Malaysia

This talk will include data interpretation covering disorders of the pituitary and adrenal glands as well as islet cell tumours. It will also include disorders of water and sodium homeostasis. Appropriate dynamic function test results will be discussed. It is hoped that by the end of the talk the participants will have more confidence in interpreting biochemical data and dynamic function test results in the endocrine conditions covered by this talk.

Symposium 4B

Patient-Based Real-Time Quality Control: Review and Recommendations

Loh Tze Ping
Department of Laboratory Medicine, National University Hospital, Singapore

Patient-based real time quality control (PBRTQC) is a laboratory quality control practice that harnesses patient data for monitoring of performance of the analytical system. It has recently gained renewed interest with increasing sophistication in the underlying algorithms as well as the software supporting such practice. In this talk, we will walk through the general concepts of PBRTQC and recommendations surrounding the implementation in routine clinical laboratories.

Indirect Reference Range Establishment

Loh Tze Ping
Department of Laboratory Medicine, National University Hospital, Singapore

Reference intervals are the most commonly used tool assisting a clinician interpreting a quantitative laboratory result. Traditionally, reference intervals are derived by measuring the biomarker of interest in a representative reference population and calculating the statistical boundary for a central subpopulation. More recently, the testing of laboratory tests in large patient populations has opened up the possibility of deriving reference intervals from routine clinical laboratory database - the indirect approach. In this talk, we will walk through key concepts related to indirect reference intervals and its application in routine clinical laboratory.

Delta Checks in Clinical Laboratory

Loh Tze Ping
Department of Laboratory Medicine, National University Hospital, Singapore

Delta check is a verification rule that is applied to identify sequential laboratory results with larger than expected variation, which may be indicative of an error. Delta check is a powerful tool in the repertoire in the laboratory quality system as it detects error at individual patient level. In this talk, we will walk through the key concepts in delta check, including recently developed theories and tools, to allow laboratory practitioners to set up objective delta check rules with a priori defined performance characteristics.
Symposium 5B

LC-MS/MS Technology and Applications in the Clinical Lab

Fionn B Quinlan
APAC Division, Waters Corp, Taipei, Taiwan

After decades of being seen as a complex technology more suited for research areas, Liquid Chromatography Mass Spectrometry has steadily been making in-roads into Clinical and Toxicology laboratories worldwide. This trend has accelerated over the last decade. Learn why it’s often become the platform of choice for areas such as Expanded Newborn Screening, Endocrinology, Therapeutic Drug Monitoring and Clinical Toxicology. Even for Coronavirus viral load quantitation, LC-MS/MS now offers an alternative technique to PCR. By integrating sample prep automation systems, robotic handling, LIMS and rapid instrument set-up and self-calibration, this technology is getting easier to implement every day. Seamless sample to report output is now becoming a reality.

Application of LCMS/MS in Newborn Screening

Salina Abdul Rahman
IEM & Genetic Unit, Institute for Medical Research, NIH, Setia Alam, Malaysia

The development and introduction of electrospray ionization into the LCMS/MS system has embarked a new technology for newborn screening purposes. Newborn screening using tandem mass spectrometry from dried blood spots was first proposed by Millington et al. in 1990. MS/MS is capable of identifying and quantifying many metabolites in a single run within less than two minutes. It is robust, sensitive and specific that enables it to screen multiple disorders simultaneously from one dried blood spot for Inborn Errors of Metabolism (IEM). IEM is a group of heritable disorders which may present as emergency cases and can cause death if not treated promptly. Screening of newborn for IEM before they become symptomatic allows early diagnosis and treatment of affected neonates, resulting in normal growth and development and reduction of financial costs for families and society. Due to advances in technology and treatment, more disorders are proposed to be included in newborn screening. In conclusion, mass spectrometry provides a rapid, sensitive, and specific screening method that ultimately gives clinical laboratories ability to measure and screen many disorders for early diagnosis and treatment.

Haematology and Transfusion Medicine

Symposium 1C

Use of banked cord blood to create a clinically compliant iPSC Masterbank for potential cellular therapies

Ngaire Elwood
BMDI Cord Blood Bank & Cord Blood Stem Cell Research Laboratory, Murdoch Children’s Research Institute, Parkville, Australia

We aim to establish a bank of clinical grade induced pluripotent stem cell (iPSC) lines from banked unrelated CB. CB stored within the BMDI Cord Blood Bank (CBB) has met strict donor eligibility and quality requirements and is therefore an ideal source of well-characterised, Good Manufacturing Practice (GMP)-grade starting material for the creation of iPSCs. To this end, we have established an Animal Component Free protocol to generate iPSC lines from 50 μl of cryopreserved CB buffy coat, using defined reagents manufactured under GMP. Thawed CB cells are expanded in culture prior to reprogramming using the non-integrating Sendai Reprogramming system. iPSC colonies are picked and cell lines then maintained long-term under xeno-free conditions. Karyotype integrity of the generated iPSC lines is confirmed and flow cytometry used to show that iPSCs express known pluripotency markers. In vitro differentiation experiments indicate that cord blood derived iPSCs can differentiate into cells representing the 3 germline lineages: beating cardiac cells (mesoderm), neuronal cells (ectoderm) and endodermal precursor cells. CB donors with common homozygous HLA haplotypes have been identified and we are currently in the process of re-consenting these donors to create and store GMP-compliant iPSC lines from a fraction of their stored CB. Appropriate Quality Assurance parameters have been established to ensure the safety and quality of the lines produced. Once manufactured, we believe this bank of clinical grade iPSCs will be an important source of stem cells to derive cells for therapeutic use.
CAR T-cell Therapy: A New Era in Cancer Immunotherapy

Chang Kian Meng
Sunway Medical Centre, Malaysia

Chimeric antigen receptor T (CAR-T) is an innovative immunotherapy in the treatment of malignancies. The current CD19-CAR-T is approved for the therapy of refractory/relapsed B-cell ALL and B cell lymphomas. A high remission rate of 60 – 90% can be achieved in some cases that have even failed autologous or allogeneic transplantation.

CAR-T cells are produced by transducing a genetically engineered CAR fusion protein into T cells by means of a retrovirus or lentivirus. The recognition of tumor cells by the CAR molecule overcomes the evasion of tumor by HLA loss. A CAR construct consists of a single-chain variable fragment (scFV) antigen-recognition domain, a CD3-derived T cell activation domain and a co-stimulatory domain (CD28 or 4-1BB). The first-generation CART however had poor responses due to poor activation and limited persistence but the addition of the co-stimulatory domain has improved this problem with more potent cytotoxic activity, longer persistence and memory T-cell formation.

The use of CAR-T cells is most successful in haematological malignancies and less in solid organ tumours. There are still many unresolved issues including upscaling the manufacture and production of commercial CAR T cells, affordability, regulation and ensuring quality control for institution-made products. At the clinical level, there is a learning curve on managing the acute phase toxicity including cytokine release syndrome, immune effector cell associated neurotoxicity syndrome, the protracted cytopenia, macrophage activation syndrome as well as tumour lysis syndrome. The long-term toxicities remain to be elucidated with longer experience and survival of patients. These include prolonged B cell aplasia, T cell deficiency, infections and long term impairment of memory and fatigue. There are still limitations to this therapy including loss of the CAR-T cells after a few months as well as tumour escape and tumour relapse involving the loss of CD-19 expression.

Some of the new developments include the manufacture of double antigen CAR-T (expressing both anti CD19 and anti CD20), the third and fourth generation CAR-T and the combination of CAR-T therapy with checkpoint inhibitors, and other immunomodulators. There are also issues with T cell harvesting in patient who have undergone multiple cycles of therapy with poor T cell quality. This can be overcome with the development of off-the-shelf CAR T (allogenic CAR T) and CAR NK cells.

Symposium 2C

Haematology Parameters in Infections, Practicality & Trend

Ida Parwati
Department of Clinical Pathology, Dr. Hasan Sadikin General Hospital, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia

Peripheral blood as a minimally invasive source has been widely used as biomarker for many diseases. In the case of infection, when the microbiological examination takes a long time and is more expensive, the hematology examination can be immediately used as a screening tools. Each cell such as RBC, neutrophils, lymphocytes, monocytes, platelets has a specific role in infectious diseases. The classically used hematologic parameters are the number of leucocytes and the differential count. Using modern hematology analyzer, hematological parameters, such as white blood cell (WBCs) and their subpopulations, red cell distribution width (RDW), mean platelet volume (MPV), and plateletcrit (PCT), and derived biomarkers such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), are easily measured at low cost. A combination of multiple parameters with measuring phenotypic changes in activated leukocytes contain such as lipid rafts in their cell membrane and altered intracellular DNA/RNA levels can be used as novel diagnostic algorithm for different infectious diseases called Infectious Management System (IMS). Early diagnosing of infection in a timely manner at low cost can improve infection management and reduce unnecessary antibiotics usage.

Illustrative cases in Multicolour Flowcytometry

Mimi Azura Aziz
Pathology Department, Hospital Tunku Azizah (WCHKL), Kuala Lumpur, Malaysia

Immunophenotyping using flow cytometry has become the method of choice in identifying and sorting cells within liquid suspension. It has wide usage in laboratory services for haematological diseases. Flow cytometric immunophenotyping allows comprehensive assessment of both surface and intracellular cell antigens. The new generations flow cytometry enables rapid analysis of massive cell volumes. The phenotypic capabilities of flow cytometric immunophenotyping facilitate the identification of cell population, identification of potential therapeutic target, prediction of genetic lesion and detection of rare cells. The cases presented will be illustrating some of these flow cytometric immunophenotyping functions in our clinical flow cytometry lab.
Symposium 3C

Parallel bimodal single-cell sequencing of transcriptome and chromatin accessibility

Jonathan Loh
Institute of Molecular and Cell Biology, Singapore

Joint profiling of transcriptome and chromatin accessibility within single cells allows for the deconstruction of the complex relationship between transcriptional states and upstream regulatory programs determining different cell fates. Here, we developed an automated method with high sensitivity, assay for single-cell transcriptome and accessibility regions (ASTAR-seq), for simultaneous measurement of whole-cell transcriptome and chromatin accessibility within the same single cell. To show the utility of ASTAR-seq, we profiled 384 mESCs under naive and primed pluripotent states as well as a two-cell like state, 424 human cells of various lineage origins (BJ, K562, JK1, and Jurkat), and 480 primary cord blood cells undergoing erythroblast differentiation. With the joint profiles, we configured the transcriptional and chromatin accessibility landscapes of discrete cell states, uncovered linked sets of cis-regulatory elements and target genes unique to each state, and constructed interactome and transcription factor (TF)-centered upstream regulatory networks for various cell states.

Symposium 4C

Understanding of MDS/MPN based on Pathogenesis & Approach to Diagnosis

Raja Zahratul Azma Raja Sabudin
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Myelodysplastic syndrome/myeloproliferative neoplasm is a group of chronic clonal myeloid malignancies with overlapping features of both myelodysplastic syndrome and myeloproliferative neoplasm at the time of presentation. These overlapping features complicates the diagnosis of patient with myelodysplastic syndrome/myeloproliferative neoplasm. This group includes the entities chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, BCR-ABL1 negative atypical chronic myeloid leukemia, myelodysplastic syndrome/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis and myelodysplastic syndrome/myeloproliferative neoplasm, unclassifiable. Advancements in next generation sequencing have begun to reveal the molecular abnormalities of these diseases, identifying an array of recurrently mutated genes involved in epigenetic regulation, RNA splicing, transcription, and cell signaling. Mutually exclusive gene combinations have been observed between specific subtypes of patients with myelodysplastic syndrome/myeloproliferative neoplasm that have an impact on patient outcomes, including TET2-SRSF2 in chronic myelomonocytic leukemia, ASXL1-SETBP1 in atypical chronic myeloid leukemia, or SF3B1-JAK2 in myelodysplastic syndrome/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis. The understanding of the pathogenesis of these clonal myeloid malignancies will provides aid in determine their prevalence, diagnosis and surveillance. Development of targeted therapy in near future will also help in improvement of their survival.

NGS for MRD Detection in Acute Leukaemia

Rosline Hassan
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The purpose of Measurable residual disease (MRD; also referred to as minimal residual disease) testing is to determine the clearance of disease following chemotherapy or stem cell transplant. Different methods are available to follow up patients with Acute Leukemia. MRD can be assessed by flow cytometry and few molecular techniques. The molecular methods have been dramatically improved over the last 20 years, paralleled by a significant knowledge growth in the molecular aspect of acute leukemia. There are 2 general approaches to molecular MRD assessment: real-time PCR-based approaches and sequencing approaches wherein sequences from individual DNA/complementary DNA (cDNA) molecules are generated.

The PCR approach includes classical real-time qPCR using fluorescent probes, and digital PCR. This approach is usually of high sensitivity and therefore currently considered the gold standard. However, its applicability is limited to the 40% of AML patients that have specific translocation or mutation. Theoretically, NGS for MRD assessment can be applied to all subtypes of AML and with the improvement in bioinformatics approaches, it is applicable for those leukemia without specific translocation or mutation.

Next-generation sequencing (NGS) can simultaneously detect various mutations and be applied to the majority of patients with Acute Leukemia. Recently, it was shown that NGS MRD of mutants other than the common mutations occurring in clonal hematopoiesis, including the DTA (DNMT3A, TET2, and ASXL1) mutations, carry prognostic impacts on relapse rates and overall survival (OS) in AML patients. However, the proper time point for NGS MRD detection after treatment is still unclear. It is hypothesized that NGS MRD detected at different time points might have different clinical implications. In acute lymphoblastic leukemia, with this high-throughput NGS technology, a more in-depth analysis of IG and/or TCR gene rearrangements will be able to reach. In conclusion, standardization, quality control, and validation of this new technology as a tool for MRD in acute leukemia are warranted prior to its incorporation into clinical routine practice.
Liquid biopsy: The future in Haemato-Oncology Diagnosis

Yuslina Mat Yusoff
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In the era of precision medicine, ‘liquid biopsy’ is increasingly being studied as a potential tool for refining diagnosis and disease monitoring. The term “liquid biopsy” means accessing circulating tumour cells or tumour DNA through a blood sampling, without the need of an invasive tissue biopsy. In 1977, scientists identified the presence of abnormally high levels of cell-free DNA (cfDNA) in the plasma and serum of cancer patients relative to health control patients and this cfDNA was presumed to represent mainly circulating tumor DNA (ctDNA).

Liquid biopsy has promising clinical utility in haemato-oncology particularly lymphomas. Today, the management of lymphoma is typically guided by the results of a needle biopsy at diagnosis, then monitoring through and after chemotherapy treatment by PET-CT scans. However, this relies on the presence of macroscopic tumour burden in order to detect areas of lymphoma involvement. Due to this limitation, patients can be incorrectly labelled as having a complete remission even though microscopic disease may still be present.

Furthermore, limitation in accessing fresh tumour material from tissue biopsies has prevented the rapid translation of lymphoma gene mutations into prognostic or predictive tools for clinical practice. Recent studies have demonstrated the use of ctDNA assessment across many lymphoma subtypes. Compared with conventional tissue biopsy or other commonly used complex imaging techniques, liquid biopsies have a lower risk and relatively easy to operate. Latest update on liquid biopsy including its clinical utility, technical issues, standardization and limitations will be discussed.

Symposium 5C

Patient Blood Management in Malaysia: Challenges and Way Forward

Nor Hafizah Ahmad
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Patient Blood Management (PBM) is the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome. This clinical practice started to be implemented in surgical patients and currently it has been expanded for clinical use in medical department. The primary concepts of PBM are: (1) optimizing red cell mass, (2) minimizing blood loss and (3) maximising patients’ tolerance of anaemia. (Ishister, James P. 2013). Literatures have shown that peri-operative morbidity and mortality are markedly reduced for patients whose hemoglobin are well optimized before surgery and when restrictive transfusion practice were being practiced. The success of PBM implementation requires a holistic and multidisciplinary approach with contribution from all levels involved. Setting up a national framework, empowerment of early anemia recognition and treatment at the primary care centres, implementation of PBM clinical practice at hospital levels, having a national guideline and also continuous education or awareness program in undergraduate and post graduate training which shall be focused on to build a strong foundation towards the success of implementation of PBM in Malaysia.

Non-homologous use of cord blood

Ngaire Elwood
BMDI Cord Blood Bank & Cord Blood Stem Cell Research Laboratory, Murdoch Children’s Research Institute, Parkville, Australia

The BMDI Cord Blood Bank (CBB), one of three public cord blood banks in Australia, has released nearly 600 CBU for treatment of patients with leukaemia and other blood disorders; cord blood (CB) is an important donor source for bone marrow transplant. The CBB is licensed by the Therapeutic Goods Administration (TGA) and holds international accreditation through the Foundation for the Accreditation of Cellular Therapy (FACT). CB stored within the bank has met strict donor eligibility and quality requirements and has a high success of donor follow-up. Banked CB is therefore an ideal source of well-characterised, GMP-grade starting material for non-homologous clinical use beyond bone marrow transplant. We have been exploring the use of CB for cellular therapies involving cardiac and neurological repair. We have also been exploring the use of banked CB as the ideal starting material to create GMP-grade induced pluripotent stem cell (iPSC) lines from donors with a homozygous haplotype (ie. ‘super-donors’). To this end we are able to generate stable iPSC lines from stored CB under “GMP-like” conditions. Once manufactured, we believe this bank of clinical grade iPSCs will be an important source of stem cells to derive cells, such as nerve, cardiac and T-cells, for potential therapeutic use. Looking towards the future, public unrelated CBBs will play a key role in provision of CB for regenerative and immuno-therapies, thereby value-adding to the vital role the banks already serve for the bone marrow transplant community.
Passenger lymphocyte syndrome

Nurasyikin Yusof
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The passenger lymphocyte syndrome (PLS) refers to the clinical phenomenon of alloimmune haemolysis resulting from the transfer of viable lymphocytes from donor during hematopoietic stem cell transplant and solid organ. It is caused by donor B lymphocyte production of antibodies causing a primary or secondary immune response to recipient erythrocytes. Most commonly, it is in the setting of minor ABO mismatches. Sometimes, it is very severe and may cause “unexplained” haemolysis post transplantation. It is a recognised complication of minor incompatibility but the incidence of haemolysis associated with this is waning because anti-B-cell immunosuppressive therapy is increasingly a component of graft versus host disease prophylaxis. The impact of ABO mismatching on stem cell recipient survival remains as an area of research interest. Clinicians must be vigilant in order to recognize haemolysis and implement appropriate therapy to combat this phenomenon.

Forensic Medicine, Paediatric and Perinatal Pathology

Symposium 1D

Challenging Cases - Do We Really Know?

Philip Beh
Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Forensic pathologists frequently find themselves in the national or international media over cases that they may have been involved in directly or indirectly. The casual observer would often feel that the pathologists involved should have foreseen that those cases are going to be challenging, but is that really true?

This paper will discuss the issues and factors that may make a case challenging. It is hope that the audience can reflect on them and perhaps be better prepared foe challenging cases in future.

Symposium 2D

Placental Infection and Stillbirth

Tan Geok Chin
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Infection may result in stillbirth due to direct infection, injury to placental and severe maternal illness. Infection is more likely associated with early (20–28 weeks) compared with late stillbirths (after 28 weeks). Estimated 10 -25% of stillbirth may be a consequence of infection and this is higher in developing countries. Organisms that result in stillbirth include bacteria like Escherichia coli, group B streptococci, Ureaplasma urealyticum, Listeria monocytogenes and syphilis. Others are parasites like malaria and toxoplasma gondii, viruses like parvovirus, coxsackie virus and cytomegalovirus. Different types of infection produce specific histological changes to the infection, for examples, microabscesses at the subamniotic region of umbilical cord is a characteristic feature of candida infection, lymphoplasmacytic villitis is seen in syphilis and cytomegalovirus infection, and intervillous microabscesses in listeria infection. The complications of chorioamnionitis include hypoxic-ischaemic encephalopathy, cerebral palsy, periventricular leukomalacia, respiratory problems, intrauterine growth restriction, neonatal sepsis and stillbirth. Placental histological chorioamnionitis can be divided into the following stages: Acute subchorionitis (stage 1), acute chorioamnionitis (stage 2) and acute necrotising chorioamnionitis (stage 3). This is known as the maternal inflammatory response. In addition, there are specific histological features that indicate a fetal inflammatory response, namely chorionic vasculitis or umbilical phlebitis (stage 1), umbilical arteritis (stage 2) and necrotising funisitis (stage 3). Study showed that histological chorioamnionitis with fetal inflammatory response had a higher risk of spontaneous labour, while those without fetal inflammatory response had unexplained death. The latter was suggested that these fetuses were unable to mount a sufficient inflammatory response and were more likely to die in-utero.
Placental Causes of Stillbirth - Sharing Local Experience
Nur Syahrina Rahim
*Faculty of Medicine and Health Science, USIM*

Placenta, often at time a neglected specimen by the pathologists and clinicians particularly in non-specialised centres. Nevertheless, the evaluation of placenta is essential in stillbirth and is performed with or without perinatal autopsy. A thorough gross examination of the placenta can often identify a likely cause of stillbirth. Still, several factors may hamper the clinicopathological assessment, leading to limited interpretation and frustration amongst pathologists. Notably, the placenta is not an uncommon organ to be encountered in forensic practice. In unusual fateful circumstances, the stillbirth befalls together with maternal death. Hence, placenta examination not just possibly explained the stillbirth, but may offers insight into maternal events. The shared cases illustrate the value and relevant issues of placenta examination of stillbirths in varied clinical settings.

Forensic Significance of Intrauterine Death
Khairul Anuar Zainun
*Forensic Medicine Department, Hospital Serdang, Selangor*

Intrauterine death, when it occurs, is a real tragedy. It warrants proper investigation. More often than not, when intrauterine death investigation relates to existing laws of the country, the process may pose its own challenges. It requires detailed awareness of death circumstances, understanding of pregnancy physiology and knowledge of fetal developmental including placenta. Autopsy approach and procedures can be different from that commonly performed in death involving infants and children.

This presentation highlights the significance of intrauterine death from forensic pathologist perspectives in Malaysia. It will discuss relevant laws pertaining to intrauterine death, livebirth in abandoned fetus, timing of death in relation to delivery and role of trauma in the causation of death. It is essential to have all the information required prior to autopsy examination including access to relevant obstetric notes when intrauterine deaths occur in hospital settings. This is to ensure interpretations and opinions are rendered by the pathologists correctly.

Symposium 3D

Role of 2nd Autopsy - Malaysia’s experience
Siew Sheue Feng
*Department of Forensic Medicine, Kuala Lumpur Hospital, Malaysia*

An autopsy is a procedure that involves an examination of a dead body. It is destructive in nature and known to produce artefacts. Most forensic medicine experts will agree that a comprehensive, good quality autopsy will provide the most valuable information to the investigation of death. A second autopsy is not a prioritized choice and shall be avoided.

Most of the second autopsies involve disputed deaths occurred in lockups and detaining centres, whereas some were associated with actions of enforcement agencies. A distrust to the original post-mortem is perhaps the main factor calling for a second autopsy, especially when the original findings went against the wishes of a certain party. The role of a second autopsy in such cases is highly questionable.

An incomplete autopsy, which fails to address the issues surrounding a death is another common factor for a second autopsy. Many medical officers, forensic medicine specialists have been taught and believe that a full autopsy is not required once the cause of death has been identified and determined. They are unaware of the legal standard of proof in criminal cases and the meaning of “cause of death” as according to the laws of Malaysia. A second autopsy may also be beneficial in certain cases conducted by inexperienced medical officers.

In conclusion, a second autopsy is no better than the first autopsy, if the latter is properly conducted. A re-interpretation of the first autopsy findings together with new evidence evolved should be considered before proceeding for a second autopsy.
Reviewing Autopsy/ Autopsy Reports in Hong Kong

Philip Beh
Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Hong Kong, despite the handover back to China in 1997 still practices death investigation under legislation largely similar to the UK’s Coroners System. Similar to many jurisdiction in the world, the number of autopsies performed are declining not just for hospital autopsies but also for Coroner’s autopsies. Despite this decline over 3,000 autopsies are still performed annually.

Worldwide, autopsy systems are promoting peer reviews of autopsies and autopsy reports. This is however not formalized in Hong Kong. Such reviews an take many forms and the value of such reviews will be illustrated in this talk.

Symposium 4D
Forensic Anthropology: Challenges and the Way Forward
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Department of Forensic Medicine, Kuala Lumpur Hospital, Malaysia

Forensic anthropology is the application of the knowledge of physical anthropology to solve medicolegal issues. The forensic anthropologist assists the police in locating and exhuming skeletal remains and performing an anthropological analysis on the remains to determine the biological profile i.e sex, age-at-death, ancestry and stature of the deceased. Presently forensic anthropologists are also involved in the identification of victims of mass disasters and genocide and are an integral part of any Disaster Victim Identification (DVI) team. Although well established in many developed countries this discipline is still in its infancy in Malaysia. This presentation will discuss the current practise of forensic anthropology in Malaysia and its place within the general inquiry into death as a provision under the Criminal Procedure Code. This presentation will also cite some well profiled local cases over the past 10 years where forensic anthropology played a major role in the investigation. The Malaysia DVI team was also involved in the identification of the victims of the MH17 air tragedy in 2014 and the victims in multiple clandestine graves along the Malaysia-Thailand border in 2015. This paper will also identify some of the challenges faced by the forensic anthropologist which has resulted in the slow acknowledgement of this discipline in an investigation into death – they are practical reasons as well as religious and sociocultural constraints unique to this country. Finally, this paper will propose steps to address these challenges with the hope that forensic anthropology in Malaysia will garner as much interest and be as developed as in other countries.

Result of toxicology analysis - Interpret it wisely
Khairul Adli bin Nikman
Forensic Medicine Laboratory, Department of Forensic Medicine, Hospital Sungai Buloh

A number of factors could influence the interpretation of toxicology analytical results, especially when post-mortem samples are concerned. Possible factors may be associated with: 1) the nature of the drug/poison detected, 2) the method of sampling, transport and storage, 3) the method of analysis applied, 4) the circumstances of exposure to contaminant, and 5) the circumstances that are related to death (if the medical and drug use history of the deceased person is made available) and postmortem changes. In certain situations, the interpretation of analytical measurement can be simplified by regulation. Terms such as ‘therapeutic’, ‘normal’, ‘normally expected’ or ‘target ranges’ have been conventionally used when analyzing the concentrations of many drugs and their metabolites presented in whole blood, plasma or serum. The interpretation of the toxicological results can sometimes be straightforward, but most of the time is difficult. It depends on the understanding of the principles of the analysis, the specimens used and their suitability for the analysis, the stability of the substances detected, and other relevant factors that could influence the results. The result of analysis can offer an objective evidence of the exposure of the drugs/poisons. However, the interpretation made in the knowledge of the possible effects of the detected drugs/poisons might influence the outcome of the investigation.

Forensic DNA Analysis - Challenges and the Way Forward
Nor Aidora Saedon
Forensic DNA Division, Department of Chemistry, Malaysia

Forensic DNA analysis in Malaysia had gone through a marvelous advancement since it was first launched in 1995. It used to be the RFLP techniques using radioactive isotopes to the HLA DQα and straight to PCR-STR technique. The process of hands on extraction via organic or Chelex, has evolved to automated platform via Solid Phase Extraction (SPE) methods. Since the extraction step has been shortened, the technology is no longer about the ability to extract but the quality of the extracted DNA. The quantitation process is coupled with extraction to ensure sufficient amounts of extracted DNA as well as the ability to detect male DNA and the rate of degradation. The amplification process in a single multiplex has increased from 9 to 24 loci for individual identification. Last but not least, interpretation of DNA profiles especially mixtures is another laborious task for Forensic DNA scientists worldwide.
Although it has progressed tremendously, there are still numerous challenges directly impacted on the quality of the samples submitted which leads to inability to generate interpretable DNA profiles, such as climate, storage conditions and sampling procedures. We may have the latest innovative technology in Forensic DNA analysis but it is futile when these destructive challenges are not dealt with accordingly. The understanding of basic fundamentals of Forensic DNA samples and the cooperation of inter-agencies are required to overcome some of these challenges.

Symposium 5D

Histology - Supportive or Detrimental Evidence in Court

Mohd Suhani Mohd Noor
Department of Forensic Medicine, Sultanah Bahiyah Hospital, Alor Setar, Malaysia

Forensic histopathology is the application of histological techniques and examination in forensic pathology practice, and like any other findings garnered during an autopsy, postmortem histological findings form part of the autopsy evidence presented in court. Because the applied histological techniques are similar to clinical histopathology, it is not unusual for some forensic pathologists who lack training in histopathology to defer entirely to the anatomical pathologists for their histological examination; a flawed practice, not least because anatomical pathologists are usually unfamiliar with histothanatology. It is crucial that the forensic pathologists themselves must be competent and comfortable in conducting a forensic histopathology examination and be aware of the limits of what histology can offer to a forensic pathology investigation. Although the scope and practice of autopsy tissue sampling for histology varies between centers, postmortem histology has proven to be an invaluable primary ancillary tool in the investigation of sudden natural deaths, dating of lesions and injuries, and in the detection of sequelae in delayed unnatural deaths. As histology provides permanent documentation of the pathologies identified at autopsy, it is also a valuable tool for auditing a forensic pathology service and can be made available for reexamination by other experts in subsequent case reviews. This presentation will illustrate by case examples how histology can be indispensable evidence in court and how, either through erroneous reporting or overinterpretation, it can prove to be detrimental to justice.

Forensic Imaging - Destructive or Supportive Evidence in Court

Mansharan Kaur A/P Chainchal Singh
Faculty of Medicine, Universiti Teknologi MARA

Advances in technology have led to the use of various digital techniques including the use of radiological imaging in the presentation of evidence to the courts. In some cases, these techniques have allowed the court to gain more valuable information than would otherwise have been evident. In other cases, it has allowed the court to receive evidence that it would not have been able to receive without the assistance of digital technology. Radiological imaging which includes the use of x rays, post mortem computed tomography (PMCT and PMCTA) as well as Magnetic Resonance Imaging (MRI) enables a complete and permanent recording in real time of the images it produces and these images can readily be transmitted. Further, the process occurs before the body is subject to surgical intervention which may reveal important factors demonstrating the cause of death that can be missed in autopsies.

Medical Microbiology, Parasitology and Immunology

Symposium 1E

Mass Spectrophotometry Application in Infectious Diseases

Kartina Mohd Nor
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Mass spectrophotometry has been used for many decades but only in the 1970s, it was proposed for bacterial characterization. As a result, matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) was developed. It is a rapid, accurate, cost effective method in microbial characterization and identification. It is used to identify bacteria and fungi in laboratory settings in main public hospitals in Malaysia. The experiences, advantages as well as disadvantages and important practical issues will be presented.
Current Trends in Microbiological Diagnostics and Clinical Application of Rapid Diagnostic Tests in Infectious Disease

Alex van Belkum
bioMérieux, Open Innovation & Partnerships, La Balme Les Grottes, France

Rapidity is one of the most important parameters and central pillars of modern diagnostics in infectious diseases management. Next to speed, also costs, availability, technical complexity and quite a few other parameters are important parameters when making local choices for in vitro tests. Classical culture-based technologies have continued to suffer from lack of speed, although modulation of media has resulted in improvements over the years. Still, in order to improve on the overall speed of testing, lengthy procedures should be circumvented and there is an obvious need for more direct methods. Serology has proven to be one of those candidate technologies and with the advent of miniaturized testing formats both the rapidity and efficacy of immunological testing has been improved. Better, molecular diagnostics has now facilitated the reliable and (semi-)quantitative detection of essentially all pathogens that carry nucleic acids. Single tests have been developed for all clinically relevant pathogens, but currently multiplexed tests that target specific syndromes (respiratory infections, sexually transmitted infections, gastrointestinal infections etc) are rapidly gaining in usefulness and popularity. New trends in IVD are laboratory automation, consolidation of labs and the development of dedicated satellite laboratories, inclusion of omics technologies (mostly next generation sequencing) and, last but not least, optimized data management using artificial intelligence and machine learning components. All technological and data management development will work in concert for further improvement in the adequate application of IVD in clinical microbiology and infectious diseases.

Next to the mostly laboratory-oriented developments sketched above, improved diagnostics will have an impact on the medical sector. The use of tests will result in better diagnosis, surveillance application of tests will result in better assessment in infectious epidemiology and, most importantly, antimicrobial resistance testing will result in better, more targeted use of therapeutic antibiotics. The impact of the newer diagnostic tests will be discussed in the context of increasing numbers of infectious disease outbreaks (antimicrobial resistance spread, coronavirus outbreaks, the annual influenza waves etc) and the better protection of increasing numbers of susceptible individuals (elderly, immune-compromised, transplant patients etc).

This one hour-presentation will be split in two sections as based on the two-component title. The first part will be on test quality, the second on test application in specific infectious diseases. The references below provide current state-of-the-art information on several of the topics covered above.

Symposium 2E

Genetic Approaches in Diagnosing Patients with Primary Immunodeficiency Diseases

Siti Mardhiana Mohamad
Immunology Unit, Advanced Diagnostic Laboratory, Advanced Medical and Dental Institute, Universiti Sains Malaysia

Primary Immunodeficiency Diseases (PIDs) are a heterogeneous group of genetic disorders characterised by malfunctioning of the immune system that predisposes to different patterns of infections, allergy, autoimmunity and cancer. To date, more than 400 gene defects have been identified to cause PIDs. PIDs are considered to be ‘experiments of nature’ as they provide in vivo assessment of the functional consequences when specific genes are defective and help our understanding of the basic cellular pathways and mechanisms of host defence in the human immune system.

There have been several approaches that have been used to identify the genetic defects that cause the diseases in PIDs patients. The three major approaches that are currently favoured are: 1) targeted sequencing - investigating candidate genes within pathways that are known to be important and shown to be dysfunctional, 2) genomic approaches such as next generation sequencing (NGS) and/or linkage analysis and 3) comparative genetics, i.e. similarity of the clinical phenotypes to mouse models.

The identification of a genetic defect provides a huge impact for the patients and family members. Importantly, it helps to provide precise diagnosis and accurate prognosis for the patient. Since patients with PIDs are associated with increased morbidity and mortality, the molecular diagnostics enable the appropriate therapy and treatment to be given to the patients so that a permanent curative can be given and lifesaving for the patients.

Updates in Allergic Testing

Amir Hamzah Abdul Latiff
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Allergic diseases pose huge economic burden and adverse effects on quality of life. Serum specific IgE has been considered a surrogate allergy marker for decades. An overview on current status of allergy testing is discussed in this presentation, including molecular testing. Other modalities of allergy testing include skin prick tests which are useful for aero-allergies whereas oral challenge tests are best for identifying suspected food allergies. An allergy test should be individualised based on clinical features, diagnostic efficacy, and cost-benefit analysis.
Anti-nuclear Antibody Test - An Update

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Anti-nuclear antibody (ANA) test is a common laboratory test requested particularly for the working diagnosis of systemic autoimmune rheumatic diseases. There are many laboratory methods available for the detection of ANA, but indirect immunofluorescence (IIF) has been considered as the gold standard. Usually for ANA-IIF positive reporting, it requires the report of the pattern and titration. However, the significant ANA-IIF positive titration is different between the laboratories and similarly the report of the pattern may differ from one individual to another. To add to these challenges, the recognition of the new pattern such as dense-fine speckled requires further evaluation to determine their clinical significance. Recently, the introduction of the International Consensus on ANA Patterns (ICAP) helps to provide the platform towards education and standardization of ANA reporting. Furthermore, the encouraging performance of the digital imaging software in interpreting ANA pattern will further reduce the gap towards the standardization of ANA-IIF testing and reporting.

Symposium 3E

What We Should Know About SARS Coronavirus 2

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On March 11th, 2020, WHO has declared SARS-CoV-2 pandemic which has to date globally infected 73 million and killed 1.6 million people. It has affected virtually all countries including Malaysia. Various methods were employed by all countries to control the pandemic which include lockdowns, quarantine and complying with standard operating procedures such as social distancing, wearing masks and good hand hygiene. The pandemic has also a severe impact on global economy and has increased poverty rates and therefore pose serious threats to human health in a big way.

The virus which originates from animals and bats were implicated as the natural reservoir. However, intermediate hosts was never confirmed to link to the current pandemic. Coronavirus generally mutate at a slower pace compared to other viruses. This may be a good thing but a minor mutation on D614G was postulated to increase its efficiency in transmission. However, this mutation has not shown to increase its virulence.

Initially thought to be only limited to the respiratory tract, it is now shown that the virus had gone to infect other organs and even creating havoc to the immune system and thus many patients died because of the overwhelmed immune overreaction. Long term immunity has been debatable and cannot be proven at the moment. The reduction in antibodies in recovered patients may indicate loss in immunity but one must not rule out the role of T cells in preventing future infections. Studies on T cells are ongoing and preliminary, there is a promising role of T cells in coronavirus infections.

Diagnostic Challenges of Hepatitis B Escape Mutant

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Hepatitis B (HBV) viral infection causes acute and chronic liver disease, preventable by vaccination. One third of the world population have serological evidence HBV infection. In 2015 an estimated 257 million people were living with chronic HBV infection. Worldwide it is a primary cause of cirrhosis and hepatocellular carcinoma. Hepatitis B belongs to the Hepadnaviridae family, the smallest DNA-enveloped virus, with a unique genome and replication mechanism. The genome has four overlapping open reading frames (ORFs): preS/S, precore/core, pol and X ORF. High mutation rate results in genetic variability or production of viral variants, known as “quasi-species”. Viral selection depends on factors such as viral fitness, host immune response and external factors ie vaccination and antiviral therapy. Laboratory diagnosis is based on the detection of HBsAg, the antigen that induces protective antibody (anti-HBs). In most cases, serological markers including anti-HBcore and anti-HBs, can identify different clinical stages of viral persistence; chronic hepatitis B, “healthy carrier” or occult hepatitis B infection. Mutations within HBsAg alter the antigenicity of HBsAg, which give rise to s-gene mutants or “escape mutants”. These mutants escape neutralising anti-HBs antibodies including vaccine-induced immunity, affect the success of vaccinations using HBsAg, escape from anti-HBV immunoglobulin therapy, and affect detection by diagnostic immunonoassays. Escape mutants form a subset of occult hepatitis B infection (OBI), which are HBsAg-negative with detectable HBV DNA in liver and/or blood, by a sensitive molecular method. Mutations were also detected among immunosuppressed patients who developed HBV reactivation, who previously had anti-HBs. Pol gene mutations have also been described, causing resistance to nucleo(s)tid analogues antiviral therapy. Precore/core mutants cause HBeAg-negative chronic hepatitis B with presence of anti-HBe, where viral replication continues, and HBV DNA is detectable. X-gene mutations may alter the function of the nonstructural X protein, with possible role in HBV replication and carcinogenesis.
Molecular Diagnostics for Viral Meningitis and Encephalitis

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Viral meningitis and encephalitis have traditionally depended on serology and culture for diagnosis of causative agents. These methods are insensitive and slow and have been largely superseded by molecular methods. This talk will cover available molecular diagnostic assays and their advantages and disadvantages, as well as clinical impact.

Symposium 4E

Update on Parasitic Infections: Conventional and Advanced Diagnostic Approaches

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Parasitic infections continue to be one of the most devastating diseases affecting humans worldwide. Appropriate anti-parasitic agents and sustainable preventive measures are the main key implementation for successful reduction of mortality and morbidity of parasitic diseases. However, these are largely dependent on the timely and accurate detection of the parasitic agents. For many decades, the diagnosis of parasitic infections relies on the microscopic examination which is very labour-intensive and time-consuming. Nonetheless, in situations where clinical samples or affected tissues are not readily available, non-microscopic methods such as immunological and molecular approaches can be considered. In addition, as misdiagnosis of several parasitic diseases would significantly influence the impact on the optimum care of the patient, several advanced methods of diagnosis have been developed and have gained much attention by the parasitologist.

Molecular Diagnosis of Malaria: What’s New?

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Malaria is a mosquito-borne disease caused by five species of Plasmodium parasites. People infected with malaria often experience fever, chills and flu-like illness. Left untreated, they may develop severe complications and die. Prompt and accurate diagnosis of malaria play an essential part in malaria treatment, control and elimination. While the sensitivities of conventional diagnostic methods i.e. light microscopy (LM) is generally sufficient to diagnose acute malaria cases, it has important limitations in low-endemic settings, as substantial proportion of infections might be asymptomatic and sub-patent. By increasing sensitivity of malaria parasites detection compared to LM, molecular techniques provide a more sensitive approach to diagnose very low parasite density infections. Molecular techniques, such as polymerase chain reaction (PCR) enables the specific identification of malarial parasites up to the species level. With conventional diagnostic methods falling short in terms of practicality or having incomplete coverage of all medically important Plasmodia, PCR-based methods seem promising as the new gold standard in malaria diagnosis, especially in the cases with low parasitaemia or in the case of mixed species. In this talk, I will discuss a comprehensive overview of the currently available molecular malaria diagnostics, ranging from well-known tests to practical issue for the application of molecular tests in malaria identification. Indirect reference range establishment.

Symposium 5E

The role of non-cultural technique in yeast infection

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Fungal infections caused by various yeast pathogens have been reported to be increasing worldwide. The emergence of antifungal resistance among yeast warrants accurate, reliable laboratory diagnosis to ensure prompt, targeted treatment. As culture technique is time-consuming and has low sensitivity, there is a crucial role for alternative, non-culture diagnostic methods. A number of methods including multiplex-PCR analyses, T2 magnetic resonance and fungus-specific DNA microarrays are reviewed, with regard to their principles, advantages and current applications.
Current Microbiological Techniques for the Diagnosis of Nontuberculous Mycobacterial Infections

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The majority of nontuberculous mycobacteria (NTM) isolated in diagnostic microbiology laboratories are respiratory isolates. Although the isolation of NTM from respiratory sites usually reflects environmental contamination/colonisation, their growth in culture may also represent a clinically significant lung infection. Due to factors such as cost as well as lack of appropriate laboratory facilities, technical skills and expertise, diagnostic methods/tools for the identification of NTMs may not be widely available, especially in resource-limited settings. Hence, the diagnosis of NTM infections remains a challenge in developing countries. In this presentation, I will give an overview of and updates on the different microbiological techniques currently available for the diagnosis of NTM infections, including line probe assay and gene sequencing, with emphasis on their advantages and limitations.

Sepsis Biomarkers

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Sepsis is one of the major causes of death in Malaysia and globally. The results of the Global Burden of Disease Sepsis Study were published 17 January in The Lancet and presented at the Critical Care Reviews meeting in Belfast. It is the fact that twice as many people are dying from sepsis worldwide than previously estimated, with 48.9 million cases and 11 million deaths in 2017 alone. One in every 5 deaths worldwide are associated with sepsis. Two out of every 5 cases are in children under 5. About 85% occur in low- or middle-income countries. It is also the third principle cause of death in Malaysia in the year 2016, which is about 13.3% out of other causes of death. However, sepsis is the second-leading cause leading to intensive care unit (ICU) admission in the year 2016 in Malaysia. Given the morbidity and mortality associated with sepsis, the ability to risk stratification in early phase of their illness may assist the physician to more effectively manage the care and to improve their outcome. Bacteraemia sepsis is a condition in which patients have systemic inflammatory response syndrome associated with infection. Early diagnosis of a bacterial infection is necessary because it can evolve rapidly, and treatment depends on antibiotic administration. Clinicians are in need of good diagnostic and prognostic biomarkers to identify infected patients who would benefit from prompt antibiotic therapy as early as possible, thus, improve the survival rate. Traditionally, the white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are utilised as common screening laboratory tests, but these have poor sensitivity and specificity. Therefore, there is a need to explore other biomarkers that are specific and sensitive in correlation to sepsis diagnosis, prognosis and differentiate bacterial infection.

ABSTRACT

ANATOMIC PATHOLOGY

AP01 Orbital Kimura’s disease: a collection of 7 case reports

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Introduction: Kimura’s disease (KD) is a chronic inflammatory disorder. The orbit is one of the most common sites of occurrence. Case Series: A total of seven cases of orbital KD were retrieved from the database of Department of Pathology, Hospital Serdang. Orbital KD occurred in four male and three female patients (age: 12-67 years old, mean age: 38.4 years old). All cases were presented as painless eye swelling of various duration (2 months to 6 years). Upper or lower eyelid of either eye was involved. One of the patients developed new lesion at contralateral eye a year after first surgery. All patients were associated with eosinophilia and increased absolute eosinophilic count in peripheral blood. The tumour size varied from 1 to 5 cm grossly. Histologically, all cases showed lymphoid hyperplasia, eosinophils infiltrates and fibrosis. Discussion: Orbital KD occurs in a wide range of age groups and presents as slow-growing nodular masses. One should raise the possibility of KD before a diagnosis of nonspecific reactive lymphoid hyperplasia is made. A helpful guide is eosinophilia and increased absolute eosinophilic count in peripheral blood.
AP02 Expression of oestrogen-α receptor in papillary thyroid carcinoma and its association with metastasis

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Introduction: Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy, which is more prevalent in females than in males. Although the disease prognosis is good, less favourable outcomes are predicted in those with higher disease stages and nodal metastasis. Oestrogen-α (ER-α) has been proposed as a predictor for lymph node metastases due to its association with greater disease progression. This study aims to evaluate the association between ER expression and clinicopathological features, which include lymph node metastasis, tumour size, extrathyroidal extension, histological variants of PTC, age groups, ethnicity and gender. Materials & Methods: We studied immunohistochemical expression of ER-α in 84 PTC cases obtained within an eight-year period (2011-2018) in Hospital Pulau Pinang. Fisher’s exact test was used to evaluate the associations between ER-α expression and clinicopathological features. The statistical significance was set at p <0.05. Results: ER-α was expressed in 13.1% of all the PTC cases examined (n=11/84). There were no associations observed between ER-α expression and lymph node metastasis (p=1.000), tumour size (p=0.970), extrathyroidal extension (p=0.677), variants of PTC (p=1.000), age groups (p=0.188), gender (p=0.725) or ethnicity (p=0.920). Discussion: There was no evidence in this study to support the application of ER-α as a prediction marker for lymph node metastasis or disease aggressiveness in PTC. We suggest a prospective study integrating detailed clinical and radiological findings together with proper follow up data to be conducted for future research, to better evaluate ER-α expression association with lymph node metastases and disease progression.

AP04 Immunexpression of retinoblastoma protein in uterine carcinoma of urinary bladder

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Introduction: Expression of retinoblastoma gene protein (pRb) has been observed in the genesis of many types of human cancers. The study aims to determine the immuno-expression of pRb in primary uterine carcinoma cell carcinoma of urinary bladder and its association with different histological grades. Materials & Methods: Expression of pRb was studied by immunohistochemistry in 45 cases of uterine carcinoma of urinary bladder. Mouse monoclonal antibody against human pRb was used for immunohistochemistry on formalin fixed paraffin embedded tissue sections. Positive immune-reactivity was observed in the nuclei of tumour cells as brown staining. The intensity of immune-reactivity was classified based on the percentage of tumour cell nuclei with positive staining: negative = no immune-reactive cells, weak = 1 - 50% of tumour cells showing nuclear reactivity, strong = >50% of tumour cells showing nuclear reactivity. pRb immunexpression was correlated with the different histological grades of uterine carcinoma. Results: Positive pRb immunexpression was observed in 39 cases (86.7 %) and negative in 6 cases (13.3%). Intensity of pRb expression was well correlated with histological grades of transitional carcinoma of urinary bladder. Strong pRb expression was seen in 82.4% of histological grade I (14 out of 17) and negative or weak expression was seen in histological grade III (15 out of 17). Discussion: These data suggest that pRb expression plays an important role in the genesis of bladder cancer and has an inverse relationship with histological grades.

AP05 Programmed death ligand 1 expression in endometrial carcinoma: an immunohistochemical study

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Introduction: Endometrial carcinoma is the 3rd most common gynaecologic cancer in Malaysia. It is the only gynaecologic malignancy with a raising incidence and mortality and poses a major health concern worldwide. PD-L1 is a transmembrane protein that modulates T-cell response. The up-regulation of PD-L1 expression on tumour cells causes T-cell suppression, which impedes anti-tumour immunity, promote immune cell evasion and enhance tumour survival. The aim of this study was to evaluate PD-L1 expression in endometrial carcinoma and correlate with survival rate. Materials & Methods: A total of 59 cases of endometrial carcinoma were retrieved from the archive of department of Pathology in a period of 5 years. Thirty-two cases of non-neoplastic endometrial tissue were included as control. PD-L1 immunohistochemistry was performed on all cases. PD-L1 expression was evaluated on tumour cells and immune cells. Results: The average age of patients with endometrial cancer (53.5 years) was slightly higher than control (48.9 years). PD-L1 was positive in 62.7% (37/59) and 28.8% (17/59) of immune cells and tumour cells, respectively. PD-L1 expression in immune cells was significant higher in endometrial carcinoma than non-neoplastic endometrium (p= <0.001). Among the patients with endometrial carcinoma, PD-L1 expression in tumour cells was significantly higher in patients who died (10/15, 66.7%) compared to those who survived (7/44, 15.9%) (p= <0.001). Discussion: It is noteworthy to point out that the expression of PD-L1 in tumour cells was significantly associated with a poor survival. This suggests that immunomodulation using PD-L1 inhibitors may be useful in advanced endometrial carcinoma.
AP06  Correlation of E-cadherin expression in endometrial carcinoma with tumour grade and stage

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Introduction: Endometrial carcinoma (EC) is among the common malignancy in female with adverse prognosis in the advanced stage. Prediction of its prognosis is important in stratifying EC patients in order to achieve optimum treatment and improve clinical outcomes. This study is aimed to evaluate the prognostic significance of E-cadherin expression in patients with EC.

The present study investigated the correlation of E-cadherin expression in EC with its tumour grade and stage. Materials & Methods: A total of 70 cases of EC were included in the study within the duration of eleven-year period comprising of 56 cases of endometrioid carcinoma, 2 cases of mucinous carcinoma, 10 cases of serous carcinoma and 2 cases of clear cell carcinoma. E-cadherin expression was immunohistochemically analysed and compared with clinicopathological parameters. Results: Loss of E-cadherin expression shows significant association with non-endometrioid EC (p=0.003), high tumour grade (p=<0.001) and tumour with distant metastasis (p=0.028). Loss of E-cadherin expression shows significant predictor for high tumour grade (Grade 3: aOR 8.400, 95%CI 2.534-27.842). There were no significant association between E-cadherin expression with myometrial invasion, FIGO stage, lymph node status and lymphovascular invasion. Conclusion: E-cadherin expression correlates with high grade EC. This may serve as potential prognostic marker for EC.

AP07  Intensity of stromal CD10 expression: a useful tool in differentiating grades of fibroepithelial neoplasms

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Introduction: The application of the WHO criteria to distinguish fibroadenoma and phyllodes tumour can be ambiguous with inter-observer variability among pathologists. The aim of this study is to evaluate stromal CD10 expression in fibroepithelial neoplasms as a tool to differentiate fibroadenoma and different grades of phyllodes tumour. Materials & Methods: We analysed stromal CD10 expression in 100 cases of fibroadenoma and 60 cases of phyllodes tumour (30 benign, 21 borderline and nine malignant) including eight recurrent phyllodes tumour using tissue microarray blocks. The staining intensity was graded into 0, 1+, 2+ and 3+, respectively and only considered positive if more than 20% stromal cells stained for CD10. Results: There was a significant increase in the age and tumour size of the patients, from fibroadenoma to phyllodes tumour group (p < 0.001). Stromal CD10 expression were positive in 25 of 100 fibroadenomas (13 cases 1+, 11 cases 2+, one case 3+), 23 of 30 benign phyllodes tumours (four cases 1+, 13 cases 2+, six cases 3+), 13 of 21 borderline phyllodes tumours (five cases 1+, six cases 2+, two cases 3+) and nine of nine malignant phyllodes tumours (one case 2+, eight cases 3+). Stromal CD10 expression was significantly increased in the higher grade fibroepithelial lesions (p < 0.001). Stromal CD10 expression had a high specificity (91%) for differentiating between benign (fibroadenoma and benign phyllodes) and malignant tumours (borderline and malignant). Conclusions: Stromal CD10 expression can be a helpful adjunct in distinguishing fibroadenoma and different grades of phyllodes tumour.

AP08  A diagnostic challenge of orbital Kimura disease: a case report

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Introduction: Kimura disease is a benign, chronic inflammatory disorder of subcutaneous tissue of unknown aetiology. Patients usually presented with tumour-like swellings, mainly in the head and neck region. Its occurrence in the orbital region has been reported although it is extremely rare. Case report: A 68-year-old gentleman presented with worsening proptosis, diplopia on primary gaze and blurring of vision of right eye for the past 6 years. On examination, the right eye shows non-axial proptosis with fullness over upper and lower eyelids. There is a subconjunctival mass at the supero-temporal region. Computed tomography of the brain, orbit and thorax revealed a right retrobulbar enhancing mass encircling the optic nerve with poor fat plane with the surrounding extraocular muscles and lacrimal gland. Possible differential diagnoses include orbital lymphoma, vascular mass, haemangioma or pseudotumour. Right eye incisional biopsy was performed. Histopathological examination showed heterogenous lymphoid infiltration of the fibrous tissue, composed of admixture of mature lymphoid cells, eosinophils and plasma cells. Several lymphoid follicles with germinal centres are seen. Hyalised vessels are noted interspersed between the lymphoid cells. Immunohistochemical studies show the admixture of B and T cells is highlighted by CD3 and CD20. CD30, CD15, Bcl-2 and CD1a were negative. Discussion: Despite its rarity, Kimura disease should be considered as one of the possible differential diagnoses of orbital lesion. Because of the peculiar location and variability of histologic patterns, it may cause diagnostic problems clinically, radiologically and histologically. Although the case of Kimura disease is regularly reported and is now clearly defined, it still constitutes a diagnostic challenge. This case highlights the importance of awareness for this entity, the characteristic morphological features and immunohistochemical profile that may help prevent a misdiagnosis.
AP09 NUT midline carcinoma – a distinct new entity of an aggressive and poorly-differentiated sinonasal carcinoma predicated by NUT immunohistochemical stain

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Introduction: NUT midline carcinoma (NMC) is a highly aggressive carcinoma with poor prognosis that is caused by translocations involving the NUT gene on chromosome 15q4, most commonly with BRD4 (19p13); forming a fusion gene. The histological features of this tumour are indistinguishable from various other tumours. Identification of the translocation or NUT fusion protein confirms the diagnosis. Case report: We present a case of an 18-year-old Malaysian, who presented with hyposmia, nasal congestion, thiorrhoea, epistaxis and headaches. Nasal endoscopy revealed a mass in the right nasal cavity, completely occluding the space. In addition, another mass is seen on the hard palate. Imaging (CT) of the head and neck region reveals a mass arising from the septum, extending to the skull base, posterior nasopharyngeal wall and turbinates. The tumour was debulked with recurrence detected 13 days post-operatively at the base of the left nostril. The tumour was initially reported as poorly-differentiated squamous cell carcinoma. The patient was referred to a tertiary centre and underwent transcranial and transcranial tumour resection. Microscopically, the tumour was poorly-differentiated, with non-specific immunohistochemical findings. The list of differential diagnoses was inexhaustive and was finally confirmed by outsourcing the case for NUT immunohistochemical stain, which was positive and confirmed the presence of NUT fusion protein. Discussion: The unequivocal diagnosis of NUT midline carcinoma is established through diffuse nuclear staining using NUT immunohistochemical stain, rather than through histology, which is indistinguishable from many poorly differentiated tumours. Awareness of this new entity helps in early confirmation of this lethal tumour.

AP10 Leiomyosarcoma of the retroperitoneum with liver metastasis: a case report

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Introduction: Leiomyosarcoma is a high grade malignant soft tissue sarcoma with high rate of local recurrence. It has propensity for hematogenous spread and infrequently metastasize to lymph nodes. Up to 16% of all patients with retroperitoneal sarcomas develop hepatic metastases. Case report: A 51-year-old woman presented with painless right sided abdominal mass of three months duration, associated with loss of weight. Computerised tomography (CT) abdomen revealed a large right retroperitoneal mass causing right ureteric obstruction and right hydrenephrosis. A laparotomy was performed and intraoperative findings revealed a huge lobulated mass (21.0 x 19.0 x 12.0 cm) attached to the right kidney. Histopathological examination confirmed leiomyosarcoma. After 18 months, follow-up CT scan noted enlarging liver nodule at segment V. Subsequently, a liver segmentectomy was performed. The nodule measured 6.0 x 4.5 x 4.7 cm and histological examination showed circumscribed tumour composed of malignant spindle cells arranged in intersecting fascicles and focal storiform pattern. Numerous mitotic figures including aberrant form are seen. The cells were diffusely positive for desmin and smooth muscle actin (SMA) with negativity for S100 and MyoD1, confirming the presence of NUT fusion protein. Conclusion: The unequivocal diagnosis of NUT midline carcinoma is established through diffuse nuclear staining using NUT immunohistochemical stain, rather than through histology, which is indistinguishable from many poorly differentiated tumours. Awareness of this new entity helps in early confirmation of this lethal tumour.

AP11 The eyes don’t see what the mind doesn’t know: a story of calciphylaxis

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Introduction: Calciphylaxis, or calcification uremic arteriolopathy, is a rare but fatal medical condition due to subcutaneous vascular calcification and cutaneous necrosis. The pathogenesis is complex and poorly understood. Calciphylaxis is most often occurred in patients with renal failure and affecting mostly the lower extremities. Case report: We report a case of a 60-year-old gentleman with multiple comorbidities including end-stage renal failure presented with multiple painful gangrenous and necrotic patches involving the abdomen, inner thighs and tips of glans penis. The initial skin biopsy was too superficial and reported as hyperpigmentation with chronic inflammation. Tissue culture and sensitivity reported growth of Proteus houseri and Enterobacter cloacae. Dermatologist in a tertiary centre was consulted and calciphylaxis was suspected based on the clinical presentation and laboratory findings. The patient was managed by multiple disciplinary teams and wound debridement was planned. The removed tissue was sent for histopathological examination and subsequently, reported as features consistent with calciphylaxis and panniculitis. However, one week after the wound debridement, he developed sepsis and succumbed to death. Conclusion: Calciphylaxis is a challenging medical condition to both physician and histopathologist. Strong clinical suspicion and adequate tissue sampling are important for accurate diagnosis.
AP12 The user interface evaluation of Integrated Cancer Diagnosing System

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Introduction: Statistics shows that numbers of new cancer patients are increasing and this means more work to an already high workload for pathologist. This study report testing and evaluation result for the Integrated Cancer Diagnosis System (ICDS).

Materials & Methods: A workshop on digital pathology concepts and artificial intelligence role has been carried out with participation of twenty pathologists. The ICDS alpha version comprises of automated breast and prostate cancer diagnosing functionality were presented. Workshop participant were asked to explore the system intuitively and rate the system on the user interface. The breast cancer diagnosing system applies Decision Rules algorithm to combine knowledge from General Surgical Ward, Radiology and Histopathology text record. Mamdani-fuzzy algorithm was used to grade radiology images into BIRADS grading. The prostate cancer diagnosing on the other hand, uses Production Rule and Random Tree algorithm to combine knowledge from Urology, Radiology and Histopathology departments. An automated Gleason Score grading for histopathology images which uses ensemble learning algorithm has been fused as well into the ICDS. For record, the BIRADS grading module as well as prostate cancer grading and Gleason score modules has been evaluated by experts in their own evaluation session.

Results: The ICDS interface has been rated as 3.4 stars out of 5. Discussion: The medical officers prefer to be guided first rather than self-exploratory method in navigating new system. Improvement on the ICDS interface was suggested, particularly on help and information button to facilitate and provide guidance to user.

AP13 Comparative evaluation of immunofluorescence technique on paraffin embedded and fresh frozen sections in renal biopsies

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Introduction: Immunofluorescence (IF) technique is essential for diagnosis of glomerular disease to detect immune deposits in renal biopsies. This technique is routinely done on fresh frozen tissue (IF-F) for optimal and reliable results. However, variable success rates were reported for IF study on formalin fixed and paraffin embedded (FFPE) tissue sections (IF-P). Materials & Methods: We studied the IF expression of immunoglobulin IgG and IgA in the FFPE of renal biopsies. Proteinase-K enzymatic treatment was carried out on the FFPE tissue of renal biopsies for antigen retrieval. Direct and indirect IF was done on FFPE for immunoglobulins IgG and IgA and the result were compared to the routine IF-F study. Results: When compared to the IF-F, the IF (direct method) carried out on the IF-P cases show 19% positivity (of 1+ and 2+) for IgG and no positivity for IgA. However, using IF (indirect method), 34% cases show positivity of 1+ in IgG. In general, the intensity of the IF staining is weaker compared to the routine IF-F. Discussion: Overall, the detection of immunoglobulin on IF-P was very low in terms of quantity and staining intensity compared to those of routine IF-F samples. Therefore, the IF staining on IF-P must be interpreted with great caution. Further studies are needed to improve the methodology used to enable the use of IF-P as a salvage technique in renal biopsies.

AP14 EBV positivity and lipid signalling molecules Sphk1 and S1pr1 protein and mRNA expression in Hodgkin Lymphoma

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Introduction: Lipid signalling molecules, particularly Sphk1 and S1pr1 have been correlated with increasing clinical grade of Hodgkin lymphoma (HL), suggesting possible targets for therapeutic intervention. The role of EBV is still poorly defined in HL. Materials & Methods: This study aims to determine the EBV positivity by EBER in situ hybridization and the immunohistochemical expression of Sphk1 and S1pr1 in 61 cases of Hodgkin lymphoma, retrieved from the Pathology Department, Queen Elizabeth Hospital, Birmingham. mRNA expression of Sphk1 and S1pr1 in HL cell lines were determined by RT Q-PCR. Results: EBV was found to be positive in 24/61 cases (39.3%), however EBV positivity did not show any significant correlation with clinicopathological parameters and overall survival of HL patients. Sphk1 was expressed in HRS cells in 25/61 (41%) cases and was localised to the cytoplasm of HRS cells. S1pr1 was strongly expressed in HRS cells in 48/61 cases (78.7%) and was localised to the cell membrane of HRS cells. Most tumours which were positive for Sphk1 were also significantly positive for S1pr1 (p =0.018). Sphk1 and S1pr1 mRNA were highly expressed in a few HL cell lines. Discussion: High levels of Sphk1 and S1pr1 are associated with increased proliferation and resistance to chemotherapy in a few cancers. High levels of Sphk1 and S1pr1 in primary HL tissue and cell lines might shed some lights on their significance in lymphomagenesis and maybe promising targets in HL.
AP15 Determination of EBV gene latency pattern in EBV-positive diffuse large B cell lymphoma using EBER in situ hybridization, LMP1 and EBNA2 immunohistochemistry and correlation with clinical outcome

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Introduction: EBV-positive cases comprise about 2-7% of DLBCL and they are associated with poorer outcome compared to their EBV-negative counterparts. EBV can establish different latent state and there are three types of latency patterns. Various EBV associated cancers exhibit different EBV latency pattern. Burkitt lymphoma expresses latency type 1 and nasopharyngeal carcinoma exhibits latency type 3. Materials and Methods: This study aims to determine EBV gene latency type and correlate them with clinical outcome. We analysed 300 cases of DLBCL cases and determine their EBV positivity by EBER in situ hybridization followed by LMP1 and EBNA2 immunohistochemistry to determine the latency type. Results: Out of 300 DLBCL cases, 14 cases showed EBV positivity. Out of these 14 cases, eight (57.1%) patients showed EBV latency III (EBER+, LMP1+, EBNA2+), 2 (14.3%) latency II (EBER+, LMP1+, EBNA2-) and 4 (28.6%) latency 1 (EBER+, LMP1-, EBNA2-). Statistical analysis showed that EBV latency type did not correlate with overall survival (p=0.194) and event free survival (p=0.221).
Discussion: EBV latency III was most frequently seen in EBV-positive DLBCL. This is in line with most reports which showed that latency II and III are the most common forms of latency seen in EBV-positive DLBCLs. Previous study observed a worse survival outcome for patients with latency type III compared to latency type II and I. The reason for EBV latency pattern not having any prognostic impact or a worse survival rate could be due to the low number of EBV-positive cases in our series.

AP16 CD3-positive plasmablastic lymphoma in an immunocompetent individual: a potential diagnostic caveat

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Introduction: Plasmablastic lymphoma (PBL) is a rare aggressive subtype of mature large B cell lymphoma involving almost exclusively the extranodal regions in immunocompromised patients. Aberrant immunoexpression of CD3, a T cell marker in PBL, in the absence of other B-cell markers is exceptionally rare, may potentially lead to incorrect interpretation as high grade T-cell lymphomas. Case report: A 51-year-old man presented with two-month history of painful, rapidly enlarging right alveolar mass associated with significant weight loss. Computed tomography of paranasal sinuses concluded a locally aggressive malignant lesion. The right alveolar mass was biopsied, revealing diffuse sheets of malignant cells displaying large pleomorphic vesicular nuclei with prominent nucleoli and moderate abundant cytoplasm. Mitotic figures were easily seen, Tumour necrosis was focally noted. Immunohistochemically, the malignant cells demonstrated CD3 immunopositivity; while cytokeratin AE1/AE3, SI100, CD20, CD79a and PAX5 were negative. Ki67 proliferative index was high, approximately 80%. Intriguingly, the rest of the T-cell markers (CD2, CD5, CD7 and CD8) other than CD4 were negative, but strongly expressed CD138 and MUM-1. CD30, TIA-1 and ALK were negative. Epstein-Barr encoding region (EBER) in situ hybridisation for EBV was positive. A diagnosis of PBL was rendered. Discussion: Applications of other T-cell and B-cell markers in addition to routine CD3 and CD20 with appropriate molecular studies are sometimes essential in assigning the malignant lymphoid cell lineage. Knowledges of the characteristic clinical presentation, sites of tumour involvement, careful scrutinised histomorphological and immunohistochemical pattern evaluation with a high index of suspicion are the key to achieving an accurate diagnosis.

AP17 Interpretation of FISH assays according to the latest ASCO-CAP guidelines 2018 in breast cancers

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Introduction: Recommendations on human epidermal growth factor receptor 2 (HER2) testing on invasive breast cancers by in situ hybridisation have recently been updated by the American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP). In this preliminary retrospective study, we aim to investigate the impact of the new guidelines on invasive breast cancers with equivocal (HER2 2+) and positive (HER2 3+) immunohistochemistry (IHC) results diagnosed in the past one year in a local tertiary institution. Materials and Methods: 24 breast cancer cases with equivocal HER2 IHC and 25 positive HER2 IHC cases between January 2019 and December 2019 were enrolled in this study. Results: According to the 2018 guidelines, of all equivocal HER2 cases, 3 cases were categorised into group 1, 4 cases were group 4 and 17 were group 5. Therefore, 21 out of 24 HER2 IHC-equivocal cases were confirmed to be negative. All 25 HER2 IHC-positive cases fell into group 1, except for one case, where the case was re-categorised as negative (group 5). Conclusion: The latest 2018 guidelines provide a reduction in false-positive and equivocal HER2 cases which result in accurate selection of patients for HER2-targeted therapy.
AP18 The use of WHATSAPP® instant messaging in histopathology

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Introduction: To evaluate whether instant messaging application such as WhatsApp® is a reliable tool for obtaining quick second opinion on routine histopathological cases. Materials & methods: Seven histopathologists working in the public and private laboratories were engaged in a what app communication sharing histopathological images and case discussion over a period of 26 months. Microscopic images of hematoxylin and eosin or immunohistochemistry findings were sent as WhatsApp® messages and discussed among the pathologists involved. At the end of the 26 months, a google form survey containing 14 questions was conducted among the involved histopathologists. Results: There were a total of 40 histopathology cases discussed comprising 215 hematoxylin and eosin as well as immunohistochemical images posted on the WhatsApp® by participating pathologists. All seven histopathologists responded to the survey of 14 multiple choice questions. The majority of the histopathologists found the WhatsApp® application a useful and important tool in obtaining second opinions and discussing difficult cases. Discussion: Histopathological images shared on WhatsApp® instant messaging application is a reliable tool and provide a fast method in obtaining quick second opinion and discussing difficult cases in this era of social media. However, diagnostic accuracy is highly dependent on the resolution of shared images and the technical competence of operator in adjusting the smartphones to acquire the best representative image.

AP19 High grade myxofibrosarcoma: a case report with cytologic, histologic and molecular study

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Introduction: Myxofibrosarcoma is a common neoplasm of the soft tissue of the elderly. It is mainly diagnosed on histology with typical features. Nevertheless, diagnosis on fine needle aspirates is often challenging, due to overlapping cytological features with other differential diagnoses. Case report: We report a case of 50-year-old woman with a progressively enlarging, painless soft tissue mass in the left anterior chest wall. Initial trucut biopsies of the mass performed in a private centre were interpreted as extraskeletal myxoid chondrosarcoma. Fine needle aspirates of the mass performed in HUKM showed a cellular atypical lesion comprising of high grade spindled to pleomorphic, multinucleated cells in a background of myxoid-like stroma. The cytological features could represent a myriad of high grade entities including high grade myxofibrosarcoma, myoepithelial carcinoma and high grade extraskeletal myxoid chondrosarcoma. However, fluorescence in situ hybridisation (FISH) studies on the trucut biopsy showed no evidence of EWSR1 gene rearrangement, thus consistent with diagnosis of high grade myxofibrosarcoma. Discussion: Although myxofibrosarcoma display typical features on histology, cytologic features can be non-specific. Ancillary studies such as FISH can aid in the confirmation of the diagnosis resulting in the best line of management for these tumours.

AP20 A rare spindle cell lesion in stomach

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Introduction: Gastrointestinal tract spindle lesion is not uncommon and need panels of immunohistochemistry to reach the accurate diagnosis. Diagnostic pitfalls may occur if we did not consider all differential diagnosis. Although gastrointestinal stromal tumour is the commonest spindle cell tumour in stomach, we recently encounter angiosarcoma, a rare soft tissue sarcoma arising from endothelial cells. Case report: A 32-year-old lady presented with symptoms of upper gastro-intestinal bleeding. On examination, she is pale. No palpable mass upon abdominal examination. An esophagogastroduodenoscopy was done and show a bleeding ulcerated tumour at antrum. Partial gastrectomy was done the next day. Gross examination shows a submucosal tumour with mucosal ulcer at posterior wall of the stomach measuring 50 x 40 x 35mm. No tumour perforation is seen. The tumour has greyish cut surface with area of hemorrhage and necrosis. Microscopic examination shows the ulcerated tumour is hemorrhagic composed of anastomosing blood vessels lined by atypical endothelial cells. The atypical endothelial cells are positive to SMA, CD31 and FLi1. CKAEl/AE3, CD34, CD117, DOG1, S100, Desmin and H-caldesmon are negative. Discussion: Angiosarcoma is a rare and aggressive soft tissue tumour. Until now, there is no consensus regarding the management among clinician. Thus, this rare entity should be considered when dealing with spindle cell lesion in gastrointestinal tract for patient benefit.
AP21  *Gardnerella vaginalis* induced accelerated cellular death of syncytiotrophoblasts in placenta may explain preterm births and fetal growth restriction

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**Introduction:** Increased syncytiotrophoblast cell death (apoptosis) is seen in placental aging and other conditions e.g., pre-eclampsia. It is unclear if it is associated with intrauterine infection and specifically, with *Gardnerella vaginalis* (GV) that causes bacterial vaginosis, a recognised risk for preterm delivery and fetal growth restriction. **Materials and Methods:** Placenta tissues were stained on routine H&E and the ratio of SK per villous was analysed on light microscopy. GV infection was determined by PCR from vaginal swabs of women with bacterial vaginosis. The mRNA levels in placenta tissue for IGF1R, TGFBR1, PDGFA, PDGFB and TLR2 normalized to GAPDH were determined. The apoptosis rate of human chorionicarcinoma cells (BeWo), exposed to GV (MOI 500) for 12h was stained with TUNEL and analysed on flow cytometry. **Results:** Placenta of GV-positive cases (n=11) showed higher mean SK ratio than controls (n=11) (36.18%±15.25 vs. 25.54%±11.24) (p=0.07). SK ratio was positively correlated with gestational age (r=0.787, p=0.004) but not in cases with GV-infection (r=0.062, p=0.86). In GV-positive cases (n=15), placenta IGF1R appeared to decrease when TLR2 increased (r=-0.305, p=0.27). In vitro, BeWo cells exposed to GV showed 20-fold increased apoptosis (0.55%±2.01) above baseline control (0.03%±0.131) (p=0.05). **Discussion:** That SK formation increased with GV-infection irrespective of gestation, suggests accelerated syncytiotrophoblast apoptosis may occur earlier in pregnancy. The reduction of IGF1R with increased TLR2 activation by GV and increased apoptosis of trophoblasts may explain the underlying placental dysfunction that causes preterm births and fetal growth restriction in pregnant women with bacterial vaginosis.

AP22  Effects of saffron, crocin and crocetin on atherosclerotic plaque: a systematic review

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**Introduction:** Atherosclerosis is characterized by the narrowing and hardening of arteries following the buildup of plaque. Saffron, crocin and crocetin (SCC) have been shown to have positive effects on attenuating atherosclerotic plaque histologically. The study aims to systematically review the effects of SCC on atherosclerosis at tissue level. **Materials & Methods:** We searched English articles up to January 2020 using three online databases (PubMed, SCOPUS and WOS). Reviewers independently screened all reports to identify in vivo studies that evaluated SCC for the treatment of atherosclerosis. Outcomes of primary interest include histological findings on atherosclerotic plaque. Only English language articles were reviewed. This study was performed in accordance to PRISMA guidelines. **Results:** 5 studies met inclusion criteria. Of these studies, crocetin (n=3), crocin (n=1) and saffron (n=1) were used. Duration of the studies ranging from 4-10 weeks and the doses range from 15-100mg/kg/day. Types of animals used were NZW rabbits (n=2), Wistar rats (n=1), ApoE-/- mice (n=1) and quails (n=1). Of 3 studies that used crocetin (dose ranging from 15-50mg/kg), 15mg/kg/day for 8 weeks decrease up to 45.5% of atherosclerotic lesions while 50mg/kg/day for 10 weeks could reduce up to 42% fatty streak lesions. Crocetin(25mg/kg/day) for 10 weeks could reduce the atherosclerotic lesions up to 15% while the same dose of crocin for 9 weeks could reduce the aortic lesions up to 36.7%. Saffron (30-90mg/kg/day) could decrease the atherosclerotic plaque ranging from 8.93%-14.21% while crocin (25-100mg/kg/day) showed percentage decrease of aortic lesions ranging from 36.7%-60.1%. **Discussion:** Crocin has the highest ability in attenuating the aortic lesions. Thus, crocin would be the most effective compound to attenuate atherosclerosis.

AP23  RB transcriptional corepressor 1 (RB1) protein as an alternative biomarker in distinguishing complete from partial hydatidiform moles

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**Introduction:** Complete moles (CMs) are a type of androgenetic fertilization without an ovum. Because CMs lack a maternal genomic component, an absence of p57 immunohistochemical (IHC) staining in the cytotrophoblast is specific for CMs. With the p57 being a paternally-imprinted gene and expressed maternally, this gene is a suitable to distinguish between complete and partial hydatidiform moles (HMs). The purpose of this study is to evaluate the role of RB1, another paternally-imprinted gene, as an alternative to p57. **Materials & Methods:** Immunohistochemistry (IHC) using the RB1 antibody was performed on 39 formalin-fixed paraffin embedded tissue sections (FFPEs), consisting of 13 CMs, 14 PMs and 12 product of conception (POCs). The diagnosis of all the samples was confirmed by p57 IHC. **Results:** The expression of RB1 was repressed in the inner cytotrophoblast of all 13 CMs. Likewise, RB1 showed expressions in cytotrophoblasts, syncytiotrophoblasts, and villous stromal cells of all 14 PMs and 12 POCs. **Discussion:** In a HM, the presence of paternally derived chromosomes without maternal components will leads to an abnormal expression pattern of these imprinted genes. Since the RB1 is paternally-imprinted like p57 and operates downstream of p57, thus, there is a lack of protein expression in CMs. This similarity in expression pattern of RB1 to p57 indicated that RB1 could potentially be an additional marker for differential diagnosis of HMs.
AP24 Retina degeneration of retinal pigment epithelial cells: possible involvement of oxidative stress by inducing senescence

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Introduction: Retinal pigmented epithelial (RPE) cells constitute a key component of the blood-retinal barrier (BRB), oxidative insult to RPE leads disruption of the BRB or loss invariably results in pathogenesis of retinal degeneration due to formation of reactive oxygen species (ROS). The response of the RPE to oxidative stress has been examined with the use of RPE cell lines. Therefore, we sought to investigate the effects of sodium iodate (NaIO₃) as an oxidative compound to induced oxidative stress. Materials & Methods: Treatment with a variety of NaIO₃ concentrations (1-20 mM) for 24 hours has thus shown to affect the cell viability, MTT assay was used to evaluate the of exposed NaIO₃ on human RPE cell line (ARPE-19). Immunofluorescence and western blot analysis were used to investigate tight junction, and senescence marker. qPCR used to quantify the absolute amount of CDNA of the two classical cadherins. Senescence-associated-β-galactosidase (SA-β-Gal) assay used to detect galactosidase activity. Results: Structural changes appearing in senescent cells causes changes in the shape and size of RPE cells insulted with NaIO₃. RPE cells integrity was determined by immunofluorescence analysis of tight junction, and senescence marker. qPCR used to detect galactosidase activity. Conclusion: Our results support the hypothesis that NaIO₃ insulation plays a role in the induction and progression of AMD.

AP25 Correlation between poorly differentiated clusters (PDC) grading with lymphovascular invasion and nodal metastasis in colorectal carcinoma

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Introduction: Poorly differentiated clusters (PDC) of 5 or more cancer cells lacking a gland-like structure represent sequential steps in tumour growth in colorectal carcinoma (CRC). The counting of PDC has been associated with poor prognosis. The objective of this study is to correlate between PDC grade with prognostic factors (nodal metastasis, lymphovascular invasion and perineural invasion). Material & Methods: 47 colectomy of confirmed CRC cases diagnosed from November 2014 until December 2017 in Hospital Selayang were selected. CRC tissues stained with hematoxylin and cosin were reviewed under x20 magnification and graded based on the PDC count (Grade 1: less than 5, Grade 2: between 5 and 9 and Grade 3: 10 or more PDC clusters). Association between PDC grade and other prognostic factors were studied. Results: Out of 47 CRC cases, 7 were PDC grade 1, 13 PDC grade 2 and 27 were PDC grade 3. 6. 4% and 93.6% were <50 years old and > 50 years old respectively. 57. 5 % were males and 42.5% were females. There were 66% Chinese, 29.8% Malay, 2.1% Indian and 2. 1 % others. Most cases were left sided tumours (32 cases; 68%). There were significant associations between nodal metastasis (p=0.00087) and lymphovascular invasion (p=0.029) with PDC grades. No significant associations between perineural invasion and PDC grades (p=0.0538) was identified. Discussion: This study shows that the grade of PDCs may predict nodal metastasis and hence the N staging of TNM. It also shows close relation with lymphovascular invasion. PDC grading can be used for patient selections in situations where suboptimal number of lymph nodes were obtained and as neoadjuvant treatment options.

AP 26 Kikuchi-Fujimoto disease: a clinical and histological mimic of lymphoma

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Introduction: Kikuchi-Fujimoto disease is a condition of uncertain aetiology characterized by subacute necrotizing lymphadenitis. It commonly affects young Asian adults. Multiple lymph nodes involvement and the rare occurrence of hepatosplenomegaly associated with fever, weight loss and elevated serum lactate dehydrogenase may clinically mimic hematolymphoid malignancies. Furthermore, proliferation of large immunoblast cells and high proliferative index may histologically be mistaken for malignant lymphoma. Case report: A 29-year-old man presented with multiple enlarged lymph nodes involving the cervical, axillary, inguinal and supraclavicular lymph nodes for two-months duration associated with fever and muscle aches. Biopsy of the supraclavicular lymph node was performed and reported as suggestive of diffuse non-Hodgkin lymphoma. The case was then referred for further immunohistochemistry studies for subtyping of lymphoma. Microscopically, the biopsy showed geographical necrosis containing pale histiocytic clusters which was CD68 and MPO-positive with preserved normal reactive lymphoid follicles in the unaffected area. Clusters and sheets of CD3-positive large lymphoid cells were noted in the background which also showed high Ki67 proliferative index of 80%. These atypical T-cells are mainly CD8-positive with no aberrant loss of CD5 or CD7 are seen. Based on the morphology and its immunoprofile, a final diagnosis of Kikuchi disease was made. Discussion: Awareness of the morphology and immunoprofile of Kikuchi disease is paramount as the clinical presentation and histology may mimic lymphoma.
AP27 Primary extragonadal vaginal yolk sac tumour: its potential diagnostic caveat in immunohistochemistry

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Introduction: Yolk sac tumour (YST) or endodermal sinus tumour is rare and typically seen in gonads. We described a case of extragonadal vaginal YST in a one year and seven months old girl who presented with vaginal discharge and bleeding, and discuss its differential diagnosis and potential pitfalls in immunohistochemistry. Case Report: She was found to have a suprapubic mass on examination. The serum alpha fetoprotein was 11919.4 ng/mL. Computed tomography of the pelvis revealed a large 6.4 cm heterogeneous pelvic mass. Colposcopic examination of the pelvis showed a fungating vaginal mass that was subsequently confirmed as a yolk sac tumour. Immunohistochemically, the malignant cells were positive toward CAE1/AE3, AFP and glypican-3, as well as CD117. Discussion: Solid pattern extragonadal vaginal YST may morphologically resemble dysgerminoma and clear cell carcinoma. Being mindful of these potential diagnostic caveats is necessary to prevent misdiagnosis.

AP28 The incidence and histological diagnosis of Barrett oesophagus at Hospital Canselor Tuanku Muhriz

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Introduction: Barrett oesophagus is a change in normal stratified squamous epithelium of the distal oesophagus to metaplastic columnar epithelium. It is highly associated with gastroesophageal reflux disease (GERD). This retrospective study aimed to determine the demography and to assess histological diagnosis of patients with Barrett oesophagus in Hospital Canselor Tuanku Muhriz (HCTM). Materials & Methods: 131 cases of endoscopic biopsies of gastroesophageal junction (GOJ) suspicious for Barrett oesophagus were histologically confirmed from January 2018 to June 2020. The retrospective data were retrieved from archived histological material and medical records. All biopsies ensured a maximum of 6 haematoxylin and eosin (H&E) sections and equivocal cases were subjected to Alcian Blue-Periodic Acid Schiff (ABPAS) stain. Results: Out of 131 patients, 78 (59.5%) cases were confirmed to have Barrett oesophagus histologically. Majority of the patients are Malays (55%) with more males (65.6%) than females (34.4%). The mean age is 58 years old. 31 (39.7%) cases had GERD, 43 cases (55.1%) had more than 2 GOJ biopsy fragments and 3 cases (2.3%) required ABPAS. Chi square and t-test analysis showed significant relationship between Barrett oesophagus with gender (p=0.039; p<0.05), age (p=0.00; p<0.05) and number of fragments (p=0.000; p<0.05) but not with race (p=0.062; p>0.05) or gastroesophageal reflux disease (p=0.291; p>0.05).

Conclusion: Barrett oesophagus is seen in middle-aged populations with male predominance. Multiple GOJ biopsy fragments improves detection of Barrett oesophagus and adequate H&E multilevel sections is sufficient for the diagnosis. Identification and documentation of GERD may improve suspicion and diagnosis of Barrett oesophagus.

AP29 Peripheral funisitis: a distinct feature not to be missed

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Introduction: Acute funisitis is a form of fetal inflammatory response, characterised histologically by the presence of neutrophilic infiltration within the umbilical cord, involving the umbilical vessels with or without migration into Wharton’s jelly. Peripheral funisitis is defined as small punctate microabscesses with neutrophils at the peripheral or outer surface of the umbilical cord. This distinct pattern of inflammation when occurs diffusely is virtually pathognomonic for Candida species infection, a feature should not be disregarded as bacterial-associated acute funisitis. Case report: A 28-year-old primigravida, a known case of gestational diabetes mellitus on diet control, presented with maternal pyrexia in labour at 39 weeks and 3 days of gestation. No history of abnormal discharge per vagina. Light meconium-stained liquor was noted during delivery. High vaginal swab and placenta was sent for further investigation. Histopathological examination of placenta revealed mature chorionic villi appropriate for gestational age with no evidence of villitis. Acute nectrotizing chorioamnionitis was evident. There were multiple foci of neutrophilic microabscesses seen within Wharton’s jelly, most pronounced at the periphery. Umbilical phlebitis and arteritis were also noted. Fungal organisms with cytomorphological features consistent with Candida species were demonstrated with Gomori methenamine (GMS) histochemistry stain. Candida albicans was isolated from HVS, confirming the diagnosis of Candidal intrauterine infection. Discussion: Peripheral funisitis is a distinct type of umbilical cord inflammation, most frequently associated with Candida species infection. Careful examination of the umbilical cord and the role of GMS histochemistry stain in demonstrating the presence of fungal organisms with pseudohyphae cannot be overemphasized.
AP30  Case report of atypical meningioma with nodal metastasis

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Introduction: Meningiomas are common and usually benign central nervous system (CNS) neoplasms derived from meningotheial cells. These neoplasms are graded into three groups which differ in biological behaviour. Atypical meningioma is an intermediate grade tumour which is rarely associated with metastases compared to higher grade (Grade III) meningiomas. Case Report: 68 years old lady with history of multiple craniotomies and hemifacial resections for meningotheial meningioma. Subsequent histopathological examination following the first surgery showed features of atypical meningioma. Follow up serial magnetic resonance imaging (MRI) brain showed increasing tumour size despite postoperative radiotherapy. At current presentation for tumour recurrence, she underwent orbital exenteration, tumour debulking and cervical nodal excision. Unfortunately, patient succumbed to disease in the postoperative period. Macroscopic examination showed a skin-covered tumour with part of mandible, and intact eyeball encased by tumour. The tumour had whitish fleshy cut surface with necrosis. Lymph nodes were received in separate container. Microscopically, tumour cells seen in sheets, with hypercellularity, mitoses 8/10 HPF and necrosis. Tumour cells were present within the lymph nodes. The cells of the main tumour and nodal metastases were reactive for EMA and PR. Ki67 proliferative index around 60%. Discussion: Previous history of surgical resection is a known risk factor for iatrogenic metastasis for low to intermediate grade meningioma. Other factors include: venous sinus invasion, local recurrence, high grade, and papillary morphology. Extranodal metastasis is more common in atypical and anaplastic subtypes. The most common sites of extracranial metastases are lung, abdominal viscera, pleura, lymph nodes and bones. Surgical intervention is one of the factors contributing to metastasis, in addition to tumour grade. Due to its rare nature, it remains a challenge to diagnose and manage. No standardised management protocol has been developed and prognosis remains unknown.

AP31  A heavy burden: case report of atypical carcinoid tumour of the scrotum

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Introduction: Scrotal swellings are a common presenting complaint with a wide aetiology, including neoplasms. Tumours within the scrotum may be of testicular primary or extratesticular origin. Among testicular primaries, carcinoid tumours are rare, constituting less than 1% of testicular tumours. Case Report: 69 years old gentleman with no known medical illness, presented with painless and irreducible unilateral scrotal swelling for more than 20 years. Clinical impression prior to surgery was irreducible unilateral inguinal hernia. Intraoperatively, a unilateral scrotal tumour could be delineated from the testis and spermatic cord, however exact tumour origin could not be ascertained. Testis was preserved and orchidopexy with tumour excision done. Macroscopic examination showed a 1.8kg tumour measuring 21cm in largest dimension. Cut section showed solid whitish to yellow tumour with degenerated myxoid and necrotic areas. Microscopic examination showed solid sheets of tumour cells with characteristic salt and pepper chromatin, which were immunohistochemically reactive for CD56, NSE and INSM1. Areas of necrosis were noted within the tumour. The mitotic count was 14/10 HPF. No other teratomatous elements or non tumoural tissues identified in the sections. Discussion: Distinction between testicular primary and metastasis is important to determine further patient management. A primary testicular carcinoid and those with teratomatous elements is associated with better prognosis compared to metastatic tumours. Metastatic origin is commonly from the gastrointestinal tract and lung. Factors favouring metastasis are bilaterality, large size, carcinoid syndrome and multifocality. Atypical carcinoid tumour has higher metastatic potential and thus requires longer follow up. We report a rare case of indolent, large atypical carcinoid tumour which was present within the scrotum, with pathologic features. Determining the tumour origin is the key to further patient management.

AP32  Reverse teaching - a strategy for undergraduate medical education in pathology

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Introduction: Of late much attention is targeted towards reverse teaching as tool of integrated medical education. These studies have focused on the application of digital technology rather than exploring the students’ knowledge on a particular topic. The purpose of this study was to explore the effectiveness of reverse teaching in learning the basic medical sciences in undergraduate pathology course. Materials & Methods: Study design was interventional case –control. Participants were 150 first year medical students of University of MAHSA, Malaysia 2017-18. We used quantitative content analysis in pre and post teaching sessions and a delayed test score after 5 months. This result was compared with control group who were exposed to traditional pathology teaching. Results: There was no significant difference in the pre test scores between control group and test group (independent sample t –test, t=-0.836, p=0.404). There was a significant increase in the test scores between the two groups for the immediate post- test (independent sample t –test, t=-23.705, p<0.001), test group performed much better when compared to control group.
A significant difference in the test scores between the two groups was noticed in the delayed post-test after 5 months (independent sample t-test, t = -6.440, p < 0.001), test group performed slightly better than the control group. Discussion: Reverse teaching based on clinical scenarios has significantly increased score compared to control group (P < 0.001 vs P > 0.072).

AP33 The challenges in diagnosing mediastinal lymphoma with peculiar morphological features from small biopsies; immunohistochemistry to the rescue

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Introduction: Primary mediastinal B-cell lymphoma (PMBL) is a mature aggressive large B-cell lymphoma of thymic B-cell origin arising in the mediastinum. This rare entity is commonly occurring in young female adults. Case Report: We present 3 cases of PMBL, presenting with peculiar morphological features in which immunohistochemical stains (IHC) have aided in the correct diagnosis. Case 1: 26-year-old female with anterior neck swelling associated with dyspnoea on exertion and chest tightness upon lying down. Case 2: 44-year-old female presented with multiple neck swellings and reduced effort tolerance. Case 3: 22-year-old male presented with dyspnoea. Both cases 2 and 3 also had constitutional symptoms for 3 months. All patients had a mediastinal mass which were biopsied. There was no generalized lymphadenopathy. Pathological findings. The specimens obtained were 8-17 mm strips of tissue. Microscopic examinations revealed the following: Case 1- Diffuse infiltration of discohesive atypical, pleomorphic lymphoid cells with large nuclei and prominent nucleoli and inconspicuous cytoplasm. There is surrounding infiltration by mixed inflammatory cells. Case 2- Crushed tissue with small to large neoplastic cells in nests and islands separated by thick bands of stromal sclerosis. Case 3- Crushed fibrocollagenous tissue infiltrated by discohesive sheets of mononuclear cells with angulated hyperchromatic nuclei, some with distinct nucleoli. IHC were positive for B-cell markers (CD20, CD79a) with variably-positive CD45. The diagnosis of PMBL was concluded in these cases. Discussion: PMBL can present with a variety of morphologic appearance. In addition, small amounts of tissue with artifacts provide additional challenges. IHC and clinical correlation are crucial in arriving to the diagnosis.

AP34 Endocan-microvascular density as the novel biomarker of neoangiogenesis in primary ovarian carcinoma

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Introduction: Epithelial ovarian cancer is one of the leading causes of death in women. The progression of ovarian carcinoma is influenced by angiogenesis. High expression of endocan in tumour endothelial cells is a promising biomarker of neoangiogenesis. Microvascular density (MVD) is an index of angiogenic activity. Materials & Methods: This was a cross-sectional study constituting 89 epithelial ovarian cancer cases diagnosed in Hospital Universiti Sains Malaysia from January 2008 to December 2018. The formalin-fixed paraffin-embedded tissue blocks were retrieved from the pathology archives. Sectioned samples were stained immunohistochemically with endocan. Quantification of MVD was done using Weidner counting method. The number of microvessels immunostained by endocan was counted in the three hot spots at 200x magnification. The average microvessel count in the three hot spots was obtained and recorded as ‘endocan-MVD’. The endocan-MVD level was divided into a low and high group using the mean value (21.63) as a separating point. Results: High endocan-MVD level was significantly associated with the older age group (p value = 0.009), smaller tumour size (p value < 0.001), type II tumour (p value < 0.001), high-grade tumour (p value < 0.001), advanced FIGO stage (p value = 0.002), and presence of tumour recurrence (p value = 0.017) among primary epithelial ovarian cancer. Discussion: Endocan-MVD was significantly associated with age, tumour size, type, tumour grade, FIGO stage, and recurrence in primary epithelial ovarian cancer. Thus, endocan MVD could be a reliable marker to predict prognosis in epithelial ovarian cancer in the future.

AP35 Sporadic young-onset colorectal cancer: two cases from Hospital Universiti Sains Malaysia experience

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Introduction: Colorectal cancer (CRC) is the third most common cancer worldwide, occurring mainly in the older population. However, the prevalence in younger patients has recently increased. Although it is commonly linked to genetic predispositions, there has been an increasing trend in the prevalence of sporadic type young-onset CRC. They have shown to be associated with late presentation and poorer prognosis. This report aims to discuss the clinicopathological characteristics and molecular signature of young-onset CRC. Case report: We reported two cases, a 23-year-old male (case 1) and a 22-year-old female (case 2) who presented with worsening of right-sided abdominal pain and altered bowel habit. There was no significant past medical, family history or established risk factors. Colonoscopy showed an intraluminal mass on the right side of the colon in both cases. CT scan revealed bowel thickening in case 2. Both cases were subjected to the right hemicolectomy. Histopathological
examination revealed signet-ring carcinoma with loss of MLH1 protein expression for case 1 and mucinous adenocarcinoma with loss of MLH1 & PMS2 protein expressions for case 2. Both cases were found to have positive BRAF V600E expression by immunohistochemistry method and the tumour was already at an advanced stage due to late presentation. **Discussion**: Young-onset CRC has its characteristic features which are different from the hereditary type. They have loss of MLH1 protein expression with positive BRAF V600E and have a poorer prognosis. BRAF V600E is found to be associated with worse prognosis in CRC. These findings should promote further studies to explore the immune checkpoint in young-onset CRC for future targeted therapy.

**CHEMICAL PATHOLOGY**

**CP01 Treatment resistant hypothyroidism**

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**Introduction**: Persistent elevation of thyroid stimulating hormone (TSH) even with levothyroxine (LT4) dose exceeding the usual weight-adjusted required dose is a common clinical issue in outpatient clinics. This may prompt further assessment of LT4 malabsorption and poor compliance, the latter being a diagnosis of exclusion, which is difficult to confirm as it is based on a patient’s voluntary self-report. **Case report**: A 35-year-old lady was initially diagnosed with Graves’ disease and multinodular goiter before undergoing radioactive iodine (RAI) therapy in 2016. Post RAI, she was put on oral thyroxine and remained euthyroid for the next one year. In 2018, she started experiencing hypothyroid symptoms despite claiming to be compliant to medication. Pseudo-malabsorption was suspected after excluding digestive, liver and kidney diseases and a LT4 absorption test was done. Her free thyroxine (fT4) increased substantially, reaching a peak of more than 50% from baseline at 4 hours while TSH fell appropriately from 0 minute to 360 minutes during the test; hence enabling us to conclude that persistent hypothyroidism was due to poor medication compliance. **Discussion**: Although there is an absence of standardised methodology, all versions of the LT4 absorption test showed good utility in distinguishing between malabsorption versus non-compliance. This test is a fast and inexpensive tool to rule out true LT4 malabsorption, as a positive test negates the need for investigating other causes of refractory hypothyroidism, reduces unwarranted referrals for subspecialty care, as well as justifies the lowering of LT4 dosage to the expected weight-adjusted requirement.

**CP02 The hook effect in non-gestational choriocarcinoma**

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**Introduction**: Non-gestational choriocarcinoma is a rare component of choriocarcinoma which is invasive with early haematogenous spread. However, 90% of patients are cured by treatment. Human chorionic gonadotrophin (hCG) is an important biomarker for diagnosis and follow-up. Nonetheless, the significantly large amount of hCG in choriocarcinoma may lead to a false-negative or low result due to a phenomenon known as the ‘high dose hook effect’. **Case report**: A 35-year-old lady, presented with vaginal bleeding of one-month duration. She was diagnosed with persistent trophoblastic disease and suction curettage was done. Serial serum hCG showed increasing pattern. She was planned for CT scan and chemotherapy but defaulted. Later she presented again with cough, haemoptysis and shortness of breath which raised a suspicion of choriocarcinoma with metastasis to the lung. However, serum hCG result showed a level of 1125.68 IU/U which was much reduced compared to previous result. This raised the possibility of hook effect. After manual dilution, hCG level was >1342000 IU/U. CT thorax was done, and she was diagnosed with non-gestational choriocarcinoma. She was subsequently started on chemotherapy and showed good response evidenced by the reduced hCG level. **Discussion**: We highlight the possibility of hook effect in measuring β-hCG level in choriocarcinoma using a chemiluminescent method with a two-step immunoenzymatic assay. When the concentration of antigen is extremely high, the binding capacity of the two antibodies is saturated causing falsely reduced level. When the values are plotted on a dose-response curve, they do not ascend proportionately to the antigen concentrations. Dilution testing of specimen may counteract this effect.

**CP03 Performance comparison between Roche c513, Bio-Rad D100, Abbott Alinity ci-series and Trinity Biotech Premier Hb9210 automated HbA1c analytical platforms**

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**Introduction**: Haemoglobin A1c (HbA1c) is an established and reliable biomarker in the diagnosis and monitoring of diabetes mellitus. Therefore, the reliability and comparability among different automated analytical platforms for its detection have become very important. This study aims to compare four analytical methods in determining HbA1c. **Materials & Methods**: A
comparative evaluation of the analytical performances using precision, accuracy, method comparison, interferences (including haemoglobin variants and dialysis samples) and sample stability studies were performed on Cobas c513 (Roche Diagnostics, Germany), D100 (Bio-Rad, USA), Alinity ci-series (Abbott, USA), Premier Hb9210 (Trinity Biotech, Ireland) and Capillarys 2 Flex Piercing (Sebia, France). Results: A good precision was shown at both low and high HbA1c levels on all four systems, with all individual CVs below 2% (IFCC units). Among the four analysers, the c513 and D100 showed the best accuracy achieved based on analytical bias against the IFCC targets of ±5%. Method correlation showed good agreement between methods with absolute bias and bias at HbA1c decision limit of 6.5% to be <5% by NGSP guideline. The average bias for HbF, HbE and alpha thalassaemia trait were <±5% by NGSP guideline. Correlation between methods for dialysis sample was acceptable with (R²>0.95) with Bio-Rad D100 having the best correlation against c513. Sample stability showed good recovery (>95%) for a period of 5 consecutive days. Discussion: All four HbA1c automated analysers showed acceptable reliability and comparability with Bio-Rad D100 and Roche c513 having the best correlation. These findings imply that these commonly commercial platforms are comparable with one another in terms of performance.

CP04 Reducing rework with Multi Vision Cameras technology
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Introduction: Barcode labeling is widely used for automatic identification especially in patient and sample identification process. There are many challenges in barcode identification such as low contrast printing, distorted barcode details or even misalignment of barcode placement on sample tubes that will lead to detection error. Siemens Atellica Solution consists of 3 unique Multi Vision Cameras that are able to read barcode accurately at high speed. In contrast with the commercial laser barcode reader in most of the healthcare diagnostic system, reading barcode using the camera is able to maximize the reading capability leading to a higher percentage of barcode identification success rates. Universiti Malaya Medical Center (UMMC) reported 14% of barcode rejection rate based on 4000 tubes received per-day using commercial laser barcode reader. Materials & Methods: This study is designed to verify the success rate of multi vision cameras to capture different scenarios of barcode labeling. Six scenarios were created to test the barcode identification success rate of Atellica Vision Cameras such as Improper Reading Position, Print or Mark Inconsistency, Orientation, Moisture, Damage or Distortion and Multiple Layers. Results: Results showed that the Atellica Solution’s unique Multi Vision Cameras were able to give 100% reading success rate on the six barcode labeling scenarios created and were eventually able to decrease barcode rejection rate as well as prevent unnecessary reworking and reprinting efforts. Discussion: This will increase the workflow efficiency, decrease sample turnaround time and significantly save the costs in laboratory settings.

CP05 Assessment of a technology driven analyzer in reducing turnaround time
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Introduction: Space constraint and high demand on faster result delivery is the main challenge faced by the worldwide healthcare service provider. One of the key performance indicators that represent the high quality laboratory performance is the turnaround time (TAT). Two independent TAT studies have been designed to assess Atellica® Solution performance on TAT. Materials & Methods: In study 1, four runs with a total of 220 tests in each run were assayed. These four runs consisted of different mixtures of short and long analyzing assays, ranging from 5%-62% of long assays in each run. There were 11 high volume assays involved comprising of tumor markers (AFP, total HCG, PSA, CA19.9, CA125), thyroid function markers (TSH, FT4), Vitamin D, and infectious disease markers (AHAVM and AHCV). Results: This study showed that there was no impact on TAT even when 137 tests out of 220 tests were long assays. It was proven that Atellica® IM1300, met the claimed throughput of 220 tests per hour. This finding suggests that laboratory management can consider test consolidation in integrated laboratory to maintain less number of analyzers and save operation cost without impacting the TAT. Study 2 compared the TAT of STAT and routine samples. STAT mean TAT for chemistry tests is 37% faster while that of the immunoassay tests is 17% faster. Discussion: The featured single sample management, a 10-second STAT samples recognition time, bi-directional capability of Magline™ transport, software intelligence embedded in Atellica® Solution, have shown that the TAT for both STAT and routine samples can be consistently achieved.
CP06 Acute kidney injury (AKI) electronic alert in paediatric population

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Introduction: Electronic alert (e-alert) are intended to enable early detection of acute kidney injury (AKI). AKI e-alert is generated by lab information system (LIS) based on creatinine reference value (RV) ratio. It was introduced in Great Ormond Street Hospital for Children in August 2017. Materials & Methods: This was a retrospective three months data collection through EPIC information system from July to September 2019, two years after AKI e-alert implementation to identify the number of AKI alerts generated according to stages, underlying medical condition and the action taken by the paediatrician once alerted. Results: A total of 1812 AKI alerts were generated within 3 months; 64% stage 1, 26% stage 2 and 10% stage 3. AKI is more common in children aged less than 12 years old with the mean age of 5. Common causes of AKI observed from this study included in-patients with underlying cardiac abnormality undergoing cardiac surgery (24% in stage 1, 32% in stage 2 and 53% in stage 3) followed by patients with underlying haematological malignancy either on chemotherapy or post hematopoietic stem cell transplantation (20% in stage 1 and stage 3 respectively and 29% in stage 2). More than 60% of patients that required nephrology referral were in AKI stage 3. One false positive alert generated as stage 3 AKI was observed in this study. Discussion: AKI is common in children. The introduction of AKI e-alert allows early recognition and intervention to be delivered within appropriate time to prevent progression of kidney injury.

CP07 Weight status as a predictor for microalbuminuria among the Samarahan district rural community in Sarawak

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Introduction: Obesity and chronic kidney disease (CKD) have emerged as important public health problems. Microalbuminuria is a known early predictive factor for renal disease. This study aimed to determine the association between weight status and microalbuminuria among the rural adult community in Sarawak. Materials & Methods: A cross-sectional study was carried out among 610 subjects. A pre-tested questionnaire was used for social demographics, personal lifestyle and family history of CKD. The urine dipstick examination was used for detection of microalbuminuria and a measurement of 20 mg/L or above was considered as positive for microalbuminuria. Body mass index (BMI) was classified according to the Ministry of Health Malaysia criteria. Logistic regression analysis was performed to evaluate the relationship between the presence of microalbuminuria and BMI. Results: One-fourth (26.9%) of the rural adult population had microalbuminuria. A hierarchical binary logistic regression analysis revealed that BMI status of underweight (Adj. OR= 4.072, 95% CI=1.334, 12.427) and obese (Adj. OR= 2.715, 95% CI=1.492, 4.942) appeared to be important predictors of microalbuminuria. However, age, and gender had no association with microalbuminuria (p>0.05). Discussion: Among the studied subjects, 26.9% had microalbuminuria. Microalbuminuria in a rural adult community in Sarawak was associated with BMI status of underweight and obese in both men and women. We recommend further research to shed more light on the association between underweight and microalbuminuria among the high risk group in this community.

CP08 Detection of abnormal urine findings among asymptomatic pre-clinical medical students in Universiti Malaysia Sarawak

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Introduction: Renal disease may be an incidental finding during urinalysis. A dipstick urinalysis was conducted to estimate the prevalence of abnormal urine findings among asymptomatic pre-clinical medical students in the Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak. Materials & Methods: A cross sectional study involving 286 students was carried out from November 2018 to August 2019. First morning midstream urine samples were obtained from students and were tested by dipstick method. Students with abnormal urine findings were retested after 15 days. Results: Thirty-three (11.5%) students had urinary abnormalities at the first screening; 54.5% of them still had abnormal results at the second screening. Ketonuria was the most common abnormality found with a prevalence of 2.4%, followed by glycosuria (1.4%), leukocyturia (1.4%), haematuria (0.7%) and nitriuria (0.3%). In microscopic examination, leukocyturia was the most common abnormality detected in four students (1.4%) followed by isolated haematuria in two of them. Among students with leukocyturia, two were diagnosed to be due to urinary tract infection. There was statistically significant association between glycosuria and males. The prevalence of ketonuria was higher in females; however, no significant difference was observed between male and female students. Proteinuria was not present in any participant. Discussion: Urinary abnormalities were detected among asymptomatic preclinical medical students on dipstick and microscopic analyses. Further investigations are needed to elucidate the underlying aetiology of these abnormal findings.
CP09 Evaluation of analytical quality using sigma metrics and quality goal index in a Chemical Pathology laboratory

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Introduction: Sigma metrics or better known as six sigma is the current method used widely in clinical laboratories for benchmarking of analytical quality. Quality goal index (QGI) is an approach to ascertain the reasons for quality shortcomings. This study aimed to assess the analytical performance of our laboratory using the sigma metrics and QGI for quality improvement purposes.

Materials & Methods: The analytical performance of 25 biochemistry analytes were evaluated using internal quality control (QC) data over a six-month period extracted from the laboratory database. Sigma metrics were determined using the equation $\sigma = \frac{\text{total allowable error (TEa)} - \text{bias}}{1.5 \times \text{coefficient of variation (CV)}}$. QGI was calculated using the formula $QGI = \frac{\text{bias}}{1.5 \times \text{CV}}$. A QGI value of <0.8, 0.8-1.2 and >1.2 indicates imprecision, both imprecision and inaccuracy, and inaccuracy, respectively. Results: Six analytes (24.0%) achieved world-class performance, while 3 analytes (12.0%) had $\sigma$-value <3. The best and worst performing analytes were creatine kinase and calcium, respectively. QGI analysis indicated that imprecision was the major factor in failure to achieve six sigma quality for most (84.2%) analytes. Discussion: Sigma metrics and QGI are valuable quality management tools to evaluate the performance of analytical processes and customize analyte-specific QC strategies in a clinical laboratory.

CP10 IgD plasma cell myeloma: a rare case report

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Introduction: Plasma cell myeloma is one of the haematological malignancies in which abnormal B cell lymphocytes proliferate and secrete abnormal immunoglobulins (M-protein). Plasma cell myeloma derived from IgD monoclonality accounts for less than 2% of all multiple myeloma cases. Case report: A 60-year-old lady presented with lower back pain for two months and constitutional symptoms. Her investigations revealed a moderate normochromic, normocytic anaemia with leukoerythroblastic picture, significant hypercalcaemia, and impaired renal function, supported with generalised lytic lesions on skeletal survey. An extended panel of serum and urine protein electrophoresis showed IgD lambda. She was on haemodialysis in view of deterioration of her renal function. On recent admission, her condition was complicated with MRSA bacteraemia and paravertebral abscess.

Discussion: Patients with IgD myeloma present with similar clinical findings as other subtypes of plasma cell myeloma. However, it is difficult to detect IgD myeloma in the early stage due to its lower synthesis rate. IgD myeloma has been reported to have a poor prognosis despite its good response to treatment. The early recognition and diagnosis of rare variants of plasma cell myeloma is essential for prompt treatment in order to improve patient prognosis and prevent complication such as renal failure.

CP11 A possible case of transient biclonal light chain paraproteinaemia

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Introduction: Serum transient paraproteins are small monoclonal immunoglobulins that are induced by a self-limiting regulatory defect in the control of certain terminally differentiated B-cell clones. Case report: A 74-year-old man presented to the hospital complaining of back pain with multiple episodes of fall due to weakness for the past one month. Laboratory investigations revealed leukocytosis, thrombocytosis and anaemia. Inflammatory markers (ESR, CRP and procalcitonin) were raised. Hypercalcaemia and reversed albumin:globulin ratio were noted. Urinalysis showed leukocyturia with presence of nitrate and pus cells. Blood and urine cultures were positive for Staphylococcus aureus, Morganella morganii, Enterobacter species and Pseudomonas aeruginosa. MRI of the spine revealed multilevel spondyloisitciscis with cord compression and nerve root impingement secondary to psoas abscess. Serum protein electrophoresis (PE) and immunofixation (IFE) showed presence of two monoclonal bands of kappa and lambda light chains clonality with concentrations of 3.6 g/L and 4.2 g/L, respectively in the gamma region. Alpha-1 and alpha-2 globulin fractions were elevated. Urine PE showed one paraprotein band of 51.4 mg/L. IFE revealed presence of kappa and light chains. Discussion: We highlight a possible case of transient biclonal kappa and lambda light chains gammopathy due to severe infection postulated to have stimulated the increased production of immunoglobulins. A repeat serum and urine PE (SUPE) after the resolution of infection is recommended to confirm the presence of true paraproteinaemia. Unfortunately, a repeat SUPE was not done in this patient as he passed away two months after admission. Recognition of this condition is important to prevent unnecessary ancillary testing and expense.
CP12 Evaluation of analytical quality in clinical biochemistry using six sigma at Hospital Sultan Ismail Petra, Kelantan

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Introduction: Accuracy of clinical biochemistry test results is crucial for patient management. The evaluation of laboratory performance is critical in maintaining accurate laboratory test results. We aimed to use sigma metrics in assessment and management of our clinical biochemistry laboratory performance. Materials & Methods: Internal quality control and external quality assessment data for 20 clinical biochemistry analytes performed on Beckman Coulter AU680 analyser were analysed retrospectively over a period of six months from July 2019 to December 2019. For all analytes, the average of coefficient variance for 2 levels of IQC was calculated and mean of percentage bias was calculated from EQAS. Sigma metrics were calculated using total allowable error, average of coefficient variance and mean of percentage bias. Results: Five analytes with sigma ≥6 achieved world-class performance. They were urea, creatine kinase, direct bilirubin, high density lipoprotein and lactate dehydrogenase. Sigma values of albumin, alanine aminotransferase, amylase, aspartate aminotransferase, total cholesterol, creatinine, glucose, magnesium, total bilirubin, triglyceride, total protein and uric acid were between 3 to 6. Alkaline phosphatase, calcium and phosphate performed poorly with sigma <3. Discussion: Action should be taken to improve method performance for those analytes with sigma below 3. Application of six sigma principles would help in evaluating the performance of biochemistry analytes and providing the scientific basis for recommendation of QC strategy and planning of QC frequency.

CP13 Tales of non-IgM monoclonal gammopathy-associated neuropathy

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Introduction: Monoclonal gammopathy-associated neuropathy is believed to be the result of excess immunoglobulin deposition at the nervous tissue. Neuropathy is a well-recognised complication rather than an initial presentation of monoclonal gammopathy. Hence, monoclonal gammopathy presenting solely with neuropathy may be a challenge to the diagnosis of plasma cell myeloma. Case report: Case 1: A 76-year-old man was screened for malignancy after presenting with progressive imbalance requiring assisted daily routine for the past one year. Nerve conduction study (NCS) reported length-dependent sensorimotor axonalpolyneuropathy. Serum and urine protein electrophoresis (SUPE) and immunofixation electrophoresis (IFE) reported the presence of IgG lambda. Bone marrow aspiration (BMA) report was consistent with plasma cell myeloma. Other myeloma defining events (MDEs) were absent. Chemotherapy was initiated, and his neuropathy improved. Case 2: A 34-year-old woman presenting with progressive bilateral lower limb weakness for three months associated with numbness and tendinopathy, was diagnosed with chronic inflammatory demyelinating polyneuropathy. NCS showed predominant motor axonal polyneuropathy. However, the symptoms persisted despite intravenous immunoglobulin administration. SUPE and IFE revealed IgA lambda. BMA report was consistent with plasma cell myeloma. MDEs were absent. Chemotherapy was planned for this patient. Discussion: Neuropathy is caused by many diseases, least commonly by non-IgM monoclonal gammopathy. Both cases highlighted the occurrence of neuropathy in non-IgM monoclonal gammopathy as the initial presentation, albeit rare. Although the association between neuropathy and non-IgM plasma cell myeloma is still uncertain, screening with SUPE for the disease in a patient presenting with any type of neuropathy is still crucial.

CP15 Mitochondrial fatty acid oxidation disorders: is it a common cause of death in Malaysian children

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Introduction: Mitochondrial fatty acid oxidation disorder (FAOD) is a group of clinically and biochemically heterogeneous disorders of inborn errors of metabolism (IEM). Estimated prevalence of FAOD worldwide is 1 per 10 000 infants. The clinical presentation can mimic other IEM and common diseases in childhood. Since the introduction of selective screening for IEM in 2008, we have detected increasing number of high probable cases of FAOD. Materials & Methods: Data from January 2009 to December 2019 from 50,515 dried blood spots was reviewed. Patients’ biodata, clinical characteristics and laboratory results were kept confidential and analysed using Microsoft excel. Results: 90 probable positive cases of FAOD were detected from tandem mass spectrometry (TMS) or organic acid analysis by gas chromatography mass spectrometry (GCMS). Most detected cases were multiple acyl CoA dehydrogenase deficiency; MADD (68%) with others being primary carnitine deficiency (4%), CPT1α deficiency (6%), CACT (6%), CPT2 (2%), medium chain acyl CoA dehydrogenase deficiency; MCAD (1%), MTP (2%), LCHAD/VLCAD/MTP (10%), SCHAD/SCAD (1%). Discussion: Distribution of race 70% Malay, 23% Pribumi Sabah/Sarawak, 4% Indian, 1% Chinese and 2% others. 73% of patients were alive at the time of diagnosis. Most alive patients had transmigris with metabolic acidosis. Clinical characteristics; 30% hypoglycaemia, 23% hepatomegaly and 9% cardiomyopathy. Screening by TMS showed a characteristic acylcarnitine profile although occurrence of false positive due to fasting and parental nutrition. Most but not all FAOD patients had dicarboxylic aciduria. Due to inadequate DNA sample, many cases did not undergo full mutation analysis. FAOD is rare in Malaysia, however correct diagnosis may prevent another death in the affected families. As adequate DNA sample is usually an issue for disease confirmation, next generation sequencing looking at targeted gene panel may help to confirm the diagnosis.
CP16 Patient moving average as an additional quality tools in medical laboratory

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Introduction: Achieving high quality and productivity with automated testing processes require optimised process control systems for error detection and minimum false rejection. It typically uses artificial control specimens and can detect some, but not all analytical defects. Implementation of real-time patient initiated moving average may become useful not only in monitoring assay performance but to complement the existing quality control procedures and assisting in troubleshooting. We compared the pattern between Levy-Jennings (LJ) chart for the Patient Moving Average (PMA) and the conventional internal quality control (IQC). Materials & Methods: PMA protocol was established using three months patients’ data across routine and immunonassay testing, and used to determine the target mean, standard deviation and sample block size for each analyte. A mean determined from patient samples block which exceeds the predefined control limits indicate the possible presence of error. It was then compared to the IQC chart pattern on that particular day. Results: Five sets of LJ charts were compared, in conditions where shifts were detected in PMA monitoring. In three conditions, the IQC chart did not show any violation despite shifts in PMA monitoring. Shifts were caused by reagent contamination, extreme result, and ISE electrode error. Two other conditions demonstrated shift of PMA monitoring and violation of IQC-LJ chart, caused by calibrator master curve change and reagent lot change. Discussion: PMA is useful as an additional quality tools in medical laboratory. It allows error detection and early troubleshooting despite non-violated IQC-LJ chart. In addition, it also assists in troubleshooting for systematic error and monitoring of analytical performance.

CP17 Haematuria as a presentation of light chain myeloma

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Introduction: Multiple myeloma (MM) is a clonal plasma cell malignant neoplasm constituting 10% of haematological malignancies and accounts for 1% of all malignancies with an annual incidence of 7.74 per 100,000 population. Light chain multiple myeloma (LCMM) is a variant of plasma cell dyscrasias and accounts for 15% of reported cases. Fatigue and bone pain are the most common initial clinical symptoms reported by patients. Case report: A 42-year-old woman presented with acute onset of frank haematuria. She was initially diagnosed with urinary tract infection (UTI) and was given intravenous fluids and antibiotics, and subsequently the pain and haematuria resolved. Initial blood investigations revealed bicytopenia with urinalysis positive for blood and protein. The renal profile, however, was normal. Her renal profile deteriorated on day four and progressively worsened. Pelvic and hip X-rays revealed lytic lesion at the intertrochanter of left femur. Serum and urine protein electrophoresis and immunofixation electrophoresis tests revealed the presence of lambda light chain myeloma. She underwent a series of chemotherapy. However, she developed neutropaenic sepsis and succumbed to her condition one year after her initial diagnosis. Discussion: Generally, not all patients with plasma cell myeloma present with the classical signs and symptoms. What could be easily misdiagnosed as UTI can in fact be an indication to a more grave diagnosis. Therefore, we highlighted this case to reiterate the importance of clinical findings and baseline investigation to avoid missing a crucial diagnosis.

CP18 A case report of bleeding disorder and hyperlipidaemia in an infant

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Introduction: Hyperlipidaemia is usually detected incidentally during a health check-up without causing any apparent symptoms. A high index of suspicion is especially required to diagnose it in a young infant. Case report: A two-month-old baby boy without any family history of bleeding disorder developed a gradual swelling of the right thigh. He was hospitalised for further investigation. There was no history of preceding trauma. However, two weeks prior to this, he received his vaccination at the same site and passed bloody stool one week after. On examination, the swelling was warm and tender without overlying skin redness. His coagulation profile was prolonged and radiological investigation revealed intramuscular haematoma. The blood sample was found to be lipaemic. Analysis showed elevated triglycerides with a mild increase in total cholesterol. Further testing such as genetic study to rule out primary hyperlipidaemia could not be done as the parents requested for follow up at a different centre. He was then provisionally discharged with the diagnosis of hyperlipidaemia. Discussion: We highlight a case of hypertriglyceridaemia in a baby who presented with bleeding and deranged coagulation results. High levels of lipid could cause hyperviscosity of the blood and is associated with abnormal coagulation profile which may lead to bleeding problems as seen in this case. The presence of a high amount of triglyceride in the blood sample might interfere with other laboratory measurements. Thus, it is important to process the sample properly and interpret its result cautiously to avoid reporting error and misdiagnosis.
Case report: A rare cause of primary adrenal insufficiency

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Introduction: The X-linked form of adrenal hypoplasia congenita (AHC) is a rare genetic disorder, characterised by failure of the definitive zone of the fetal adrenal cortex to develop. This condition should be differentiated from congenital adrenal hyperplasia (CAH), as the treatments and prognoses differ. Case report: A 1-month old male infant presented with biochemical features of primary adrenal insufficiency (PAI). CAH due to 21-hydroxylase deficiency was initially suspected but further investigations revealed low baseline as well as ACTH-stimulated 17-hydroxyprogesterone levels, with undetectable dehydroepiandrosterone sulfate (DHEAS). The definitive diagnosis is yet to be determined but the early onset of PAI and adrenal steroid profiles suggest the diagnosis of X-linked AHC. Genetic testing should be done for definitive diagnosis. Discussion: AHC is a rare condition, mainly inherited in an X-linked recessive pattern due to mutations in the nuclear receptor DAX1 (NR0B1), but also occur in autosomal recessive form or as part of an underlying syndrome. Irrespective of the underlying genetic aetiology, conditions with adrenal hypoplasia are associated with deficiencies of all adrenocortical hormones. Despite the distinctive adrenal steroid profiles, children with AHC are sometimes misdiagnosed as CAH. Accurate distinction is imperative for further patient care as well as for genetic counselling.

A systematic review of the effect of saffron extract on lipid profile in hyperlipidemic experimental animal model

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Introduction: Saffron is widely used in traditional medicine to treat various medical disorders including hyperlipidaemia, which is an important risk factor for cardiovascular diseases. This study aims to review the effects of saffron extract (SE) on lipid profile in in-vivo studies. Materials & Methods: A strategic literature search was done according to the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)”. Database from SCOPUS, PubMed and Web of Science, and hand searching method were included. Results: A total of six articles met the inclusion criteria. The methods of extraction were aqueous (n=4), ethanolic (n=1), and hydroalcoholic (n=1) extracts. Five doses of SE ranging from 10 to 100 mg/kg were administered to Sprague-Dawley rats (n=2), Wistar rats (n=3) and hamsters (n=1) with duration ranging from 10 days to 8 weeks. SE at 10mg/kg/day for 4 weeks intervention showed no significant difference between treated group and untreated group. SE at doses 40mg/kg/day and 80mg/kg/day significantly decreased level of TC(21.4-35.4%), LDL(38.7-50.0%) and TG(29.1-45.0%) and markedly increased level of HDL(36.6-65%) between treated group and untreated group with minimum 3 weeks duration of intervention (p<0.05). SE at 100mg/kg/day for 10 days intervention did not show significant difference of lipid profile from untreated group(p>0.05). Discussion: SE has anti-hyperlipidaemic properties. However, the most effective dose, types of intervention and duration of intervention are not yet clarified. Further studies should be done to define the minimum effective dose of SE, the minimum duration of intervention and the best preparation method of SE to achieve the maximum benefit of anti-hyperlipidaemic effect of saffron.

Usage of high-sensitivity cardiac Troponin I in evaluation of cardiac pathology in systemic lupus erythematosus

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune mediated connective tissue disease affecting multiple systems with an unknown cause. Case report: A 39-year-old woman with an underlying thalassemia trait and SLE with antiphospholipid syndrome (APS) for the past 14 years. She was admitted for menorrhagia secondary to over-warfarinisation. Hemoglobin (Hb) concentration upon admission was 10.6g/dL, consistent with her baseline Hb. Further history and physical examination revealed that the patient had episodes of fluid overload but never complained of any typical angina symptoms. Upon admission, her high-sensitivity cardiac Troponin I (hs-cTnI) was 10000 pg/ml, peaking at 15000 pg/ml which eventually reduced to 3000 pg/ml within a week. Electrocardiogram (ECG) and coronary angiography were normal but echocardiogram showed ejection fraction of 24% with several moderate-severe valvular regurgitation. A diagnosis of coronary vasculitis with non-ischaemic dilated cardiomyopathy was made. She was treated with pulses of methylprednisolone and subsequently underwent aortic valve replacement operation two months later. Discussion: Cardiac diseases in SLE can range from asymptomatic to overt, involving pericardium, myocardium, endocardium, valves, conduction system and coronary arteries. Cardiac pathology in SLE can be directly affected by the disease itself, secondary to other organs (e.g., lupus nephritis) or treatment such as steroids. Despite the inconsistency of clinical history, ECG and coronary angiogram findings, the acute trend of hs-cTnI and echocardiogram findings suggested type II myocardial infarction. Although interference of troponin I by heterophilic antibodies in SLE is still under-studied, it is unlikely to occur in hs-cTnI assay and patient never had blood transfusion or monoclonal antibodies.
Case report: (1) A 51-year-old man presented with a two-month history of upper limbs neuropathy associated with bony lytic lesions of T3-T5 vertebrae without other end organ damages. Serum and urine protein electrophoresis (SUPE) and immunofixation (IFE) showed IgG kappa and IgG lambda biclonality. He was treated with instrumentation, decompression and tumour debulking operation and radiotherapy. However, he died secondary to nosocomial infection before chemotherapy was initiated. (2) A 59-year-old woman presented with one-week history of severe back pain. Investigations showed hypercalcaemia, anaemia with leuкоerythroblastic picture, multiple bone lytic lesions and normal renal profile. SUPE and IFE showed IgA kappa and IgG lambda biclonality. After multiple cycles of chemotherapy, the initial dominant paraprotein (IgA kappa) was reduced by 50% while the second paraprotein (IgG lambda) disappeared. Discussion: BGM involves two different heavy or light chain classes of paraprotein in the serum and/or urine, detected on immunofixation. BGM accounts for 1-6% of total plasma cell dyscrasia cases, with IgG and IgA combination being the commonest (53%). BGM of two similar heavy chains and/or light chains is the rarest (10%). Typically, BGMs are more symptomatic than its monoclonal counterpart. However, there is no significant differences in terms of diagnosis, treatment and outcome between monoclonal and BGMs. We suggest further molecular studies to determine their clonality and pathogenesis that might be useful in treating and prognosticate this disease.

Ethnic differences in HbA1c as an index of glycaemic control and its associated factors among type 2 diabetes mellitus patients in a Malaysian tertiary hospital

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Introduction: Glycated haemoglobin (HbA1c) is used for monitoring glycaemic control in type 2 diabetes mellitus (T2DM). Several studies have demonstrated variation in HbA1c value among different ethnicities at the same glucose level. This study aimed to determine ethnic differences in HbA1c as an index of glycaemic control and its associated factors among T2DM patients. Materials & Methods: This was a retrospective cross-sectional study involving 293 T2DM patients in Hospital Kuala Lumpur (HKL) from 2017 to 2018. Electronic data of demographic characteristics and laboratory parameters of T2DM patients were extracted. Results: There was significant difference in ethnicity between T2DM patients with HbA1c ≤ 6.5 and HbA1c > 6.5. At lower fasting plasma glucose (FPG), Malays had lower HbA1c compared to Chinese, but at higher FPG, Chinese had lower HbA1c compared to Malays, with cross-over at FPG 2.8 mmol/L. Indians remained at higher HbA1c values compared to Malays and Chinese. Independent predictors of HbA1c were FPG and ethnicity. Every 1 mmol/L increase in FPG was associated with 0.44% increase in HbA1c. Malays and Indians had 0.47% and 0.60% higher HbA1c respectively, compared to Chinese. Discussion: This is the first study in Malaysia examining ethnic differences in the relationship between HbA1c and FPG among T2DM patients. Since at any given FPG, HbA1c is higher in Malays and Indians compared with Chinese, the risk of hypoglycaemia may be increased in Malays and Indians when efforts are made to treat Malays, Chinese and Indians using similar target HbA1c values.

Isolated elevated alkaline phosphatase level in prolonged neonatal jaundice

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Introduction: Alkaline phosphatase (ALP) is a marker of bone and hepatobiliary disease. Nevertheless, ALP enzyme also identified as a biomarker for a diverse range of diseases and physiological processes. During infancy, vitamin D deficiency (VDD) is common however often over-look. Case report: 45-day-old baby girl who was investigated for prolonged jaundice had elevated ALP from 495 to 605 U/L since day 17 of life. Her TSB had normalised and other liver enzymes were normal. She was a term baby and exclusively breastfed. She was otherwise thriving well and not dysmorphic. There was no organomegaly. FBC, TFT and other liver enzymes were normal. Serum 25(OH)D was analysed at private laboratory showed a low level of vitamin D at 19.8 mmol/L. Syrup Appleton 1 ml once daily was prescribed and a repeat ALP at day 90 of life showed normalised ALP to 466 U/L. Thus, this finding supported a diagnosis of isolated elevation of ALP secondary to VDD. Discussion: Detection for vitamin D should raise a suspicion in infant presented with isolated elevation of ALP without any apparent sign and symptoms. As VDD has become a major public health concern due to its higher prevalence during infancy, ALP activity can be suggested as a screening tool for VDD even though conflicting findings regarding correlation between increased ALP with serum vitamin D status has been reported. Serum 25(OH)D is preferred for screening as it reflect the vitamin D status and selected over 1,25(OH)D based on its stability and less affected to fluctuation by PTH.
CP25  Dimeric IgG kappa in monoclonal gammopathy of unknown significance

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Introduction: Monoclonal gammopathy of undetermined significance (MGUS) is a premalignant plasma-cell disorder characterised by presence of paraproteinaemia without the typical end organ damage seen in multiple myeloma (MM). MGUS is more common in the older age group and has a risk of progression to MM of 1 - 8% per year. Case Report: A 79-year-old man with underlying hypertension and established kidney failure (EKF) on regular haemodialysis was admitted to the hospital with fever, chesty cough and mild dyspnoea. He was diagnosed with pneumonia. He has had previous recurrent admissions for parapneumonic effusion. During this admission, anaemia and reversed albumin:globulin ratio were noted. A CT-thorax incidentally revealed presence of multiple lytic lesions in the left humerus and ribs. Serum protein electrophoresis showed presence of two distinct paraprotein bands in the gamma region with a concentration of 2.29 g/dL. Both bands were confirmed to be dimeric forms of IgG Kappa on immunofixation and electrophoresis. Bone marrow aspiration showed presence of 5% plasma cell. In view of all the results, he was subsequently diagnosed with MGUS. The patient and the family members were not keen for chemotherapy and opted for supportive care. Discussion: We highlight a case of MGUS in an elderly man with recurrent hospital admissions due to infection. The postulated underlying mechanism is hypogammaglobulinaemia. Other MGUS-related complications include vertebral fracture, renal complications (monoclonal gammopathy of renal significance), neuropathy and thrombosis. Annual follow up is recommended to monitor progression of disease as well as to manage and improve outcomes from MGUS-related complications.

CP26  Lambda light chain disease co-migrating in the beta region with normal renal profile

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Introduction: Light chain multiple myeloma (LCMM) is seen in 15% of multiple myeloma cases and frequently causes rapidly progressive renal failure. Patients with lambda light chain disease have a three times worse prognosis than kappa light chain disease. Case report: A 73-year-old woman was referred from a private hospital for progressive back pain and kyphosis for the past two years. Magnetic resonance imaging of the spine showed presence of pathological compression fracture suggestive of vertebral metastasis. Full blood picture showed bicipotopenia of normochromic normocytic anaemia and thrombocytopenia with no rouleaux formation. Other haematological indices were normal. Her calcium, ALP, renal and liver function tests were normal. Urinalysis was positive for proteinuria (1+) and haematuria (1+). Serum protein electrophoresis revealed the presence of a 6.8 g/L paraprotein band co-migrating in the beta region. Immunofixation electrophoresis showed that it is of lambda light chain. Urine protein electrophoresis also exhibited lambda light chain of 2417 mg/L. Bone marrow aspirate displayed the presence of 23% plasma cells. Serum free light chain (sFLC) assay from a reference lab showed a significant increase of serum free lambda compared to serum free kappa with abnormal serum free Kappa/Lambda ratio. The diagnosis of lambda LCMM was made. Chemotherapy was initiated and she showed good response with normalisation of sFLC assays. Discussion: We highlight a case of lambda LCMM caught at an early stage presenting with bone pain, haematuria, proteinuria and normal renal profile. The sFLC assay is more sensitive in monitoring LCMM response to treatment and progression of disease.

CP27  5-year cost analysis of specimen rejection in Chemical Pathology Laboratory of UiTM Medical Specialist Centre

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Introduction: Specimen rejection rate is an important quality indicator of clinical laboratory. High rate of specimen rejection may not only affect patient’s management, but it also contributes to financial implication to patient and healthcare provider. Thus, we aimed to analyse the cost involves in specimen rejection in our healthcare setting. Materials & Methods: Retrospective data of specimen rejection registry from 2015-2019 were analysed. All costs include tangible and nontangible cost were identified. Results: A total of 2818 blood tubes, 326 specimen container and 357 heparinised syringe were rejected for various reasons according to specimen rejection criteria in our laboratory. Data was recorded and analysed using Microsoft Excel. All these consumable materials costed about RM 2086.20. Other cost that were identified but unable to be measured objectively include the cost for printing test order forms, syringes, needles, specimen collection plastic bags and electricity. Discussion: Even though the cumulative cost of specimen rejection for 5 years seems low, but the financial implication not only chargeable to healthcare institution, but also to the patients. In most cases, patients have to bear cost of the rejected test. As most of the specimen rejection causes can be controlled, training of phlebotomists, nurses, doctors and transporter regularly could keep the specimen rejection at low rate thus increased the quality of laboratory services and efficiency of the healthcare institution.
CP28 Challenges in interpreting discordant thyroid function test results

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Introduction: Thyroid function test (TFT) is a commonly requested laboratory investigation in primary or secondary care. However, although rare, immunoassay interference may impart challenges in diagnosis and management. Further investigations are necessary to ensure correct interpretation. Case Report: A case of a 48-year-old Malay woman was brought to our attention due to possible assay interference based on repeatedly incongruent results. History revealed that 10 years ago she presented to the hospital with diffuse neck swelling plus palpitation and was diagnosed with hyperthyroidism. She was put on carbimazole. After eight years of defaulting follow up, her TFT showed hypothyroidism biochemically, hence L-thyroxine was started at the Health Clinic. Upon assessment at Hospital Ampang, TFT showed elevated thyroid stimulating hormone (TSH) with inappropriately raised fT4. In view of the results, thyroxine dose was increased; however, similar results were seen on four subsequent different occasions. Discussion: After demonstration of non-linearity of results following serial dilutions, serum samples were sent to two other Specialist Centres with different platforms; Hospital Putrajaya- Beckman Coulter, Siemen and Hospital Serdang-Architect, Abbott to elucidate the presence of interference. Results from both platforms revealed hypothyroidism biochemically. Anti-thyroglobulin and anti-thyroidperoxidase were positive. She was the followed up for hypothyroidism accordingly. This case report highlights the possibility of thyroid hormone assay antibody interference when results are incongruent with clinical picture. Following reassessment and consideration of possible confounding factors, if TFTs remain discordant, assay interference as a possible cause should be considered.

CP29 Association of serum ferritin with demographic factors and laboratory parameters among severe dengue patients in Hospital Kuala Lumpur

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Introduction: Hyperferritinaemia in severe dengue is believed to be secondary to overwhelming activation of monocytes and macrophages. Serum ferritin has been proven as a predictor of dengue severity. The aim of this study was to determine the prevalence of hyperferritinaemia and its associated factors among severe dengue patients. Materials & Methods: A retrospective cross-sectional study was conducted among 120 severe dengue patients admitted to Hospital Kuala Lumpur from January 2017 to December 2018. Demographic data (age, gender, race, nationality) and laboratory parameters [serum ferritin, platelet count, haematocrit (HCT), aspartate transaminase (AST), alanine transaminase (ALT)] of the patients were extracted. Results: Prevalence of hyperferritinaemia among study subjects was 69.2%. There was a significant difference in gender between hyperferritinaemia and normoferritinaemia groups with males having higher serum ferritin compared to females. Thrombocytopenia, elevated AST, ALT and HCT were significantly associated with hyperferritinaemia. Correlation analysis demonstrated that platelet count was negatively correlated with serum ferritin while age, AST, ALT and HCT showed significant positive correlation. However, independent predictors of serum ferritin were only AST and HCT. Discussion: The prevalence of hyperferritinaemia among severe dengue patients was relatively low at 69.2% compared to previous studies in Asia (90.5% - 100%). AST and HCT, which are routine laboratory investigations in dengue patients are shown to be independent predictors of serum ferritin in this study population. These findings advocate the use of serum ferritin as a routine biomarker of disease severity in dengue patients, whereby hyperferritinaemia signifies severe dengue.

CP30 Determining salivary cortisol reference intervals measured on automated electrochemiluminescence immunoassay (ECLIA) for the Malaysian population at Penang General Hospital

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Introduction: Salivary cortisol has been used as an indicator of stress level and a screening tool for Cushing syndrome. The reference intervals for salivary cortisol depend on the analytical methodology and the population studied and hence the establishment of a local population-based reference interval is recommended. Materials & Methods: A cross-sectional study to determine the reference values of morning (0700 – 0800 hours) and late-night (2300 – 2400 hours) salivary cortisol levels conducted in a group of hospital staffs and blood donors aged 18 to 60 years old attending Penang General Hospital from June 2018 till May 2019. Paired (morning and late-night) saliva samples were collected from 129 individuals with no history of chronic medical illness. Salivary cortisol was assayed using electrochemiluminescence immunoassay (ECLIA) technique. Non-parametric statistics were used for calculation of reference intervals and 90% confidence intervals. Results: The subjects had mean age of 32 ± 9 years and mean BMI of 25.7 ± 5.5 kgm⁻². The reference intervals for morning and late-night salivary cortisol among the subjects were 2.09 – 22.63 mmol/L and <12.00 mmol/L, respectively. Discussion: The locally-derived reference intervals for morning and late-night salivary cortisol vary from those reported previously emphasising the need in establishing individual laboratory reference interval according to the recommendations by Clinical & Laboratory Standard Institute (CLSI) guideline.
CP31  Effect of sample storage duration and temperatures of -20°C and -80°C on stability of HbA1c concentration analysed using Bio-Rad D-10 in Hospital Tengku Ampuan Afzan, Kuantan

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Introduction: Glycated haemoglobin (HbA1c) is widely used for monitoring long-term glycaemic control. The accuracy of its measurement is, however, affected by sample storage conditions. Hospital Tengku Ampuan Afzan (HTAA) laboratory receives samples for HbA1c test request from clinics in HTAA and district hospitals in Pahang; at which, prior to analysis, the samples may be stored beyond the manufacturer’s recommendation (i.e., seven days at 2-8°C). This study aimed to determine the effects of storage duration and temperature on the stability of HbA1c measurements. Materials & Methods: A total of 222 HbA1c samples were collected from healthy blood donors and HTAA patients with type 2 diabetes mellitus. Each sample was aliquoted into four aliquots and stored at -20°C and -80°C for 15 and 30 days. HbA1c analysis was performed using an ion-exchange high-performance liquid chromatography (HPLC) assay (Bio-Rad D-10). Results: The mean±SD HbA1c at baseline was 6.65±2.18%. Following sample storage, HbA1c concentrations decreased from baseline; a mean difference of 0.091% on day 15 and 0.271% on day 30 when stored at -20°C and mean difference of 0.06% on day 15 and 0.04% on day 30 when stored at -80°C. The number of samples with clinical significant HbA1c change on storage, defined as a concentration change of >0.5% from baseline, was 10 (4.5%) at -80°C and 51 (23%) at -20°C. Discussion: Duration and storage temperature affect HbA1c concentration. In cases where prolonged storage of HbA1c sample is required, samples should preferably be stored at -80°C and up to 30 days.

CP 32  Elevated free thyroxine (fT4) and non-suppressed thyroid stimulating hormone (TSH): a clinical conundrum

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Introduction: Increased free thyroxine (fT4) is often associated with suppressed thyroid-stimulating hormone (TSH). Occasionally, hyperthyroxinaemia occurs in the presence of inappropriately non-suppressed TSH. Case report: A 2 years and 6 months old boy was followed up for persistently elevated fT4 ranging between 27–35 pmol/L with non-suppressed TSH ranging between 1.23–2.87 mIU/L. It was identified incidentally at day 19 of life following admission for prolonged jaundice secondary to glucose-6-phosphate dehydrogenase deficiency. His cord blood TSH was normal. He was clinically euthyroid, had no goitre and hence, investigations for euthyroid hyperthyroxinaemia were performed. A repeat TFT, sample dilution for non-linearity and measurement of TFT on another immunoassay platform excluded assay interference. Patient was also negative for anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies and anti-TSH receptor antibodies. The mother had normal TFT, and measurement of TFT on another immunoassay platform excluded assay interference. Hospital Tengku Ampuan Afzan (HTAA) laboratory receives samples for HbA1c test request from clinics in HTAA and district hospitals in Pahang; at which, prior to analysis, the samples may be stored beyond the manufacturer’s recommendation (i.e., seven days at 2-8°C). This study aimed to determine the effects of storage duration and temperature on the stability of HbA1c measurements. Materials & Methods: A total of 222 HbA1c samples were collected from healthy blood donors and HTAA patients with type 2 diabetes mellitus. Each sample was aliquoted into four aliquots and stored at -20°C and -80°C for 15 and 30 days. HbA1c analysis was performed using an ion-exchange high-performance liquid chromatography (HPLC) assay (Bio-Rad D-10). Results: The mean±SD HbA1c at baseline was 6.65±2.18%. Following sample storage, HbA1c concentrations decreased from baseline; a mean difference of 0.091% on day 15 and 0.271% on day 30 when stored at -20°C and mean difference of 0.06% on day 15 and 0.04% on day 30 when stored at -80°C. The number of samples with clinical significant HbA1c change on storage, defined as a concentration change of >0.5% from baseline, was 10 (4.5%) at -80°C and 51 (23%) at -20°C. Discussion: Duration and storage temperature affect HbA1c concentration. In cases where prolonged storage of HbA1c sample is required, samples should preferably be stored at -80°C and up to 30 days.

CP33  Icteric index as a front-line to determine total bilirubin analysis

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Introduction: Total bilirubin (TB) is overzealously requested and although reasonably priced individually, results in a whopping cost to consumable expenses of a laboratory. In comes Icteric Index (II), a zero reagent cost test indicating semi quantitative index value for bilirubin concentration. The objective of this study is to find correlation between II of blood samples with TB levels and the reliability of using II as a screening tool to decide when TB is required. Materials & Methods: 6900 TB values and their corresponding II results analysed in Hospital Pulau Pinang in January 2019 were retrospectively reviewed. Both TB concentrations and II were measured on Cobas c 702. Linear regression analysis was used to determine the optimal II cut off value which gives elevated bilirubin value that is above the clinical decision limit. Results: Regression analysis suggested 2mg/dl as the optimal II threshold to identify abnormal bilirubin values and gives a R2 of 0.989. There is positive association between II and TB. The sensitivity was greater than 98% and the specificity was greater than 95%. Positive predictive value of II is 88% and negative predictive value is 99%. Discussion: Our study shows excellent correlation between II and TB results. Using 2mg/dl II as a cut off allows recognition of samples that require bilirubin measurement. As the icteric index gives a high sensitivity and low false negative results, it can be utilized to avoid inappropriate requests of total bilirubin measurement. Additionally, it is cost effective as it could reduce reagent and consumable expenditure of RM 23 894 per year.
CP34 The relationship between serum magnesium and type 2 diabetes mellitus among adult patients in Hospital Melaka

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Introduction: Magnesium (Mg) acts as a cofactor for many enzymatic reactions and plays an important role in glucose metabolism. Hypomagnesaemia is common in type 2 diabetes mellitus (T2DM) although Mg insufficiency often goes unnoticed. This study aimed to determine the relationship between serum Mg with demographic, clinical and laboratory variables of T2DM subjects.

Methods & Methods: A cross-sectional study was conducted among 365 T2DM adult patients who attended the specialist clinic, Hospital Melaka from December 2017 to 2018. Patients who were pregnant or with a history of alcohol abuse, malabsorption, chronic diarrhoea, critical illness, T1DM, on Mg supplement or diuretics were excluded. Results: Prevalence of hypomagnesaemia was 21.5%. A significant, linear relationship was seen between serum Mg with T2DM duration (p=0.001), fasting blood glucose (FBS) (p=0.001), total cholesterol (p=0.043), triglyceride (p=0.001), non-high density lipoprotein cholesterol (p=0.009), retinopathy (p=0.001), nephropathy (p=0.001), stroke (p=0.013) and coronary heart disease (p=0.001). However, only HbA1c, FBS and T2DM duration remained independent predictors of serum Mg after stepwise multiple linear regression. With every 1 mmol/L increase in FBS, 1% increase in HbA1c and 1 year increase in diabetes duration, Mg level will significantly decrease by 0.012 mmol/L, 0.018 mmol/L and 0.008 mmol/L, respectively (p=0.001). Discussion: The prevalence of hypomagnesaemia in this study population was comparable to that of previous studies (13.5-47.7%). T2DM duration, HbA1c and FBS being independent predictors of serum Mg among this study population advocate the use of serum Mg as a routine biomarker of glycaemic control whereby hypomagnesaemia in T2DM signifies poor control.

CP35 Prevalence of T2DM patients with abnormal haemoglobin and RBC indices in HbA1c samples measured in Hospital Kuala Lumpur from January to December 2017

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Introduction: HbA1c is used for monitoring glycaemic control and diagnosis of type 2 diabetes mellitus (T2DM). The reliability of HbA1c result is affected by abnormal red blood cell (RBC) indices with or without anaemia. The study aimed to determine the prevalence of T2DM patients with abnormal haemoglobin (Hb) and RBC indices during HbA1c measurement. Materials & Methods: This was a retrospective cross-sectional study involving patients who had HbA1c and concurrent full blood count (FBC) measurements in Pathology Laboratory, Hospital Kuala Lumpur from January 2017 to December 2017. Demographic characteristics and laboratory parameters (total Hb, MCV, MCH, MCHC, HbA1c) of these patients were extracted from the laboratory information system. Results: Out of 305 patients, 113 (37%) had anaemia with the majority being normocytic normochromic anaemia (n=63, 55.8%) while 50 (44.2%) were microcytic hypochromic anaemia. Out of 305, 131 (43%) had abnormal RBC indices. The median HbA1c was significantly lower (7.52%) in those with anaemia compared to those without anaemia (8.3%), (p=0.03). HbA1c levels significantly differed between those with microcytic hypochromic anaemia (7.9%) and normocytic normochromic anaemia (7.2%), (p=0.025). HbA1c correlated negatively with age, MCV and MCH while positively with Hb and MCHC. Discussion: The presence of anaemia and the types of anaemia affect HbA1c results and must be taken into consideration during interpretation of results. When possible, HbA1c results should be reviewed together with FBC, given the known high prevalence of anaemia in Malaysia.

CP36 Biochemical findings in a rare case of inborn error of ketogenesis defect

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Introduction: Mitochondrial 3-hydroxy-3-methylglutaryl-CoA synthase (mHS) deficiency is a rare inborn error of ketogenesis. Patients usually present with non-(hypoketotic) hypoglycaemia, lethargy and hepatomegaly during acute infection and/or prolonged fasting. The diagnosis is challenging because of poor biochemical markers and molecular diagnosis is not available in Malaysia. Case presentation: We report the case of a 10-month-old Malay boy with mHS deficiency who presented with fever, poor feeding and seizure. Persistent severe metabolic acidosis was observed in this case. Blood spot acylcarnitine analysis showed mild elevation of C4OH with slightly low level of free carnitine (C0). Urine organic acid analysis revealed small but significant peak of 4-OH-6- methyl pyrone (4HMP). Moderate increase excretion of 3-OH butyrate together with 2 peaks of acetacacetate along with significant excretion of dicarboxylic acids (adipate-> suberate-> sebacate) including the hydroxylated form indicated ketosis. Increased excretion of glutarate with mild to moderate excretion of 3-OH-glutarate was also observed. This finding strongly suggested an inborn error of ketogenesis defect. Mutation analysis was not sent for further confirmation of the diagnosis. Patient recovered with glucose infusion and was discharge home. Discussion: This patient presented with severe metabolic acidosis with inborn error of metabolism as one of the differential diagnosis. The presence of 4HMP in the urine organic acid analysis had been reported to be a characteristic of mHS deficiency during acute crisis. It is a very rare disease but most of the patients had a good prognosis after a proper treatment.
CP37 CircularRNA (circRNA) expression profiles associated with Osimertinib resistance in EGFR L858R/T790M mutant NSCLC cell line

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Introduction: Lung cancer contributes to high cancer mortality worldwide with 80% of total cases diagnosed are non-small cell lung carcinoma (NSCLC). Epidermal growth factor receptor (EGFR) tyrosine kinase (TK) domain serves as a druggable target in NSCLC patients with exon 19 deletion and L858R mutation. However, patients gain resistance to first- and second-generation EGFR-TK inhibitors through activation of T790M mutation. Third generation EGFR-TKI, Osimertinib exhibits high efficacy in patients with L858R/T790M mutation but they experienced intrinsic resistance thereafter. CircRNA, a non-coding RNA thought to be splicing error by-products, recently discovered to have functional role in cancer initiation and progression. CircRNA derived from back-splicing of pre-mRNA forming closed loop structure lacking free 5’ and 3’ end. Due to its unique structure, circRNAs are highly stable in plasma than linear mRNAs. Hence, we aim to identify circRNAs enriched in Osimertinib resistant (OR) cells involved in NSCLC progression. Materials & Methods: OR clones were established via increasing Osimertinib concentrations and characterized from H1975 cell line. H1975 and OR clones then subjected to circRNA-Next Gene Sequencing (NGS). CircRNAs enriched in OR clones extracted from bioinformatic analysis and validated. Results: OR clones showed increased drug resistance potential than H1975. Total of 479 circRNAs were enriched in OR clones. CircRNAs showed consistent expressions in qPCR analysis further confirmed our NGS data. Discussion: We generated OR clones in-vitro as evidenced by increased drug resistance potential. CircRNAs identified in our OR clones warrant further functional analysis downstream molecular analysis. Nevertheless, circRNA can be used as prognostic and non-invasive biomarker in clinical settings for NSCLC patients.

CP38 Diagnostic concordance between HbA1c and OGTT in diagnosing diabetes mellitus

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Introduction: Traditionally, fasting plasma glucose (FPG) measurement and the oral glucose tolerance test (OGTT) were the primary methods used to diagnose diabetes mellitus (DM). However, recently glycated haemoglobin (HbA₁c) value of ≥6.3% has been added in local guidelines as an additional diagnostic test. This study aimed to determine the diagnostic concordance between HbA1c when compared to OGTT as a reference test in identifying dysglycaemic status among subjects in an out-patient setting. Materials & Methods: The OGTT and HbA1C results from 2017-2018 were analysed. The prevalence of prediabetes and diabetic patients using OGTT and HbA1c were compared. The diagnostic agreement between HbA1c and OGTT was examined. Results: A total of 106 subjects were reviewed. According to the HbA1c criterion, 13 patients (12%) were normoglycaemic, 37 patients (35%) were in the prediabetes group, and 56 patients (53%) were in the diabetes group. An HbA₁c value of ≥6.3% detected DM with a 63% sensitivity and 85% specificity. However, by using OGTT, normoglycaemia was found in 23 patients (22%), prediabetes in 39 patients (37%) and diabetes in 44 patients (41%). Therefore, the prevalence of diabetes using HbA1c was approximately 1.3 times higher than those defined by OGTT (53% versus 41%). Discussion: Marked discordant between measured HbA1c and OGTT should raise the possibility of haemoglobin variants and plasma blood glucose criteria should be considered in order to diagnose diabetes mellitus, as stated in American Diabetes Association guideline.

CP39 Molecular mimicry between human chorionic gonadotrophin (hCG) and thyroid stimulating hormone (TSH) in gestational trophoblastic disease

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Introduction. The association between thyroid function abnormalities and high human chorionic gonadotrophin (hCG) in normal pregnancy due to molecular mimicry of the α-subunit hCG and thyroid stimulating hormone (TSH) leading to cross-reactivity with the TSH receptor is well established. However, it is rarely reported in gestational trophoblastic disease (GTD). Case Report. A 51-year-old woman presented to the hospital complaining of abdominal pain and distention for one month and was admitted to the ward. Transabdominal scan showed honeycomb appearance of the intrauterine cavity. Laboratory investigations revealed a markedly raised β-hCG level of 1,035,928.1 mIU/mL. Thyroid function test (TFT) results showed suppressed TSH (0.01 uIU/mL) and raised fT4 (25.29 pmol/L) levels. However, she was clinically euthyroid. The following day, suction and curettage was done. Approximately 200 ml of vesicle-like tissue was evacuated and was reported as complete hydatidiform mole on histopathological examination. She was started on chemotherapy consisting of etoposide, methotrexate and actinomycin D.
CP40  A pilot study to determine glycerol concentration among obese subjects in a small medical institution

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Introduction: Previous studies have shown that glycerol metabolism contributes to the pathophysiology of obesity through the discovery of aquaglyceroporin channel mutations present in adipose tissues. In this pilot study, fasting glycerol concentration in obese and normal subjects were investigated in a small cohort. Materials & Methods: One hundred subjects were recruited for this study and divided into two groups: obese group (n=50, body mass index ≥ 23 kg/m²) and normal control group (n=50, body mass index 18.5–22.9 kg/m², non-diabetic, normotensive and normal lipid profile). Plasma glycerol concentration was measured by colorimetric method using a free glycerol assay kit (Cell Biolabs). Results: Both obese and normal groups consisted of 16 males and 34 females each. The median plasma glycerol concentration for obese and normal groups were 0.86 mg/dL and 0.42 mg/dL, respectively, representing a 51% difference between them. In the obese group, median plasma glycerol concentration for males and females were 1.18 mg/dL and 0.74 mg/dL, respectively. Obese group showed significantly higher plasma glycerol concentration compared to the normal group (p < 0.01). Correlation analysis demonstrated strong and positive correlation between plasma glycerol concentration and body mass index. Discussion: This pilot study showed higher plasma glycerol concentration in obese compared to normal group. This may be explained by the increased glycerol release from abundant adipose tissue present in obese subjects. Further studies on aquaglyceroporin channel mutation will highlight its role in glycerol transport leading to the development of obesity and metabolic diseases.

CP41  A case of persistent negative bias on haemoglobin A1c external quality assurance program

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Introduction: Regular assessments of external quality assurance (EQA) programs allow comparison of laboratory performance against set standards and peer group laboratories. We report a case of persistent negative bias for haemoglobin A1c (HbA1c) EQA program. Case report: The chemical pathology laboratory at our institution participates in the Glycohaemoglobin (lyophilised) and Whole Blood Glycohaemoglobin programs from The Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP) Pty Limited. HbA1c is measured on Bio-Rad D-10 Haemoglobin analyser using high performance liquid chromatography method. Throughout Cycle 50 to 51 of the Glycohaemoglobin (lyophilised) program, we noted a persistent negative bias for our HbA1c results. Fifteen out of twenty-four samples showed lower results compared to target medians and exceeded the analytical performance specification. However, these results were still within acceptable performance when compared to peer group. Comparison with Cycle 8 2019 of Whole Blood Glycohaemoglobin program showed acceptable performance. Although the glycohaemoglobin (lyophilised) results did not require further investigations, we discussed with manufacturer and EQA provider to identify possible causes for the persistent negative bias. Analyser breakdown, faulty parts, unsatisfactory maintenance, human factor, internal quality control rule violation, calibrator and reagent lot-to-lot variation were ruled out. Recently, Bio-Rad Laboratories have announced the release of a new re-labelled D-10™ Haemoglobin A1c Program reagent kit (known as diagnostic kit), with enhanced claims to aid the diagnosis of diabetes. Following the use of this new reagent kit, our Glycohaemoglobin (lyophilised) results for Cycle 52 2020 were found to be within acceptable performance compared to target median. In view of resolved bias for Glycohaemoglobin (lyophilised) program with a normal Whole Blood Glycohaemoglobin results, it may be postulated that our persistent HbA1c bias may have been contributed by change in reagent kit or matrix effect of previous lyophilised EQA material. Discussion: Participants of EQA programs should be aware of various factors that can affect EQA performance.
CP42  Reduced hands-on maintenance time with Atellica Solution in Pathology Department, Hospital Ampang

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Introduction: Hospital Ampang has been established as a turn-key project under the Seventh Malaysia Plan (RMK-7) with a total of 17 wards and up to 562 bed capacity. The Pathology Department, Hospital Ampang is dedicated in delivering the highest quality laboratory testing to the patients. Many laboratories are facing an increasing analyser hands-on maintenance time which requires laboratory personnel to be attentive to the system during maintenance. This study reviewed the total hands-on maintenance time after the Pathology Department converted from System R to Atellica Solution in April 2019. One of the features offered in this new technology is auto-maintenance. Materials & Methods: This study was performed on both Atellica Solution and the previous used platform; with the total hands-on time during daily, weekly, and monthly maintenance were recorded for comparison. Results: Result showed a total of 67% and 60% reduction on daily and weekly hands-on maintenance, respectively but 31% increase on monthly hands-on maintenance on Atellica Solution relative to previous used platform. However, in total, the hands-on maintenance time was reduced by 62.3% after converting to Atellica Solution. Discussion: Shorter hands-on maintenance time is important to reduce staff utilisation and saves operator time. In conclusion, Atellica Solution has proven to reduce operator intervention with the use of the latest technology which automates system maintenance. This feature increase system uptime and improve the overall laboratory efficiency.

CP43  Improved laboratory turnaround time (LTAT) with Atellica Solution in Hospital Ampang

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Introduction: One indicator of efficiency in a diagnostic laboratory is timeliness in producing results. Laboratory turnaround time (LTAT) has become a key indicator to measure a laboratory’s performance in timeliness. The Pathology Department of Ampang Hospital has always been striving to deliver the highest quality of service with support of trained staff and effective technology. Continuous monitoring of LTAT demonstrates the effort of a laboratory commitment to provide high quality service and to greater user satisfaction. The objective of this study was to evaluate the LTAT after switching to a new platform of Atellica Solution in April 2019 and to compare with the LTAT when using the previous system. Materials & Methods: LTAT of three tests from urgent and routine test categories were selected and compared between the previous system and Atellica Solution. Two tests from the urgent category are Serum Bilirubin for neonates (SBN) and Troponin I, and one test from routine testing, which is Total Cholesterol. Results: The data showed improvement in LTAT when using Atellica Solution. 80.11% of urgent SBN achieved LTAT within 45 minutes compared to 74.57% when using the previous system. 95.90% of Troponin I achieved LTAT less than 60 minutes compared to 88.28% before. As for total cholesterol, 100% LTAT is within three hours compared to 96.20% when using the previous system. Discussion: The study showed that Atellica Solution can help to improve LTAT and laboratory’s efficiency.

CP44  Analytical performance evaluation of the Atellica IM SARS-COV-2 Total Antibody assay

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Introduction: Several studies have demonstrated that serological tests can improve the overall sensitivity of COVID-19 detection among infected patients. Evidence suggests that measuring the total antibody against S1 Receptor Binding Domain (RBD) may be a good measure. Therefore, we evaluated and verified the performance of the Siemens Healthineers Atellica IM SARS-CoV-2 Total antibody (COV2T) assay among COVID-19 patients in Hospital Sungai Buloh. Materials & Methods: 374 blood samples from RT-PCR confirmed COVID-19 patients taken from June to July 2020 were used in this study. Atellica IM COV2T assay was used for qualitative detection of total antibodies to S1-RBD of SARS-CoV-2 and validation was performed according to modified Clinical and Laboratory Standards Institute (CLSI) EP10 protocol for the preliminary evaluation of bias and imprecision. Results: The analytical performance demonstrated acceptable precision and bias against the sample pools whereby the sensitivities for the 1st and 2nd week of illness were low; 32.6% and 62.9% respectively. However, the sensitivity increased up to 80% in the 3rd week of illness. This evaluation also showed the specificity was 100% (using samples from pre-SARS-CoV-2 period). Discussion: We concluded that the intended clinical use of Siemens Healthineers Atellica IM COV2T for the detection of SARS-CoV-2 antibodies alone may be more useful in the later phase of infection. However, it must be used complementary to PCR testing.
CP45 Biochemistry and haematology samples handling of Covid-19: Hospital Sungai Buloh experience

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Introduction: Hospital Sungai Buloh as the main Infectious Disease referral centre has been chosen as the Coronavirus 2019 disease (COVID-19) centre in Malaysia for screening, isolating & treating suspected or confirmed patients. Here, we portray our experience on handling biochemistry and haematology COVID-19 samples received from our hospital throughout the outbreak with the hopes of sharing some insight to further improve laboratory preparedness in the future. Materials & Methods: This is a compilation of our experience in handling biochemistry and haematology samples of COVID-19 patients involving risk assessment, workflow and tests offered, the recommended personal protective equipment (PPE) as well as decontamination and waste management processes. Results: The Pathology Department of Hospital Sungai Buloh receives numerous biochemistry and hematology samples of COVID-19 patients monthly. Although we see a reducing trend in the numbers of COVID-19 samples received from Mac till May, it is crucial for all laboratory personnel to adhere to the recommended guidelines while handling potentially hazardous specimens. Conclusion: A good laboratory practice, including the use of standard biological safety precautions, personal protective equipment (PPE), regular staff training, and adherence to detailed standard operating procedures consisting of pre-analytical, analytical and post analytical safety practices, will help minimise potential transmission risks.

CP47 Determination of reference interval for midnight salivary cortisol among healthy adults in Kinta Valley region

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Introduction: Midnight salivary cortisol (MSC), urinary free cortisol and overnight dexamethasone suppression test are recommended screening tests for Cushing syndrome. The reference intervals (RI) for serum and urinary cortisol are widely obtainable and commonly provided by various assay manufacturers. However, RI for MSC lacks availability due to poor assay harmonisation. Thus, this study aimed to determine the RI for MSC among healthy adults in our local population. Materials & Methods: This was a cross-sectional study that took place in November 2018 involving 125 participants in Kinta Valley region. Participants refrained from teeth brushing, eating or drinking 1 hour prior to sample collection. Saliva specimens were taken using Saliva Bio Oral Swab. MSC analysis was performed on Roche Cobas e620 analyser employing the electrochemiluminescence immunoassay. Research protocol was based on the CLSI-IFCC C28-A3c Guideline, which defines the RI as the 95% central range of 2.5th and 97.5th percentiles. Results: There were 86 (68.8%) females and 39 males (31.2%) with median age of 19 years old and median [interquartile range (IQR)] body mass index of 22 (5) kg/m². The median (IQR) MSC was 2.2 (1.9) nmol/L; the lower and upper reference limits of MSC were 1.5 [90% confidence interval (CI):1.5,1.5] nmol/L and 12.6 (90% CI:18.4, 15.8) nmol/L, respectively. Binary regression analysis and Spearman’s rank correlation analysis showed no association between MSC and gender (p>0.05) and age (p>0.05), respectively. Discussion: The findings in this study are evident that RI for MSC are not gender- or age-dependent.

CP48 Alpha-mangostin increases endothelial cell migration in an in-vitro diabetic wound healing model

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Introduction: Diabetes mellitus affects 17.5% of Malaysians; poor wound healing is a complication of the disease, culminating in diabetic foot ulcers. The pericarp of the mangosteen fruit is traditionally used to treat wounds. It is reported that its biological active compound, α-mangostin has healing properties in non-diabetic wounds. However, in diabetic wound healing especially in diabetic foot ulcers, its effect is not well established. Hence, data on the effects of α-mangostin on endothelial migration in diabetic wound healing is scarce. We investigated the in vitro effect of α-mangostin on endothelial cell migration in a diabetic wound healing model. Materials & Methods: Human carotid artery endothelial cells (HCAECs) were incubated with 35 mM glucose solution for 72 hours. A scratch assay (wound healing simulation assay) was performed by manually scratching the HCAECs monolayer using a pipette tip. The cells were then incubated with α-mangostin (0.15, 2.5 and 5 µg/ml), positive control [carboxymethyl cellulose (CMC)] and negative controls (high glucose and culture medium alone). Cell migration were photographed at 0, 6, 12, 18, 24, 48 and 72 hours. The percentage of migration was calculated using an image analysis software. Results: α-mangostin at 0.15 ug/ml showed the fastest rate of endothelial cell migration at 6, 12, 18, 24 and 48 hours compared to negative controls (p<0.001); equivalent to that of the positive control. Treatment with 2.5ug/ml α-mangostin showed the second-best effect (p<0.001). The negative control showed the slowest HCAEC migration at all-time points. Conclusion: α-mangostin at 0.15 µg/ml significantly increase endothelial cell migration in an in vitro diabetic wound healing model.
**CP49** The anti-cancer effects of Curcumin on breast carcinogenesis in rats: a preliminary study

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*Introduction:* Curcumin has demonstrated anticancer properties in various studies but the mechanism behind these effects has yet to be fully understood. We investigated the effects of curcumin in the form of a prevention study on the breast tumorigenesis in rats. *Materials & Methods:* Thirty nulliparous female Sprague-Dawley rats were grouped as follows: NC (negative control, untreated rats), PC (positive control), CUR1 (50 mg/kg curcumin treatment), CUR2 (100 mg/kg curcumin treatment) and CUR3 (200 mg/kg curcumin treatment). The rats in groups PC, CUR1, CUR2 and CUR3 were subjected to intraperitoneal injection of 1-methyl-1-nitrosourea (MNU) (80 mg/kg) to promote mammary tumour growth. The experiment was carried out for 120 days. Rats were sacrificed and histopathology analysis of both non-treated and treated tumours were carried out. *Results:* There were no significant differences between the positive control group and the curcumin treated groups in terms of the tumour grade, number of histological patterns, tumour incidence, tumour latency, tumour multiplicity, size of tumour mass and the weight of the tumour mass. Histological examinations using the modified Bloom-Richardson grading system revealed the histological types of the tumours produced in both curcumin-treated and untreated groups consist of a variation of single and a combination of two or more patterns including papillary, cribiform, tubular and non-special type (NST). *Discussion:* Previous intervention studies have shown that curcumin has a positive, significant effect on breast carcinogenesis rats. In contrast, no significant evidence regarding the role of curcumin in the prevention of breast carcinogenesis in rats was found in this study.

**CP50** Establishment of reference interval for thyroid-stimulating hormone, free thyroxine and free triiodothyronine

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*Introduction:* Reliable reference interval (RI) is important for proper interpretation of laboratory results. In Malaysia, laboratories utilize automated immunoassay analyzers for measurement of thyroid hormones with slight difference in immunoassay methodology steps. The objective of the study is to establish RI for thyroid-stimulating hormone (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) on four commonly used immunoassay analysers in Malaysia. *Materials & Methods:* This was a cross sectional study involving 156 healthy Malaysian subjects aged 18 to 60 with negative thyroid peroxidase antibody measured on Beckman Coulter DxI-800. The RI for TSH, FT4 and FT3 were established on Beckman Coulter Dxl-800, Roche Cobas e601, Siemens Centaur XPT and Abbott Architect i1000SR according to the EP28-A3c guideline. Non-parametric statistics were used for determination of RI with confidence intervals of 90%. *Results:* RI established were as follows: TSH: 0.44-3.24 mU/L, FT4: 9.35-14.80 pmol/l, FT3: 3.23-5.66 pmol/l (DxI-800); TSH: 0.32-2.80 mU/L, FT4: 11.00-21.40 pmol/l, FT3: 3.50-6.80 pmol/l (Centaur XPT); TSH: 0.41-3.04 mU/L, FT4: 11.75-20.85 pmol/l, FT3: 3.35-5.65 pmol/l (Cobas E601) and TSH: 0.34-2.63 mU/L, FT4: 10.68-16.14 pmol/l, FT3: 2.76-6.42 pmol/l (Architect i1000SR). *Discussion:* In general, FT4 and FT3 showed comparable results with manufacturer RIs. TSH upper limit was lower compared to manufacturer’s RI. This is most probably contributed by the higher number of relatively younger subjects recruited (less than 50-year-old). The locally derived RI help to verify the validity of using manufacturer derived RI in our population and may serve as a reference or further larger scale studies in future.

**HAEMATOLOGY AND TRANSFUSION MEDICINE**

**HM01** Drone technology in maternal healthcare in Malaysia: a narrative review

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*Introduction:* The vast advancement of technology and breakthrough in high-tech disciplines created multiple areas of research activities, including the innovation of medical drones. Malaysia, a rapidly developing country in Southeast Asia is on track to achieving high-income status. The stagnant growth of Malaysian maternal healthcare doesn’t run parallel with the aspirations. This review paper assessed and reported narratively the current condition of maternal healthcare in Malaysia, the possible application of drone in improving the sector, exploring in detail key challenges, and provide recommendations for experts in studying the rising technological phenomena. *Materials & Methods:* Literature search was done from June 2019 to November 2019 with restriction to the English language. The search was performed in ScienceDirect, PubMed, and EMBASE databases, using a combination of search terms related to drone, Unmanned Aerial Vehicles (UAV), Unmanned Aerial Systems (UAS), maternal, obstetric, healthcare, medical products transportation and Malaysia. A discourse analysis was follows and a narrative review was provided on this subject. *Discussion:* The ability of drones in delivery of blood products is highlighted as a possible application in improving maternal healthcare in Malaysia, particularly in the state of Sabah. Five key challenges are
HM02 Molecular Modifiers of Fibrinolytic Disorders

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Introduction: The constant deposition and removal of fibrin clots in the blood circulatory system are very vital for the regulation of haemostasis. This is provided by the extremely regulated fibrinolytic system that combines with the coagulation cascade through several molecular mechanisms. Fibrinolysis is a well-coordinated enzymatic activity that prevents the excessive deposition of fibrin clots while facilitating the removal of generated thrombi in the blood circulatory system. Main Body: Modification of the fibrinolytic activities can be achieved through a wide range of serine proteases, their cofactors, inhibitors, activators, and receptors, including some factors of the coagulation cascade. Other regulators of the fibrinolytic system are also available either on the fibrin-containing thrombus or on cells that express profibrinolytic receptors. Abnormalities of the fibrinolytic system are attributed to various severe phenotypes, including both acquired and the rarer congenital fibrinolytic defects, which contribute to the disease’s increased morbidity and mortality globally. The regulation of the fibrinolytic system is also essential as it was reported to be implicated in the cell signalling pathways, inflammation, and several types of malignancies. Although the pathophysiology of fibrinolytic disorders has been studied extensively, a compiled and well-summarised literature on the molecular modifiers of fibrinolytic disorders is still limited. Discussion: In this review, several potential molecular modifiers of the fibrinolytic disorders were discussed. Knowledge of the molecular modifiers of fibrinolytic disorders through normal and pathophysiological haemostatic states will create a room for progress to the new therapeutic interventions.

HM03 The clinicopathological factors associated with bone marrow infiltration among adult lymphoma patients in Hospital USM

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Introduction: Bone marrow (BM) assessment for lymphoma infiltration is crucial for lymphoma disease staging. It can influence management and disease prognosis. This study aimed to determine the risk factors associated with BM infiltration among adult lymphoma patients in our centre. Materials & Methods: This was a cross-sectional study using retrospective clinical and laboratory data, collected from 132 adult lymphoma patients (103 of non-Hodgkin, NHL and 29 of Hodgkin, HL) investigated for BM infiltration from January 2010 to September 2017 in Hospital USM. BM infiltration was determined by trephine marrow biopsy with or without BM aspiration. Simple and multiple logistic regression were used for statistical analysis and a p-value of less 0.05 was considered significant. Results: The mean age of patients was 48.6 (18.1) years with the majority were Malay (94.7%), male (61.4%) and B-NHL (63.6%). BM infiltration was found in 30 (22.7%) patients whereby 29 of them were suffering from NHL. The only independent factors for BM infiltration were T-NHL, indolent lymphoma and haemoglobin level, with the odds ratio of 23.167 (p=0.006), 4.433 (p=0.009) and 0.770 (p=0.022) respectively. The other selected factors (age, gender, race, disease stage, WBC and platelet count and LDH) were not significant. Discussion: We observed that the majority of lymphoma patients who had bone marrow infiltration were NHL, indolent type of lymphoma and at an advanced stage of the disease. However statistically, patients with T-NHL and indolent lymphoma were significantly at risk for having BM infiltration. Meanwhile, higher haemoglobin level will reduce the risk of BM infiltration.
HM04 Family Study of a rare haemoglobinopathy, Hemoglobin Arya in a Malaysian family

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Introduction: Thalassaemia and haemoglobinopathies are relatively common among Malaysians. One of the rare haemoglobinopathies reported is Haemoglobin Arya (Hb Arya). This Hb variant was first detected in 1975, in an Iranian female. This hemoglobinopathy occurs due to substitution of aspartic acid at residue 47 of the alpha chain by asparagine. Here, we report the detection of Hb Arya in a Malaysian family, which was detected incidentally during family screening. Case report: A 16-year-old girl was noted to have low mean corpuscular haemoglobin (MCV) levels of 26.3 pg with normal haemoglobin and raised red blood cell counts of 5.14×10^6/dl during the National Thalassaemia Screening Program. Hb analysis using capillary electrophoresis showed reduced Hba of 76.5%, HbaA2 of 1.6% with presence of small peak at Zone 1 likely A2*. There was a small peak noted at HbD zone and HbS zones which quantified as 1.5% and 20% respectively. However, supplementary test by high performance liquid chromatography showed a prominent peak at D-window (19.6%) and a small peak at S-window (0.6%). DNA analysis for alpha variant possibility revealed a heterozygous state of alph2 codon 47 Hb Arya mutation. Similar mutation was identified in her father and elder sister. While, her mother and younger brother both were confirmed with heterozygous of (αα4.2) deletion. Discussion: Among the haemoglobinopathies, Hb Arya is an extremely rare disease. Indeed, given the diversity of haemoglobin variants found in the population, we highlighted this rare disease in Malaysia contributes to the growing literature of the disorder and helps to eliminate possibility of interaction with other thalassaemic syndrome in the future.

HM05 Evaluation of platelet microparticles as a cardioprotective markers in healthy overweight subjects supplemented with EPA DHA

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Introduction: EPA DHA consumption has been known for its cardiovascular benefit. Yellow stripe scad (YSS) is a local Malaysian fish, with good quality nutritional value especially EPA+DHA. Literature showed that platelet microparticles (PMPs) were increased in obesity and overweight which increases the thrombotic risk. We evaluated the expression of platelet activation markers (CD41, CD62P and PS-annexin-V) after consumption of YSS and salmon among healthy overweight subjects. Materials & Methods: Overweight Malaysian adults recruited were equally randomized to receive steamed YSS or salmon for 3days/week for eight weeks with approximately 1000 mg EPA+DH/day in a cross-over study of 6-months. After an eight-week washout period their diets were switched. Blood was collected at the baseline and after treatment of each exposure and subjected for PMPs markers by flow cytometer. Results: Subjects in this study comprised of 17 males and 33 females with their mean age of 25.47±6.87 and 31.24±8.18 years old, respectively. Findings showed PMPs identified by CD62P, CD41 and annexin-V were significantly reduced in post treatment both groups of YSS and Salmon when compared to the baseline. Discussion: Harmonisation of the EPA+DHA on platelet phospholipid membrane might decrease the PMPs and its activation markers thus reducing the thrombotic risk. Current study provides an alternative option for salmon as YSS is a local and cheap source of EPA DHA with comparable cardioprotective effect. Further investigation on EPA+DHA phospholipid membrane analysis from platelets is required to establish the health benefits of YSS.

HM06 Comparison of red cell indices between alpha plus and alpha zero thalassaemia carriers in Hospital Kuala Lumpur (HKL)

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Introduction: α-thalassaemia is a common genetic disorder in Malaysia. The recommendation for α-thalassaemia screening should focus on alpha zero (α0) thalassaemia detection. Currently, MCH < 25pg has been used to screen for thalassaemia. The aim of this study is to compare the red cell indices between α2 and αα thalassaemia and determine the best MCH cut-off point for αα thalassaemia carriers. Materials & Methods: Cases of α2 and αα thalassaemia confirmed by DNA analysis were selected. RBC count, haemoglobin, MCV, MCH and HPLC results were retrieved. The differences of parameters between α2 and αα thalassaemia was tested using T-test. Receiver operating characteristic (ROC) curve was generated to determine the MCH cut-off point for αα thalassaemia carriers. Results: Out of 688 cases, 487 cases were αα thalassaemia and 201 cases were α2 thalassaemia. Comparison between α2 vs αα thalassaemia showed RBC (x 10^6/l) - 5.2 ± 0.9 vs 5.9 ± 0.7, Hb (g/dl) - 12.9 ± 1.4 vs 12.2 ± 1.5, MCV (fl) - 77.0 ± 4.5 vs 66.7 ± 3.8 and MCH (pg) was 24.9 ± 1.7 vs 20.7 ± 1.3 and all were statistically significant difference. Based on the ROC, the cut-off level of MCH in predicting αα thalassaemia carriers is 23.5pg with an area under the curve (AUC) of 0.969 with 98% sensitivity and 85% specificity. Discussion: RBC, Hb, MCV and MCH are significantly lower in αα than α2 thalassaemia. Using MCH cut-off point of < 23.5pg for alpha thalassaemia screening may reduce the cost and detect only clinically significant thalassaemia carriers.
HM07 Analysis of adverse transfusion reactions (ATR) in a teaching medical centre

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Introduction: Blood transfusion is a lifesaving treatment for some patients. Though with the advance of transfusion medicine, the incidence of transfusion risk is reducing but the occurrence of ATR still prevails. The aim of this study is to analyse the incidence and the pattern of ATR in UiTM Medical Specialist Centre. Materials & Methods: This is a retrospective study done by examining all the ATR cases reported to blood bank over a period of five years. ATR related to all types of blood components were analysed according to the type of reactions, clinical presentation, and the time of occurrence. Results: A total of 7525 transfusions were documented within the study period with the average rate of reported ATR was 0.31%. Allergic reaction was the most common type of reaction reported (41.6%). The most frequent clinical presentation reported was urticaria (29.8%). Pulmonary related complications were identified in 16.7% of reported ATR. Out of all 24 cases of ATR in this study, 42% occurred at night. Discussion: The incidence of ATR in our centre is low compared to incidence reported worldwide. However further investigation is required to determine whether the low incidence of ATR reported is accurate or under reported.

HM08 Blood group change in acute myeloid leukaemia: a case report

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Introduction: Blood group antigens are either sugars or proteins found attached to the red blood cell membrane. ABO blood group antigens are the most clinically important antigens because they are the most immunogenic. As red blood cell antigens are inherited traits, they are usually not altered throughout the life of an individual. Case report: We report a case of ABO antigen alteration associated with acute myeloid leukaemia. A 28 years old Indian male diagnosed as AML. He was grouped as O Rh(D) positive before starting on treatment. Patient was transfused with O Rh(D) positive packed cell prior to initiating chemotherapy. Patient attained remission one month of treatment. During the next follow up, ABO group result showed B Rh(D) positive. Bedside grouping was done and showed the same blood group, B Rh(D) positive. RBC genotyping confirmed that patient is B Rh(D) positive and subsequently transfused with B Rh(D) positive packed cell. Discussion: The patient had suppression of his blood group antigens during their leukaemic phase, and the antigens were re-expressed when the patient attained remission. There are two possible mechanisms for the weakening of ABO antigens in hematopoietic diseases. The first mechanism is the inactivation of A/B transferases, and the second is the inactivation of H transferase. Red blood cell (RBC) antigens are inherited traits and, as such, their expression is constant throughout the life of an individual. RBC antigen change has been occasionally described in association with haematological malignancies. These modifications of blood group antigens usually revert to normal after remission is attained.

HM09 Modulation of gene expression related to iron metabolism in iron deficient Wistar rat with consumption of date palm and goat milk

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Introduction: Despite the numerous reports on the health benefits of date palm and goat milk, there is limited information on its effects at molecular level. This study aims to assess the effects of date palm and goat milk on iron metabolism key proteins in iron deficiency anaemia (IDA) induced rats. Materials & Methods: Wistar rats were acclimatised for seven days before divided into normal control and iron deficiency anaemia (IDA) group. The IDA group was given a low iron diet for two weeks to induce iron deficient state. The IDA group were further divided into a few groups, supplemented with ferrous fumarate, date palm, goat milk and combination of date palm and goat milk for 4 weeks. Blood was collected for haemoglobin (Hb) and serum iron analysis while small intestine and liver were harvested for gene expression using qPCR. Results: Supplementation of date palm and goat milk significantly increased the Hb and serum iron level in IDA rats. The expression of Dcytb, ferroportin and transferrin in the small intestine was significantly improved. Date palm and goat milk also potentiates hepcidin expression in the liver, enhancing iron metabolism and storage. Conclusion: Date palm and goat milk modulate the expression of iron metabolism related genes, improving Hb and serum iron status in IDA rats.
**HM10 Survey of thrombophilia test ordering practices at a small healthcare facility**

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**Introduction:** Thrombophilia testing is often ordered inappropriately and can lead to misinterpretation of results. The results of the thrombophilia test may not change the patient’s clinical management. Many clinical guidelines and medical societies advocate against injudicious ordering of this test. **Materials & Methods:** We conducted a retrospective survey of all thrombophilia requests between 2019 to January 2020. The request forms and results were manually extracted and examined for demographic data, test indication, history of the thrombotic event, and anticoagulation therapy. We sent all our thrombophilia requests to the National Blood Bank for analysis. **Results:** Overall, there were only thirteen requests for thrombophilia testing from January 2019 to January 2020. There were ten female and three male patients, aged between 16 to 58 years old (mean 35.5 years old). Four requests were rejected because they were not indicated. The remaining nine cases had the test completed. Only two were weakly positive for the presence of lupus anticoagulant, with one positive result on repeated sampling. None was positive for anti-cardiolipin and anti-B2-glycoprotein-I antibody tests. **Discussion:** Thrombophilia test contributed less than 0.1% of the number of tests received by the haematology laboratory annually. Although a significant number of requests were processed, none of the request forms has stated the timing of a thrombotic event or any use of anticoagulation at the time of testing. Clinicians should be reminded of the importance of these details and screening for the appropriateness of a thrombophilia request should be performed by the laboratory personnel.

**HM11 Haemophagocytic lymphohistiocytosis in adults: a case series**

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**Introduction:** Haemophagocytic lymphohistiocytosis (HLH) is an aggressive and life-threatening syndrome of excessive immune activation. Prompt treatment is critical. Delay in diagnosis due to the rarity of this syndrome, variable clinical presentation and lack of specificity of the clinical and laboratory findings remain unresolved problem. The objective of this study is to present detailed clinical and laboratory features of a series of HLH cases in our centre. **Materials & Methods:** We retrospectively analysed the data of 5 HLH patients who were admitted between Jan 2018 and Jan 2020. The criteria for diagnosis was based on HLH 2004 diagnostic criteria. **Results:** All our 5 patients were Malay with female predominance (3/5) and majority were young adults with a median age of 24 years. All patients had fever, anaemia, hyperferritinaemia, hypertriglyceridaemia and presence of haemophagocytosis in the bone marrow. Mostly had splenomegaly, neutropenia and thrombocytopenia in 80%, 50% and 60% of the patients respectively. The underlying aetiology include pulmonary tuberculosis, systemic lupus erythematous and T-cell lymphoma while the other 2 cases were idiopathic. Three patients were in remission after being treated with HLH protocol while two patients died before specific treatments were initiated. **Discussion:** Patients with HLH often have non-specific symptoms and become progressively and critically unwell, with fever, cytopenia and multi-organ failure. Untreated HLH is almost universally fatal, even when treated, mortality is still high. Higher index of suspicion is needed in making a diagnosis of HLH syndrome. In strongly suspected cases based on clinical and laboratory findings, treatment should not be delayed as it can compromise the outcome.

**HM12 Molecular and haematological characterisation of high haemoglobin F among anaemic patients in Hospital Universiti Sains Malaysia**

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**Introduction:** Anaemia with high haemoglobin F (HbF) usually associated with a variety of inherited or acquired diseases. Single nucleotide polymorphisms (SNPs) related to HbF levels have been reported to be particularly beneficial in ameliorating the severity of anaemia by influencing the levels of adult HbF. Therefore, the aim of this study was to determine the association between HbF level and BCL11A (rs1186868) and HMIP (rs9376090) SNPs in acquired anaemic patients. **Materials & Methods:** This study involved 144 anaemia patients with HbF level ≥1.0%. High-Performance Liquid Chromatography (HPLC) was used to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. Multiplex ARMS (MARMs)-PCR and Gap-PCR were performed to detect β globin gene cluster mutation and deletion. Samples with no mutation detected by MARMs-PCR and Gap-PCR proceeded with allelic to determine the HbF and HbA2 level. **Discussion:** This study highlighted the importance of an updated data of common genetic modifiers or SNPs associated with high HbF in this population and considering their role in anaemia severity for a better approach involving the treatment and management of anaemic patients.
HM13 Seroprevalence of human immunodeficiency virus among voluntary non-remunerated blood donors in a teaching hospital: 10 years retrospective study

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Introduction: Blood transfusion is one of the routine therapeutic interventions in hospitals that can be lifesaving. However, this intervention is related to several transfusion-related infections. Human immunodeficiency virus (HIV) infection is a serious complication of blood transfusion. Therefore, the purpose of this article is to describe the seroprevalence of HIV infection among blood donors screened at our institution. Materials & Methods: A retrospective study was conducted among blood donors who donated blood at the Transfusion Medicine Unit Hospital USM from January 2011 to December 2019. Serologic screening for anti-HIV was conducted for all samples, and positive cases were confirmed. Results: During the study period, 98874 blood donors were screened for HIV infections. The majority were aged 17-24 year with a male-to-female ratio of 1:1.21. The overall seroprevalence of HIV infection in blood donors was found to be only 0.03% (n=29) in the ten consecutive years. The age groups of 21-25 years had the highest contribution of HIV infection. Twenty donors admitted they had a history of sexual promiscuity and nine donors denied on the risk factor. Discussion: The seroprevalence of HIV infection among our blood donors was low as compared to previous studies in other regions worldwide. The majority of the HIV positive donors were the young generation with a history of sexual promiscuity. Conducting further community-based studies to identify societal risk factors exposing communities for blood-borne infections and developing population-specific interventions to interrupt transmission are valuable in recruiting potential volunteer non-remunerated blood donors.

HM14 Descriptive profiling of normal cytogenetic AML in differentially expressed genes and survival rate

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Introduction: Recent molecular analyses of patients with acute myeloid leukaemia (AML) with a normal cytogenetic have revealed a striking heterogeneity with regard to the presence of acquired changes in gene expression and survival rate. This study aimed to identify descriptive profiling of normal cytogenetic AML in differentially expressed genes involved in the different pathways and survival rate. Materials & Methods: The clinico-biological parameters monitored in twenty at diagnosis patients including age, gender, initial peripheral blood counts (Hb, platelets and total white blood cells count), cytogenetic and bone marrow status were retrieved from Haematology Patient Management Information System (HPIS) Hospital USM for survival rate analysis. For gene expression analysis, blood samples from only eight out of twenty at diagnosis patients, two follow-up samples of normal cytogenetics AML and two normal healthy controls were obtained prior to RNA extractions. RNA gene expression assay was performed using NanoString nCounter4 PanCancer Pathway Panel. Results: Out of 20 patients, 55% survived more than a year with a mean survival rate of 1105.82 ± 513.92 days. Bone marrow status for one-year survival showed that patients were all in remission after first induction. We found the most enriched up regulated genes in newly diagnosed normal cytogenetic AML enlisted MPO, FLT3, MYCN, MYB and ITGA9 which are commonly found in AML cases. For highly expressed down regulated genes were GZMB, IL8, TNFRSF10C, LEF1 and IL2RB. Discussion: No significant association was detected between survival outcomes and bone marrow status. This may be due to the changes in the treatment regimes and complications of treatments over the years may have affected the overall results. Previous reports demonstrated that the groups by the MPO expression in the intermediate cytogenetic group showed a significant difference in disease-free survival (DFS) (p<0.001). The most down regulated gene was Granzyme B (GZMB) involved in cytolytic activity showed high correlation with other transcripts expressed in activated cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells as well as lymphocyte activation-related gene validating it as a robust and specific metric of active cellular immunity.

HM15 Molecular and haematological characterization of Hb Lepore: Institute for Medical Research (IMR) experience

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Introduction: Haemoglobin (Hb) Lepore is the result of a crossover between misaligned clusters of beta and delta globin genes. Hb Lepore Boston Washington is the most common Hb Lepore variant. It has been found with a low frequency in Malaysia even in Southeast Asian countries. In a heterozygote, it is associated with clinical findings of thalassemia minor but interactions with other hemoglobinopathies may lead to various clinical phenotypes and possible diagnostic challenges. Materials & Methods: We carried out a retrospective analysis of 54 cases referred to our laboratory for the confirmation of Hb Lepore during a period of 3 years. The haematological parameters and Hb analysis findings were analysed. Molecular analysis was performed using the Multiplex Gap-PCR method for Hb Lepore and variants. Data were analysed using IBM SPSS Statistic version 23. Results: Fifty-one samples were classified as heterozygous for Hb Lepore, two samples as compound heterozygous for Hb Lepore/ HbE, and one sample as compound heterozygous for Hb Lepore/Filipino deletion based on genotype findings. All of the Hb Lepore detected was of Washington Boston type (δ87/β116). Majority of the patients are Malay (n=50, 92.6%), followed by Bugis (n=3, 5.6%) and Chinese (n=1, 1.9%). Heterozygous for Hb Lepore showed mean Hb, RBC, MCV and MCH of 12.5 ±
CONFERENCE ABSTRACTS

HM16 Pertussis with lymphocytosis and cleaved nuclei. Telltale signs on peripheral blood smear: a case series

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Introduction: Despite the availability of vaccines, the growing incidence of pertussis in Malaysia has raised concern. Laboratory confirmation of Bordetella pertussis through culture and polymerase chain reaction, although readily accessible in major hospitals may still pose a potential delay. The morphological finding of mature lymphocytes with cleaved nuclei on peripheral blood smear in patients with pertussis has garnered significant interest over the past years. Case report: We report the case of two unvaccinated infants presenting with fever, cough, and respiratory distress. Both were initially treated as outpatients but subsequently referred to tertiary health care setting for bronchopneumonia with suspicion of pertussis. Case 1 is a 4-month-old infant with leukocytosis of 82.10x10^9/L and lymphocytosis of 53.10x10^9/L. Case 2, a 2-month-old infant with leukocytosis of 136.80x10^9/L and lymphocytosis of 40.30x10^9/L. A peripheral blood smear on day 2 and day 4 of admission respectively for each case demonstrated the presence of predominantly mature lymphocytes. These lymphocytes have condensed chromatin with a characteristic cleaved nuclei pattern. Both cases were treated with macrolides. A positive B. pertussis PCR result was obtained after 10 days and 13 days respectively for case 1 and case 2. Outcomes however deferred whereby case 1 recovered fully whereas case 2 succumbed to severe pertussis complicated with carditis. Discussion: Culture and molecular detection (PCR) of Bordetella pertussis may take up to several days to process. Hence, the recognition of lymphocyte morphology in a blood smear is valuable, as it can be used as a guide for early diagnosis.

HM17 Haemophagocytic Lymphohistiocytosis (HLH) secondary to Hodgkin Disease presenting as Pyrexia of Unknown Origin (PUO)

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Introduction: Hodgkin lymphoma affects mainly young adults, with a typical presentation of peripheral lymphadenopathy and mediastinal involvement. Hodgkin lymphoma in an elderly is rare and often diagnosed incidentally during work up for pyrexia of unknown origin (PUO) or uncommonly HLH. Therefore, a high index suspicion is necessary to make a prompt diagnosis and prevent fatal event. Case report: A 62-year-old Malay gentleman presented with two-month history of constitutional symptoms. Examination showed no palpable lymph nodes or organomegaly. Laboratory tests revealed pancytopenia, increased ferritin, high lactate dehydrogenase level and increased inflammatory marker of C-reactive protein. Due to persistent fever despite negative blood cultures and antibiotic treatment, bone marrow (BM) aspirate was proceeded which showed histiocytosis with evidence of haemophagocytosis, supportive of HLH. BM malignant infiltration was still considered by the presence of significant background smudge cells although no obvious abnormal cells appreciated. The trephine biopsy revealed effacement of normal marrow architecture by polymorphic infiltrates and fibrotic background. Scattered mononuclear cells observed. These cells stained positive for CD30, CD15, PAX 5 (weak). Marrow involvement by classic Hodgkin disease was diagnosed and determined to be the cause of HLH. PET-CT scan done subsequently revealed extensive uptakes of radioactive in the bone, liver, cervical, mediasternal, and abdominal lymph nodes. Discussion: This case illustrates atypical presentation of HD in an elderly patient characterized by shorter clinical history, aggressive histology and advanced stage of disease. This case highlighted that findings of HLH in elderly patient should raise suspicion of an aggressive primary disease.

HM18 Capillary 3 OCTA (CAP3) and Capillary Electrophoresis Flex Piercing (CEFP): performance assessment for Hb analysis

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Introduction: An evaluation of the capillary electrophoresis method for haemoglobin (Hb) analysis using two analysers from Sebia; Capillary 3 OCTA (CAP3) from Pathology Laboratory of HPUPM and Capillary Electrophoresis Flex Piercing (CEFP) from Pathology Laboratory of Hospital Kajang was conducted to ascertain their performance. Materials & Methods: The precision study of CAP 3 was conducted using HbA2 Normal and Pathological Controls where the samples were repeated 3 times for 5 days. As for linearity, three types of samples; low HbA2 (<2%), high HbA2 (>5%) and high HbF (cord blood) were used.
Carryover was performed using samples with low HbA2, high HbA2, normal HbA and HbE. The correlation was evaluated using 48 random patients’ samples. Results: The precision results of CAP3 for within and between run were less than the manufacturer’s claim CV. The relationship between both low HbA2 and high HbA2 and low HbF and high HbF were linear with the linearity of $y = 0.0628x - 0.1021$ ($R^2 = 0.9871$) and $y = 0.7973x + 2.1557$ ($R^2 = 0.9975$) respectively. The carryover from low HbA2 to high HbA2, high HbA2 to low HbA2, low HbE to HbE trait and from HbE trait to low HbE samples were $-0.905\%$, $0.00\%$, $-0.072\%$ and $-0.10\%$ respectively where all the results were less than $< 2\%$, fulfilling the ICSH guidelines. The results obtained on CAP3 and CE2FP were excellently correlated ($R^2 > 0.95$) with a correlation coefficient ($R \approx 1$). Discussion: CAP3 showed excellent performance and comparable to CEFP for the diagnosis of thalassaemia haemoglobinopathies.

HM19 Concomitant β-thalassaemia carriers and alpha globin gene triplication revealed variable phenotypes

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Introduction: Thalassaemia syndromes are very heterogeneous at the molecular level. Co-inheritance of α-globin cluster duplications as a genetic modifier in heterozygous β-thalassaemia leads to an increase of α/ non-α-chain imbalance which aggravates β-thalassaemia severity. The most common triplicated α-globin cluster are αααanti3.7 and αααanti4.2. However, their true prevalence in Malaysia is unknown. This report aims to describe a molecular analysis of these α-globin gene triplications and its clinical implication in thalassemia syndromes in Malaysia. Materials & Methods: Beta-globin gene mutations were diagnosed by routine diagnostic tests such as β-multiplex ARMS, Gap-PCR, and/or Sanger sequencing. The presence of α-globin gene abnormalities was tested using PCR for α-globin triplication. Results: Among β-thalassaemia carriers, sixteen and nine αααanti3.7 and αααanti4.2 were found involving ten types of β-thalassaemia mutations, respectively. Three β-thalassaemia carriers had both alpha triplication types. Six HbE/β-thalassaemia patients, four HbE carriers, and one Gγ(Aγδβ)°-thal Chinese ~100Kb deletion had one of the alpha triplications. Twelve had alpha triplication solely. In most cases, the β-thalassaemia carriers, and HbE/β-thalassaemia with single or both triplication types developed symptomatic anaemia. Severities were variables, presented from early infant to adult-onset NTDT. Two adult β-thalassaemia carriers were asymptomatic whereas one patient with HbE/β3-Filipino deletion and αααanti4.2 was converted from NTDT to TDT at the age of ten. The Chinese ~100Kb and HbE carriers with alpha triplication remained asymptomatic. Suspecting simple heterozygote for α-triplications remained obscure due to inconsistent haematological characteristics and may occur in individuals with normal and abnormal RBC. A β-thalassaemia carrier with a normal partner is still at risk of having symptomatic children. Discussion: The α-globin gene triplication was found in many β-globin mutation types. The variable phenotypes may complicate thalassaemia genotyping. In the pre-marital screening program, α-triplications and duplicated α-globin locus should be investigated if one partner is a β-thalassaemia carrier.

HM20 Identification of high oxygen affinity haemoglobin variants in Malaysian population

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Introduction: More than 100 variants of high-affinity haemoglobin (Hb) have been reported to date involving 78% and 22% of mutation occurs in β-globin gene and α-globin gene respectively. Most reported patients were heterozygous for mutations in a single globin gene however, homozygous patients have been described with more severe presentations. Materials & Methods: We analysed 47 cases referred to the Institute for Medical Research for molecular analysis of Hb variants from 2012-2019. Clinically all patients had no hepatosplenomegaly. Hb levels ranging between 10.1-24.8g/dL, haematocrit of 29.4-67.2%, red blood cell of 3.73-10.410/L, MCV, and MCH values ranging from 50.5-86.9fL and 20.1-30.1pg respectively. Presumptive diagnoses from haemoglobin analysis were suggestive of Hb variants, which subsequently confirmed at the DNA level by α or β-globin gene sequencing. Results: Twenty-five (53%) cases accounted for β globin gene variants which were found to be 15 cases of Hb Tak followed by four cases of Hb Bethesda, two cases of Hb Nottingham, a case of Hb Johnstown, Hb Crete, Hb Puttelange and Hb Genova respectively. While 22 (47%) accounted for α globin gene variants which were found to be 19 cases of Hb G-Georgia, two cases of Hb Ethiopia, and a case of Hb Tarrant. We observed that high affinity Hb variants involving a mutation in beta globin gene have more severe symptoms as compared to alpha-globin gene variants. Discussion: The diagnosis of high affinity Hb variants should be considered when the patient presented with unexplained polycythaemia. It is important that patients are not misdiagnosed as polycythaemia vera.
HM21 Blood donation program: initiatives towards attracting blood donors

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Introduction: The success of blood donation programme depends on the efforts of blood donor recruitment program. It has been shown that a good recruitment program can improve blood collections hence the blood supply. The aim of the study is to review initiatives taken by our centre in promoting blood donation. Materials & Methods: We analysed blood donation programs done between 2015 to 2019. The number of blood donors and initiatives done during each program was reviewed. Results: There were nine blood donations between these years. The total number of blood donors were 1520, with average of 168 per program. In 2016 and 2018, the blood donors increased by 251 and 191 respectively, compared to 2017 which decreased by 49. Based on 2018 and 2019 donor registry, most of the blood donors were medical student (67%), few were staff (26%) and visitors. Discussion: We focused on 1st and 2nd year medical students since they stayed in campus. The donation date was chosen based on the most relaxed day of their academic schedule. In 2018, we introduced food bazar to boost the potential blood donors crowd. In 2016, free ice cream was introduced as a catchy incentive as most of the blood donors were students. Education was given during lecture and customer education programs. We placed banner and poster at strategic area e.g., lift, main gate. We spread program information through email, WhatsApp, and social media (Facebook). Discussion: Blood donation recruitment program is continuous efforts, as it requires new ideas and strategies to attract public interest.

HM22 Machine learning approach in the morphological analysis of myeloid lineage blasts

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Introduction: The morphological analysis of peripheral blood smear plays a major role for the successful diagnosis of myeloid leukaemia. Currently, the classification of the myeloid lineage blasts is done manually with the use of bright field microscope. This method is time consuming, partly subjective and tedious. Hence, researchers have proposed automated classification methods using machine learning. Materials & Methods: This review compared ten studies that focused on machine learning models efficiency for the morphological classification and automatic detection of myeloid lineage blasts captured from peripheral blood smears with 40X magnification. All studies applied image enhancement, segmentation and feature extraction using both geometric and texture features. Meanwhile, few studies applied coloured features. These extracted features were then used as a parameter to feed into machine learning models. Amongst machine learning models reviewed in this study were support vector machine (SVM), artificial neural network (ANN), decision tree and evolutionary algorithm. Results: Results showed that prediction with SVM and ANN are potentially possible to achieve good performance. The average accuracy reported were 96 percent, sensitivity were 95 percent and specificity were 98 percent. On the other hand, fewer studies were reported using evolutionary algorithm and decision tree models. Discussion: SVM and ANN are models widely used by researchers as these models have proven significant performance, assisting the haematologist to perform efficient and fast morphological analysis of myeloid lineage blasts. They may also assist in the interpretation of some morphological features and may serve as a learning and survey tool.

HM23 Intelligent classification of blood cells with machine vision

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Introduction: Blood cell analysis can provide useful information concerning the health status of patients with hyperleucocytosis or abnormal red cell parameters. In this study, the performance of intelligent classification of blood cells with machine vision was evaluated. Materials & Methods: A hundred images of peripheral blood film for each of normal blood cells, acute lymphoblastic leukaemia (ALL) and chronic myeloid leukaemia (CML) were taken in 40X magnification under close supervision of the domain expert. Images were pre-processed to standardised the staining saturation effects, as well as artifacts removal using Thresholding, Median and Box filtering, and contrast tuning. These images were divided into a training set and test set (to test the trained model) with the ratio of 70:30. Shaped-based algorithms were fed with the train set images to learn the characteristics of lymphoblast, leucocyte, and erythrocyte. The learnt characteristics were used to detect lymphoblast cells and further improved with the rule induction method. Meanwhile, detected leucocytes were analysed with inception V3 deep learning architecture and Hough Circular transform algorithm to further classify them into granulocytes or agranulocytes, as well as detecting CML from the counting. Abnormal erythrocytes cells were classified using the Iterative Randomized Irregular Circle Detection algorithm. Results: Lymphoblast detection managed to get 86% accuracy percentage, leucocyte detection: 95.98%, leucocyte classification: 76.53%, CML detection: 88%, erythrocytes detection: 85.3% and erythrocyte classification performance is 70%. Discussion: The implementation of artificial intelligence techniques is highly potential to reduce the diagnosing time, haematology workload, and create rooms for pathologist’s advancement in new diseases.
HM24 ZACA extracts inhibit thrombus formation in hyperlipidaemia-induced Sprague Dawley rats revealed by SEM examination

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Introduction: Hyperlipidaemia is a major risk factor associated with thrombosis and subsequent progression to cardiovascular diseases. Anti-hyperlipidemia drugs such as simvastatin are currently used to treat hyperlipidaemia. ZACA extracts have never been utilised for its anti-hyperlipidemic and anti-thrombotic activities. Therefore, this study investigated the thrombotic therapeutic potential of ZACA extracts in the organs of hyperlipidaemia-induced Sprague-Dawley rats. Materials & Methods: Thirty-six male Sprague Dawley rats were grouped into six. Group A rats were fed with HFD for 12 weeks to induce hyperlipidaemia. Groups B were maintained on normal rat chows, while the remaining four groups (C-F) were fed with HFD and concurrently with simvastatin supplement, 200mg, 300mg, and 500mg /kg per body weight of ZACA extracts respectively for the same period. After the treatment, aorta and liver of the rats were harvested for histopathological studies by Scanning Electron Microscope, for the antithrombotic activity of ZACA extracts. Results: The (HFA) A rats showed significant structural changes particularly in the aorta and evidence of lipids infiltration in the liver. While simvastatin supplement demonstrated inhibition of thrombus formation, ZACA extracts at 200mg, 300mg, 500mg /kg per body weight respectively revealed intense inhibitions for thrombus formation, particularly at 300mg/kg per body weight concentration. Discussion: This study indicates that ZACA extracts have both anti-hyperlipidemia and anti-thrombotic activities and therefore, have significant therapeutic benefits to be utilized as a supplement to primary drugs in the treatment of hyperlipidaemia predisposition to thrombosis and its related cardiovascular diseases.

HM26 Study of co-inheritance of Haemoglobin E trait with Alpha Thalassaemia among Malay students in National Thalassaemia Screening Programme in HSNZ K. Terengganu from July 2016 to July 2018

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Introduction: Multiple studies had been carried out to determine deletional alpha thalassaemia in HbE trait. Meanwhile limited data available regarding non-deletional alpha thalassaemia in HbE trait. Materials & Methods: This cross-sectional retrospective study was conducted in Haematology lab HSNZ K. Terengganu. Capillary electrophoresis (CE) and gel electrophoresis is done to determine thalassaemia status and further DNA analysis conducted to determine alpha thalassaemia status. Results: The prevalence of co-inheritance of HbE trait with alpha thalassaemia was 8.9 %. The mean HbE level among HbE trait with alpha thalassaemia was 20.5 % which was significantly lower (p<0.001) than 25.3 % for HbE trait alone. The Hb A2, Hb, RBC, MCH, and MCV in HbE trait alone and HbE trait with concurrent alpha thalassaemia didn’t show significant changes in mean value. Discussion: HbE less than 23 % in CE was an acceptable criteria to be considered for further DNA analysis to detect concurrent 2 gene deletion of alpha thalassaemia or non-deletional alpha thalassaemia. HbE level was either above or below 23 % (CE) in cases of HbE trait with single gene deletion alpha thalassaemia.

HM27 Massive Transfusion Protocol: retrospective analysis of the current practice

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Introduction: Massive bleeding is associated with high mortality rates. Many institutions have implemented Massive Transfusion Protocol (MTP) to prevent haemodilution, trauma-induced coagulopathy by restoring normal coagulation function with the ultimate goal of controlling haemorrhage and reducing complications. Our institution started this protocol in 2012 with a 2:1 ratio of red blood cells (RBC): fresh frozen plasma (FFP). The aim is to study the effectiveness of the current massive transfusion protocol. Materials & Methods: Retrospective analysis of all activated MTPs cases over a 3-year period from 2017 till 2019. Data collected from the Laboratory information system and Hospital Information System. Results: There were a total of 61 cases, 29 cases were male and 32 were females. The age range was 15 years to 74 years old. Time to RBC and FFP transfusion ranges from 10 mins to 20 minutes. Time taken to control and or cessation of bleeding after initiation of MTP range from 1 hour 15 minutes to 24 hours. A total of 382 units of RBC, 363 units of FFP, and 388 units of cryoprecipitate were used. 23 of the cases were due to traumatic injury whilst the other 38 cases were due to non-traumatic injury. There were 17 death; 15 cases died within 24 hours of MTP activation. Of those 23 trauma-related cases there were 5 death. Discussion: Our results showed that the product issued was almost 1:1 ratio indicating that the current protocol was not appropriately adhered to. Revision of the protocol is needed so as the implementation for prompt and aggressive management of massively bleeding patients for better patient outcome.
HM28 An insight on dominantly inherited Beta Thalassaemia mutation (Hb Khon-Kaen): points to remember

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Introduction: Dominantly inherited β-thalassaemia is caused by a single mutation affecting HBB gene that manifests as a disease phenotype. Thirteen mutations (including frameshift, missense, nonsense, and complex rearrangements) causing dominant β-thalassemia have been reported and most of the mutation occurs in exon 3 of HBB gene. This study aims to evaluate and characterized haematological features of Hb Khon Kaen among Malaysian population. Materials & Methods: Diagnostic thalassaemia data from 2012 to 2019 were analysed. Twenty-six cases were found to have Hb Khon Kaen mutation. Strikingly all the cases were presented with a classical Hb A2 level of β-thalassaemia trait (mean=5.0±1.5%) without abnormal peak detected in haemoglobin analysis thus, all the samples were subjected for Multiplex β-ARMS PCR before sequencing analysis. Results: Fifteen cases were classified as heterozygous Hb Khon Kaen, nine cases were compound Hb Khon Kaen and Hb E while two cases were compound Hb Khon Kaen and β°-Thal Filipino deletion. The heterozygous cases presented with intermediate phenotype with mean Hb of (8.94±2.19 g/dL) and most cases have features of chronic haemolysis. Interestingly, we found that this mutation is common among Malays (76.9%) from Peninsular Malaysia and does not localize in the Northern region of Malaysia as expected after the first case being discovered in Thailand. Discussion: These findings will significantly change the understanding and planning for the molecular test required particularly in a limited resources country. The mutation should be suspected in cases of classical HbA2 range of beta thalassaemia with intermediate clinical features and inclusion bodies.

HM29 Evaluation of the effectiveness of strategy to reduce rejection rate for DNA alpha thalassaemia in Haematology Unit, Kuala Lumpur Hospital

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Introduction: Rejection rate is one of the quality indicators monitored in the accredited laboratory. The Molecular Haematology Laboratory in Hospital Kuala Lumpur encountered a high rejection rate for Alpha Thalassaemia DNA Analysis request due to various reasons. Among the highest rejection causes are redundancy and incomplete necessary attached documents or results required for the testing. For Alpha Thalassaemia DNA Analysis test, the requestor must fill in specific request form, provides patient/parents’ consent, complete clinical history information, recent full blood count within three months, haemoglobin analysis and EDTA sample. One of the strategies to reduce the rejection rate is by implementing the guideline for Alpha Thalassaemia DNA Analysis request to Hospital Kuala Lumpur (HKL). Materials & Methods: This study is carried out to evaluate the effectiveness of the guideline in reducing the rejection rate. Pre-intervention data was collected starting from January to March 2019. The guideline was distributed to all the Ministry of Health hospitals and clinics in March 2019. Post-intervention data was collected starting from June to September 2019 and analysed in October 2019. Results: The study showed reduction in rejection rate. The mean rejection rate for pre-intervention data was 10.7% and reduced to 6.7% in post intervention data. Discussion: The guideline provided had assisted the customers to adopt the correct process on the delivery of a sample for thalassaemia molecular testing and thus reduced the rejection rate and produced quality test results. However, further corrective action needs to be done to improve quality of the service.

HM30 Utilising a targeted next generation sequencing analysis in Malaysian non-small cell lung cancer patients

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Introduction: Malaysian non-small cell lung cancer (NSCLC) patients have a high prevalence of EGFR mutation i.e., 37-40% (n=4434) and positive rearrangement involving the ALK gene accounted for 19-21% of patients (n=817). In the advancement of molecular era, Next Generation Sequencing (NGS) has started to consolidate their techniques to screen lung cancer patients. We evaluated the performance of mutation detection between cobas® EGFR Mutation panel and Ion AmpliSeq Colon and Lung Cancer v2 in combination with Ion RNA Fusion Lung Cancer Panel using the Ion Torrent Personal Genome Machine. Materials & Methods: Thirty NSCLC patients were selected from our database based on previous molecular study reports and sample suitability. DNA and RNA were manually extracted from paraffin sections. Ion Torrent sequencing technology was utilized using 10ng DNA and 100ng RNA from each sample. The raw data were analysed using the torrent suite software v3.6.2 (Life technologies). Results: Among the 30 samples, 29 showed concordant results between NGS and cobas® EGFR test, with 1 discordant case for Ex20ins. Meanwhile, NGS and FISH for ALK were both informative. Further mutations in TP53, KRAS, PTEN, STK11, CTNNB1 were found in 18 patients and 2 positive ROS1 rearrangements were identified. Discussion: The NGS technology appears to be the best approach with first line NGS testing being most cost effective in the long run with more patients having targetable, actionable and druggable genetic rearrangement being established within the fastest turnaround time.
Malays J Pathol April 2021

**HM31 Cross reactivity dengue NS1 antigen in paraproteinemia**

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*Introduction:* NS1 Antigen is a non-structural protein from dengue virus. NS1 duo combo test is a highly sensitive and specific one step immunochromatographic assay for diagnosis of dengue infection. Paraproteinemia is the presence of excessive amounts of monoclonal gamma globulin in the blood. We presented a case of prolonged fever with hypoalbuminemia, and was treated as dengue infection. *Case report:* A 55 years old Malay man, not known of medical illness. Presented with a history of lethargy, low grade intermittent fever which resolved with paracetamol, loss of appetite, gradual loss of weight about 3 kg per year. He went to a private medical centre for further examination and was treated as dengue fever. NS1 antigen was positive using dengue duo combo rapid test. However, his blood investigation shows Hb level of 10.0g/dL, haematocrit level of 33%, albumin of 25 g/dL, and proteinuria 3+. Radiological investigation was normal. He was discharged with a further plan for renal biopsy. Unfortunately, 3 months later, he collapsed at his office and succumbed to death. Post mortem findings revealed an extensive amyloid deposition in the heart, lungs, both kidneys and blood vessels. Trephine biopsy showed increased plasma cells with lambda chain restriction. Serum electrophoresis and immunofixation showed presence of monoclonal IgM lambda paraproteinaemia with serum free light chain lambda involvement. *Discussion:* Cross reactivity of NS1 antigen was observed in this case as reported previously in haematological malignancy patients. The indiscriminate use of the NS1 test strip in this case results in delayed diagnosis and treatment of paraproteinemia. Thus, validation of the interference or cross reactivity between NS1 tests and haematological illnesses is important to avoid wrong or delayed diagnosis.

**HM32 Human leukocyte antigen (HLA) genes associations among Malay Beta thalassaemia major patients**

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*Introduction:* Beta (β)-thalassaemia major is a public health problem in Malaysia. It is curable by human leukocyte antigen (HLA) matched-sibling donor/HLA-matched unrelated donor stem cell transplant. As of 2018, the Malaysian Thalassaemia Registry documented about 7,984 registered patients of which 2,676 (33.52%) consists of β-thalassaemia major. Among them, Malay ethnicity is the most common (63.95%). We investigated the association between HLA genes and β-thalassaemia major in the Malay population. *Materials & Methods:* A total of 70 β-thalassaemia major patients underwent routine HLA genotyping between 2014 and 2019, and 70 unrelated and ethnically matched healthy controls from the Malaysian Stem Cell Registry were analysed. The HLA-A, -B and –DRB1 loci were genotyped using the SSO-PCR method on the LABscan3D Multiplex platform. *Results:* Our data revealed, the HLA-B*60 allele was associated with decreased risk for the β-thalassaemia major in the studied population (OR=0.09, 95% CI 0.01 – 0.70, P<0.05). No association was observed in HLA-A and HLA-DRB1 genes with a β-thalassaemia major in this study. *Discussion:* Our study showed that B*60 was negatively associated with β-thalassaemia major in the Malay population.

**HM33 Up-regulation of IGSF4 in partially methylated CD26/IVS1-5 HbE/β-thalassaemia patients**

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*Introduction:* DNA methylation in IGSF4, an immunoglobulin-like intercellular adhesion molecule is one of the potential epigenetic modifiers not fully explored in HbE/β-thalassaemia. IGSF4 is normally expressed in normal cells and its promoter not methylated. This study aimed to analyse DNA methylation profile and gene expression of IGSF4 using peripheral blood (PB) in nucleated red blood cells (RBNCs) for the source of DNA of HbE/β- and β-thalassaemia major patients. *Materials & Methods:* PB were collected from 33 transfusion-dependent thalassaemia patients from Hospital USM and Hospital RPZII, Malaysia. DNA methylation profile and gene expression of IGSF4 were examined by methylation-specific PCR and quantitative real-time PCR respectively. *Results:* 75% (9/12) β-thalassaemia major patients were fully methylated in the promoter region of IGSF4 while 95% (20/21) HbE/β-thalassaemia were partially methylated. IGSF4 expression (0.09±0.86) in β-thalassaemia major showed a significant downregulation against normal controls (p<0.05) but not against HbE/β-thalassaemia patients (0.07±1.40). The association of IGSF4 expression and DNA methylation profile was statistically significant (p<0.001). IGSF4 expression was up-regulated in 4 of 4 CD26/IVS1-5, and down-regulated in 7/7 CD26/IVS1-5 and 4/5 CD26/CD41/42 HbE/β-thalassaemia patients, in contrast to down-regulation of 5/5 IVS1-5/IVS1-5, 3/3 IVS1-1/IVS1-1 and 2/3 CD41/42 β-thalassaemia major patients. DNA methylation of IGSF4 in these patients were either partially methylated or fully methylated in CD26/IVS1-5 and IVS1-5/IVS1-5, respectively. *Discussion:* DNA methylation of IGSF4 may act as an additional modifier to gene mutation especially involving IVS1-5 in HbE/β-thalassaemia. Homozygous IVS1-5 in β-thalassaemia major may contribute to different disease presentations compared to those involving CD26 in HbE/β-thalassaemia.
HM35 Reducing red cell transfusions in patients in medical general wards in a major specialist hospital

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Introduction: Red cell transfusion has adverse effects on mortality and morbidity in hospitalized patients. Most indications for transfusion are due to anaemia which is an independent risk factor for increased length of stay in hospitals and increased mortality. In our hospital setting, we see an increasing trend of red cell transfusions in the medical department that warranted further intervention. Materials & Methods: Pre-intervention, all 43 red cell transfusion cases in medical wards for one month were studied. Exclusion criteria were ESRF/CKD, Thalassaemia and bleeding cases. Intervention including CME on Patient Blood Management (PBM) for doctors and specialists, PBM course and formation of PBM liaison officers in the Medical Department. Post-intervention, 88 cases of red cell transfusions for 2 months were analyzed. Outcome showed reduced Hb trigger from 7.4 g/dL to 6.3 g/dL, with improved CT ratio from 1.15 to 1.03. Reduction on red cell transfusion also decreased by 10%. Discussion: Intervention and activities to instill awareness regarding PBM and its practices among doctors in medical departments contributed to reduced red cell transfusions in medical general wards. This indirectly translated to lower complications and risks associated with red cell transfusions which are also cost-efficient.

HM36 Unexpected non-maternally derived autoanti-Jka in a 3-month-old patient

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Introduction: Red cell autoantibody production by newborn is extremely rare. We report a case of unexpected autoantibody with anti-Jka specificity in a previously healthy (and normal Glucose-6-phosphate dehydrogenase) 3 months old Malay male infant that was non-maternally derived. Case report: He presented with symptoms of haemolysis preceded by viral infection. His birth history and mother’s antenatal history were uneventful with no prior history of transfusion. Clinically no hepatosplenomegaly demonstrated. Laboratory investigations revealed severe anaemia (haemoglobin level of 59 g/L), reticulocytosis (3.8%), indirect hyperbilirubinemia (46.6µmol/L) and elevated lactic dehydrogenase (649U/L) without evidence of haemolysis on blood smear. Initial pretransfusion testing identified the patient as O Rh (D) positive and a negative direct antiglobulin test (DAT). Mother’s blood group was A Rh (D) positive and antibody screening was negative. Patient was transfused with 110 ml of group O Rh (D) packed red cells. DAT was positive for Immunoglobulin G (IgG) on his second sample upon planning for a repeat transfusion. Elution test showed Anti-Jka. Antibody screening on the second maternal sample was persistently negative. Patient’s antibody screening was positive, subsequently identified as autoanti-Jka. Red cell phenotyping from the initial sample showed that both patient and mother were Jka+ Jkb-. Discussion: We postulate that Anti-Jka coating the infant’s RBCs was non-maternally derived. He presented with symptoms of haemolysis preceded by viral infection. His birth history and mother’s antenatal history were uneventful with no prior history of transfusion. Clinically no hepatosplenomegaly demonstrated. Laboratory investigations revealed severe anaemia (haemoglobin level of 59 g/L), reticulocytosis (3.8%), indirect hyperbilirubinemia (46.6µmol/L) and elevated lactic dehydrogenase (649U/L) without evidence of haemolysis on blood smear. Initial pretransfusion testing identified the patient as O Rh (D) positive and a negative direct antiglobulin test (DAT). Mother’s blood group was A Rh (D) positive and antibody screening was negative. Patient was transfused with 110 ml of group O Rh (D) packed red cells. DAT was positive for Immunoglobulin G (IgG) on his second sample upon planning for a repeat transfusion. Elution test showed Anti-Jka. Antibody screening on the second maternal sample was persistently negative. Patient’s antibody screening was positive, subsequently identified as autoanti-Jka. Red cell phenotyping from the initial sample showed that both patient and mother were Jka+ Jkb-.

HM37 Prevalence of red cell alloimmunization among the transfusion recipients at a teaching hospital in Malaysia

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Introduction: Red cell alloimmunization is a complication that results from antigenic exposure by transfusion, pregnancy or transplantation. It can lead to haemolytic reaction among transfusion recipients. The alloantibody formation is influenced by ethnicity, genetic predisposition, immune status, antigen immunogenicity, transfusion frequency and others. Materials & Methods: The prospective cross-sectional study was done on 13011 patients, investigated for pre-transfusion at a teaching hospital from October-2018 to September-2019. Antibody was detected by indirect antiglobulin test. Data were collected and analysed. Results: A total of 267 unexpected antibodies were identified among 13011 patients where 231(1.8%) were alloantibodies and 36(0.3%) were autoantibodies. Among the alloantibodies, anti-Mi(26.4%) is the most frequent antibody, followed by anti-E(23.4%), anti-c(11.7%) and anti-Le(9.5%). Rare alloantibodies such as anti-Fya and anti-Jk3 were encountered with one for each. Among the autoantibodies, 63.9% were autoIgG, 25% were cold-autoantibodies and rest were antibody-against-reagent, drug-induced autoantibody and with anti-c specificity. Discussion: The prevalence of alloantibodies has increased from 0.76% to 1.8% in our hospital in comparison with the previous 2010 study. The most encountered alloantibody was anti-Mi(0.5%) and its prevalence in other Asian countries was 0.28% (Taiwan), 0.057% (Hong Kong) and 0.17% (Thailand). Rare antibodies like anti-Ik3 were identified where the compatible blood is very difficult to obtain. Since clinically significant anti-Mi is the most common alloantibody detected in this study, we recommend the following measures: i) the reagent cells used for pre-transfusion testing should able to detect anti-Mi; ii) perform Mi phenotype in patient who developed anti-Mi; iii) supply Mi negative crossmatch compatible blood to patients with anti-Mi for improved patient care.
HM38 A case of anti-Jk3 detected by double adsorption and double elution method

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Introduction: The Kidd blood group is a system consisting of three antigens, Jka, Jkb and Jk3. Individuals with (Jka-b-) phenotype are rare in the population and they can develop an antibody to a high-prevalence antigen called Jk3, which is present on any RBC positive for Jka or Jkb. Case report: We report a case of a 75-year-old lady, with background history of diabetes mellitus, hypertension, dyslipidaemia and ischaemic heart disease. She presented with symptoms of obstructive jaundice and was diagnosed with pancreatic cancer. Her haemoglobin was 6.5 g/dl and she was transfused with two units of packed cell without any adverse reaction. Her post transfusion haemoglobin level increased to 8.9 g/dl. At this time, her antibody screening panel was negative. A month later, her antibody screening was positive in all the three panel cells. Antibody identification showed pan-agglutination reaction on all 11 panel cells with enzyme enhancement. Patient’s red cell phenotype was Jk(a-b-). Anti-Jk3 was suspected and further confirmed by double adsorption and double elution method. Discussion: A previous local study showed that out of 594 blood donors, Jk(a-b-) phenotype was found in 3.5% Malay donors and 1.7% Indian. Kidd alloantibodies have a special importance in the field of blood banking as they show evanescence where the titres tend to reduce over the time. Sometimes, the detection of antibodies is difficult and it may cause haemolytic transfusion reaction. This case report highlights the importance of recognizing anti-Jk3 to provide patients with correct blood for transfusion.

HM39 Improvements in quality of metaphase spreading by improving cytogenetic harvesting procedure

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Introduction: Metaphase spreading is an essential technique for cytogenetics procedure. Results of G-banding techniques are greatly influenced by the quality of chromosome spreading. The good quality of chromosome spreading depends on good harvesting process. The objective of this study is to improve the quality of the harvesting process in cytogenetic procedures. Materials & Methods: During harvesting, the cells are treated by Colcemid to arrest cells in metaphase, and a hypotonic Potassium Chloride (KCl) solution is used to induce cellular swelling. The cells are then fixed with methanol/glacial acetic acid and chromosome spreads are prepared. This harvesting process is done twice. Results: This protocol yields good chromosome spreads from even the most difficult cell suspensions such as neonates blood sample, whereby it usually produces cloudy suspension after harvesting. With this improved harvesting technique, the suspension cloudiness disappeared and the backgrounds of metaphase spreads became clearer. Improvement in chromosome spreading is also observed in which the spreads have a larger metaphase area and fewer chromosome overlaps. Treatment with hypotonic 0.075M KCL solution done twice can swell clumped cells, remove glycoprotein in the cell membrane, and lyse non-lymphocyte cells. Fixative solution treatment done afterward will clean the suspension and fix the lymphocytes cell membrane. Discussion: The improved cytogenic harvesting procedure has been shown to enhance our metaphase chromosome spreading, with a clear background and well-spread chromosomes that is suitable for chromosome analysis.

HM40 Interaction of Haemoglobin E (HBB:c. 26 G>A) with Haemoglobin Nottingham (HBB c.98T>G) in β Thalassemia

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Introduction: β Thalassaemia Hb E disease is a common transfusion-dependent thalassaemia in Peninsular Malaysia. Interaction between Hb E (HBB:c. 26 G>A) with various β thalassaemia mutations resulting in different severity of β Thalassaemia Hb E disease. Three common β-globin mutations that account for 73% of the mutations in Malays are HbE (HBB:c. 26 G>A), IVS 1-5 (HBBG>C), and IVS 1-1 (HBB:G >T). Hb Nottingham (HBB c.98T>G), is unstable haemoglobin, results from the substitution of valine by glycine caused severe haemolysis in few reported cases. Case report: We report two cases of compound heterozygosity of the above mutation in the Malay population. Both of these probands presented at the age of 2 years with pallor, normochromic normocytic anaemia with Hb levels of 5.5 g/dl. High performance liquid chromatography (HPLC) shows an increase of Hb F and Hb A2 level in HPLC and prominent A2 and F band in gel electrophoresis system compatible with β Thalassaemia Hb E disease. Mother’s shows thalassaenic indices with normal Hb levels and father’s red cell parameters are within normal. Molecular characterisation by ARMS PCR and reverse dot blot hybridisation for both twin and mother shows only heterozygous HBe (HBB:c. 26 G>A). DNA sequencing of HBB gene confirms mutation of Hb Nottingham (HBB c.98T>G) and HBe (HBB:c. 26 G>A) in both twins. Discussion: Our case highlights the interaction of Hb E with Hb Nottingham presented in twin Malay boys and categorised as severe β Thalassaemia Hb E disease. Therefore, understanding this rare de novo mutation is important for family counselling as thalassaemia is a very common inherited blood disorder in our population.
HM41 An unusual case of a naturally occurring anti-M antibody causing ABO blood group discrepancy

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Introduction: Anti-M antibody can lead to ABO discrepancy triggering a challenge for blood bank personnel and delay in blood supply. Here, we present a rare case of naturally occurring anti-M leading to ABO discrepancy. Case report: A 2-year-old girl, admitted with right canine space cellulitis, planned for incision and drainage and tooth extraction under GA and GSH was requested. The patient had no transfusion or transplantation history. On investigation, ABO blood group showed a discrepancy. The forward grouping was A; however, reverse grouping showed 4+ reaction with ‘A-cell’ and ‘B-cell’. Repeat testing with a new sample showed similar results by tube method, gel-card method, and by pre-warm technique. The patient’s Rh phenotype was CDe/CDe with negative DCT. Technical error and the possibility of A-subgroup or any autoantibody were excluded. Antibody screening and identification revealed anti-M, reactive at 4°C, room-temperature, 37°C and at the AHG phase. MN phenotype: NN. We suspect the discrepancy could be due to the presence of M-antigen in the reagent ’A-cell’ that cross-reacts with the patient’s anti-M. Subsequent testing showed M-antigen is present in the reagent ‘A-cell’. Repeat reverse grouping using M-antigen negative ‘A-cell’ showed no reaction and matches the forward and reverse grouping. Crossmatch with M-antigen negative blood was compatible. The patient’s operation was carried out without any complication and the patient did not require any packed cell transfusion. Discussion: This is a rare example of anti-M causing ABO discrepancy. Any ABO discrepancies should be resolved before transfusion. Therefore, careful interpretation of the results and patient’s clinical history, previous blood group, or transplant or transfusions history is extremely important.

HM42 Three-way translocation in de novo myelodysplastic syndrome (t(3;5;22) (p21;q15;p12) : a case report

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Introduction: Cytogenetic abnormalities are present in about 50% of myelodysplastic syndrome (MDS). Balanced translocation is uncommon. We report a case of MDS with t(3;5;22)(p21;q15;p12). Case report: A 64-year-old, lady presented with leathargy and weakness for 1 year. Examination revealed pallor without jaundice or hepatosplenomegaly. Blood picture revealed bicytopenia (Hb:6.7g/dL, platelets:142x109/L), some macrocytosis, dysplastic neutrophils and presence of 15% blast cells. Bone marrow (BM) revealed hypercellularity, erythroid hyperplasia with reversed myeloid to erythroid ratio (0.4:1). Megaloblastic dyserythropoiesis and binuclearity were observed. Myeloblasts formed 12% of BM cells. Dysplastic neutrophils were seen. Dysmegakaryopoiesis were identified, evidenced by hypolobated and micromegakaryocytes. No ring sideroblasts noted. Chromosomal analyses revealed a female karyotype with t(3;5;22)(p21;q15;p12). Findings is consistent with MDS with excess of blast. Follow-up blood smear showed an increased blast percentage 6 months later, when disease progression to acute leukaemia was made. Discussion: Primary MDS with balanced translocations is extremely rare. Abnormality related to del(5q) defined a specific subtype, carries a favourable clinical course. Our case involved chromosome 5 abnormality in the form of three-way translocation. To date, no similar cases were described in our center and literature search respectively. The blast percentage and Hb level has stratified the patient into a high-risk group, following IPSS-R scoring system. Cytogenetic abnormality further stratified patients into very high risk, hence predicting poorer prognosis. Association between the chromosomal abnormality and morphologic subtype remains to be defined. In this respect, it involved a female patient, morphologically exhibiting hypolobated megakaryocytes with nearly normal platelets, resembling the morphologic description described in MDS with del(5q) subtypes.

HM43 Compound heterozygous state of Hb E and Hb D with hereditary stomato-ovalocytosis: a case report

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Background: Haemoglobinopathies are reported as one of the most common hereditary diseases in the world population. In Malaysia, Hb E and South East Asia are common, but HbD Punjab is rare. We report a case of a double heterozygous state of HbE and HbD, together with hereditary stomato-ovalocytosis in a 16-year-old patient. Case Presentation: A 16-year-old asymptomatic male student underwent thalassaemia screening under the school health program. Complete blood count showed normal haemoglobin with hypochromic and microcytic red cell indices. Blood film showed the presence of numerous stomatocytes and ovalocytes suggestive of hereditary stoma-ovalocytosis. Capillary electrophoresis showed the presence of a peak at D zone (65.7%) and at E zone (29.8%). A high performance liquid chromatography (HPLC) revealed raised haemoglobin in D-window (61.5%) and HbA2/E (28.5%). Cellulose acetate electrophoresis showed a prominent band at HbD and at HbE in both acid and alkaline. Family tracing revealed both parents are Malaysian Malays. Discussion: HbE is a β-haemoglobin variant that affects haemoglobin structure and synthesis rate. It is commonly seen in the South-East Asian population while HbD Punjab is prevalent in Northwestern Indian. These different geographical features contribute to the low incidence of the disease. Stomato-ovalocytosis is an autosomal dominant membrane defect disease that only needs symptomatic treatment. Eight similar cases were reported in the literature which the disease may manifest asymptomatic that may pass unnoticed up to moderate anaemia. This perhaps the first case reported together with hereditary stomato-ovalocytosis. The incidence of these rare haemoglobinopathies may be higher in the future coinciding with advancing technologies and civilization which need further socio-economic consideration.
HM44 To investigate the errors in transfusion practice of major hospitals in Kedah

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Introduction: Errors in transfusion practice can occur from near-miss to actual errors with or without harm. Objectives: This study was done to identify the incidence, major causes and associated factors of transfusion errors and near-miss events in major hospitals of Kedah. Materials & Method: This study is a retrospective and cross-sectional study which required the data collection from all requests for Group, Screen and Hold (GSH) and Group and Crossmatch (GXM) tests sent to the Transfusion Medicine Unit of the respective hospitals. This study analysed the incidence of errors, major causes, an association of causes and human factors with errors from the incident reporting form by using a proforma. Fisher’s Exact Test was utilized for the association of factors. Results: Near miss events were more in comparison to transfusion errors. Comparatively, laboratory transfusion error had a higher proportion than clinical transfusion error. As for major causes, wrong blood issue and miscollected samples contribute the most to laboratory transfusion error and clinical transfusion error respectively. Clinical near-miss events were higher in comparison to laboratory near-miss events. Mislabelling samples were the most common cause in clinical near miss and transcription errors in the laboratory. Lack of supervision resulting in error was the most common human factor. Discussion: The incidence of transfusion errors and near-miss events in major hospitals in Kedah were relatively low. However, transfusion errors were predominant in laboratory service. An improvement is a must which includes intensive training among laboratory technicians and enhancing the education of blood safety in clinical areas.

HM45 Pattern of Clot Waveform Analysis (CWA) in relation to Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT)

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Introduction: CWA is a recently developed technique that has been used for global coagulation function. Principally, CWA is done based on the routine coagulation assays such as aPTT and PT. Objective: To analyse patterns of clot wave in a spectrum of clinical disorders and their significance. Materials & Methods: A cross sectional study amongst patients’ samples sent to Hospital Serdang for routine coagulation tests was performed. The samples were tested in ACL TOP 350 which uses optical clot detection method. The clot waveform was analysed and details on three phases of clot formation was determined, correlating with underlying clinical disorders. Results: Eighty-six samples were analysed for clot wave pattern. Majority, 92% (n= 79) samples showed normal sigmoid pattern of clot wave. Others showed unstable baseline (n=4), acceleration phase seen but no endpoint (n=2) and short baseline pattern (n=1). Amongst the sigmoid pattern clot wave, the longest duration in pre-coagulation phase (54.5 seconds) was seen in bleeding-related diseases. Maximum change in optical density was seen in diseases unrelated to haemostasis disorders, whilst shortest mean duration in post-coagulation phase (24.3 seconds) was seen in disease with mixed underlying haemostasis disorders Discussion: The clot wave provides additional information on phases of clot formation apart from clotting time. Pre- coagulation phase denotes reaction before clot is formed and samples from bleeding-related diseases showed longest duration; however, rate of clot formation is highest in diseases not related to haemostasis and shortest time for clot establishment was seen in diseases related to mixed haemostasis disorders.

HM46 Evaluation of automated coagulation analyser STA Compact Max 2 in Hospital Duchess of Kent, Sandakan, Sabah

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Introduction: STA Compact Max 2 (Stago Diagnostica, Asnieres-Sur-Seine, France) is an automated coagulation analyser which utilise the chronometric principle of measurement for clotting assays and photometric principle for chromogenic and immunologic assays. The main aim of this study was to evaluate the analytical performance of two units of new STA Compact Max 2 in the department. Materials & Methods: Evaluation protocol study were done for the following coagulation tests: PT(prothrombin time), APTT(activated partial prothrombin time), fibrinogen and D-dimer concentration. This protocol includes verification of manufacturer’s precision, accuracy, sample carryover, reagent carryover and reference range, correlation study, and establishment of the reference time. Results: The manufacturer’s claim for precision, accuracy, sample and reagent carryover, and the reference range for the four tests were verified with both analyzers. Good correlation was obtained between both new analysers and existing analyser ACL TOP (Instrumentation Laboratory, Paris, France) with r value ≥0.95 for PT, APTT and fibrinogen tests. Quantitative D-dimer assay showed sensitivity and negative predictive value of 100% in comparison with the existing qualitative D-dimer test. Excellent correlation was obtained with r value ≥0.99 between the two units of new analysers, STA Compact Max-A and B. The MNPT/PT reference time for Analyser A and B are 13.1 sec and 13.2 sec, respectively. The APTT reference time for Analyser A is 34.4 sec and 34.9 sec for Analyser B. Conclusion: Both new coagulation analysers, STA Compact Max 2-A and B have good analytical performance and the performance is comparable with the existing coagulation analyser.
HM47 Determination of mean cell volume and mean cell haemoglobin cut off values for alpha thalassaemia screening in Hospital Selayang

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Introduction: Thalassaemia is an inherited disorder and in Malaysia, thalassaemia cases have been increasing. It is a major and common health problem in people of Asian descent. Haematologic or red blood cells indices have been a very useful screening method for thalassaemia. However, the screening method for alpha thalassaemia based on mean cell volume (MCV) <80fl and mean cell haemoglobin (MCH) <27pg showed many false positive results and in such a situation, the screening would require a new cut off value. Materials & Methods: 197 patients’ data were collected at Hospital Selayang, out of which 97 were diagnosed with alpha thalassaemia and 100 with normal data. The ROC curve was plotted for MCV and MCH indices by SPSS version 20 and the accuracy of the screening determined by sensitivity, specificity, positive and negative predictive value were calculated by using Excel. Results: Based on the ROC curves, the best cut off values for predicting the presence of alpha thalassaemia in the Selayang population was MCV <77.3fl and MCH <24.7pg. Discussion: Cut off values of MCV <77.3fl and MCH <24.7pg stood out as the combination of red blood cells parameters and can be used to predict alpha thalassaemia. MCV<80fl has a sensitivity of 91% and specificity of 33% whilst MCH <27pg has a sensitivity of 97% and specificity of 19%. In conclusion, based on this study, MCV and MCH can be appropriate red blood cells indices for selection of further confirmation tests for alpha thalassaemia.

HM48 Discrepancy of haemoglobin level between laboratory and POCT analyser: How to troubleshoot? Hospital Sungai Buloh experience

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Introduction: A discrepancy was noted for haemoglobin level measured by blood gas analyser GEM PREMIER 3500 in intensive care unit compared to the laboratory automated haematology analyzer Beckman CoulterUnicelDxH800. UnicelDxH800 measures haemoglobin level directly via photometric method, whereas GEM PREMIER 3500 indirectly measures haemoglobin level from haematocrit using internal algorithm. We conducted a correlation study to compare haemoglobin level between these two analysers and to obtain a new Hct ratio to overcome the discrepancy. Materials & Methods: Forty-two paired samples acquired from the intensive care units were analysed with DxH800 and GEM PREMIER 3500. Haemoglobin and haematocrit levels were recorded and divided into haematocrit 20-29%, 30-39% and 40-49%. Data obtained were analysed using SPSS Statistics. Result: The mean difference (GEM-DxH) of haemoglobin level for haematocrit 20-29% was -1.40g/dL (95% CI, -1.71 to -1.09). Whereas the mean difference for haematocrit 30-39% and 40-49% were -0.46g/dL (95% CI, -0.94 to 0.30) and 0.80g/dL (95% CI, -2.09 to 0.49), respectively. There was higher negative bias in the lower haematocrit group (9.1% vs 1.1% vs 0.9%). Regression analysis showed R square value of 0.81. Discussion: We concluded that GEM PREMIER 3500 has a significant negative bias for lower haematocrit which may affect decision for prompt treatment in the intensive care units. A new haematocrit conversion factor of 0.33 for GEM PREMIER 3500 was calculated and applied.

HM49 Transfusion related acute lung injury (TRALI) from packed cell transfusion - a case report

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Introduction: Transfusion related acute lung injury (TRALI) is non cardiogenic pulmonary oedema developing during or within 6 hours of transfusion and often confused with acute heart failure due to circulatory overload or acute respiratory distress syndrome (ARDS) of other causes. The reaction in most cases is due to passive transfer of leucoagglutinins in donor plasma that react with granulocytes in the recipient’s lung causing an acute inflammatory reaction. Case report: We present a case of a 71-year-old gentleman with the underlying head of pancreas carcinoma that underwent elective Whipple procedure. He was vitally stable initially prior to operation and suddenly deteriorated with hypotension and desaturation and subsequently succumbed post-surgery after receiving two units of packed red cells intraoperatively. He was investigated for acute transfusion reaction and diagnosis of TRALI was confirmed after laboratory investigations revealed that one of the donors had positive human leukocyte antibody (HLA class I (C 08:01, B 15:02) and HLA class II (DRB1 12:02)) that matching with the antigen of the patient. Other transfusion reaction investigation such as coombs test and antibody screening were negative. Discussion: Although TRALI is a life-threatening adverse effect of acute transfusion reaction, it is difficult to decide which transfusion recipients are at risk for it. Thus, it is important for the clinical practitioner to develop a good transfusion practice when ordering blood products and have a high suspicion for TRALI whenever a patient develops symptoms of adverse transfusion reaction.
HM50 The spectrum of bone marrow metastasis in non-haematological malignancies - a case report

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Introduction: Bone marrow infiltration is often seen in a tumour that metastasizes via bloodstream commonly in carcinomas of the prostate gland, breast and lung. A haematological abnormality that is unspecific but can suggest marrow infiltration include leucoerythroblastoid anaemia and pancytopenia. We present two patients with both marrow infiltration but different haematological findings. Case report: Case 1 describes a 67-year-old gentleman who initially presented with newly diagnosed end-stage renal failure and metastatic liver and lung cancer. Haematological findings from full blood count and peripheral blood smear showed that the patient had persistent neutrophilia since November 2020. Thus, bone marrow and trephine biopsy was initially done to look for myeloproliferative neoplasm but later revealed that there is marrow infiltration from a primary tumour which is non-haematological. While case 2 describes a 78-year-old gentleman who initially presented with gross haematuria, hard and craggy prostatomegaly with bone pain. The patient had been managed for possible prostate carcinoma with bone metastasis. Haematological findings from full blood counts and peripheral blood smear showed bicytopenia with leukoerythroblastoid features. Bone scan revealed widespread bone metastasis. Subsequently, bone marrow and trephine biopsy was done to look for marrow infiltration and revealed generalised focal infiltration by the non-haematological tumour. Discussion: These two cases are significant due to their different haematological spectrum presentation of bone marrow in which one is hypercellular while the other with hypocellular marrow although both are having marrow infiltration by non-haematological malignancy.

HM51 A case of intravascular large B-cell lymphoma in bone marrow presented with pyrexia of unknown origin

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Introduction: Intravascular large B-cell lymphoma (IVLBC) is a rare subtype of large cell lymphoma, characterised by its presence within the lumina of small blood vessels, without an obvious extravascular tumour mass or circulating lymphoma cells. Bone marrow involvement is reportedly uncommon in patients with IVLBC. We report a case of IVLBC in marrow in a patient who presented with pyrexia of unknown origin. Case report: A 68-year-old lady presented with prolonged fever and constitutional symptoms. Clinical examination was unremarkable. Full blood count at presentation showed Hb 10.3g/dL, TWBC 9.8 x 109/L and platelet count of 366 x 109/L. Peripheral blood film reported normocytic normochromic anaemia with presence of atypical lymphocytes. No significant abnormality was detected from CT scan, upper or lower scope and she initially declined a bone marrow examination. Infective and connective tissue screens were also unremarkable. However due to her deteriorating condition, she consented to a bone marrow examination that showed features of myelodysplasia. However, a relook at her trephine biopsy revealed clusters of medium to large sized neoplastic lymphoid cells seen within the sinusoids. The neoplastic cells expressed CD20, CD 79a, PAX5, MUM-1 and BCL2 and was diagnosed with intravascular large B-cell lymphoma of marrow. Discussion: This case illustrates the diagnostic dilemma in a patient with pyrexia of unknown origin. Initially suspected to have MDS but further evaluation confirmed a rare type of IVLBC. Delay in diagnosis is common due to its rarity and pathologic obscurity. High index of suspicion of this clinicopathological entity can improve diagnosis and treatment outcome.

HM52 A comparison study of red blood cell indices in Southeast Asian ovalocytosis (SAO), iron deficiency anaemia (IDA) and SAO with concomitant IDA

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Introduction: Southeast Asian ovalocytosis (SAO) and iron deficiency anaemia (IDA) are common in Malaysia. Both have specific red blood cell (RBC) parameters pattern but some overlapping morphological features. When coexist, it is challenging to differentiate them as the parameters also change. The study aimed to compare RBC parameters in those with SAO alone, IDA alone and SAO with concomitant IDA as well as identifying potential parameters in discriminating them. Materials & Methods: A retrospective cross-sectional study among 79 subjects from IPPT, Universiti Sains Malaysia (30 cases with SAO alone and IDA alone and 19 cases of SAO with IDA). Data were obtained from the Laboratory Information System from January 2010 to May 2019. One-way ANOVA (or Kruskal-Wallis test for skewed distributions) was used to compare the RBC parameters (RBC, Hb, MCV, MCH, MCHC and RDW) between the three groups. Results: Statistical significance (p-value <0.05) was found for all parameters between the three groups. In the post-hoc test, there was a significant difference in all parameters between IDA alone and SAO alone groups. For comparison between SAO with concomitant IDA group versus IDA alone, a significant difference was found for RBC and MCHC only. For comparison between SAO with concomitant IDA group versus SAO alone, a significant difference was identified for Hb, MCV, and MCH parameters. Conclusion: Three RBC parameters (Hb, MCV and MCH), were shown to be potential parameters discriminating SAO alone and SAO with concomitant IDA and may be used as a guide in ordering iron profile particularly when advanced haematology parameters are not available. For IDA cases with
possible co-presence of SAO, RBC and MCHC may add value for further investigations of SAO confirmation. However, this is a preliminary study, and larger sample size is required in future.

HM53 Generation of adenoviral vector encoding human interleukin-12

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Introduction: Interleukin-12 (IL-12) is one of the key immunomodulatory cytokines which has potential in antitumour effect through combination of immunostimulatory and anti-angiogenic mechanisms. However, the systemic administration of the cytokine at therapeutic dosage can lead to serious toxicity in cancer patients as well as in animal models due to the extremely high systemic level of interferon-γ (IFN-γ) induced by this strategy. Adenovirus is one of the most well-studied viral vectors. It has been widely used in many research studies and also in clinical trials. In this work, we constructed the adenoviral vector encoding hIL-12 which will be used for downstream work. Materials & Methods: The recombinant adenoviral vector was constructed using the Adeno-X™ Adenoviral System 3. Briefly, the hIL-12 gene was amplified by PCR and cloned into linearised pAdenoX-ZsGreen1 tagged with green fluorescent protein. Following the verification using restriction digestion analysis and sequencing analysis, the linearised recombinant adenoviral plasmid was transfected into HEK293 cells to package the recombinant adenovirus. The resulting adenoviruses were further amplified by reinfecting HEK293 cells and purified using the Adeno-X™ purification kit. Viral titers were determined using Adeno-X™ qPCR titration kit and plaque forming assay. The presence of hIL-12 gene in the recombinant adenoviruses was evaluated with PCR. Results: The DNA electrophoresis of the PCR product confirmed the successful generation of the adenoviral vector encoding hIL-12. Discussion: The adenoviral vector encoding hIL-12 can be utilised in future studies to investigate the efficacy of hIL-12 in cancer research.

HM54 Metastatic poorly differentiated adenocarcinoma presenting with bone metastasis with unknown primary

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Introduction: In metastatic cancer, the search of the primary tumour is important as it dictates treatment strategy and prognosis of the patient. However, site of primary tumour remains elusive in 10-30% of metastatic cancer despite an extensive search. Case Report: We report a 66-year-old lady who presented with back pain for 6 months. Clinical assessment revealed kyphosis but no lymphadenopathy, breast mass or organomegaly were appreciated. X-ray shows numerous lytic lesions over skull, vertebrae, ribs and pelvis. Full blood count showed leucocytosis 12.6k/μL predominantly neutrophils, normocytic normochromic anaemia with haemoglobin 5.3g/dL and normal platelet count. The leukoerythroblast picture was seen in the peripheral blood film. Other laboratory investigations were normal except raised alkaline phosphatase and lactate dehydrogenase level. No paraprotein was detected and free light chain ratio was within the normal range. Tumour markers CA 125 and CEA were marginally raised. Marrow aspirate and trephine showed infiltration by neoplastic cells which are CK positive. Further immunohistochemistry staining revealed the lineage as poorly differentiated adenocarcinoma likely breast in origin with weak ER, negative PR, but positive GaT3 and c-erb B2 with aberrant CD138 expression. Staging computer tomography showed diffuse lytic skeletal changes but no primary tumour was identified. Further investigations by endoscopies and gynaecological assessment were negative. Palliative care was planned due to the patient’s poor performance status. Discussion: Close collaboration between clinician and pathologist is required to identify the lineage of metastatic cancer to aid the investigations for the site of the primary tumour but only less than half of the cases will have the primary site identified.

HM55 Atypical presentation of plasma cell leukaemia: a case report

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Introduction: Plasma cell leukaemia (PCL) is a rare blood disorder with an aggressive clinical course and dismal diagnosis. PCL is diagnosed based on the presence of an absolute plasma count of more than 2x10^9/L or 20% plasma cells in the peripheral blood. Initial presentation (primary PCL, pPCL) is 2-4% of myelomas. Secondary PCL is a leukaemic transformation occurring in approximately 1% of previously diagnosed plasma cell myeloma. The incidence of PCL is low, and this case presents a rare opportunity to describe the clinical and pathological characteristics of this disease. Case report: We report a case of a 66-year-old lady with underlying hypertension and dyslipidaemia. She presented with a five-day history of fever, lethargy, cough, and intermittent bone pain. Laboratory findings revealed bicytopenia and leucocytosis. Peripheral blood showed lymphoplasmacytoid cells, marked rouleaux and few circulating plasma cells. Lactate dehydrogenase was raised with evidence of renal failure and extremely elevated calcium level of 4.05 mmol/L. Flow cytometry analysis of the peripheral blood showed PCL. She was
initially treated as occult sepsis with acute kidney injury where hydration and antibiotics were started. Chemotherapy was commenced upon diagnosis of PCL. Discussion: Lymphoproliferative disorder may mimic PCL clinically and morphologically, hence a comprehensive immunophenotypic and immunohistochemical evaluation is required. PCL is a rare and aggressive form of leukaemia with poor prognosis. Elucidation of the disease entity and establishment of an optimal treatment strategy is especially warranted with the introduction of novel agents in combination with stem cell transplantation to improve treatment response and overall survival.

HM56 Establishment of reference intervals in Malaysia: a performance evaluation and comparison of haematological parameters between Sysmex XE5000 and XN3000

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Introduction: The Sysmex XN-3000 is a new automated haematology analyser designed to improve the accuracy of cell counts and the specificity of the flagging events. By comparing the previous Full blood count (FBC) reference intervals in Malaysia for Sysmex XE-5000, we determined a reference interval for all parameters measured by the Sysmex XN-3000 for the Malaysia population. Materials & Methods: Three hundred ninety-seven healthy adults comprising all ages, both genders and three principal races were recruited through voluntary participation. FBC was performed on the two analysers. Qualified healthy adults were screened using questionnaires followed by determination of reference intervals, measures of central tendency and dispersion with point estimates for each subgroup. Results: Complete data were available in 397 subjects comprising of 227 women and 170 men, which were included in the reference interval calculation. Compared to other populations there were significant differences for haemoglobin, red blood cell count, platelet count including immature platelet fraction (IPF) in Malaysians. XN-3000 showed excellent precision and linearity results. Within- and between-run precisions were met for all parameters tested, except for immature platelet fraction. Less than or equal to 0.5% carry-over was seen for all parameters tested. Comparison studies showed an acceptable correlation with both XN-3000 and XE-5000. Discussion: XN-3000 showed good analytical performance and maybe a solution for laboratories with medium to high workload with evolving clinical needs. Our data also confirms the importance of population specific haematological parameters and supports the need for local guidelines rather than adoption of generalized reference intervals.

FORENSIC MEDICINE, PAEDIATRIC AND PERINATAL PATHOLOGY

FM01 A rare case of situs inversus totalis (mirror-image) with sudden death

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Introduction: Situs inversus (SI) is a rare congenital anomaly in which visceral organs are placed reversely. Although cardiac problems are more common in people with situs inversus than in general population, most people with situs inversus have no medical symptoms or complications resulting from the condition, and until the advent of modern medicine it was usually undiagnosed. This report describes the first ever case of SI with sudden death by cardiac tamponade. Case report: A 75-year-old lady was admitted to the hospital with history of fall onto the ground at home. Although resuscitation was done at emergency unit in hospital, she could not be revived and succumbed to death. The cause of death was shock due to flail chest given by the medical officer. Autopsy revealed the situs inversus totalis and the cause of death was cardiac tamponade due to ruptured-myxoma. Discussion: Our aim to do a report of this case is to impart knowledge for the young generation of professional colleague on “things are not always revealed as they are seen at first glance” and the first impression might not always be correct. It is unwise to give the cause of death before a complete and thorough post-mortem examination. When we encounter the case of situs inversus at autopsy, the concerned family should be counselled and advised to undergo screening tests as they are prone to have various cardiac abnormalities.
FM02  Fatal poisoning of glyphosate herbicide: an autopsy case report

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Introduction: Suicidal attempts with agricultural chemicals are not uncommon in our region. Glyphosate is one of the most common herbicides used as poisoning in Malaysia. It is considered to be of low toxicity to humans because the effects are specific to plants. Furthermore, glyphosate does not exhibit anticholinesterase effect although it contains a carbon phosphorus component as per organophosphate. We reported pathological features of fatal glyphosate poisoning in negative toxicological analysis. Case report: A 47-year-old man with unremarkable medical history was admitted following deliberate ingestion of approximately 400 mL of ‘Ecomax’, herbicide containing glyphosate. He revealed of taking the compound himself and witnessed by his wife. He developed persistent metabolic acidosis, hyperkalaemia with hypotension. He was pronounced dead after around 28 hours of admission. Postmortem examination revealed oedematous larynx with haemorrhagic appearance of the trachea, oesophagus and stomach. The lungs were oedematous. Histological examination showed evidence of aspiration pneumonia. Glyphosate was undetectable in toxicological analysis along with other poisons and medications. After reviewing the circumstances evidence with clinical and pathological features, the death attributed as glyphosate poisoning. Discussion: In the absence of glyphosate in the toxicological analysis, it was the reasonable explanation for the death. It was confessed by the deceased and witnessed by the family member. There was no evidence that any other substance had been taken and the clinical with pathological features were typical of other similar cases described in the literature. Knowing these clinico pathological changes creates understanding of the toxicity mechanism.

FM03  Comparison of available diagnostic methods in post-mortem pulmonary tuberculosis: a preliminary study

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Introduction: Tuberculosis (TB) caused by Mycobacterium tuberculosis remains a serious public health threat with the World Health Organisation (WHO) estimating nearly 10 million new TB cases worldwide in 2017, while in Malaysia TB claims about 1,500 to 2,000 lives annually. TB can be diagnosed by imaging, histopathological and bacteriological methods with culture remaining the gold standard. This study was performed to look at the sensitivity and specificity of post-mortem computed tomography (PMCT) imaging and histopathological examination when compared to culture in diagnosing pulmonary tuberculosis. Materials & Methods: This is a retrospective case-control study looking at post mortem cases where lung tissue samples sent for TB culture at Hospital Kuala Lumpur were compared against PMCT imaging and histopathology using both Hematoxylin-eosin (HE) and Ziehl-Neelsen (ZN) staining. Exclusion criteria included contaminated samples, decomposed cases, immunocompromised subjects and those below 18 years of age. Results: A total of 33 cases were selected for the preliminary study. Assuming results obtained from TB culture of lung tissue were accurate, sensitivity and specificity of PMCT were 68.8% and 58.8%, respectively regardless of the inter-observer factor due to the insignificant difference of their readings at observed kappa value of 0.5056 and p>0.05 using Wilcoxon Signed-Rank test. Nevertheless, the sensitivity and specificity of histopathology was 43.8% and 94.1%, respectively compared to the culture results. Conclusion: We conclude that though PMCT may be more sensitive in picking up TB cases before autopsy, HPE is highly specific. Further studies looking at a bigger sample size will be conducted to enhance the validity of these findings.

FM04  A review of a newborn with partial 13q monosomy: a result from an unbalanced translocation

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Introduction: Partial monosomy of chromosome 13q is a rare chromosomal disorder that results from the loss of all or part of the long arm of chromosome 13. New-born with partial monosomy 13q may presented with low birth weight, malformations of the craniofacial region, skeletal abnormalities especially of the hands and feet and other physical abnormalities and guarded prognosis. Case report: This proband with prenatal diagnosis of intrauterine growth restriction was delivered at 35-weeks with wide-spaced eyes and nipples, flat nasal bridge, oligodactyly over four limbs, ambiguous genitalia and anocutaneous fistula. Ultrasound of the cranium showed small lateral ventricles and bedside echocardiogram revealed presence of small atrial septal defect. Both parents and elder sibling are physically normal. Cytogenetic studies of the proband showed 46,XY, del(13)(q22), (p23;q22).pat.ish(X;13)(Y)(SRY)(1)x1,7,Y(8;13)(p23;q22). This abnormality imparts monosomy for the region 13q22 to 13qter. This is likely to be the cause of this patient’s clinical phenotype. Fluorescence in situ hybridization (FISH) studies using Sex-determining region Y (SRY) probe and Centromere specific Probe for Chromosome X (CEP X) confirmed 46, XY cell line. Mother’s karyotype was normal. Discussion: This case highlights the importance of cytogenetic studies; to assist in clinical diagnosis of syndromic babies, provide prognosis of the conditions and guide the clinician to delineate further management accordingly to the patients and the parents; in case future pregnancy is expected.
FM05 Death due to methadone poisoning in a 3-year-old boy: a case report

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Introduction: Methadone poisoning in children is uncommon in Malaysia. Methadone is supplied in syrup and the incidental consumption due to unsafe keeping of the medicine has increased the possibility of methadone poisoning in children. Case Report: A 3-year-old Malay boy was found dead during sleep. The mother discovered the boy was stiff when she tried to wake him one morning. Deceased had a medical history of upper respiratory tract illness when he was 9 months old and history of incision and drainage due to left parotid abscess when he was 1-year-old. Parents claimed their child had accidentally ingested methadone the night before. The incident scene was visited the following day to complete the investigation. Discussion: Abnormal autopsy findings include renal agenesis and the histopathology examinations showed hypoxic changes in brain, oedematous brain and congested blood vessels in kidneys. Other organs were unremarkable. All microbiology laboratory tests showed negative findings. Toxicology examination was positive for methadone in urine. Overdose of methadone had probably stopped the child from breathing; which limited the amount of oxygen to the brain and resulted in hypoxic changes and consequent inflammation had caused oedematous brain. Therefore, the cause of the death was likely due to methadone overdose. Methadone dose as low as 1 mg/kg is fatal in children. Proper keeping of methadone in places unreachable by children must be adhered by parents. The parents should be held responsible for the child’s death due to negligence.

FM06 Sexual dimorphism in foramen magnum dimensions of the Malaysian adult population using post-mortem computed tomography (PMCT): a pilot study

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Introduction: Reliability of analysing sexual dimorphism in foramen magnum dimensions using post mortem computed tomography (PMCT) needs to be evaluated prior to a larger population based study. Materials & Methods: Retrospective cross-sectional study with convenient sampling of 40 Malaysian adult decedent PMCT Brains. Standardized morphometric evaluation of three foramen magnum parameters i.e. foramen magnum anterior-posterior diameter (FMAPD), foramen magnum transverse diameter (FMTD) and foramen magnum index (FMI = FMTD/FMAPD) were performed twice by three readers at separate times. Statistical analysis included intra-observer and inter-observer relative technical error of measurement (RTEM), coefficients of reliability (R) range and p-values for significant differences. Results: Error rates (RTEM) were lowest for FMAPD with intra-observer values between 3.65-3.84% (R=0.69-0.72) and inter-observer values between 2.55-3.69% (R=0.69-0.85). Error rates (RTEM) were highest for FMI with intra-observer values between 4.83-5.81% (R=0.21-0.45) and inter-observer values between 4.18-5.02% (R=0.23-0.56). Error rates (RTEM) for FMTD were within acceptable range with intra-observer values between 4.52-5.00 % (R=0.45-0.65) and inter-observer values between 3.89-4.92% (R=0.37-0.73). P-values demonstrated generally acceptable intra-observer errors but inadequate inter-observer errors. Discussion: With reference to literature review and study limitations, recommendations for a population based study include specialised operator training in using PMCT software, a statistically computed sample size, single reading of each FMAPD and FMTD by more than one reader, considering ethnicity and age as confounders. In conclusion, this pilot study demonstrates PMCT may be used as a reliable tool to assess sexual dimorphism of foramen magnum dimensions.

FM07 Post-mortem computed tomography (PMCT) differentiation of putrefactive gas and air embolism: a case of traumatic carotid-jugular arteriovenous fistula

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Introduction: PMCT is superior to autopsy for identification of intravascular or extravascular gas pockets and their distribution. However, differentiation between air embolism and putrefactive gas can prove challenging due to overlapping imaging findings. Case Report: We report a case of a healthy young man who was involved in a fight, sustained a slash wound to the right side of his head by a kitchen knife and died at the scene. Pre-autopsy PMCT demonstrated complex fractures of the right mastoid bone extending to the right petrous apex and jugular bulb, exposing the right sigmoid sinus. There was also asymmetric intravascular air distribution suspicious of air embolism with ancillary findings of traumatic carotid-jugular pseudoaneurysm and arteriovenous fistulous formation. Post-mortem examination revealed a slash wound measuring 12x2 cm at the right side of the head, cutting through the scalp, right temporal bone, right temporal meninges, right sigmoid venous sinus and part of the right occipital lobe. No intracranial haemorrhage was found on both PMCT and autopsy. Discussion: PMCT findings of air embolism versus putrefactive air on PMCT are discussed in this case. Detailed history on mechanism, circumstances, time of death and careful analysis of intravascular and extravascular air distribution patterns on PMCT are essential in guiding differentiation of true fatal air embolism and “normal” post-mortem putrefactive air. Needless to say, it is recommended that PMCT be performed as early as possible after death to reduce the chances and presence of artifactual decomposition changes.
MM01  Diagnosing *Candida auris* fungemia: the need for heightened vigilance

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*Introduction:* The first infection caused by *Candida auris* was reported in 2009. Within just a decade, *C. auris* has attained considerable notoriety for being frequently misidentified as other yeasts. *Case report:* A 65-year-old diabetic woman had severe metabolic acidosis with inadequate respiratory compensation was first diagnosed with ventilator-associated pneumonia due to multidrug-resistant *Acinetobacter baumannii* while in intensive care. She was started on high-dose IV ampicillin-sulbactam but developed fever two weeks later and a blood culture was taken. The blood was positive for yeast, which formed pink colonies on CHRO Magar Candida medium. Cornmeal agar culture revealed oval budding yeast cells in groups with infrequent rudimentary pseudohyphae. The yeast was identified biochemically as *Candida sake* by ID 32 C (bioMérieux, France). However, due to the rarity of this species, as well as discrepancies between morphological and biochemical findings, identification using MALDI-TOF MS was attempted and the isolate was identified as *C. auris*. Sequencing of the D1/D2 region of the 28S rRNA gene reconfirmed this identity. *Discussion:* Microbiologists must possess a high index of vigilance whenever a rarely encountered *Candida* sp. (*e.g.* *C. sake*) is identified by a commercial biochemical yeast identification kit. A vital clue that *C. auris* may be present is a chromogenic and/or cornmeal agar morphology which is inconsistent with the identification result provided by the commercial identification kit. Definitive identification should then be attempted using either MALDI-TOF MS or nucleic acid sequencing.

MM02  Seroprevalence of *Bordetella Pertussis* among adult population in Malaysia

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*Introduction:* The introduction of vaccines against pertussis dramatically reduced disease incidence. However, many countries have recently experienced disease resurgence including Malaysia. As a result, many of them especially adolescence may unknowingly contract and transmit the disease to vulnerable populations such as infants and young children who are not fully vaccinated or just partially vaccinated against pertussis. This study was conducted to assess the pertussis immunity state among student and staff attending Pusat Kesihatan Universiti Putra Malaysia in relation to their socio-demographic factors, vaccination and health status. *Materials & Methods:* This was a cross-sectional study involving data and sample collection from age >18 years old attending PKU UPM. The immunoglobulin G-pertussis toxin (IgG-PT) levels were measured quantitatively with ELISA method. For qualitative assessment, IgG-PT levels more than 40 unit IU/ml were considered immune. An IgG-PT ≥ 100 IU/ml indicated recent pertussis. Data on socio-demographic factors, vaccination status and health status were gathered and analysed using SPSS software. *Results:* From the total of 113 respondents, 104 (92%) were not immune against *B. pertussis*. Only one respondent (0.9%) who got recent infection towards *B. pertussis*. However, no statistically significant difference was observed with respect to seropositivity of IgG-PT between these factors. *Discussion:* High percentage of non-immune adolescent towards pertussis suggested that they were at risk of acquiring the disease. Insufficient herd immunity among adolescent also increases the risk of transmission to others especially to newborn, immunosuppressed or elderly. A booster dose of pertussis vaccine should be considered to ensure pertussis elimination.

MM03  Broad-spectrum antibiotic administration as a predisposing factor for invasive trichosporonosis

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*Introduction:* *Trichosporon asahii* (formerly known as *T. beigelli*) is a yeast that is gaining notoriety as an important cause of invasive fungal infections in tertiary medical centers. *Case report:* A middle-aged Chinese man with no medical comorbidities presented with liver lacerations and numerous fractures after falling from a considerable height. Due to the severity of his injuries, he had to be nursed in an intensive care setting. During his first two weeks in the intensive care unit, multiple febrile episodes were recorded but blood cultures were consistently negative for microbial growth. Despite this, empirical antibiotic coverage for sepsis was administered, with ceftriaxone being given initially, followed by piperacillin-tazobactam and finally imipenem-cilastatin. On day-17, while on imipenem-cilastatin, a urease-positive yeast was cultured from the patient’s blood. The yeast grew as dry, fuzzy and wrinkled white colonies on Sabouraud dextrose agar after 48 hours of incubation, and produced blastoconidia, true hyphae, pseudohyphae and arthroconidia on slide culture. It was identified biochemically by ID 32 C (bioMérieux, France) as *T. asahii*. *Discussion:* Although *T. asahii* is known to cause disseminated infections in patients with severe granulocytopenia, our patient was immunocompetent. Thus, vigilance is needed to diagnose invasive trichosporonosis. Immunocompetent patients who are treated with broad-spectrum antibiotics can be predisposed to this infection, especially if they are also nursed in an intensive care setting. Fortunately, *T. asahii* is relatively easy to isolate on routine mycological media and identify using conventional techniques such as slide culture and/or carbohydrate assimilation.
MM04 Evaluations of rapid diagnostic tests for detection of influenza & respiratory syncytial viruses

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Introduction: Influenza and respiratory syncytial viruses (RSV) frequently cause acute respiratory infection (ARI). Many commercial rapid diagnostic tests (RDTs) are available and frequently used to aid the diagnosis of ARI. This study assess the performance of the three RDTs for detection of influenza A, influenza B and RSV in respiratory samples. Materials & Methods: It is a retrospective study of hospitalized children with ARI from September 2019 to January 2020. A total of 133 nasopharyngeal aspirates were collected and analysed with Standard™ F Influenza A/B/RSV Fluorescence Immunoassay, QuickVue® Influenza A+B and D’ Ultra Direct Immunofluorescent Assay (DFA) in comparison to real-time polymerase chain reaction (rt-PCR) assay as a reference method. Results: The sensitivity of Standard™ F, QuickVue® and DFA were 71.4%, 57.1% and 39.3%, respectively for influenza A. As for RSV, sensitivities for Standard™ F and DFA were 91.3% and 82.6%, respectively. No influenza B was detected by all RDTs. Meanwhile, the specificity of all RDTs was almost 100%. Positive predictive value of the three RDTs were 100% for influenza A, whereas for RSV were 75% and 86.4% for Standard F and DFA, respectively. As for negative predictive value for Standard™ F, QuickVue® and DFA, they were 92.8%, 88.5% and 83.7% for influenza A, respectively. Discussions: Standard™ F displayed higher sensitivity than other RDTs for influenza A and RSV detection. It is rapid, easy to use and cheap compared to rt-PCR. It can be used as a point of care testing to diagnose ARI in clinical settings.

MM05 Neonatal lupus erythematosus presented as thrombocytopenia: a rare presentation

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Introduction: Neonatal lupus erythematosus (NLE) is a rare clinical condition. This condition is caused by maternal autoantibodies. Anti-Ro and anti-La antibodies are the two most common autoantibodies associated with this condition. Anti-RNP antibody is another autoantibody associated with NLE albeit very rarely. NLE has a broad clinical manifestation but congenital heart block is the most severe presentation and it is associated with poor prognosis. Case report: A newborn girl was admitted to neonatal intensive care unit (NICU) for presumed sepsis after thick meconium-stained liquor was noticed during delivery. During antenatal period, she was noted to have a symmetrical small gestational age but all the infectious diseases screening for her mother were negative. Her mother was diagnosed to have systemic lupus erythematosus (SLE) since last year. Mother’s SLE disease activity was noted to be stable throughout the pregnancy. The baby was doing well in NICU but was noted to have persistent thrombocytopenia. The platelet level ranged between 74-89x10⁹/L. Autoimmune screening from the neonate showed positive antinuclear antibody at titration of 1:640 with speckled pattern. Anti-RNP antibody was positive but both anti-Ro/La were negative. The diagnosis of NLE was made and she was discharged home on the day 5 of life. No specific therapy was given to her and she did not have any bleeding tendency. Discussion: Thrombocytopenia can be the only clinical manifestation of NLE. Anti-RNP antibody is associated with non-cutaneous form of NLE. In this case, perhaps anti-RNP antibody is associated with thrombocytopenia. The autoantibody screening is worth to be performed in a neonate particularly in those that is born from a known SLE mother.

MM06 A rare case of brain abscess caused by Salmonella spp. in a post neurosurgical patient

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Introduction: Intracranial infections caused by Salmonella spp. are unusually reported in clinical practice. Previous reports of such cases were shown to be commonly associated with intracranial tumour excision and steroid therapy. Case report: A 56-year-old male who worked as a supervisor in an organic fertilizer production company was diagnosed with meningioma and had undergone tumor resection procedure. The operation was successful and subsequently he was also prescribed intravenous dexamethasone. He was discharged well on day seven post operation. Unfortunately, he had to be readmitted four days later with fever and pus discharged from the surgical wound. Presence of the abscess at the left fronto-temporo-parietal subdural and subgiall with adjacent cerebritis was noted in the brain CT-scan. The abscess was evacuated, and intraoperative pus specimen was sent for microbiological culture. Salmonella enteritidis was isolated from the pus specimen. The organism was susceptible to ciprofloxacin, ceftriaxone and amoxicillin-clavulanic acid. He was subsequently treated with intravenous ceftriaxone for 6 weeks and responded well to the treatment. He was discharged home once the treatment was completed. Discussion: Salmonella spp. intracranial infection should be suspected in post neurosurgical intervention patient presented with brain abscess. Given the rarity of this organism to cause this type of infection, the pus specimen should be sent for microbiological culture and antibiotic susceptibility testing in order to identify the correct causative agent and subsequently to initiate appropriate therapy.
MM07  Comparison of Kinyoun stain vs. Auramine stain in detecting acid-fast bacilli in a teaching centre, Malaysia

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Introduction: Tuberculosis (TB) caused by Mycobacterium tuberculosis (MTB) takes 6-8 weeks to grow, while screening of patient samples for acid-fast bacilli (AFB) will help to rapidly detect and thus control the spread of TB. The World Health Organization (WHO) has advocated the use of light-emitting diode fluorescent microscopy (LED-FM), which uses auramine-stained smear techniques to replace the current traditional method. This study aims to compare the results of the traditional method (Kinyoun-carbol fuchsin stain) versus Auramine stain for the detection of AFB among positive samples for MTB cultures at a teaching centre. Materials & Methods: Retrospective data of TB registry from May 2014 until September 2019 from the microbiology laboratory at a teaching hospital in Malaysia were analysed. Eighty consecutive patient’s results who had positive TB culture were included, and their AFB stain findings were compared. Results: A total of 39/80 (49%) samples were positive by at least one or both staining methods. There were 35 AFB samples positive by Kinyoun stain and only 22 samples positive by Auramine stain. Out of this, 17/39 (43.6%) patients had a false negative result when Auramine stain alone was used to screen for AFB. Discussion: AFB screening procedures using the conventional approach has lack of sensitivity as compared to Auramine staining procedure, which noted to be more sensitive and less time consuming. Since the detection of AFB is still low with Auramine stain, both Kinyoun and Auramine staining methods should be performed together until the laboratory staff has achieved satisfactory results with this new skill and is competent to verify the presence of AFB with Auramine stain.

MM09  Atypical presentation of bilateral third, fourth, and sixth cranial nerve palsies in a young adult with meningococcal meningitis: a case report

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Introduction: Neisseria meningitidis is one of the commonest causes of community-acquired bacterial meningitis worldwide. It affects mostly children and young adults. Atypical presentations of meningococcal infection may halt early diagnosis and treatment imperative to prevent morbidity and mortality. Case report: We present a unique case of meningococcal meningitis in a 30-year-old lady who presented with sudden onset of double vision for four days prior to admission. She has no underlying medical illness and nor smoking. Upon arrival, she was alert and conscious with normal vital signs. Neurological examinations showed bilateral third, fourth and sixth cranial nerve palsies with negative meningeal signs. There was no papilloedema or fever documented throughout her admission. The CSF biochemistry was normal and CSF culture was non growth. The MRI brain showed subtle diffused patchy meningeal thickening and enhancement, primarily along the right cerebral hemisphere. The diagnosis of meningococcal meningitis was confirmed by positive CSF PCR for Neisseria meningitidis. Her diplopia was improved after treatment with intravenous Ceftriaxone 2g bd for two weeks. She was discharge well after 15 days of admission. Her family members were traced and given prophylaxis antibiotic. Discussion: Diagnosing meningococcal meningitis with atypical presentation is challenging. The clinical presentations may mimic cerebral aneurysm, vascular disorder or brain tumour. Meningococcal meningitis should be considered as a differential in cases of focal neurological impairment even in the absence of fever and classical findings. Prompt antimicrobial treatment following laboratory confirmation is important to prevent irreversible complications.

MM10  Autism spectrum disorder and its relationship with coeliac antibodies in a Malaysian population: a preliminary study

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Introduction: One of the most frequently associated clinical manifestations shown by patients with Autism Spectrum Disorder (ASD) is gastrointestinal dysfunctions. Thus, a possible association between ASD and coeliac disease (CD) has been suggested by previous studies. CD is a chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed individuals. Materials & Methods: A total of 77 ASD patients and 72 healthy controls (4 – 8 years old) were recruited from a paediatric specialist clinic at the Women and Childrens Hospital Kuala Lumpur. Blood samples were tested for the presence of IgA anti-deamidated gliadin (DG), IgG anti-DG, IgA anti-tissue transglutaminase (tTG), and IgG anti-tTG via a fluoroenzyme immunoassay. The positive cut-off reading was set at >10 U/mL. Results: The majority of patients were males (96%) with a mean age of 5.2 years. Among controls, 56% were males with a mean age of 5.9 years. Only one study subject (1.3%) showed positive antibody response (11 U/mL) against IgA anti-DG antibody. No significant mean difference was observed between patients’ and controls’ IgA anti-DG antibody levels (p=0.439). None of the individuals in any group were positive for the other antibodies tested. Discussion: Although no statistical significance was reached, the observation of
one antibody positivity (IgA anti-DG) may confirm that mucosal immune response is being activated towards gliadin contained in the diet of the patient and is possibly distinct from the immunopathology of CD. This observation may be attributed to the occurrence of non-coeliac gluten sensitivity as some have reported before.

MM11 The Lucio phenomenon in undiagnosed lepromatous leprosy patient concomitant with Salmonella bacteraemia in Malaysia: a rare manifestation

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Introduction: Lucio phenomenon is a rare and severe type of leprosy reaction. It is seen in patients with longstanding and untreated lepromatous leprosy of lepromatous leprosy. Here we present a case of Lucio phenomenon in undiagnosed leprosy patient concurrent with Salmonella bacteraemia. Case report: A 73-year-old lady with underlying hypertension presented with fever for 1 week duration. She had multiple vesicles at both feet and hands which ruptured and forming ulcers. On examination she appeared dehydrated and febrile. There was leonine facies and multiple infiltrated nodules seen on face, ears and both forearms. Multiple punched out ulcers with foul smelling discharge were seen at both lower legs. A gangrenous patch was noted at left big toe. There was right ulnar claw hand with glove and stocking pattern of anaesthesia. Blood C&S sent grew Salmonella species while swab C&S grew Aeromonas hydrophila. She was initially treated with intravenous ampicillin sulbactam escalated to IV ceftriaxone. Slit skin smear (SSS) examination revealed a bacteriological index of 4.3. Skin biopsy of the ulceration area showed focal necrosis and moderate perivascular infiltration with lymphoplasmacytic cell and neutrophils. Fibrinoid necrosis of the vessel wall was present. Perivascular foamy cells were observed. Numerous AFB were seen involving endothelial cells and highlighted by Wade-Fite stain. Multidrug therapy was started for Multibacillary leprosy and later the lesions dried up and healed. She was discharged with medication and was given regular follow up. Discussion: The Lucio phenomenon in this patient is clinically diagnosed and supported by SSS examination and histopathological evidence in the setting of undiagnosed leprosy. Management and treatment is complicated by concurrent Salmonella bacteraemia and infected skin lesion. Early diagnosis and treatment prevent morbidity and mortality.

MM12 Reproducibility of Cobas CMV test using the Cobas 4800 system in comparison with COBAS AmpliPrep / COBAS TaqMan CMV (v2.0) test

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Introduction: Quantitative CMV DNA real-time PCR testing is important for the initiation of preemptive antiviral therapy, diagnosis of active disease, and monitoring response to therapy. We determine the reproducibility of the newer Roche cobas CMV real-time PCR test using the Cobas 4800 system compared to our centre’s currently in-use CMV (v2.0) test on the COBAS AmpliPrep / COBAS TaqMan system. Materials & Methods: Twenty-one EDTA-plasma samples were selected by convenience sampling from stored leftover clinical specimens previously quantified for CMV DNA on the COBAS AmpliPrep / COBAS TaqMan system within its linear range. Nucleic acid extraction and real-time PCR was performed for the Cobas CMV test on the Cobas 4800 system according to the manufacturer instructions. Reproducibility was assessed by measuring the correlation with Passing-Bablok regression analysis and agreement with Bland-Altman analysis using MedCalc software (v19.1.7). Results: Quantification of CMV DNA by the cobas 4800 test and COBAS AmpliPrep / COBAS TaqMan CMV (v2.0) test demonstrated good correlation ([log₁₀ CAP/CTM CMV test value] = 0.986 * [log₁₀ cobas CMV test value] - 0.449, r = 0.823, P < .001. 95% of data points recorded for the assay pair were within ±1.96 SD of the mean difference showing agreement. Discussion: The quantification values of the Cobas 4800 CMV test are in agreement and correlated well with values obtained from the COBAS AmpliPrep / COBAS TaqMan CMV (v2.0) test. The Cobas CMV real-time quantitative PCR test using the cobas 4800 system is suitable as a replacement viral load test in our setting.
MM13 Disseminated cryptococcosis with hepatitis in a systemic lupus erythematosus patient: a diagnostic challenge

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Introduction: Hepatitis is an uncommon presentation of disseminated cryptococcal infection among systemic lupus erythematosus (SLE) patients, and can be masked by hepatitis due to SLE itself or concurrent autoimmune hepatitis (AIH). Case report: A 34-year-old woman with past hepatitis B infection and newly diagnosed SLE on oral prednisolone since one month ago presented with fever and jaundice, and was suspected to have AIH. Blood investigations revealed elevated white cell count, C-reactive protein, alkaline phosphatase, alanine transaminase, bilirubin, IgA, IgG and IgM levels. Her C3 and C4 levels were low, anti-mitochondrial and anti-smooth muscle antibodies were negative. Hepatitis B viral load was <20 IU/mL. Initial blood cultures were negative. Chest X-ray showed bilateral perihilar haziness with bilateral pleural effusion. Liver ultrasound showed hepatomegaly without biliary obstruction. She was empirically treated with antibiotics for pneumonia and was also started on intravenous immunoglobulin and methylprednisolone. Cryptococcus neoformans was isolated from a repeated blood culture a week later. The cerebrospinal fluid culture was negative. A liver biopsy performed after completing a 14-day course of intravenous amphotericin B did not show any features of AIH, and her clinical condition improved with the antifungal treatment. Discussion: We postulate the hepatitis to be secondary to disseminated cryptococcal infection despite lacking of evidence on liver biopsy, most likely due to a response towards amphotericin B. A reactivation of hepatitis B was also unlikely due to a low viral load. Distinguishing hepatitis due to a cryptococcal infection is challenging in an SLE patient, especially in the presence of possible hepatitis B reactivation, and warrants diagnostic vigilance.

MM14 Antimicrobial susceptibility of bacteria isolated from various clinical specimens in a private hospital in Kuching – A retrospective study

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Introduction: Antimicrobial resistance is an emerging global health problem that impacts the quality of patient care. Bacterial spectrum and antimicrobial susceptibility vary among countries and regions. Selection of empirical antibiotic therapy should be guided by local microbial profile and antimicrobial susceptibility pattern. This retrospective study was conducted at Borneo Medical Centre in Sarawak to determine the profile of bacteria isolated from various clinical specimens with their antibiotic susceptibility patterns. Materials & Methods: All the clinical specimens for bacterial culture and sensitivity from January to December 2018 were included in this study. Clinical and laboratory data were extracted from the hospital digital database. Results: There were 2728 specimens of which 31.3% yielded positive cultures. Most frequently isolated gram-positive bacteria were Staphylococcus spp. (19.8%), Streptococcus spp. (5.9%) and Enterococcus spp. (3.9%); gram-negative bacteria were Escherichia coli (20.4%), Pseudomonas spp. (12.8%) and Klebsiella spp. (11.3%). E. coli was most commonly isolated from urine and blood. Klebsiella spp. and Staphylococcus aureus were most isolated from sputum and wound, respectively. Ceftriaxone was sensitive against Klebsiella spp. (94.9%), E. coli (86.0%) and Pseudomonas spp. (50.0%). Ceftazidime was sensitive against Pseudomonas spp. (94.3%), Klebsiella spp. (91.3%) and E. coli (86.4%). S. aureus and Streptococcus spp. showed 100% sensitivity to vancomycin. Discussion: Resistance rate of gram-negative bacteria to third generation cephalosporins was low (15.2%). Rates of MRSA (4.1%) and ESBL producing bacteria (1.9%) were also low.

MM15 Laboratory exposure to Brucella in a tertiary center – The experience and challenges

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Introduction: Brucellosis is one of the commonest causes of zoonotic infection and of laboratory transmitted infections worldwide. It is easily transmissible through aerosolization especially during sample handling and colony manipulation by laboratory personnel. Case report: We report our experience and challenges in managing the first laboratory exposure to Brucella spp. in a busy diagnostic laboratory in a tertiary hospital. The case was a young boy who was admitted for prolonged fever. No history was indicative of brucellosis. Blood culture was positive on day 3 of incubation, on gram stain revealed gram-negative coccobacilli, and grew pure slow-growing tiny translucent colonies on 5% sheep blood agar and chocolate agar. All tests were performed on the open workbench. Colonies sent to a reference laboratory confirmed Brucella spp. by PCR method. The exposure to Brucella spp. among microbiology laboratory staff occurred during handling and manipulation of the patient’s samples and the colonies that grew, due to inadequate history provided to the laboratory and the difficulties in identifying the organism. Discussion: This exposure led to a review and amendment of the laboratory work instructions and work etiquette, including usage of biosafety cabinets in handling blood cultures. Staff were given training on the organism. Exposed staff were required to undergo serological monitoring and high-risk exposures were advised to take post exposure prophylaxis. The diagnosis of
brucellosis is difficult to make because its symptoms are non-specific and it is a slow growing organism that can be missed out during incubation or improperly identified.

MM16 The performance of digital imaging software in predicting antinuclear antibody indirect immunofluorescence end titration through a single well analysis

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**Introduction:** Antinuclear antibody test (ANA) is a common laboratory test performed as a screening test for connective tissue diseases. Indirect immunofluorescence (IIF) technique for a long time has been considered as a gold standard for detection of antinuclear antibody. The laboratory report for ANA-IIF is usually consisted of pattern and titration. This study was conducted to evaluate the performance of a digital imaging microscope and software NOVA View\(^\circledR\) (Inova Diagnostics, San Diego, US) in predicting the end point titration for positive ANA-IIF samples. **Materials & Methods:** A prospective cross-sectional study was conducted whereby 43 consecutive positive ANA-IIF samples were included. The samples were diluted from 1:80 until 1:640 titration (traditional dilution) as per routine laboratory procedure. The single well prediction was performed on the 1:80 well in which the software will allow end titer prediction to be made. The accuracy of single well titration was then compared to the exact positive titration form the traditional dilution. The difference of +/- 2 dilutions was considered as acceptable. **Results:** The distribution of a single well titer prediction versus traditional dilution was as following; +/- 0 dilution = 25 samples (58.1%), +/- 1 dilutions = 13 samples (30.2%) and +/- 2 dilutions = 5 samples (11.7%). None of the samples had +/- 3 dilutions different. **Discussion:** The results showed that the single well titer prediction for ANA-IIF by NOVA View\(^\circledR\) performed accurately with all samples were within the acceptable range. Perhaps, single well titer prediction can replace traditional dilution for the reporting of ANA-IIF titration. This will definitely reduce the laboratory cost and turnaround time.

MM17 Defect in gene encoding CARD14 protein as the cause of combined immunodeficiency in a Malay girl

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**Introduction:** Primary combined immunodeficiency with elevated serum IgE level is a rare condition. This can be part of the hyperIgE syndrome. The genetic defects showed that this condition can be an autosomal dominant (STAT3 gene defect) or an autosomal recessive (DOCK8 defect) inheritance. **Case report:** An 8-year-old girl presented with history of recurrent middle ear effusion since 3 years old. She had underlying eczema which started when she was 6 months old. Apart from that, she also had recurrent episodes of wet cough since the age of 2 years. The cough occurred about 3-4 episodes per year usually requiring nebulizer and sometimes oral antibiotics. She was delivered at term by spontaneous vaginal delivery. She had craniosynostosis at birth which was repaired at the age of around 2 years. On examination, her height was below the 3rd centile. The immunological investigations showed that she had low serum IgG level but normal serum IgA and IgM. Serum IgE level was raised to 5000 kU/L. The CD4 and CD8 counts were also low at 216 cells/mm\(^3\) and 302 cells/mm\(^3\), respectively. Genetic analysis revealed the presence of 2 variants of genetic defect of the CARD14 gene. **Discussion:** CARD14 gene’s function is to provide instruction for making of protein that activates nuclear factor-kappa β (NF-κβ). The defect of this gene has been reported in cases of psoriasis and familial pityriasis rubra pilaris, but not in immunodeficiency. In fact, the variants of CARD14 defect in this patient have not been reported before. Further study is needed to highlight the mechanism of immunodeficiency related to this variant.

MM18 Serum neurofilament light chain in anti-aquaporin 4 negative NMO patients in Malaysia

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**Introduction:** Neurofilament light chain (NFL) is a part of cytoskeletal component of neuronal cells that is released into cerebrospinal fluid (CSF) during neuronal damage. Increase of NFL in CSF is associated with inflammatory and degenerative neurological conditions such as the neuromyelitis optica spectrum disorder (NOMS) and can be detected at lower concentration in peripheral blood. NMO is commonly characterised by the presence of anti-aquaporin 4 antibody (AQP4), a highly specific but less sensitive biomarker. Therefore, the identification of other biomarkers is warranted in the diagnosis of seronegative NMO patients. **Materials & Methods:** Serum samples from 28 NMO patients from Neurology Clinic, Hospital Kuala Lumpur, and 28 healthy control were collected. The samples were tested for AQP4 by cell-based immunofluorescence method. Patients with positive AQP4 positive were excluded from the study. Level of serum NFL was measured by ELISA method. **Results:** Majority of the NMO patients were female (85.7%) with overall mean age of 28.4 years. For the healthy control,
78.6% were female and mean age was 29.1 years. Mean level of NfL in the patients’ group (3.21 ng/ml) were lower than healthy individuals (mean of 3.60 ng/ml). Discussion: The difference of serum NfL level between NMOSD patients and controls was not significant (p=0.13). Therefore, serum NfL may not be a prominent biomarker for NMOSD in this population.

MM19 Comparing concentrated sputum smear microscopy with direct sputum smear microscopy for the detection of acid-fast bacilli in health facilities in Sabah, Malaysia

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Introduction: Acid-fast bacilli (AFB) microscopy is a standard method for tuberculosis screening. The conventional direct sputum smear microscopy (DSSM) with Ziehl-Neelsen (ZN) staining has sensitivity of 35%-75%. The replacement of light microscopy with LED-based fluorescence microscopy (LED-FM) led to a 6-10% increase in sensitivity. Recently, a concentrated sputum smear microscopy method (CSSM) was introduced to concentrate AFB by membrane filtration prior to smear preparation. In this study, we compared the performance of the CSSM with that of the DSSM. Materials & Methods: 4114 sputum samples were collected from health facilities in Sabah from February to June 2019. CSSM (Interlayer Acid-fast Bacilli Test Kits on Auto Stainer MS-AUTO20 from Hunan-Tech New Medical System Co. Ltd. China), DSSM (LED-FM) and AFB culture (Ogawa method) were performed on these samples. Demographic, clinical and epidemiological data were recorded for all samples. The sensitivity and specificity of the two smear microscopy methods were interpreted in light of culture results, sample collection/ storage/transportation conditions and clinical data such as history of anti-TB drug treatment. Results: The overall sensitivity of CSSM was higher than DSSM (79.4% versus 60.5%). This improved sensitivity was consistently seen in all participating health centres. Discussion: The CSSM is a simple and practical method to prepare AFB smears. Besides the use of membrane filtration to increase sensitivity, the advantages of the test from Hunan-Tech New Medical System also include the use of a specially-designed sputum collector with a digestive solution to inactivate microbes and dissolve mucus and contaminating cells, thus lowering infection risk during sample handling and reducing background interference with staining. The high sensitivity and affordability of the CSSM makes it a method of choice for TB screening, monitoring and intensified case finding in TB control programs.

MM20 A case of localised Histoplasma capsulatum septic arthritis

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Introduction: Histoplasma capsulatum is a thermally dimorphic soil fungus and one of the most common endemic mycoses in Asia-Pacific region. In immunocompetent individuals, initial infection of histoplasmosis is usually transient and asymptomatic. Fewer than 1% of this population will be symptomatic and most commonly presented with pulmonary disease. Bones and joints are rarely affected. Case report: An 86-year-old gentleman was presented with gradual left knee swelling for the past two years. There was no constitutional symptoms or prior history of fall or trauma. MRI left knee showed effusion with lobulated synovial proliferation suspected of synovitis or synovial sarcoma. Cultures from first open biopsy did not yield any result. Hence one month later, wound debridement of the left knee was done. Tissue culture from the left knee and left knee synovium polymerase chain reaction detected the presence of Histoplasma capsulatum. He was started on two weeks course of intravenous amphotericin B and discharged home with oral itraconazole after that. His symptoms recurred two weeks later, he succumbed to death in ward due to myocardial infarction. Discussion: Fungi that cause musculoskeletal infections can form biofilm and are resistant to antifungal with high possibility of recurrence. Fungal arthritis follows a chronic indolent course and therefore often causes delay in diagnosis and appropriate treatment. Although a rare condition, it should be considered as a differential diagnosis in culture-negative arthritis.

MM21 A post mortem case report of neuroleptospirosis

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Introduction: Leptospirosis is an infectious zoonotic disease caused by pathogenic strain of leptospires. It can present with a wide clinical spectrum ranging from mild flu-like illness to very severe disease with haemorrhage and multiorgan failure which can be fatal if not treated early. Case report: We report a case of neuroleptospirosis in a 41-year-old lady with no known medical illness that was brought in dead. She had fever for ten days associated with flu-like illness with vomiting and lethargy. There was no history of travelling or jungle trekking prior to illness. However, she had two pet dogs at home. Post-mortem examination showed oedematous brain, haemorrhagic lungs and pale liver that were consistent with histopathological examination of pulmonary haemorrhage, mild meningoencephalitis and liver pathology that supported leptospirosis. The cerebrospinal fluid (CSF) biochemistry showed turbid appearance with low glucose level (<0.6 mmol/L) and high protein (2.48g/L) while bacterial...
culture showed no growth. Even though the micro agglutination testing (MAT) was negative, polymerase chain reaction (PCR) of blood, CSF and kidney tissue were positive for leptospiral DNA detection possibly correlating with an early infection. 

Discussion: Leptospirosis can be transmitted to humans via contact with surface or water contaminated with infected urine from animal hosts such as rodents or dogs with incubation period of 2 to 30 days. The infection usually follows biphasic phase with acute leptospiraemia followed by immune phase. In this case, the cause of death was concluded as disseminated leptospirosis with evidence of central nervous system involvement.

MM22  Disseminated cryptococcosis in an immunocompromised, non-HIV infected patient

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Introduction: Cryptococcus neoformans var. grubii is an encapsulated basidiomycetous yeast that found ubiquitously in the environment particularly soil enriched with avian excreta and is the commonest cause of cryptococcosis in Malaysia. 

Case report: We report a case of 56-years-old housewife living in a rural agriculture area, with underlying myeloproliferative disease and liver cirrhosis not on long term steroid and chemotherapy treatment, who presented with a month history of body weakness and lethargy with rapid deterioration of her neurological condition a day prior to admission. She was initially admitted in a district hospital treated for decompensated liver failure and community acquired pneumonia. Her condition was partially improved with intravenous amoxicillin-clavulanic acid and discharged without antibiotic. She was readmitted four days later for acute ischaemic stroke and nosocomial infection. The presence of fever and persistent intermittent cough with the evidence of generalized consolidation on chest radiograph and isolation of yeast from blood culture with positive urease and Indian ink tests support the diagnosis of pulmonary cryptococcosis. She was treated with monotherapy of intravenous fluconazole 400mg and succumbed to death due to multiple comorbidities precede with multiorgan failure. 

Discussion: Cryptococcosis should be consider as a differential diagnosis although it is less common in non-retroviral disease, immunocompromised patients. Disseminated cryptococcosis is unable to be ruled out in this case due to abrupt onset of altered consciousness with radiological evidence of cerebral oedema - a common non-specific finding of CNS cryptococcosis. Delayed onset of in the diagnosis may results in poor prognosis with high mortality rate.

MM23  The up-regulation of three efflux genes may be associated with the MAB_3542c mutation which confers tigecycline resistance in Mycobacteroides abscessus

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Introduction: Tigecycline is presently acknowledged as one of the most effective treatments for Mycobacteroides abscessus infections, known to be resistant to many antibiotics. Three genes (MAB_1395, MAB_1396 and MAB_1299c) annotated as putative drug/multidrug transporters were found to be up-regulated alongside the point mutation in MAB_3542c (encoding a stress-response anti-sigma factor) possessed by 7C, a tigecycline-resistant M. abscessus mutant derived from the previously sensitive ATCC 19977. This study aimed to determine if the up-regulation of these efflux genes is caused by the MAB_3542c mutation which confers tigecycline resistance. 

Materials & Methods: cDNAs were prepared from the RNA samples of 7C-MAB_3542c wt (7C complemented with the pMV261 plasmid carrying the wild-type MAB_3542c gene and reverted back to tigecycline-sensitive phenotype upon complementation) and 7C-pMV261 (the empty plasmid control). RT-qPCR was carried out in biological triplicates to quantify the cDNA levels of the three efflux genes. MAB_4107c, previously identified as the most suitable “housekeeping” gene in this condition, was selected as the reference gene for normalisation. Results: The three target genes, MAB_1395 (fold-change -1.92193), MAB_1396 (fold-change -1.85218) and MAB_1299c (fold-change -8.4995) were found to be significantly down-regulated (p values < 0.05) in 7C-MAB_3542c compared to 7C-pMV261. Discussion: The RT-qPCR results suggest that the up-regulation of these efflux genes in 7C may be a direct outcome of the MAB_3542c mutation. Over-expression of these efflux genes will be carried out in the tigecycline-sensitive ATCC 19977 strain to verify their biological roles in tigecycline resistance.
MM24 *Aureobasidium pullulans* peritonitis in a patient with a continuous ambulatory peritoneal dialysis (CAPD): a case report

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**Introduction:** Fungal peritonitis is an uncommon complication of peritoneal dialysis. *Aureobasidium pullulans* is a dematiaceous fungus that is found in humid environments and can be a skin commensal, however deep infections like peritonitis are rare. **Case report:** We report the first case of fungal peritonitis caused by *Aureobasidium pullulans* in our centre. A 47-year-old gentleman with end stage renal failure on continuous ambulatory peritoneal dialysis (CAPD) for one year, presented with turbid peritoneal dialysate associated with diarrhoea and abdominal pain for one day duration. He was treated as peritonitis and started on intra-peritoneal antibiotics, but the turbid dialysate persisted. Culture of the dialysate grew yeast-like pinkish black colonies that had pseudo hyphae seen on wet mount. Colonies sent for molecular testing by polymerase chain reaction (PCR) revealed the organism as *Aureobasidium pullulans*. The peritoneal catheter was removed and his renal replacement therapy changed to haemodialysis. He completed intravenous Amphotericin B for 3 weeks duration. The patient is currently asymptomatic and tolerating haemodialysis. **Discussion:** The patient responded well to treatment as the diagnosis was made promptly and treatment was given early. However, there is no standard management for *Aureobasidium pullulans* peritonitis as it is rare with only a handful of cases reported. Though a skin commensal, in the presence of pure colonies isolated from sterile body fluids with associated clinical symptoms, this fungus should be considered as a pathogen and treatment must be initiated.

MM25 A rare case of *Streptococcus anginosus* parotid abscess

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**Introduction:** *Streptococcus anginosus* group (SAG) are normal flora of the human oral cavity and gastrointestinal tract. Since its ability to cause abscess and systemic infections, it must be carefully interpreted. To date, only few cases of SAG isolated in parotid abscess have been reported. **Case report:** A 41-year-old gentleman presented with a painful right infra auricular swelling which had been progressively increasing in size for two weeks. Physical examination showed a 10cm x 6cm swelling which was tender, fluctuant with erythema of the overlying skin in the patient’s right parotid gland. Full blood count showed leucocytosis with neutrophils predominant. Computed tomography scan of the right parotid gland demonstrated a minimally rim enhancing multiseptated collection with impression of abscess. He was hyperglycaemic with high anion gap metabolic acidosis at presentation, thus was treated as diabetic ketoacidosis secondary to right parotid gland abscess. Surgical incision and drainage was performed. The pus specimen was sent for culture and sensitivity. The organism showed characteristic alpha lysis with caramel-like odour and identified by Vitek 2 system as SAG (97%). The isolate was susceptible to ampicillin, clindamycin, ceftriaxone, erythromycin and penicillin G. Patient was treated with ceftriaxone and metronidazole. Patient responded well to treatment and was discharged home on day 9 of admission without complication. **Discussion:** Being a commensal flora of the oropharynx, the SAG might be under evaluated during identification. Nonetheless, the SAG can be an aggressive pathogen in the head and neck with a propensity for abscess formation.

MM26 Primary biliary cholangitis: frequency of anti-mitochondrial antibody (AMA) seropositivity among suspected patients in Malaysia

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**Introduction:** Primary biliary cholangitis (PBC) is an autoimmune liver disease characterized by destructive lymphocytic cholangitis, and presence of specific anti-mitochondrial antibodies (AMAs) targeting mitochondrial autoantigens. PBC clinical presentations range from asymptomatic biochemical cholestasis to cholestatic itching and severe life-threatening events, biliary end-stage cirrhosis. It has a distinctive serological signature, which is AMA, and complex bile duct pathology with progressive intrahepatic destruction leading to cholestasis. **Method:** This study was conducted retrospectively using serum samples from suspected PBC patients sent from hospitals all over Malaysia from January 2018 until December 2019. A total of 4735 samples were tested using indirect immunofluorescence (IF) assay for AMA. The statistical analysis of the data was performed using SPSS 26. **Results:** From a total sample of 4735, 2.5% (118) were tested positive for AMA with 65.3% (77) were female and 34.7% (41) were male. The mean age of patients with positive AMA was 58 years (±16 years). Results showed that female gender (65.3%), adults (35 to 59 years old; 33.1%) and elderly (above 60 years old; 53.3%) age groups have significant association (p < 0.05) with the presence of AMA. Female gender was 1.601 times the odds compared to male gender to have PBC (95% CI: 1.092 to 2.350, p = 0.016) when other confounders were not adjusted. Chinese (41.5%) and Malay (33.1%) were the most common ethnicities with positive AMA. **Conclusion:** In Malaysia, the frequency of AMA seropositivity among suspected PBC patients was found to be higher in elderly females compared to males.
MM 27 Case series of morphological different *Klebsiella pneumoniae* infection in patients admitted at major specialist hospital

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Introduction: *Klebsiella pneumoniae* is colonizer of gastrointestinal tract and may lead to infection as gains entry into circulation or other tissues. Classically, *Klebsiella pneumoniae* appears as short and stout gram-negative rod. Morphological changes in Gram-negative organisms are associated with inhibition of cell wall synthesis by beta-lactam antibiotics. The authors noted such morphological changes in *Klebsiella pneumoniae* isolation from blood culture specimens in our patients. Case report: Two unrelated blood culture specimens were collected at different time periods and circumstances. Case 1: A 69-year-old gentleman with underlying diabetes mellitus without previous antibiotic exposure, was admitted due to drowsiness and generalised weakness for a duration of 4 days. He was treated as cholangitis with multiorgan failure. Case 2: A 56-year-old gentleman with underlying decompensated congestive cardiac failure, nephrotic syndrome, hypertension, dyslipidemia was discharged 2 weeks prior to the current hospital visit, in which patient was administered IV cephalosporin and oral macrolide, presented to emergency department (ED) with complaint of fever, shortness of breath and pleuritic chest pain for a duration of 2 weeks. He was treated as septic shock secondary to hospital acquired pneumonia. Discussion: In both cases, *Klebsiella pneumoniae* was isolated from blood culture aerobic bottle. However, the morphological appearance on Gram stain showed Gram-negative bacilli with central bulge, dissimilar to other cases in which *Klebsiella pneumoniae* were isolated. This case series of *Klebsiella pneumoniae* been reported as to draw the attention of microbiology personnel to the existence of atypical morphology of this strain, which could be less aware of.

MM28 Intestinal hookworm infection in a young immunocompetent patient

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Introduction: Hookworm infection is common in endemic areas. It can be prevented by good sanitation and personal hygiene practices. The manifestation is rarely seen in immunocompetent individuals unless in prolonged exposure to the parasite or heavy infection. Case report: In this case study, we reported a case of hookworm infection in a young immunocompetent male patient, presented with gastrointestinal symptoms after exposure to contaminated soil and cats at home. He suffered generalised abdominal pain associated with foul-smelling loose stool for 10 days. He was initially prescribed home with an oral antibiotic for five days, however, the condition did not improve. Subsequently, he was referred to hospital and was admitted. During admission, the laboratory examination showed leukocytosis with eosinophilia, whilst hookworm ova was seen in stool ova and cyst examination. The patient was treated with oral albendazole and covered for bacterial infection with oral ciprofloxacin. He was discharged well with the medications with no subsequent follow-up. Discussion: This case suggests the possibility that hookworm infection can occur in a healthy person with prolonged exposure to the parasite and it can happen all over the places whether in the remote or urbanized regions.

MM29 Profile of virulence genes among Methicillin Resistant *Staphylococcus aureus* (MRSA) strains isolated from a tertiary medical centre in Malaysia

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Introduction: *Staphylococcus aureus* is known to produce a variety of virulence factors. Data on the profile of the virulence genes among the MRSA isolates is very limited in our setting. We aimed to determine the virulence genes in MRSA isolates and the association with the types of infections. Materials & Methods: Sixty MRSA isolates were obtained from patients admitted to a tertiary public hospital in Malaysia over a six-month period in 2018. PCR was used for the detection of five virulence genes i.e., enterotoxin gene (*sea*), exfoliative toxin *A* (*eta*), toxic shock syndrome toxin 1 (*tst*), lukS-Panton-Valentine (*lukS-PV*) and alpha haemolysin (*hla*). The types of infection were correlated with the types of staphylococcal genes present by statistical analysis. Results: The types of MRSA infections were cellulitis 18(30%), diabetic foot ulcer 17(28.3%), necrotizing fasciitis 8(13.3%), osteomyelitis 9(15%), catheter-related bloodstream infections 6(10%) and pneumonia 2(3.3%). The three main virulence genes were *lukS-PVL* gene (60%) *sea* gene (45%) and *tst* gene (43.3%). The genes that were significantly associated with all types of MRSA infections were *sea* (p=0.049) and *hla* (p=0.006). Other virulence genes tested showed no associations with the types of infection. Discussion: In our study we found the *lukS-PVL* gene was the most common gene detected among the MRSA isolates strains which indicated the MRSA isolates were mainly community-associated. The staphylococcal enterotoxin (*sea*) and alpha haemolysin (*hla*) genes were significantly associated with all types of infections.