The 20th Annual Scientific Meeting, College of Pathologists, Academy of Medicine of Malaysia; Bridging Frontiers: Transforming Laboratory Diagnostics for Tomorrow 5th-6th August 2024, Swiss-Belhotel, Kuantan, Pahang

K. Prathap Memorial Lecture: Is there a Role for Haematologists in the Emerging Field of Regenerative Medicine?

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Regenerative medicine is an emerging field which focuses on developing and applying new treatments to restore normal functions in diseased or damaged cells, tissue, and organs. Pathologists play crucial roles in this field in four major areas: 1. Understanding tissue growth and vascularization in health and diseases – to facilitate identification of biomarkers for diagnosis or prognostication, and druggable targets for prevention or treatment; 2. Evaluation and characterisation of tissue-engineered and regenerative medicine (TERM) products and their banking – to facilitate optimal regeneration from substandard repair outcomes; 3.Contributing to clinical trials as a vital member – to ensure regulatory compliance, perform imaging & molecular analysis at cellular, tissue and organ levels; 4. Contributing to ex vivo production of cells, tissues or organs and its automation under Good Manufacturing Practice environment. Among the pathologists, haematologists are particularly suited to play a significant role in driving the field by virtue of their prior expertise in stem cell biology and transplantation, cell characterisation and banking, and involvement in preclinical studies and clinical trials to ensure safety and efficacy of the new treatment approaches. Perhaps it is high time that the haematology fraternity would now consider a sub-specialty to train medical specialists as practitioners as well as guardians for safe and effective regenerative medicine practices.

Plenary Lecture 1: AI powered WES (Whole Exome Sequencing) – Making Sense out of Nonsense

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Artificial Intelligence (AI) has revolutionised pathology diagnostic landscape unveiling unparalleled possibilities not only for early detection, accurate diagnosis, personalised treatment strategies and prognosis. AI technologies include machine learning (ML) algorithms, deep learning (DL) models, and computer vision techniques, applied across various domains of diagnostic pathology. ML identifies patterns in data, while DL employs neural networks for intricate processing. Predictive modelling challenges, such as data labelling, are addressed by transfer learning (TL), leveraging pre-existing models for faster training. TL have great potential in diagnostics and genetics research of gene expression analysis, mutation detection, genetic syndrome recognition, and genotype-phenotype correlations. This presentation will discuss the profound impact of AI on congenital anomalies, genetics of disabilities and cancer and their management within the field of pathology. AI application in genomics, its challenges and AI dialogue with WES is addressed (variant calling, annotation & prioritisation & interpretation. Illumina e.g. of DRAGEN software methods of improved variant identification are highlighted. Invitae EMP (evidence modelling platform) which assess DNA variant, generates prediction and final variant classification will be discussed. Remarkably AI had shown its extraordinary potential starting even from fresh untreated tissue samples during surgery. AI enables a much faster tissue diagnosis way ahead of fresh frozen sections procedure. In neurosurgery where goal is to achieve maximum safe tumour removal within a tight lapsed time interval, delineation of tumour tissue from healthy tissue during surgery is particularly difficult, and in some cases residual tumour can therefore be observed after surgery. A new AI technology is able to more accurately detect the tumour boundary. Surgeons can thus examine tissue samples taken during surgery at the suspected tumour boundary for the presence of residual tumour tissue. Besides machine learning software using specific histological features recognises over 93 % of specific genetic tumour features within a few minutes. Future possibilities include increasing the domains of AI ie ML, DL, Computer Vision and data science. As AI evolves it is important to be always mindful of ethical considerations. WES Case reports in congenital anomalies & cancer are discussed.

Plenary Lecture 2: The Science of CAR-Immune Cell Therapy

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Cell-Based Immunotherapy has evolved from transplanting the whole immune system via haemopoietic stem cell transplantation as pioneered by the Father of bone marrow transplant, Dr Donall Thomas, in the seventies. Therapeutic approach is now single immune cell focused such as using T cells, NK cells, Macrophages or Dendritic cells. In fact, these immune cells are genetically engineered for more precise targets to achieve optimal results. One outstanding effort is the creation of artificial Chimeric Antigen Receptor (CAR) in these immune cells. CAR-T cells, CAR-NK cells and CAR-Macrophages are now available for clinical studies. In fact, to date 6 CAR-T cells are FDA approved for market authorisation for treating blood cancers. This lecture will focus on the development of CAR-T cells and their successful application in the treatment of blood cancers. There

5.2 mmol/L, and at 60 hours post-admission potassium level normalised to 4.6 mmol/L. The patient was discharged 5 days later. *Discussion:* The hyperkalaemia was caused by prerenal failure due to hyperglycaemic polyuria which led to volume depletion and partly contributed by the patient's tobacco chewing habit as it is known to contain a significant amount of potassium.[2] It can be postulated that the accompanying hyperglycaemia is a potential mechanism by which the patient might have had a survival benefit under such extreme hyperkalaemia. While it is an independent risk factor for hyperkalaemia, it may have protected this patient from fatal cardiac consequences.[3] *Conclusion:* To our knowledge, this is the highest described hyperkalaemia treated conservatively and survived without cardiopulmonary resuscitation.

CP19. Urinary 5-Hydroxyindolacetic Acid Measurements in Patients with Neuroendocrine Tumour-Related Carcinoid Syndrome

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Introduction: Neuroendocrine tumours (NETs) are a heterogeneous group of neoplasms arising from neuroendocrine cells. Functioning NETs produce excessive serotonin and contribute to carcinoid syndrome (CS), characterised by facial flushing, diarrhoea, and wheezing. 5-hydroxyindoleacetic acid (5-HIAA), the urinary breakdown metabolite of serotonin, is an established biomarker for the diagnosis of NETs with CS. Here, we aim to study the 5-HIAA excretions in NETs with CS and evaluate potential factors influencing 5- HIAA excretion. *Material and Methods:* 768 clinical requests for 24-hour urine 5-HIAA assessments received at the Institute for Medical Research from June 2015 until May 2024 were retrospectively reviewed. Age, gender, site of lesions and 24-hour urine 5-HIAA levels were evaluated. Parametric and non-parametric data were expressed as mean and median respectively. Statistical analysis was performed using Mann-Whitney U test. *Results:* 50 cases of NETs with CS were identified. Patients' ages ranged from 23 to 76 years old, with mean of 51 years. Female (n=28; 56%) were slightly more than male (n=22; 44%). 24-hour urine 5-HIAA excretion ranged from 43 to 13,252 umol/24 hour with a median of 190 umol/24 hour (normal range: <40 umol/24 hour). Most tumours were of unknown site (n=27; 54%, followed by intestinal (n=9; 18%). Patients with metastatic tumour had significantly higher 5-HIAA excretion (p=0.005). *Conclusion:* Our study revealed a wide variation of 24-hour urine 5-HIAA excretion in NETs with CS. Urinary 5-HIAA excretions could be influenced by disease status, location of tumours, and the size of the tumour.

CP20. Differentiating Non-compliance from Malabsorption: A Case Study With Rapid Levothyroxine Absorption Testing

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Introduction: Levothyroxine (LT4) is the treatment of choice for primary hypothyroidism. Persistent elevation of thyroid-stimulating hormone (TSH) despite supraphysiological LT4 doses requires further investigation. A rapid LT4 absorption test helps differentiate between non-compliance and the co-existence of malabsorption as the cause of high LT4 requirement. *Case presentation:* A 48-year-old Malay woman with underlying type 2 diabetes mellitus, obesity, hypertension, and dyslipidaemia was diagnosed with primary autoimmune hypothyroidism in 2011, necessitating lifelong LT4 treatment. She was also diagnosed with autoimmune atrophic gastritis associated with vitamin B12 deficiency (pernicious anaemia). However, despite daily doses of 200-350 mcg of LT4, her TSH levels remained high. A rapid LT4 absorption test was conducted. Blood samples for serum free thyroxine (FT4) and TSH were taken at 0, 60, 120, 180, 240, 300, and 360 minutes after administering 1000 μg of LT4 orally. The results showed a >60% increase in FT4 at 240 minutes and a corresponding decrease in TSH, indicating normal LT4 absorption and excluding malabsorption. *Discussion:* LT4 absorption primarily occurs in the small intestine. Typical LT4 doses range from 1.6 to 1.8 mcg/kg/day; doses exceeding 300 mcg/day suggest non-compliance or malabsorption. The rapid absorption test aids in distinguishing between these conditions. *Conclusion:* This case highlights the utility of rapid LT4 absorption test in differentiating non-compliance and co-existing malabsorption as a cause of persistently elevated TSH in a patient with underlying autoimmune gastritis despite high dose of LT4. To ensure patient compliance, 'direct observation' of weekly LT4 doses at the outpatient clinic may be considered.

CP21. Establishment of Reference Intervals for Aldosterone and Renin in Malaysian Community Using Chemiluminescence Immunoassay (CLIA)

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Introduction: Primary aldosteronism (PA) is the most common cause of secondary hypertension, characterised by elevated plasma aldosterone (PAC) and suppressed renin (PRC) concentrations. There is lack of uniformity in PA diagnostic criteria due to variability in cut off values. PAC and PRC vary between whites, blacks and Hispanics, but there is no data in Asian community. This study aimed to establish reference intervals (RI) of PAC and PRC for our local community. *Material and Methods:* A total of 301 multi-racial healthy adults aged 19-63 years with equal male-to-female ratio were recruited. They comprised Chinese (40.5%), Borneo Bumiputera (24.3%), Malays (25.9%), mixed heritage (7.6%) and others (1.7%). PAC and PRC were determined using an

automated CLIA analyser (Liaison XL). In this study, reference intervals (RI) of PAC (2.35- 26.21 ng/dL) and PRC (5.99-90.27 µIU/mL) differed from manufacturer's ranges (PAC: 2.21- 35.3 ng/dL, PRC: 4.4-46.1 µIU/mL). PAC and PRC were significantly higher in females (PAC: $p<0.001$; PRC: $p=0.026$) and younger adults (<40 years; PAC: $p=0.016$; PRC: $p<0.001$), suggesting the need of gender-specific and age-specific RI. Linear regression demonstrated predictors for PAC and PRC were gender and age, respectively. No significant difference of PAC and PRC among different ethnicity (PAC: $p=0.203$; PRC: $p=0.554$). *Conclusion:* To the best of our knowledge, this was the first report of RI for PAC and PRC of a multi-ethnic population in Southeast Asia. The findings enhanced our understanding on the need of appropriate RI in different cohorts of population. Larger population-based future studies are required to investigate the effect of genetic variation on PAC and PRC.

MEDICAL MICROBIOLOGY

MM02. Evaluation of a Lipopolysaccharide-Based Enzyme-Linked Immunosorbent Assay (ELISA) as a Potential Diagnostic Tool for Acute Leptospirosis

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Introduction: Leptospirosis is a zoonotic infection caused by the genus *Leptospira*. The disease is widespread especially in the tropics including Malaysia. During the early infection phase, leptospirosis manifests as an acute undifferentiated febrile illness, of which timely and accurate diagnosis are pivotal. Thus, this study is designed to evaluate lipopolysaccharide (LPS) as a potential biomarker that could be used in developing diagnostic assays for leptospirosis. *Materials and Methods: Leptospira biflexa* serovar Patoc was cultured in EMJH medium, harvested, and washed. Crude LPS was extracted by hot-phenol method and lyophilised. Two micrograms of LPS were coated on microtiter plate and blocked with skimmed milk. Twelve sera from positive-leptospirosis patients ($n = 6$) and negative-leptospirosis patients ($n = 6$) were evaluated. Reactive IgM was then detected using HRP-conjugated goat anti-human IgM. Finally, optical density (OD) was measured at 450 nm. *Results:* Upon testing, all six sera from positive-leptospirosis patients reacted with the coated LPS with $OD_{450\,nm}$ values between $0.4250 - 0.8039$. On the other hand, the remaining six sera from negative-leptospirosis patients had OD450nm values between $0.0020 – 0.2096$. *Discussion/Conclusion:* In this study, it is found that the *L. biflexa* serovar Patoc LPS was able to distinguish positive- and negative-leptospirosis sera using ELISA at OD450nm value of 0.3. Further validation using larger set of sera is necessary to determine its potential for rapid and timely diagnosis of acute leptospirosis.

MM03. The COVID-19 Antibody Level Three Months After Discharge from The Intensive Care Unit: Results from A Northern Klang Valley Hospital

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Introduction: Since its emergence in Wuhan, China, the COVID-19 pandemic has recorded over 14.9 million deaths within 2 years and infected 44% of the global population. Without vaccination, immunity conferred by infection decreases after 1 year. However, it remained consistently higher in those who were subsequently vaccinated. We wanted to explore the effect of age, gender, infection category, type of vaccine and duration from the last vaccination on the antibody level. *Materials and Methods:* We measured the levels of anti-SARS-Cov-2 S-RBD IgG antibodies in patients diagnosed with severe COVID-19 infection. We used one- and two-way ANOVA to compare the levels and effects of the variables on the level of antibody. *Results:* There was a total of 43 participants, most of whom were males (60%). The mean age for males and females were 46.8 and 52 years old, respectively. Most patients completed the second dose of vaccination at the time of blood sampling, where the longest duration from vaccination was 12 weeks. There were almost equal numbers of patients in categories 4 (51%) and 5 (46.5%). Patients who received Cominarty® recorded a higher antibody level (mean=165.17BAU/ml, SD=19.3) compared to those receiving CoronaVac® and ChAdOx1-S ($p<0.05$). The mean level of antibody was 175.34BAU/ml (min= 123.68, max=244.20, SD=21.5). *Discussion/ Conclusion:* The antibody levels were more than 100 BAU/ml, months after infection, regardless of the timing of vaccination, category of infection, gender or age groups. This study did not explore the levels of neutralising antibodies, which would be protective against future COVID-19 infection.