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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

remain limitations of this modality of treatment such as serious side effects, financial toxicity due to high cost of production, secondary malignancy and disappointing results for solid cancers. Recognising their safety and efficacy, continuous efforts are being made to overcome these limitations. We look forward to newer generations of these live drugs which would be more affordable and showing wider efficacy including the solid cancers.

Plenary Lecture 3: Future Direction of Pathology Training in Malaysia

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Viewed in a historical perspective, the focus of pathology training in post-independence Malaysia has been largely in human resource development. The efforts of the predominant fully-supervised Master of Pathology (MPath) Programmes: UM (1973), UKM (1988), USM (1992), UPM (2009) and UiTM (2013) have collectively led to the laudable achievement of almost 1000 pathologists in the National Specialist Register (NSR) by 2024. However, the turn of the millennium has seen a rapid evolution of the healthcare and technology scene and the needs of the wider Society, demanding a rethinking of the future of pathologists as diagnosticians, medical doctors and world citizens in an interdependent global world, as articulated in the Social Determinants of Health, commitments to the Sustainable Development Goals, Universal Health Coverage and the quest for personalised precision medicine. The MPath Curriculum Review Workshop under the National Pathology Conjoint Board, hosted by UM in August 2019, can be viewed as marking a new direction in Pathology Training. The workshop, with 68 participants from all pathology disciplines from the 5 training universities, the Ministry of Health Malaysia, the College of Pathologists-Academy of Medicine Malaysia and for the first time, Master of Pathology student representatives, was to provide strong direction and mandate to 5 Pathology Specialty Writing groups (AP/HM/CP/MM/FP) to develop the Pathology Curricula of the National Postgraduate Medical Curriculum (NPMC) Project – the latter being a collaboration of all stakeholders (MOH, MOHE, the Universities, MQA, MMC, AMM and Conjoint Boards), to unify the curricular structure of postgraduate medical specialist training (both the Master's Programmes and alternative pathways) in Malaysia. The 5 NPMC pathology curricula were launched in October 2023. UM adopted it for its June 2024 MPath intake. It is expected that all other MPath programmes will adopt it soon after. In essence, all NPMC curricula charted not just the knowledge and skills syllabi, but incorporated pedagogical advancements to monitor essential learning activities and inculcation of personal qualities (communication, integrity, responsibility, commitment to continuous learning, adaptability to change, leadership) for patient-centric and competent practice. Assessments (formative and summative) were standardised, as were e-portfolios, train-the-trainer courses and applicant guides, to meet NSR and MQA requirements. In addition, the pathology curricula introduced some specialty specific changes to strengthen adaptability to evolving needs, namely, STRUCTURE: a monodisciplinary Part 1 examination, ADVANCES: incorporation of molecular pathology, digitalisation and AI into diagnostic practice, OPTICS: enhanced visibility and leadership of pathologists in healthcare, and METRICS: defined competence indicators and workplace-based formative assessments. Going forward, the future of pathology training will require the pathology profession to have a finger on the pulse of Society (national and global), so that it can be a valued partner in the healthcare arena.

Plenary Lecture 4: Revolutionising Diagnostic Microbiology

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The current advancements in technology have made it possible to fully automate the bacteriology culture laboratory, encompassing sample processing, result analysis, and storage, with the use of artificial intelligence for intuitive data analysis. This innovative automation system has been proven to enhance efficiency and reduce costs by requiring fewer personnel. Furthermore, the utilisation of advanced technologies like mass spectrometry and molecular diagnostics is rapidly revolutionising our capacity to diagnose infections. Techniques such as multiplex PCR assays and microarrays enable rapid identification of pathogens based on their genetic material, thereby improving accuracy and speed compared to traditional culture-based methods. Point-of-care testing has been transformed with the adoption of isothermal molecular diagnostic kits and CRISPR-based diagnostics, streamlining molecular diagnostics from sample to result. Syndromic panels have also improved laboratory diagnosis by detecting pathogens with similar clinical features using a single testing platform, which facilitates prompt treatment decisions. Additionally, T2 Magnetic Resonance (T2MR) technology, which combines magnetic resonance with nanotechnology, offers a powerful diagnostic approach. Targeted sequencing for resistance detection through whole genome sequencing (WGS) has expedited the delivery of personalised care. Ongoing advancements, education, and consideration of ethical implications are crucial to fully harness the potential of automated and genomic techniques in medical microbiology.

ANATOMIC PATHOLOGY

AP01. Rare Entity of Mesonephric-like Endometrial Carcinoma: A Diagnostic Challenge

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Introduction: Mesonephric-like adenocarcinoma (MLA) is a rare subtype of endometrial cancer which accounts for 1% of all endometrial tumours. We report a case of MLA with initial diagnosis of endometrioid adenocarcinoma. *Case Presentation:* A 44 year-old lady with dysmenorrhoea underwent TAH with clinical impression of fibroid without a formal CT scan. Based on histomorphological features and immunohistochemistry diagnosed as endometrioid adenocarcinoma. Subsequently completion surgery ensued and bilateral ovaries and pelvic lymph nodes were removed. Characteristic histomorphological features of the tumour with extensive endometriosis and positive tumour cells for GATA 3, ER, TTF 1 with inverse staining pattern and CD10 luminal staining with expert opinion from consultant gynaecological pathologist a final diagnosis of uterine MLA was concluded. *Discussion:* MLA are high grade carcinoma with a low grade morphology and usually seen in post-menopausal age groups. The diagnostic challenges of MLA was age and limitation of available immunohistochemistry and molecular tests in our centre. After reviewing the initial hysterectomy specimen, we found the tumour arising from uterine wall with mixed histological patterns and areas showing small glands and tubules with luminal eosinophilic colloid-like material in the pelvic lymph nodes. Diagnostic stains are required and outsourced. We also required expert opinion due to the rarity of the occurrence. *Conclusion:* The diagnosis of rare carcinoma is established by characteristic histomorphological features which requires a thorough examination of the entire resected specimens with the help of relevant immunohistochemistry and experienced pathologist. It is important to make a correct diagnosis due to the aggressive behaviour of the tumour.

AP02. Uncommon but Crucial: Neuroma of Appendix as a Rare Aetiology of Acute Appendicitis

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Introduction: Acute appendicitis is the most common surgical emergency globally. Neuroma of the appendix, a rare neural-origin tumour, often mimics the symptoms of acute appendicitis. *Case Presentation:* We report a case of a 39-year-old female who presented with sudden right lower abdominal pain associated with vomiting, reduced oral intake, and nausea. Examination revealed right iliac fossa tenderness, positive rebound tenderness, and a positive Rovsing's sign. Laboratory tests showed leukocytosis with neutrophilia, and abdominal ultrasound indicated acute appendicitis. An appendicectomy was performed, revealing an inflamed retrocecal appendix forming a mass clump with the tip embedded in the cecum. Microscopically, the appendiceal lumen was obliterated by uniform spindle cell proliferation in a myxoid background, with mild neutrophilic infiltration at the serosa. Immunohistochemistry revealed spindle cells positive for S100 and negative for SMA. The final diagnosis was neuroma of the appendix with serositis. *Discussion:* Acute appendicitis is a common surgical emergency, typically resulting from luminal obstruction. While the common causes include fecaliths, lymphoid hyperplasia, and infections, rare etiologies such as neuroma of appendix are seldom reported. Neuroma of appendix are benign nerve tissue tumours within the mucosal layer, often associated with genetic syndromes but can occur sporadically. Their presence in the appendix leading to acute inflammation presents a unique diagnostic challenge and clinical interest. *Conclusion:* Neuroma of appendix, though rare, should be considered a potential cause of acute appendicitis. Recognition of this entity is crucial for pathologists and surgeons to ensure accurate diagnosis and appropriate management.

AP03. Uncommon Side Effect Of A Commonly Prescribed Oral Kalimate (Calcium Polystyrene Sulfonate): A Case of Kayexalate Induced Gastropathy

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Introduction: Calcium polystyrene sulfonate (CPS), commonly known as oral kalimate, is a resin utilised in clinical settings to address hyperkalaemia by binding potassium and facilitating its elimination through faeces. However, its oral administration is linked with gastrointestinal mucosal injuries, which can escalate to severe complications such as bowel ischaemia and perforation, predominantly affecting the colon. While upper gastrointestinal involvement is rare, it's not unheard of. *Case Report:* This report presents the case of a 70-year-old Malay man with underlying chronic kidney disease (CKD), who underwent oesophagogastroduodenoscopy (OGDS) for anaemia investigation to rule out upper gastrointestinal bleeding. The endoscopic examination revealed focal gastric erosion with a suspicion of fungal lesion at the fundal area. Histopathological analysis of biopsy specimens from the fundus exhibited features of reactive gastropathy induced by Kayexalate, characterised by the presence of rhomboid basophilic crystals with a mosaic pattern embedded within the mucosal layer. Further history revealed recent ingestion of oral kalimate prescribed for hyperkalaemia within 3 days prior to OGDS procedure. *Discussion:* Hyperkalaemia, a critical electrolyte imbalance, necessitates prompt intervention. Oral kalimate has been a longstanding treatment option for mild to moderate hyperkalaemia. However, it can induce gastrointestinal injury through vascular vasospasm and inflammatory reactions especially in patients with predisposing factors like underlying chronic kidney disease, uraemia, gastropathy, ileus, hypotension, or immunosuppressed. *Conclusion:* In

conclusion, the administration of oral kalimate for hyperkalaemia treatment carries significant gastrointestinal risks, especially in patients with the aforementioned predisposing factors. Therefore, its usage warrants careful consideration and monitoring to prevent adverse events.

AP04. Patterns of Seminal Fluid Analysis In A Tertiary Centre In Sarawak

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Introduction: Routine seminal fluid analysis is a prominent and globally used laboratory investigation for the evaluation of male infertility. However, limited studies have been conducted to identify the pattern of seminal fluid parameters, especially in Malaysia. This study aimed to study the seminal fluid analysis (total seminal fluid volume, total sperm count, sperm motility and viability) pattern and determine the association of age, cigarette smoking and body mass index (BMI) with the seminal fluid analysis. *Materials and methods:* This retrospective study was conducted in an infertility centre in UNIMAS [Ethical Approval: UNIMAS/TNC(PI)/09-65/01(26)] for a year (1 October 2021 – 30 September 2022). A total of 127 patients' data were included in this study. The patients' data were recorded using a predesigned form and analysed using IBM SPSS version 28.0. *Results:* The mean age of the subjects was 35.26±5.61 years old. Overall, non-smokers were found to have lower seminal fluid volume and reduced sperm motility compared to non-smokers. A statistically significant correlation between age and the total sperm count (p=0.028) and between BMI and sperm viability (p=0.037) was observed in this study. However, no statistically significant correlations were observed between BMI and seminal fluid volume, total sperm count and total sperm motility. Similarly, no statistically significant correlation was noted between smoking and the seminal fluid analysis. *Discussion/Conclusion:* Our findings suggest a significant association between age and total sperm count, BMI and sperm viability, which in turn may affect the fertility status.

AP05. Unveiling A Rarity: Myoepithelial Neoplasms of Soft Tissue

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Introduction: Myoepithelial neoplasms of soft tissue represent a heterogeneous group of tumours classified as benign (myoepithelioma and mixed tumour) or malignant (myoepithelial carcinoma). *Case Presentation:* We report the case of a 42-year-old woman with no prior medical conditions who presented with a right arm mass persisting for 15 years. Despite its gradual increase in size, she remained asymptomatic. Examination revealed a substantial mass in her right arm, with well-defined borders, a soft to firm texture, and a smooth surface covered by normal skin. MRI of the right humerus showed a lobulated solid-cystic mass, predominantly cystic, at the postero-medial aspect of the proximal humerus, measuring 7.1 × 7.6 × 11.5 cm. The mass was surgically excised. Gross examination revealed a well-circumscribed, lobulated-brownish mass measuring 120 × 80 × 60 mm. Cut section showed a mixture of solid and cystic components, with the solid areas displaying a brownish surface without necrosis. The cystic areas were multiloculated, ranging from 1-5 mm in diameter, and contained brownish fluid. Microscopic and immunohistochemical analysis indicated features of a myoepithelial neoplasm of soft tissue. *Discussion:* Myoepithelial neoplasms of soft tissue exhibit a spectrum of morphologic patterns, making them difficult to distinguish from other neoplasms. There are no definitive criteria for malignancy for this tumour. While most morphologically benign myoepithelial neoplasms of soft tissue behave in a benign manner, there is approximately a 20% risk of local recurrence. Therefore, complete excision with clear margins is crucial. *Conclusion:* Recognition of this rare tumour is essential for planning management and predicting prognosis.

AP06. Renal Neuroendocrine Carcinoma: The Diagnostic Challenges of Small Round Blue Cell Tumours In The Kidney

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Introduction: Diagnosis of a small round blue cell tumour in the kidney can be challenging. The differential diagnosis includes primary renal neuroendocrine tumours (PRNETs), primitive neuroectodermal tumour (PNET) and nephroblastoma. We report a difficult case of small round blue cell tumour of the kidney. *Case presentation:* A 26-year-old lady who presented with generalised abdominal pain and vomiting. CT colonography shows incidental findings of renal mass which was subsequently confirmed by CT Abdomen and Pelvis. Gross findings show a well circumscribed solid tumour at the lower pole measuring 65 × 56 × 40 mm with a homogenous tan cut surface. Microscopy shows small round blue cells and the immunohistochemical studies show positive staining for neuroendocrine markers, CD99 and NKX2.2 while negative for FLI1 and ERG. The Ki67 proliferative index is 20-30% which leads to a diagnosis favouring neuroendocrine carcinoma. *Discussion and Conclusion:* PRNET is a rare entity and more profoundly scarce in the genitourinary system. The difficulty in diagnosing PRNET is due to significant histological overlap with its differentials with minimal differences in immunohistochemical staining. NKX2.2 immunopositivity can significantly support the diagnosis of PNET. However, PRNETs also exhibit variable NKX2.2 expression. Hence, NKX2.2 expression should be interpreted

in the context of an appropriate immunohistochemical panel and morphology for the accurate diagnosis of PNET. PNET is often confirmed with molecular testing. The accurate diagnosis of PRNET requires awareness of the rare occurrences of this case with clinical correlation and immunohistochemical staining with molecular analysis to rule out its differentials.

FORENSIC PATHOLOGY

FP01. Title: "Caught Beneath The Cage"- Unveiling A Rarely Encountered Asphyxial Death

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Introduction: Fatalities due to occupational hazards are all too common in our society. According to the Department of Occupational Safety and Health (DOSH), the rate of occupational injury was 2.22 per 1,000 workers in 2022. Following work-related fatalities, autopsies are conducted to determine the cause of death and uncover any safety deficiencies that may have triggered the incident. A rare occurrence of traumatic asphyxia death due to being trapped under an elevator is presented here. *Case report:* A 50-year-old man was found lying on his back trapped under the wooden floor of an elevator. Eyewitnesses reported that the elevator was moving slowly downward while the deceased was working beneath it and subsequently fell to the floor while attempting to push the bottom of the elevator frame to save himself. The autopsy revealed signs of asphyxia, including severe congestion to the face and neck, conjunctival petechial haemorrhage with sub-scleral haemorrhage, contusions, abrasions, and indentation marks to the chest, abdomen, and limbs. *Discussion/Conclusion:* The main purpose of this case report is to describe the pattern of injury in entrapment under an elevator. It also emphasises the importance of proper safety measures to prevent similar incidents from happening again.

HAEMATOLOGY

HM01. Fast And At The Far-End: A Case Report Of Compound Heterozygous State Of α^0 (--SEA) Deletion And α2 Codon 16 (AAG>GAG) Hb I Mutation ($--^{SEA}/\alpha^{CD16\ AAG>GAG}\alpha$)

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Introduction: Haemoglobin (Hb) I is a rare alpha 2 (α) variant, resulting from a point mutation in Codon 16 which leads to protein changes, from Lysine to Glutamine. Contrarily, the Southeast Asian deletion is the most observed α^0 deletion in this region, causing complete loss of both functional α globin genes in *cis* on the same chromosome. Here, we report a case in an asymptomatic girl, involving interaction of these two genetic alterations. *Case presentation:* A 16-year-old girl, noted to have mild hypochromic microcytic anaemia, during Thalassaemia screening program. Hb analysis was performed after failure of iron challenge. Capillary electrophoresis using Capillarys2, Sebia, revealed an anomalous, unmeasurable high peak, migrated at zone 15 thus produced inaccurate percentages of Hb A and Hb A_2. HPLC analysis using Bio-Rad-Variant II showed 53.1% of abnormal Hb at P2 window. Sanger sequencing of *HBA* gene with multiplex GAP PCR for common α deletions identified $\alpha^{CD16\ AAG>GAG}\alpha$, Hb I mutation with α^0 ($--^{SEA}$) deletion and no abnormality in β globin gene. *Discussion:* This case illustrated the interaction of an α variant with deletional α0 thalassaemia. The proportion of α2 variant is estimated around 25-28% of total Hb. The level is increased when it is co-inherited with α thalassaemia. Similarly, as in this case, the percentage of the variant in HPLC doubled, which falsely led to a presumed diagnosis of a β variant. Concurrent interaction of α^0 with a benign Hb I does not worsen the phenotype and resembles an α0 thalassaemia trait.

HM02. COVID-19-Associated Thrombotic Thrombocytopenic Purpura: A Case Report

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Introduction: COVID-19 infection is one of the newly recognised aetiologies of Microangiopathic Haemolytic Anaemia (MAHA) manifesting as thrombotic thrombocytopenic Purpura (TTP). ADAMTS13 physiologically cleaves von Willebrand factor into small multimers. Reduced ADAMTS13 activity causes large multimers to bind to platelet resulting in platelet-rich thrombi causing intravascular haemolysis. Post-viral infection triggers autoantibodies towards ADAMTS13 activity resulting in TTP. Plasma exchange remains the mainstay of treatment for TTP alongside with high dose of IV steroids. *Case report:* We report a case of a 19-year-old healthy and vaccinated female who presented with weakness, numbness of upper limbs and fever. She had COVID-19 infection 13 days prior to the symptoms. Laboratory investigations demonstrated severe anaemia (5.9 g/dL), thrombocytopenia (15x109/L), elevated LDH (899 U/L) and bilirubin level (62 umol/L). Peripheral blood smear showed marked schistocytes and reticulocytosis suggestive of MAHA. This was supported by reduced activity of ADAMTS13 (1%) with high inhibitor titre (58.1 U/mL) indicating an acquired form of TTP. Based on high clinical suspicion of MAHA, plasma exchange was initiated early and thus lifesaving. Patient's symptoms and haemolytic parameters improved significantly and discharged well. *Discussion/Conclusion:* COVID-19 infection is proposed to be a trigger for endothelial injury by activation of the complement pathway. Increasing evidence has shown

that this is the postulated pathogenesis for association of TTP and COVID-19. This case emphasises the need of keeping TTP in the list of differential diagnoses when COVID-19 patients develop neurological symptoms associated with severe thrombocytopenia and renal failure. Prompt diagnosis and treatment can be made to gain favourable outcomes.

HM03. Bone Marrow Fibrosis in A Young Patient with Chronic Myeloid Leukaemia

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Background: Patients with chronic myeloid leukaemia (CML) frequently have some degree of bone marrow fibrosis, but younger age groups are more likely to have advanced fibrosis (WHO Grades MF 2 and 3). *Case report:* 15-year-old male, presented with fatigue, weight loss and easy bruising for three months duration. Full blood count findings showed severe anaemia with hyperleukocytosis, and the peripheral blood film revealed a bimodal peak of granulocytic maturation suggestive of CML in chronic phase. Bone marrow examinations were consistent with CML in chronic phase. FISH analysis and RT-PCR showed evidence of *BCR::ABL1* fusion gene. The patient was started on tyrosine kinase inhibitor (TKI) but did not achieve a cytogenetic response despite increasing the dose of Imatinib. Thus, the TKI was changed to Nilotinib. After two weeks on Nilotinib, he developed TKI-induced pancytopenia which required red-cell and platelet transfusions. Bone marrow trephine biopsy was repeated a month later and showed hypercellular marrow with no excess of blast and fibrosis grade III (WHO grading 0-III). The diagnostic trephine biopsy traced, also showed fibrosis grade III. Subsequently, Nilotinib was withheld, and Imatinib restarted with the addition of Danazol. One year post-diagnosis, the patient presented with a COVID-19 infection, and progressively enlarged spleen. The peripheral film and blood immunophenotyping identified 45% blast population which is consistent with the transformation of CML to Acute myeloid leukaemia. *Discussion/Conclusion:* This case report focuses on the challenges in managing young CML patients with myelofibrosis because it is linked to poor prognosis. The evaluation of fibrosis grading, particularly in younger patients, may aid the physician in anticipating the necessities of an early bone marrow transplant.

HM04. A Case of Acute B-Lymphoblastic Leukaemia Masked As Juvenile Idiopathic Arthritis

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Introduction: Acute lymphoblastic leukaemia (ALL) is the most common type of cancer in children. Meanwhile, Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood. Thirty per cent of patients with leukaemia can present with initial complaints related to musculoskeletal pain. In some cases, only the joint symptoms are present, which could lead to a misdiagnosis of JIA and indirectly delayed diagnosis of leukaemia. We present a patient with B-ALL who was initially diagnosed with JIA. *Case report:* A 15-year-old boy, first presented and treated as right hip tendonitis and non-specific musculoskeletal pain. No constitutional symptoms. First full blood count (FBC) was normal (haemoglobin 12.4g/dL, platelet $190x10^9$/L, absolute neutrophil count (ANC) $6.0x10^9$/L). After 2 months of symptoms, he presented to another hospital and relabelled as JIA. He was started with Prednisolone and Sulfasalazine. Despite medications, he presented again, four months later with persistent multiple joint pain and symptomatic anaemia. His FBC revealed haemoglobin 3.2g/dL, platelet $42x10^9$/L, and ANC $3.0x10^9$/L with 2% blast cells in blood film. He was diagnosed with B-ALL following bone marrow examination. The diagnosis is only made six months after his initial symptoms. *Discussion/ Conclusion:* ALL can be misdiagnosed as JIA in children presenting with arthropathy but with fewer classical signs of leukaemia. A high index of suspicion needs to be exercised in a child with arthritis, and full blood count and smear examination should be routine tests. A low threshold for bone marrow examination should be advocated in any suspicious case.

HM05. Validity of Kleihauer Test within 24 Hours in Hospital Tengku Ampuan Rahimah

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Introduction: Haemoglobin F is resistant to acid elution, and based on this principle, the Kleihauer-Betke test (KBT) is used to screen maternal blood for fetal red cells when fetomaternal haemorrhage (FMH) is clinically suspected. While HTAR frequently requests KBT, it's not essential to conduct it urgently in cases of neonatal anaemia, as it doesn't significantly influence treatment decisions. *Aim:* To evaluate the validity of KBT if it was not done immediately. *Method:* This study was conducted from February to November 2019; a total of 16 samples in EDTA tube were received. KBT was performed according to the modified Shepard's method. The sample of all positive (>4mls) KBT was kept at room temperature and the test was repeated at 24 hours of sample collection. Two observers compared the slide that was processed immediately and at 24 hours. The quality of the slides was determined by comparison to control slides. Samples of mothers with alloantibodies and with known haemoglobinopathy were not included. *Result:* 5 samples were positive, and 11 samples were negative on the immediate process. Upon repeating the process at 24 hours, all five positive samples remained positive, and the stain quality remained intact. *Discussion:* Since the slides remained positive with the same staining quality & intensity at immediate and 24 hours, KBT need not be done immediately when there are

other urgent tests to be prioritised, especially in laboratories with limited manpower. *Conclusion:* Sample collected for KBT to establish FMH in an anaemic neonate can be processed within 24 hours.

HM06. Insights into BCR-ABL1 Negative MPNs with JAK2 Mutation: A Case Series

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Introduction: Chronic myeloid leukaemia (CML) is characterised by clonal granulocytic proliferation of various maturation stages and positive *BCR-ABL1* fusion gene. Most patients presented with splenomegaly. Basophilia and eosinophilia are common, and blasts usually account for <2%. However, similar presentation may be seen in other Myeloproliferative Neoplasms (MPNs). Here, we present 2 cases, highlighting the diagnostic challenges. *Case 1:* A 68-year-old male presented with constitutional symptoms and hepatosplenomegaly. Full Blood Picture (FBP) and bone marrow aspirate (BMA) showed granulocytic proliferation, eosinophilia, basophilia with blasts <5%. Trephine biopsy revealed marked fibrosis. Cytogenetic analysis was inconclusive. JAK2 mutation was identified but CALR and MPL genes were not tested. The diagnosis of Post-Polycythemia Vera (PV) Myelofibrosis was made since the patient had a history of polycythaemia. *Case 2:* A 68-year-old male presented with lethargy and splenomegaly. FBP revealed hyperleucocytosis with neutrophilia, eosinophilia, basophilia and 3% blasts. BMA demonstrated hypercellular marrow with granulocytic proliferation and mild dysplasia. Trephine biopsy showed a mild increase in fibrosis. The cytogenetic study revealed no Philadelphia Chromosome. JAK2 mutation was detected but CALR and MPL mutation study were not done. Differential diagnoses include Early Primary Myelofibrosis or Chronic Neutrophilic Leukaemia. *Discussion/Conclusion:* These cases underscore the challenges of differentiating CML from other MPNs since they have similar presentations. Therefore, the detection BCR-ABL1 fusion gene or Ph chromosome is crucial. However, the diagnosis can be delayed as cytogenetic and molecular analyses are not widely available. It is also important to look into the patient's history and previous investigations in establishing correct diagnosis.

HM07. Analysis of Platelet Clumps Flags Using Mindray BC6200: What's the Verdict?

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Introduction: The 'Platelet Clumps' (PC) flag generated by the mainstream haematology analyser (HA) is a critical indicator for potential platelet clumps or other interfering particles in blood samples. This study aims to assess the reproducibility of the PC flag generated by our specific HA model, the Mindray BC6200. *Materials and Methods:* This descriptive study evaluates all full blood count (FBC) samples flagged with the PC indicator by the Mindray BC6200 HA during the study period. Each flagged sample underwent a microscopic examination to confirm the presence of actual platelet clumps. Data from these samples were tabulated and analysed using Microsoft Excel. *Results:* Out of 47,761 processed FBC samples, 3.4% (1,612) were flagged for platelet clumping by the Mindray BC6200. Microscopic examination revealed that 38.6% (623) exhibited fibrin clots (FC), 8.1% (131) showed platelet clumps, and 1.6% (26) exhibited both FC and platelet clumps. Additionally, 18.3% (295) of flagged samples showed neither FC nor platelet clump. Conversely, analysis of sample rejection data indicated that out of 930 samples rejected due to clotting, only 42.3% (393) were visually identified by laboratory staff, with the remaining cases detected by the HA. *Discussion/ Conclusion:* The findings highlight that our HA frequently flags samples for potential platelet clumping, and a significant proportion of these flagged samples contain fibrin and blood clots. The high incidence of clotted samples processed by the HA indicates possible deficiencies in staff pre-analytical inspection, highlighting reliance on the HA for clot detection and suggesting continuous monitoring to improve staff training and oversight.

HM08. Comparison Study between HemaVision®-28N and HemaVision®-28Q kits for Leukaemia Translocation Study at Molecular Haematology & Stem Cell laboratory, Pathology Department, Hospital Tunku Azizah (HTA), Kuala Lumpur.

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Introduction: HTA has provided leukaemia translocation studies for acute leukaemia using the HemaVision®-28N on a nested PCR platform since 2019. The updated version of this test i.e. HemaVision®-28Q, has been introduced. Similar to HemaVision®-28N, the HemaVision®-28Q is also a CE IVD test for qualitative screening of 28 chromosome translocations in leukaemia. This study aims to compare the performance of these two kits. Material and Methods: HemaVision®-28Q detects RNA transcripts from fusion genes using one-step RT-qPCR, while HemaVision®-28N uses two-step nested RT-PCR followed by gel electrophoresis. A correlation study was performed using seven acute leukaemia cases and two RCPA samples. We also compared the duration of the test from reagent preparation to the availability of the results. *Results:* Results from all nine samples tested with both HemaVision®-28Q and HemaVision®-28N were well correlated, Cohen's k=1. Seven samples showed the presence of the same fusion genes, while two samples showed negative results. RCPA sample results were satisfactory for both methods. No contamination was found in any of the samples. The tests using HemaVision®-28Q can be completed within 4 hours. Test using HemaVision®-28N requires 7 hours

and 25 minutes for the screening panel and 14 hours and 50 minutes for positive cases, where screening needs to be followed by a confirmation panel. *Discussion/Conclusion:* The HemaVision® 28Q kit contains ready-to-use cDNA and qPCR reaction tubes for testing. It is simpler, with fewer steps than HemaVision®28N; therefore, less time is needed to perform the test. This is important when the result is urgent and trained laboratory personnel are limited. In addition, batch testing is not required for cost reduction. This rapid and cost-effective process ensures fast and accurate results for better patient care.

HM09. A possible Hypertriglyceridemia Thalassaemia Syndrome in Compound Hereditary Persistent Foetal Haemoglobin (HPFH) with Beta Thalassaemia Complicated by inherited South-East Asian Ovalocytosis (SEAO): A Rare Case Report

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Introduction: Hypertriglyceridemia thalassaemia syndrome is a rare condition and mostly reported in beta thalassaemia major. We report a case of possible hypertriglyceridemia thalassaemia syndrome in a patient who had compound Hereditary Persistent Foetal Haemoglobin (HPFH) with beta thalassaemia and hereditary SEAO concurrently. To date, compound HPFH with beta thalassaemia interaction usually known to have less severe clinical presentation. *Case Presentation:* A 6-month-old baby boy presented with fever, cough and rhinorrhoea for 2 days. Clinically, he appeared very pale with hepatosplenomegaly. Initial haemoglobin level was 11.2 g/dL appeared discordant with clinical presentation. A mildly turbid sample observed in EDTA tube and after lipemic layer removal, Hb was 8.0 g/dL. Lipid profile showed triglyceride level of 9.82 mmol/L and rapidly resolved after multiple transfusions. Both parents' lipid profile was normal. Peripheral smear showed morphological features of SEAO and Thalassaemia. Hb analysis and DNA study confirmed inheritance of compound heterozygous HPFH with beta thalassaemia trait. The patient inherited SEAO and HPFH from his father, whilst beta thalassaemia trait was inherited from his mother. *Discussion:* Clinical manifestation of compound HPFH with beta thalassaemia trait range from mild to moderate features. Co-inheritance of SEAO may aggravates haemolytic crisis. Interestingly, high triglyceride level observed. This may be attributed by severe haemolysis caused by concomitant thalassaemia and hereditary SEAO. Despite pathogenesis of hypertriglyceridemia thalassaemia syndrome remains unknown, this condition interferes with automated haemoglobin quantitation, hence special considerations in sample handling are crucial. *Conclusion:* Phenotypic manifestation of thalassaemia can be aggravated by concomitant red cell membrane disorders and hypertriglyceridemia resulting from haemolytic crisis may potentially interfere with the automated Hb quantitation.

HM10. Comparison of variant callers for BCR::ABL1 Kinase Domain mutations detection

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Introduction: Next Generation Sequencing (NGS) is advised for accurately determining the mutation status of BCR::ABL1 Kinase Domain (KD), particularly in cases where the variant allele frequency (VAF) is low. The software tools for detecting somatic mutations have been developed to analyse sequencing data. The present study applied three variant callers, BCFtools, VarScan 2, and GATK Mutect2, to the sequencing data from 85 tyrosine kinase inhibitors (TKIs) resistant patients. *Materials and Methods:* To detect point mutations in BCR::ABL1 KD, a sequential process was developed, including assessment of sequencing reads quality, alignment to the Reference Genome, identification of mutations using three-variant callers, and annotation of variants. Single-nucleotide variants (SNVs) with VAF greater than 3% were identified for further analysis. *Result:* The present study identified 10 missense mutations relevant to TKI resistance. Moreover, six mutations, Y253H, E255K, T315I, F317L, K357T, and F359C, were identified by more than one variant calling tool. The sequencing data analysis indicates that GATK Mutect2 demonstrates optimal performance in detecting SNVs. *Discussion/ Conclusion:* GATK Mutect2 appears to be the most effective tool for detecting SNVs, given its extensive use and validation in numerous research studies. However, the current findings suggest that combining the capabilities of BCFtools, VarScan 2, and GATK Mutect2 would be valuable to maximise the detection of genetic variations. Our results offer guidance to researchers in choosing appropriate workflows for extracting SNVs from NGS data of BCR::ABL1 KD mutation screening.

HM11. Plasmablastic Myeloma versus Plasmablastic Lymphoma: How to Differentiate?

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Introduction: Plasmablastic myelomas (PBM) and plasmablastic lymphomas (PBL) are aggressive haematological malignancies with common pathological features, thus posing a diagnostic dilemma. Albeit challenging, a precise diagnosis is essential, as their treatments differ significantly. *Case presentation:* We describe an interesting case of bone marrow infiltration by plasmablasts in a 51-year-old male with initial presentation of lower back pain and lytic lesion in lumbosacral X-ray. The patient had impaired

renal function and hypercalcaemia. Full blood count (FBC) showed bicytopenia (anaemia with a haemoglobin level of 77 g/L and thrombocytopenia with a platelet count of 46 × 10^9/L). Full blood picture showed 35% abnormal cells with lymphoid appearances; few were blastic-looking and plasmacytoid. Bone marrow aspiration and trephine biopsy revealed >90% moderate to large plasmablasts displaying basophilic cytoplasm, eccentric nuclei and prominent nucleoli. All three cell lines were markedly suppressed. These malignant cells expressed CD138+ (strong), CD79a+, and CD56+ with lambda light chain restriction. Ki67 was 50-60%. Meanwhile, CD20 and CD30 were negative. Immunophenotyping identified 46% of clonal plasma cells. Unfortunately, the patient succumbed to death before the commencement of treatment. Serum protein electrophoresis and serum-free light chains later revealed evidence of lambda paraproteinaemia and lambda/kappa FLC ratio of >100, respectively. *Discussion:* The presence of myeloma-defining events, significant serum monoclonal immunoglobulin, negative CD30 and Ki67 staining < 80% may support a diagnosis of PBM. Other pertinent distinguishing features (not demonstrated in this case) which are more common in PBL are MYC overexpression and HIV/EBV co-infection. *Conclusion:* Correlation of the clinical, radiological and relevant laboratory findings is vital to differentiate between PBM and PBL.

HM12. Fibroblast-Originated iPSCs Demonstrate Superior Differentiation Capabilities in Haematopoietic Differentiation

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Background: Haematopoietic stem cells (HSCs) are important candidates for cell-based therapy. Induced pluripotent stem cells (iPSCs) offer an alternative clonal source for deriving targeted cells, overcoming the ethical controversy associated with the use of human embryonic stem cells (hESCs). Fibroblasts are highly available, easily propagated *in vitro,* and exhibit 10 to 50 times higher reprogramming efficiency for iPSCs than blood cells. The key question is whether non-blood-derived iPSCs exhibit differentiation potential in deriving haematopoietic lineages. *Methods:* Prior to reprogramming, the pluripotency of two pluripotent stem cell (PSC) lines, Normal Human Dermal Fibroblast-derived iPSCs (NHDF-iPSCs), and H9-hESCs were evaluated. The PSC lines were differentiated into haematopoietic lineages using the STEMdiff™ Haematopoietic kit. Immunophenotyping analysis was performed at different stages. *Results:* NHDF-iPSCs expressed higher levels of TRA-1-60 ($p = 0.04$), SSEA4 ($p = 0.03$), and TRA-1-81 ($p = 0.04$) compared to H9-hESCs before differentiation. Compared to H9-hESCs, NHDF-iPSCs-derived haemogenic endothelial (HE) showed significantly higher expression in endothelial markers [CD144 ($p < 0.001$); CD31 ($p = 0.02$)], and haematopoietic markers including [CD43 ($p < 0.001$); CD34 ($p = 0.02$)], and CD34/CD144 co-expression (19.57 ± 0.66% vs 4.96 ± 0.29%, $p < 0.001$). NHDF-iPSCs-derived HE subsequently gave rise to a marginally higher suspension of $CD34^+CD43^+CD45^{+/-}$ haematopoietic stem and progenitor cells (HSPCs), with 53.58% ± 1.57 versus 35.69% ± 3.22 ($p = 0.13$) compared to H9-hESCs. Interestingly, NHDF-iPSCs exhibited better pluripotency and superior haematopoietic differentiation propensity than H9-hESCs. *Conclusion:* Our study highlights the promising potentials of fibroblast-origin iPSCs as an inexhaustible source for deriving $CD34^+$ HSPCs for therapeutic applications.

HM13. Transcriptomic Analysis of Tyrosine Kinase Inhibitor Resistance in Chronic Myeloid Leukaemia Patients

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Introduction: Chronic Myeloid Leukaemia (CML) is driven by the BCR::ABL1 fusion gene, promoting oncogenesis through constant tyrosine kinase activity. Despite the effectiveness of tyrosine kinase inhibitors (TKIs), resistance poses a major clinical challenge, underscoring the need for a better understanding of molecular mechanisms. This study aimed to compare CML patient transcriptomes based on TKI response. *Materials and methods:* Sixty-four CML patients were enrolled, comprising Group 1 (TKI-responsive, n=32) and Group 2 (TKI-resistant, n=32). Bone marrow and peripheral blood samples were collected. RNA sequencing was conducted, and bioinformatics analyses followed to study differentially expressed genes (DEGs) using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment. *Results:* A total of 4,746 DEGs were identified, comprising 1,747 upregulated and 2,999 downregulated genes in Group 2 compared to Group 1. GO analysis revealed upregulated DEGs enriched in protein binding, cytoplasm, and nucleoplasm, while downregulated DEGs were associated with cytosol, protein binding, and chromosome segregation. KEGG pathway analysis highlighted upregulated pathways, including T cell receptor signalling, primary immunodeficiency, Th17 differentiation, BCR signalling, and Wnt signalling. Conversely, downregulated pathways included cell cycle, metabolic processes, and DNA replication. *Discussion/Conclusion:* Our study reveals unique molecular profiles in TKI-resistant CML, indicating the roles of immune activation, survival signals, and metabolic adaptations in resistance. These findings suggest the potential for targeted therapies to improve treatment outcomes. Future research will focus on a detailed analysis of alternative splicing and validation of identified targets. These steps are crucial for fully understanding TKI resistance mechanisms and developing personalised treatments for CML.

HM14. A Young Patient with Small Lymphoid Aggregates In Bone Marrow Trephine: Benign Hyperplasia Or Malignant Lymphomatous Infiltration?

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Introduction: Benign lymphoid aggregates may be seen in trephine biopsies and making clear-cut distinction from focal lymphomatous infiltration is of utmost clinical importance. This can be challenging especially when assessing small infiltrates with small-to-intermediate size lymphoid cells, simulating benign nodules. *Case Presentation:* A 42-year-old man presented with a three-weeks history of symptomatic anaemia. Clinically, there was no hepatosplenomegaly or lymphadenopathy. Blood film showed pancytopenia with no blast or abnormal lymphoid cell. Bone marrow aspirate was dry. Trephine biopsy demonstrated hypercellularity with multiple small lymphoid aggregates consisting of a mixture of B and T-lymphoid cells with the latter slightly predominant. They are irregular at the intratrabecular region along with scattered infiltrates at the interstitial and paratrabecular areas. B-cells are small to intermediate size, expressing CD20, PAX5 and negative for CD5, CD10, Cyclin D1 and CD138. No demonstrable light chain restriction. T cells are small and regular-size, predominantly CD4 positive with no loss of T-cell markers. Ki67 proliferative index is low, about 5% within the nodules. A diagnosis of marrow infiltration by low-grade B-cell lymphoma, in favour of marginal zone lymphoma was made. *Discussion:* Distinction between benign nodules and malignant lymphoma in our patient is difficult. Studies have suggested differentiating features based on histotopography (localisation and infiltration pattern), demarcation and distribution of B and T-cells. The haphazard mixture of B and T-cells may point towards benign origin but his age factor and other infiltrative features are strongly supportive of malignancy. *Conclusion:* This case illustrates the diagnostic challenge in assessing small irregular lymphoid aggregates in trephine biopsy.

HM15. Neuroblastoma with Bone Marrow Infiltration in Early Adolescent Patient: A Case Report

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Introduction: Neuroblastoma is an embryonal cancer of the peripheral sympathetic nervous system. It is the most common extracranial tumour of childhood. Neuroblastoma in older children and adolescents are extremely rare and it carries a bad prognosis. *Case presentation:* A 14-year-old Malay girl with an underlying Nephrotic Syndrome presented with lethargy, shortness of breath and body aches. She also had abdominal distension, loss of appetite and loss of weight for 6 months. No bleeding tendency, hepatosplenomegaly or lymphadenopathy. Ultrasound abdomen and CT scan abdomen revealed a huge left suprarenal mass likely arising from the left adrenal gland. FBP showed severe normochromic normocytic anaemia with thrombocytopenia. Bone marrow aspirate showed haemodiluted marrow with the presence of many clusters of abnormal mononuclear cells. Trephine biopsy revealed marrow spaces diffusely infiltrated by malignant cells. These cells are positive to Synaptophysin, Chromogranin, NSE, CD56 and negative to CKAE 1/3, CK7, CK20, Melan A, Inhibin, S100, Vimentin, WTI, PAS and PAS-D. CD99 and LCA are negative. Pseudo rosette formation is seen. Morphological and immunohistochemical findings favour neuroblastoma. She received a total of 14 cycles of chemotherapy and underwent surgical excision of left suprarenal neuroblastoma. She also underwent a bone marrow transplant recently and subsequently planned for radiotherapy. *Discussion:* Making a diagnosis for a tumour of neuroblastic origin should be approached with caution. Correlation with clinical findings and proper investigations should be done thoroughly to identify the underlying pathology. *Conclusion:* Early diagnosis and prompt management are crucial in this fast-growing tumour. Hence, bone marrow tissue biopsy must be considered in any patient presented with cytopenia.

HM16. Mantle Cell Lymphoma with Burkitt-like Morphology: A Case Report

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Introduction: Mantle cell lymphoma (MCL) is a rare and aggressive type of non-Hodgkin lymphoma, often challenging to diagnose due to its varied presentation and overlapping features with other lymphoproliferative disorders. Accurate diagnosis is crucial, as MCL requires specific therapeutic approaches. *Case report:* An 82-year-old man with diabetes and hypertension presented with an unstable gait. He experienced lethargy, appetite loss, and a 10 kg weight loss over one month. Examination revealed hepatosplenomegaly whilst CT imaging showed a para-aortic mass with multiple abdominal lymphadenopathies. The blood film showed bicytopaenia with occasional abnormal mononuclear cells. Bone marrow revealed numerous abnormal mononuclear cells, described as moderate to large in size, with irregular nuclear outlines, prominent nucleoli, and moderate basophilic cytoplasm with vacuolation and projections. Burkitt Leukaemia/Lymphoma was initially suspected, based on the morphology. However, the immunophenotyping (IPT) showed an abnormal lymphocyte population which is CD19+, CD20+, CD5+, FMC7+, CD22+, CD79b+, cyCD79a+, CD10-, CD23- with lambda light chain restriction. The IPT results and cytogenetic finding of t(11;14) (q13;q32) confirmed the diagnosis of mantle cell lymphoma. Together with the CT scan findings of widespread lymph node involvement,

the patient was staged at Stage III Ann Arbor staging. He had a concomitant left cerebellar stroke and succumbed to death 10 days later. *Discussion:* Discrete vacuoles in blasts can indicate Burkitt lymphoma, non-haematologic infiltration, or lysosomal storage diseases. However, B symptoms and lymphadenopathy suggested lymphoproliferative disease. Integrating clinical features, morphology, and ancillary tests confirmed mantle cell lymphoma in this challenging case.

HM17. Additional Fusion Genes Beyond BCR::ABL1 in Blast Phase Chronic Myeloid Leukaemia: 15 Years' Experience

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Introduction: Chronic myeloid leukaemia (CML) is characterised by the chromosome translocation t(9;22) (q34;q11) which results in the formation of *BCR::ABL1* fusion gene. CML progresses from chronic phase (CP) to blast phase (BP) within 3-5 years after diagnosis. Here we analysed 8,245 bone marrow aspirate and peripheral blood samples from January 2008 to December 2023 where 17 cases of CML in BP with additional fusion genes besides *BCR::ABL1* fusion gene were identified. *Materials and Methods:* The extracted RNA of cases with blast count more than 20% analysed using HemaVision screening kit from Jan 2008 to July 2020 and Quandx screening kit from August 2020 to December 2023. *Results:* The break-point cluster region of 15 cases were in the major BCR (M-BCR) and 2 cases in the minor BCR (m-BCR). Five (5) cases had additional fusion genes of t(3;21), while inversion 16 and t(9;11) were each observed in 4 cases. One (1) case was identified with t(9:9), t(9;12), t(6;11) and t(1;19) respectively. *Discussion/ Conclusion:* Clonal evolutions such as cytogenetic changes like extra Ph chromosome, isochromosome 17q, gain of chromosome 8 or 19 observed in 80% of CML cases transformed to BP. Translocations of known oncogenes in blast crisis occur rarely in less than 5% cases where the most notable of these recurrent translocations are t(3;21) and t(7;11). The t(3;21) is also notable in our Malaysian populations. The emergence of additional fusion genes in these patients is a sign of disease progression and outcome. Further study needs to be conducted to prognosticate response to treatment.

HM18. Haemoglobin J (Hb J) Variants in Malaysia Population Based on Ethnicity and Characteristic in Haemoglobin Analysis: Case from Institute for Medical Research (IMR)

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Introduction: Haemoglobin J (Hb J), known as 'Fast Moving Haemoglobin' (FMH), exhibits rapid anodal movement on gel electrophoresis compared to HbA on gel electrophoresis. With over 50 reported variants, mutations occur in the *HBA or HBB* genes. This study aims to characterise Hb J variants in Malaysia by ethnicity and their haemoglobin analysis characteristics. *Materials and Methods:* This retrospective study includes a total of 17,177 cases referred to IMR from 2017 to 2023. The cases were subjected to direct sequencing of the *HBA1, HBA2* and *HBB* genes for variant detection. Alpha thalassaemia screening was done using multiplex Gap-PCR for seven common deletions. *Results:* Out of 162 Hb J variant samples, four HBA variants were identified: Hb J-Singapore (n=118), Hb J-Meerut (n=18), Hb J-Rajappen (n=5), and Hb J-Wenchang-Wuming (n=3), averaging 22.3% Hb X. For *HBB* variants, Hb J-Bangkok (n=17) and Hb J-Taichung (n=1) accounted for 51.1% abnormal Hb X, detected in zone 12 (CE) and peak 3 (HPLC). Hb J-Singapore and Hb J-Bangkok were the most prevalent alpha and beta types of Hb J variant among Malaysians, respectively. *Discussion:* Specific Hb J variants were unique to Malaysian ethnic groups: Hb J-Singapore among Malays, Hb J-Rajappen among Indians, and Hb J-Wenchang-Wuming, Hb J-Taichung, and Hb J-Bangkok among Chinese. This geographical and ethnic specificity enriches our understanding of Hb J variant distribution in Malaysia.

HM19. Role of Cell Activation Parameters in Predicting Severity of COVID-19 Patients

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Introduction: Prompt recognition and intervention for critically severe COVID-19 patients play a vital role in lowering mortality rates. This study seeks to explore routine and extended haematological parameters (Haemoglobin, Neutrophils, NLR, IG, RET, etc.), including cell activation indicators (AS-LYMP, RE-LYMP, NEUT-RI, NEUT-GI, and IG) to enhance their utility as predictive biomarkers for assessing COVID-19 severity. *Methods:* This prospective cohort study involved 118 COVID-19 patients admitted to two tertiary hospitals between December 2022 and December 2023. The patients were classified into ICU and non-ICU groups based on their admission status. Their blood samples collected for full blood count analysis were retrieved and reanalysed using

an automated haematological analyser, Sysmex XN1000 (Sysmex Corporation, Kobe, Japan). Receiver operating characteristics assessed parameter performance in predicting ICU admission, while logistic regression examined associations between cell activation parameters and disease mortality. *Results:* NEUT-RI and NLR emerge as the most promising predictors for ICU admission (AUC:0.719 and AUC:0.760, respectively), both with $p<0.001$. NEUT-RI displayed borderline significance for disease mortality in the univariable model ($p=0.050$) but was not significant in the multivariable model. Both NLR and IG emerged as significant predictors of disease mortality in univariable models ($p<0.001$ and $p=0.048$, respectively), yet only NLR remained significant in the multivariable model. Other cell activation parameters did not exhibit significant associations in either model. *Conclusions:* NLR emerges as the foremost predictor for ICU admission among COVID-19 patients, with NEUT-RI, Neutrophils, and IG following suit. Additionally, NLR stands out as the most impactful marker for predicting disease mortality in this patient.

HM20. Comparison of Manual and Automatic Cell Count Methods for Evaluation of Body Fluid among Patients in Hospital Tengku Ampuan Rahimah

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Introduction: The differential count of body fluid offers useful insight into the diagnosis and management of a wide range of medical conditions. In recent years, there have been multiple analysers available that allow for the assessment of body fluid cellularity. However, chamber cell counts and light microscopy analysis are still widely considered the gold standard for cell counting. *Aim:* To compare the differential count of body fluid by a haematology analyser with manual cell counting using light microscopy. *Method:* This study was conducted from 1st June 2022 until 30th September 2022. A total of 47 body fluid samples were received and differential cell count was performed using a Sysmex SP-10 haematology analyser on the day the specimen was received. Smears of these body fluid samples were also prepared on the same day and assessed by two observers. Comparison was made between the automated and manual differential count for polymorphonuclear and mononuclear cells using coefficient of determination (R^2) calculation. Result: Manual and automated counts for all polymorphonuclear and mononuclear cells showed an R^2 value of more than 0.9. However, the data points with an eosinophil count >30% were relatively far from the regression line. *Discussion:* Manual and automated counts for polymorphonuclear and mononuclear cells show good correlation, but careful interpretation is needed for eosinophil count >30%, especially in peritoneal dialysis patients to accurately differentiate conditions such as spontaneous bacterial peritonitis (SBP) from eosinophilic peritonitis as the management differs greatly. *Conclusion:* Verification using the manual method is recommended when the eosinophil count is >30% by the automated analyser.

HM21. The Role of Thalassaemic Red Cell in the Mechanism Process of Hypercoagulable State in Thalassaemia Intermedia and Major Patient

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Introduction: Thromboembolic events (TEEs) are a known complication in thalassaemia patients, stemming from a hypercoagulable state with various proposed mechanisms. Objectives: To compare and correlate the fragmented red blood cells (FRCs), hypercoagulable protein markers, and erythrocyte phosphatidylserine (PS) exposure in thalassaemia patients in our centre. *Methods:* This 12-month prospective case-control study at HUSM involved 34 cases (21 Major Thalassaemia, 13 Intermedia Thalassaemia) and 10 controls. The percentage of FRCs, PS, protein C, free protein S, and antithrombin III were measured and statistically analysed (Independent t-tests, ANOVA, Kruskal-Wallis, and Pearson correlation). P-value <0.05 is significant. *Results:* 44 subjects were recruited with a mean age of 22.43(±10.45), male (61.4%) and Malay (86.4%). The FRC and PS% were significantly higher in both thalassaemia groups compared to control (p-value< 0.001 for FRC and p=0.048 for PS exposure). The mean protein C and free protein S levels were significantly lower (55.00 ± 10.20% and 65.77 ± 8.66% respectively) in Thalassaemia Major and in Thalassaemia Intermedia patients (61.23 ± 16.99% and 61.11 ± 14.65% respectively) as compared to controls (101.60 ± 18.97% and 95.12 ± 23.57% respectively) with p-value of <0.001 for both comparisons, whereas mean ATIII levels were not significant. Significant correlations were found between PS exposure and protein C (p=0.014), as well as between protein C and free protein S (p=0.021) and antithrombin III (p<0.001). *Conclusions:* The PS exposure, protein C, and free protein S levels were significantly different in the thalassaemia groups than in the controls. These findings advocate for early prophylactic measures against TEEs in vulnerable populations.

HM22. Prevalence and Epidemiology of ETV6::ABL1 Fusion Gene in Malaysia: Insights from a 14-Year Study

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Introduction: Leukaemia involves various genetic abnormalities, including the fusion gene of the rare *ETV6::ABL1* t(9;12)(9q34;p13). This gene occurs from the reversed orientation of *ETV6::ABL1*, causing in-frame fusion and unbalanced translocation.

These transcripts show tyrosine kinase activity similar to *BCR::ABL1*, making them responsive to tyrosine kinase inhibitors (TKIs). This study aims to determine the prevalence of the *ETV6::ABL1* in the Malaysian population using data from the Institute for Medical Research (IMR) from 2008 to 2022. *Materials and Methods:* We analysed 8,842 leukaemia samples for fusion genes. RNA was extracted using the QIAamp MINI kit, followed by Multiplex RT-PCR using Hemavision-28Q and QuanDX-30. *Results:* Of the 8842 samples, 2317 (26%) tested positive for various leukaemia fusion genes, with only 13 (0.6%) positive for *ETV6::ABL1*, highlighting its rarity. The 13 cases included six males and seven females, with an average age of 38 years. The racial distribution included 5 Malays (39%), 2 Chinese (15%), 1 Indian (7%), and 5 Bumiputra individuals from Sabah and Sarawak (39%). Among the cases, adults (n=11) were more affected than children (n=2). The majority of cases exhibited acute leukaemia, with 4 cases of B-cell acute lymphoblastic leukaemia (B-ALL) and 5 cases of acute myeloid leukaemia (AML), along with 4 cases of chronic myeloid leukaemia (CML). *Discussion/Conclusion:* Our findings underscore the rarity of the *ETV6::ABL1* fusion gene in Malaysia, providing essential epidemiological insights that will guide future research and clinical strategies. Identifying this fusion gene is crucial due to its genomic and expression profile similarities to *BCR::ABL1*. Additionally, it is associated with a spectrum of malignancies and clinical behaviours resembling those of *BCR::ABL1*, including the unfavourable prognosis observed in acute leukaemia. Importantly, the *ETV6::ABL1* fusion gene represents a promising and relevant therapeutic target.

HM23. Understanding Haemophilia A Inheritance: Insights from a Non-Carrier Mother, a Haemophiliac Son, and a Carrier Daughter

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Introduction: Haemophilia A (HA) is an X-linked recessive inherited bleeding disorder. Approximately 70% of cases have a family history, while the remaining 30% are sporadic cases. Here, we explore the possibility of a mother passing down the pathogenic variant (PV) to their children, even when routine molecular testing shows no mutation in the mother. *Case presentation:* A 3-month-old male presented with severe HA. Interestingly, there was no family history of bleeding disorders. PCR and Sanger sequencing revealed a point mutation (with a nonsense effect) in the Factor VIII gene. Remarkably, the elder sister also carried a similar point mutation in the heterozygous state, but the mother did not have an identical mutation. *Discussion:* Research suggests that 70% of sporadic patient's mothers are carriers, as confirmed by genetic studies. However, in some seemingly non-carrier mothers, PV can be detected through low-level somatic, germline, or gonosomal mosaicism. In this case, it's possible that the mother had somatic and/or germline mosaicism, which routine genetic testing failed to identify. Detecting mosaicism is not a standard practice in molecular diagnostic labs due to cost and time constraints. Nevertheless, comprehensive analysis using multiple tissue samples (such as buccal brushings) and advanced techniques like Next-generation sequencing and Droplet digital PCR are necessary to identify the PV in apparently non-carrier mothers. *Conclusion:* When reporting spontaneous mutations in haemophilia A, caution is essential due to the potential presence of somatic, germline, or gonadal mosaicism. Genetic counselling should incorporate comprehensive testing approaches.

HM24. Chronic myeloid leukaemia in chronic phase with marked bone marrow fibrosis: A case report

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Introduction: Chronic myeloid leukaemia (CML) is a Myeloproliferative Neoplasm (MPN) characterised by the presence of the Philadelphia chromosome or translocation t(9;22)(q34;q11.2) resulting in the formation of the hybrid BCR-ABL1 protein. Marrow fibrosis of varying degrees is not uncommon in CML, ranging from mild to severe fibrosis and carries a prognostic factor of the disease. *Case presentation:* Case of CML in chronic phase with marked bone marrow fibrosis at diagnosis is described. A 64 years old gentleman presented with abdominal mass, associated with anaemic symptoms and constitutional symptoms. Full blood count and peripheral blood film shows hyperleukocytosis with presence of all stages of granulocytic series as well as eosinophilia and basophilia with presence of 3% blast cells. Bone marrow trephine biopsy shows hypercellular bone marrow with marked fibrosis. Molecular test was negative for BCR-ABL1 fusion genes, but Philadelphia chromosome was detected during cytogenetic analysis. Treatment was not commenced as the patient succumbed to death before diagnosis was established. *Discussion:* Bone marrow fibrosis in CML, though more common in accelerated phase and particularly severe fibrosis in younger age group, a small percentage can present in chronic phase in older age group with aggressive behaviour. Assessment for severity of the fibrosis within bone marrow is essential to tailor the management of the patient with an effective targeted therapy. Cytogenetic studies and other markers of MPNs also play an important role in establishing the diagnosis especially in CML with negative common BCR-ABL mutations.

HM26. Unravelling A Rare Case of Severe Pertussis with Hyperleukocytosis in A 30 Day–Old Infant

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Introduction: Pertussis, a highly contagious respiratory illness caused by *Bordetella pertussis*, can lead to hyperleukocytosis, an elevated white blood cell count often associated with severe outcomes in young infants. We report a case of a 30-day-old Malay infant with severe pertussis and hyperleukocytosis, who eventually died from complications. *Case presentation:* A 30-day-old Malay female infant presented with a five-day history of cough, fever, and rapid breathing, following exposure to her sick mother. The infant had not been vaccinated against pertussis. Examination revealed fever, tachycardia, and respiratory distress. Complete blood count showed hyperleukocytosis with a white blood cell count of 101.3 $\times 10^9$/L, dominated by lymphocytes and neutrophils. Peripheral blood analysis showed numerous mature lymphocytes. The diagnosis of severe pertussis was confirmed by multiplex PCR for *Bordetella pertussis*. Despite immediate medical intervention, the infant's condition worsened, leading to a fatal outcome. *Discussion and Conclusion:* Pertussis remains a significant global health issue, particularly for infants, with complications such as respiratory failure, seizures, encephalopathy, and death. Leucocytosis with lymphocyte predominance is key in diagnosis and prognosis, linked to pertussis toxin release, though mechanisms are not fully understood. Diagnosis relies on cultures and PCR, and treatment includes macrolides and leukapheresis in severe cases. Vaccination starting at two months is crucial, with subsequent doses at four months, six months, 15-18 months, and a booster at four to six years. This case highlights the severity of pertussis in infants and the critical role of early detection, treatment, and vaccination in mitigating its impact.

HM27. A Rare Case of Co-inherited Haemoglobin Constant Spring and Haemoglobin C in a Young Patient

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Introduction: Thalassaemia and haemoglobinopathies are common inherited blood disorders in Southeast Asia. This case report explores the clinical and laboratory findings of a rare co-inheritance of Haemoglobin Constant Spring (Hb CS) and Haemoglobin C (Hb C) in a patient. *Case Presentation:* A previously healthy 7-year-old Malay boy presented with acute polyarthritis secondary to a streptococcal infection. Laboratory tests revealed a thalassaemia trait with hypochromic microcytic red blood cells. High-performance liquid chromatography (HPLC) and capillary electrophoresis (CE) indicated low Hb A levels, normal Hb A2 and Hb F levels, and the presence of additional peaks corresponding to Hb CS and Hb C. DNA analysis confirmed heterozygosity for both Hb CS and Hb C mutations. Despite his genetic profile, the patient remained asymptomatic, active, and had no history of blood transfusions. *Discussion:* Co-inheritance of Hb CS and Hb C is uncommon and leads to unique haematologic manifestations. The interaction between these variants can result in distinctive haematologic profiles with potential implications for clinical management. The mechanisms underlying these interactions are not fully understood but may involve the preferential binding of globin chains and the relative instability of mutant chains. *Conclusion:* This case highlights the importance of comprehensive evaluation and genetic counselling for individuals with rare co-inheritance of Hb variants. Understanding these genetic interactions is crucial for accurate diagnosis, effective management, and informed family planning.

HM28. Lytic Lesions - Multiple Myeloma or Metastatic Tumour?

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Introduction: Bone lytic lesions can be seen in multiple myeloma and metastatic tumours. It can be challenging to differentiate between these two conditions, especially when there is an inadequate bone marrow sample and there is no trephine biopsy for immunohistochemical staining. *Case report:* A 59-year-old lady presented with right arm deformity, back pain and constitutional symptoms for 2 months. Blood investigation showed anaemia, hypercalcaemia and renal impairment. Upper limb x-ray showed fracture of the right humerus. Lytic lesions were seen in the skull and spine x-rays. A provisional diagnosis of multiple myeloma was made, and relevant investigations were sent. A bone marrow examination was performed but only a suboptimal sample was obtained. Bone marrow smear was haemodiluted and showed the presence of abnormal cells resembling plasma cells. No trephine biopsy is available. A breast lump was noticed on examination and a trucut biopsy was done. Histopathology examination of the breast biopsy tissue was reported as carcinoma. Flow cytometry, serum and urine electrophoresis were not in favour of multiple myeloma. A diagnosis of breast carcinoma with bone marrow metastasis was concluded for this patient. *Discussion:* Identifying the

cause for lytic lesions which can be seen in multiple myeloma and metastatic tumours is crucial since both disease entities require different treatment modalities. Besides relevant biochemical investigations, bone marrow examination plays an important role in determining the origin of the abnormal cell population seen in the marrow. Thus, an adequate bone marrow sample is needed for flow cytometry and immunohistochemical staining to differentiate between these clinical conditions.

HM29. Secondary Haemophagocytic Lymphohistiocytosis (HLH) in DLBCL, an aggressive disease: A Case report

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Introduction: Haemophagocytic lymphohistiocytosis (HLH) is a severe hyperinflammatory disorder, that causes widespread organ damage and mortality. HLH-associated lymphoma is common in adults and is often observed in Natural Killer/T cell lymphoma. However, non-Hodgkin's B-cell lymphoma is a relatively uncommon trigger of HLH. Despite advances in diagnostics and management, patients with lymphoma-associated HLH (LA-HLH) harbour poor prognoses. *Case presentation:* A 61-year-old Malay male, presented with prolonged fever prior to hospitalisation. He had cervical lymphadenopathy, pancytopenia, hyperferritinemia, elevated AST level, and biopsy-proven haemophagocytosis (demonstrated by bone marrow aspirate and trephine biopsy). The nasopharyngeal scope performed to look for the hidden cause of HLH showed an ulcerative fungating mass at the left tonsil with an unhealthy vallecula. Biopsy of the left tonsil identified Diffuse Large B Cell Lymphoma (DLBCL), ABC subtype. HLH regime (etoposide, cyclosporin, and dexamethasone) was administered but unfortunately, he succumbed on day 9 of treatment due to neutropenic sepsis. *Discussion:* HLH is associated with sustained pathologic immune dysregulation: increased activity of cytotoxic T and NK cells subsequently activates the macrophages' activities. Lymphoma is the most common malignancy triggering HLH, albeit LA-HLH cases secondary to B-cell lymphoma are rarely seen. The diagnosis of HLH is quite challenging due to vague presentation and high suspicion of LA-HLH is prompted in the advancing age group. Patients with B-cell lymphoma had longer survival times compared to T-cell types. However, cytokine storms that occur in HLH could be an indicator of treatment resistance in patients with malignant lymphoma causing aggressive clinical course and early death.

HM30. Comparative Analysis of Chimerism Monitoring Techniques in Post-Allogeneic Haematopoietic Stem Cell Transplantation: Next-Generation Sequencing versus Real-Time PCR

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Introduction: Chimerism monitoring plays a crucial role in assessing engraftment status and predicting outcomes after allogeneic haematopoietic stem cell transplantation (HSCT). In this study, we compare the effectiveness of two techniques, Next Generation Sequencing (NGS) and real-time Polymerase Chain Reaction (PCR), in post-allogeneic HSCT scenarios. *Materials and methods*: We collected 25 DNA specimens from five donor-recipient pairs at specific time points (day 0, day 30, day 60, and day 90) post-HSCT. The tests were conducted using quantitative Real-Time PCR (qPCR) (GenDX®KMRtrack and KMRtype, Netherlands) and NGS (AlloSeq HCT by CareDx). The qPCR method quantifies patient-specific polymorphisms using primer probe systems, while NGS involves library preparation through a multiplex one-step PCR-based solution followed by sequencing. Results were obtained by analysing nucleotide variations at single nucleotide polymorphism (SNP) locations. *Results:* We evaluated the sensitivity, precision, and linearity of both assays. Proficiency testing demonstrated reliable results (ranging from 0.1% to 50%) for both methods. Additionally, they exhibited high sensitivity (0.1%), with a perfect correlation (100%) between NGS and qPCR. The NGS assay's limit of detection for artificially created chimerism mixtures was 0.3%, while qPCR achieved 0.05%. *Conclusion:* NGS and qPCR methods exhibit excellent performance and sensitivity. NGS provides a broader range of informative markers, but both techniques offer rapid and accurate analyses with shorter turnaround times. This timely information is crucial for early clinical intervention and predicting relapse. Further validation studies are necessary to fully integrate NGS into clinical routines.

HM31. Rare Occurrence and Phenotypic Heterogeneity of Haemoglobin Zurich-Langstrasse In-Cis with IVS II-654 (C>T) mutations: Case Series from Malaysian Population

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Introduction: Haemoglobin (Hb) Zurich-Langstrasse (*HBB*: c.151A>T; dbSNP: rs63750336) is a rare variant haemoglobin worldwide, and limited report was documented in the literature. This report describes a series of cases with Hb Zurich-Langstrasse *in-cis* with IVS II-654 (C>T) [HBB: c.316-197C>T; dbSNP: rs34451549] mutations and associated clinical phenotype in Malaysia

population. *Case presentation:* Retrospective review of cases with thalassaemia syndromes from 2011 until 2023 was done. Three cases (two related; F1-1 and F1-2 and one unrelated; F2-1) with Hb Zurich-Langstrasse were identified. Two cases (F1-1 and F2-1) presented with beta-thalassaemia trait and one case (F1-2) presented with beta-thalassaemia major. Haematology analysis of both F1-1 and F2-1 showed microcytic hypochromic (Hb 8.4 – 10.2 g/dL; MCV 64.9 – 67.2 fL; MCH 20.6 – 20.7 pg) anaemia with elevated HbA2 (5.9 – 6.4 %) and HbF (2 – 4.9 %). Molecular analysis using sanger sequencing reveals single nucleotide change at codon 50 (ACT>TCT) *in-cis* with IVS II-654 (C>T) in the *HBB* gene. Case F1-2 was noted to have history of blood transfusion and hepatomegaly, whilst case F2-1 had multiple blood transfusion during pregnancy. Further molecular analysis of case F1-2 and F2-1 found the presence of (δβ□-thalassaemia Thai ~12.5kb deletion and ααα3.7(anti3.7) triplication respectively. *Discussion and Conclusion:* Understanding the pathophysiology of thalassaemia and awareness of their associated clinical phenotypes may help prompt and accurate diagnosis especially in rare variant haemoglobin. In summary, this study identified cases of Hb Zurich-Langstrasse *in-cis* with IVS II-654 (C>T) and described the associated clinical phenotypes. In comparison with the reported data in HbVar, our case series supported that the coinheritance of Hb Zurich-Langstrasse *in-cis* with IVS II-654 (C>T) does not modify the severity of IVS II-654 (C>T) however, presence of other mutations may affect disease severity.

TRANSFUSION MEDICINE

TM01. ABO Blood Group and Their Association with Body Mass Index (BMI) in A Tertiary Higher Institution

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Introduction: Numerous disorders have been linked with certain ABO blood groups. The ABO antigens exhibit an important role in cell physiology and pathology, including infectious diseases, cardiovascular diseases, cancer and metabolic diseases. With the increasing prevalence of overweight and obesity in Asia, the use of BMI as a disease predictor has grown in importance. This study aimed to determine the association of the ABO blood group with BMI among the Sarawakian medical undergraduates in UNIMAS. *Materials and methods:* A total of 104 Sarawakian medical undergraduates participated in this cross-sectional study [UNIMAS/TNC(PI)/09-65/01 Jld.2 (75)]. The BMI of each participant was measured and categorised as underweight, normal, overweight or obese. The ABO blood groups were determined using the tile method and recorded onto a data collection form. All data was analysed using the IBM SPSS version 28.0. *Results:* Blood group B (n=36) was found to be the most prevalent blood group, followed by O (n=34) and A (n=24). Most of the students were classified as being overweight (n=35), and 23 students were classified as being obese. The highest prevalence of obesity and overweight were observed in blood group B (n=7) and A (n=12), respectively. *Discussion/Conclusion:* A significant association between ABO blood groups and the different BMI classes ($p<0.05$) was observed, suggesting a possible link between the ABO antigens and BMI.

TM02. Practices and Perception of Voluntary Blood Donation Among University Students

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Introduction: Blood donation remains the only source of blood and its components. This study aimed to assess the practices and perception of voluntary blood donation among Year 2 medical students of University Malaysia Sarawak and identified factors that hinder their willingness to donate. *Materials and Methods:* This cross-sectional study involved 118 respondents. A self-administered questionnaire was used, and data were recorded and analysed by using SPSS version 22. *Results:* Only 27.1% of the respondents had donated blood, while 72.9% never donated blood. Of 32 respondents who had donated their blood, 90.6% were on a voluntary basis. Barriers to donation included unfit to donate (37%), fear of needles (27%), not approached to donate (24%), religious restrictions (3%), fear of knowing health status after donation (3%), no remuneration (1%) and fear blood might be sold (1%). The majority of the respondents (92.4%) perceived that blood donation is a good act, 5.1% of respondents considered it a neutral act, while 2.5% perceived it as a bad act. A majority (79.7%) knew that voluntary donation was the best source of blood. *Discussion and Conclusion:* Despite the good perception towards blood donation, unfortunately, very few respondents had donated blood. Therefore, it is suggested that awareness-raising programs on the importance of voluntary blood donation should be planned and done so that more donors can be recruited and sufficient blood supply can be maintained.

TM03. Unmasking the Culprit: Differentiating Alloantibody, Autoantibody, or Mimicking Anti-E in a Complex Case

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Introduction: The Rhesus (Rh) system, includes the clinically significant anti-E antibody. The alloantibody is formed after pregnancy or transfusion and can cause haemolytic reactions. Autoantibodies to the Rh system, on the other hand, is common in

autoimmune haemolytic anaemia. *Case report:* We report a case involving a 55-year-old Malay woman with endometrial cancer who has undergone a tumour resection with total abdominal hysterectomy and salpingectomy. Despite her E-positive phenotype (R2r, DcEce), anti-E antibodies were detected, suggesting a complex case of alloantibody, autoantibody, or mimicking antibody. Upon hospital admission, the patient's haemoglobin was 9.2 g/dl, with no evidence of haemolysis. She had a history of transfusion three months prior. Routine blood grouping confirmed her as B Rh(D) positive. Antibody screening indicated the possible presence of anti-E, anti-c, and anti-Fyb antibodies. Subsequent antibody identification confirmed anti-E, despite her E-positive phenotype, raising questions about the nature of the antibody. Repeated testing with an 11-cell panel and additional serological tests, including a direct Coombs test, supported the presence of anti-E autoantibody. The autoadsorption of the patient's serum with her RBCs (R2r) showed no reactivity, confirming the autoantibody nature. The patient received six units of E antigen-negative packed red cells, with compatible crossmatching results, except for a 1+ incompatibility with R2R2 RBCs. *Discussion:* Mimicking antibodies, seen in medications, pregnancy, autoimmunity, or malignancy, can resemble true alloantibodies but require different transfusion approaches. This case challenged us to identify E-negative RBCs instead of compatible E-positive ones, highlighting the complexities of managing these antibodies for safe blood transfusion.

TM04. Subgroup B: Unravelling ABO Discrepancies in Plasma Cell Myeloma

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Introduction: Plasma cell myeloma (PCM) is a haematologic malignancy characterised by clonal proliferation of plasma cells in the bone marrow, often accompanied by monoclonal gammopathy. *Case presentation:* A 51-year-old male presented with symptoms suggestive of PCM, including lethargy, exertional dyspnoea, and weight loss, along with laboratory findings indicative of severe anaemia, hypercalcemia, and renal impairment. Diagnostic workup confirmed PCM with bone marrow biopsy revealing extensive plasma cell infiltration. During management, the patient required blood transfusions, prompting ABO blood typing. An unusual discrepancy between forward and reverse blood grouping tests was observed. Further investigation, including incubation at elevated temperatures and adsorption-elution assays, confirmed the presence of B antigens on the patient's red blood cells attributed to a variant B subgroup. *Discussion and conclusion:* This case underscores the importance of recognising rare ABO blood group variants in PCM, particularly in the context of malignancy-associated antigen alterations. Such discrepancies can complicate transfusion management, necessitating meticulous serologic techniques and comprehensive understanding of haematologic malignancy effects on blood group expression.

CHEMICAL PATHOLOGY

CP01. Establishment of Quality Control (Positive Control) for Serum Protein Gel Electrophoresis

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Introduction: Protein electrophoresis is a well-established semi-quantitative technique routinely used in clinical laboratories for screening of serum and some other fluids for protein abnormalities. Good and reliable quality control is very important to ensure that the protein electrophoresis process and operation run efficiently and are able to produce accurate and reproducible patients' results. *Objective:* To determine the best in-house quality control procedure (positive control) for serum protein electrophoresis in Unit Patologi Kimia, Jabatan Perkhidmatan Makmal Diagnostik, Hospital Canselor Tuanku Muhriz. *Materials and Method:* A prospective study was carried out using four serum samples of patients with paraproteinaemia and with different total proteins (76 g/L, 81 g/L, 104 g/L and 120 g/L). The samples then were labelled and stored at both -20 ^{O}C and -70 ^{O}C freezer. The samples were analysed by running protein electrophoresis every month using H2SCAN for 6 months to determine their stability. *Results:* All samples at both storage temperatures of -20 ^{O}C and -70 ^{O}C maintain their stability of six months duration; being able to provide all five protein fractions within analytical specification performance (APS). All samples provided desirable selection for a positive control material for serum protein electrophoresis. Conclusion: Positive control materials with total protein of more than 70 g/L stored at both -20^{o}C and -70^{o}C are suitable for use up to 6 months duration.

CP02. 5-Year Insights into Porphyria's Diagnostic in Malaysia

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Introduction: Porphyria is a heterogeneous group of metabolic disorders characterised by various clinical manifestations, ranging from non-acute to acute types. It poses diagnostic challenges owing to its diverse presentations of cutaneous photosensitivity and severe neurovisceral symptoms. In Malaysia, the awareness of porphyria diagnosis is limited. Therefore, this study aims to elucidate underreported porphyria cases to shed light of porphyria prevalence in Malaysia. *Methodology:* A five-year retrospective analysis (2019 –2023) integrated biochemical and molecular techniques to diagnose porphyria in Malaysian patients. Biochemically, porphyrins were quantified in urine using High-Performance Liquid Chromatography (HPLC) and porphobilinogen (PBG) detected via colourimetry. Molecular analysis was conducted using Sanger Sequencing for the Hydroxymethylbilane Synthase (HMBS) gene. *Results:* Among 532 subjects screened for porphyria, 28.2% (n=150) were presumptive positive. From 150 cases, 57.3% (n=86) were non-acute types, 56.7 % (n=85) were female, and 36.7% (n=55) aged 21-40 years. Notably, 53.3% (n=80) of cases originated from the central region of Peninsular Malaysia, with government hospitals contributing 55.3% (n=83) of samples. Molecular analysis confirmed mutated HMBS genes in four cases. *Discussion & Conclusion:* This study reveals a slight predominance of non-acute porphyria types in Malaysian patients. Whilst PBG and total porphyrin analyses is sufficed for acute porphyria diagnosis, the quantitation of porphyrin separation and molecular analysis provide confirmation of different types of porphyria. This underscores the pressing need to improve laboratory diagnostic tools by exploring additional biochemical markers and leveraging advanced molecular techniques. In addition, by bridging interlaboratory multidiscipline, the accuracy and efficiency of diagnosis can be improved, which ultimately enhancing patient care and outcomes.

CP03. Beyond Initial Presentation: Unveiling SIADH in a Euvolemic Patient with Prior Hypovolemia

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Introduction: Accurate diagnosis of hyponatraemia poses significant clinical challenges, often complicated by overlapping symptoms and the necessity for precise assessment tools. This report illustrates the diagnostic dilemmas encountered in investigating a case of severe hypoosmolar hyponatraemia. *Case Presentation:* A 60-year-old man with recurrent deep vein thrombosis and a chronic left lower limb venous ulcer, receiving warfarin and amitriptyline, presented with vomiting, dizziness, and confusion following a fall. Initially admitted for hypovolaemic hyponatraemia secondary to vomiting, his serum sodium remained persistently low despite achieving euvolaemic status, prompting consideration of syndrome of inappropriate antidiuretic hormone secretion (SIADH). Laboratory investigations revealed severe hypoosmolar hyponatraemia with concentrated urine, hypernatriuresis, and normal kidney, thyroid, and adrenal function. Fluid restriction exacerbated the hyponatraemia, resulting in a negative fluid balance exceeding 1 L/day and persistent hypernatriuresis, which prompted consideration of renal salt wasting (RSW) syndrome. Intravenous fluid replacement gradually increased serum sodium levels to a plateau between 110-113 mmol/L. Following reassessment, the diagnosis reverted to SIAD, and treatment with tolvaptan alongside reinstated fluid restriction led to increment of serum sodium to a baseline of 125 mmol/L. The patient was finally discharged after 32 days of hospitalisation. *Discussion and Conclusion:* This case highlights the challenge in differentiating SIAD from RSW based solely on volume status. Accurate differentiation is crucial to avoid inappropriate treatment and associated complications. Suggesting fractional excretion of urate (FEUrate) offers promise in this regard. SIAD typically shows a normalised FEUrate post-treatment, whereas RSW exhibits sustained elevation.

CP04. Performance of artificial intelligence-based pathogenicity prediction tools for Mucopolysaccharidosis type II

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Introduction: Mucopolysaccharidoses Type II (MPS II) is characterised by deficiency in iduronate-2-sulphatase (IDS) which caused by mutations in *IDS* gene. Missense mutations are common in MPS; thus, it is crucial to accurately categorise them as pathogenic, benign, or unknown. Here, we aim to evaluate the accuracy of three AI-based prediction tools for missense mutations: Evolutionary Model of Variant Effect (EVE), Evolutionary Scale Modelling (ESMFold), and AlphaMissense (AM). *Method:* We compiled a database of IDS gene missense mutations and their corresponding IDS enzyme activity from literature, excluding duplicates. The IDS enzyme activity serves as the gold standard. We divided our datasets into two groups; dataset A contain the entire database (n=60) and dataset B includes variants from East Asia countries only (n=35). We calculated the diagnostic parameter (sensitivity, specificity and accuracy) for the three AI models, correlation between AI model values and IDS activity and overall performance by receiver operating characteristic (ROC) curve. *Results:* Overall, we found that EVE and AM had the highest diagnostic parameter for both datasets. The AI tools also outperformed the widely used PolyPhen-2 in almost all parameters. Interestingly, a moderate

correlation was observed between prediction values produced by AM with IDS enzyme activity (r=-0.288, $p<0.05$) in dataset A and a moderate-to-strong correlation (r=-0.381, $p<0.05$) in dataset B. Conclusion: AI-based tools accurately predict missense variant pathogenicity, particularly for IDS. One AI tool, AM shows potential in predicting the IDS enzyme levels and this could be useful for many missense mutations where IDS levels is not known.

CP05. Turning the Tables: A Rare Case of Immunoglobulin Switching in IgD Multiple Myeloma

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Introduction: Immunoglobulin D-secreting multiple myeloma (IgD MM) comprises less than 2% of MM cases, with relapsed MM typically maintaining the original immunoglobulin type, yet rare instances of complete isotype class switching have been documented. Here, we share a case of complete immunoglobulin switching in IgD MM. *Case presentation:* A 61-year-old woman with IgD Lambda MM R-ISS Stage II achieved complete remission after four cycles of velcade, cyclophosphamide, and dexamethasone. Ineligible for transplant due to end-stage kidney failure, she continued chemotherapy until the eighth cycle when paraproteinaemia reappeared, now manifesting as IgM Kappa Lamda. With subsequent monitoring, the paraprotein concentration increased, prompting treatment adjustment to velcade, thalidomide, and dexamethasone, resulting in complete remission after the second cycle. Presently, she remains well, undergoing her 15th cycle of chemotherapy without detectable IgD lambda or IgM kappa lambda paraproteinaemia. *Discussion:* IgM and IgD are the initial antibody isotypes expressed during B-cell development. After leaving the bone marrow, B cells acquire surface IgD through alternative RNA splicing, diversifying further upon encountering antigens in secondary lymphoid organs through somatic hypermutation and class switch recombination. Isotype class switching, typically attributed to random mutations in plasma cell genomes, may also occur during post-high-dose chemotherapy and stem cell transplants. Notably, patients with complete isotype switching upon recurrence exhibit a prolonged median overall survival compared to those with light chain escape. *Conclusions:* Isotype class switching in relapsed MM patients may indicate a favourable prognosis, though its clinical significance remains uncertain due to limited reports.

CP06. The Correlation of High-Sensitive C-Reactive Protein in Gestational Diabetes Mellitus: A Prospective Study

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Introduction: High-sensitivity C-reactive protein (hs-CRP) has been extensively studied in cardiovascular disease, but its specific role in gestational diabetes mellitus (GDM), a chronic low-grade inflammatory state, requires further investigation. This study examines the association between maternal hs-CRP levels and GDM risk factors and diagnosis. *Materials & Methods*: This prospective study recruited singleton pregnant women under follow-up at Hospital Canselor Tuanku Muhriz who underwent a modified Oral Glucose Tolerance Test (mOGTT) before 18 weeks' gestation. Demographic data were gathered through interviews following patient consent. Blood samples for hs-CRP were collected during the mOGTT and analysed using a nephelometric method on the Alinity c system. Statistical analysis was carried out using SPSS Version 29. *Results:* The study comprised 221 participants; 71.2% had GDM risk factors other than age above 25. GDM was found in 22.6% of the participants. Median hs-CRP levels were significantly higher in those with GDM risk factors (0.52 mg/dL) than those without (0.32 mg/dL) (p=0.001). GDM participants had significantly higher median hs-CRP (0.66 mg/dL) than those without GDM (0.39 mg/dL) (p=0.028). Moreover, hs-CRP levels were strongly correlated with pre-pregnancy BMI (rs=0.572, $p<0.001$) and GDM (rs=0.148, p=0.028). *Discussion/ Conclusion:* Excess adipose tissue macrophage production after physiological gain in adipose tissue mass in early pregnancy, increases pro-inflammatory cytokines, raising hs-CRP. This low-grade inflammation reduces insulin receptor tyrosine kinase activity, degrades insulin receptor substrate-1 (IRS-1) protein, or increases IRS-1 serine phosphorylation, causing insulin resistance and GDM. Our study concluded that higher maternal hs-CRP levels are significantly correlated with increased GDM incidences, with strong correlations to pre-pregnancy BMI.

CP07. Behind the Bands: A Single-centre Retrospective Analysis on Technical Impact of Immunofixation Electrophoresis Results

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Introduction: The presence of parallel bands in all heavy and light chain lanes of immunofixation electrophoresis (IFE) gel obscures paraprotein isotyping. This study aims to determine the association of total protein, albumin, globulin, and total paraprotein

concentrations with the presence of parallel bands in all lanes of IFE. *Materials and Methods:* Following ethical approval, serum protein electrophoresis (SPE) and IFE gels conducted between 2015 and 2022 were retrospectively reviewed, with data retrieved from the Department of Medical Diagnostic Laboratory. Demographic information and final diagnoses were extracted from discharge records. Plasma cell myeloma diagnoses were confirmed using the International Myeloma Working Group criteria. Data analysis was performed using SPSS® version 29. Results: Among 1,138 subjects, 44 (3.9%) exhibited parallel bands in all lanes, with 34 (77.3%) diagnosed with plasma cell myeloma. IgG Kappa paraprotein was most frequently associated with parallel bands (n=21 (47.7%)). No significant differences were found in total protein, albumin, globulin, and paraprotein concentrations between those with and without parallel bands (p>0.05). Additionally, the presence of parallel bands was not significantly linked to the studied biochemical parameters (p>0.05). *Discussion/Conclusion:* The occurrence of parallel bands is primarily attributed to the technical proficiency of the operator rather than associated with other biochemical parameters. Although chemotherapy decisions are unaffected by paraprotein clones, parallel bands often necessitate repeat SPE and IFE tests, increasing laboratory costs and workload. The adoption of immunotyping on capillary electrophoresis, which offers higher specificity, may alleviate this issue.

CP08. A Case Report of Thyroid Stimulating Hormone (TSH) Interference: Macro-TSH

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Introduction: Macro-TSH is caused by the binding of thyroid stimulating hormone (TSH) to other plasma proteins, often immunoglobulins, forming a macromolecule that results in falsely elevated TSH level measurements. *Case Presentation:* A 30-year-old male, a chronic smoker with no known comorbidities, presented with intermittent hand tremors and occipital headaches for two months. Despite being clinically euthyroid, his initial thyroid function test (TFT) showed elevated TSH (15.45 mIU/L) and borderline high serum free thyroxine (FT4) (25.1 pmol/L) levels, which were confirmed upon repeat testing. Differential diagnoses included subclinical hypothyroidism, TSH assay interference, and TSH-oma. Assay interference was suspected after discordant TSH results were obtained across multiple immunoassay platforms, prompting further evaluation. An MRI revealed a pituitary microadenoma and a thyrotropin-releasing hormone (TRH) stimulation test suggested the possibility of a TSH-oma. However, comprehensive hormonal evaluations, including his family's TFTs were normal. His anti-thyroid antibodies were also negative. A significant reduction in his TSH levels post-polyethylene glycol (PEG) points to the presence of macro-TSH. *Discussion:* Discordant TFT results necessitate consideration of immunoassay interference as it can lead to misdiagnoses and inappropriate treatment. In this case, macro-TSH, which interacts with antibodies used in immunoassays, resulted in elevated TSH levels. Various immunoassays show different sensitivities to macro-TSH, complicating the diagnostic process. *Conclusion:* This case highlights the importance of considering macro-TSH in the context of discordant TFT results. Comprehensive investigations, including measurements on different immunoassay platforms and specific tests like PEG precipitation, are essential for the identification of assay interference.

CP09. Hyperthyroxinemia with Non-suppressed Thyrotropin: A Case Report

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Introduction: Hyperthyroxinemia with non-suppressed thyrotropin will lead to thorough laboratory tests and radiological imaging. Among the most likely cause is assay interference which should firstly rule out. Once excluded, TSH-secreting tumour (TSH-oma) and Resistance to thyroid hormone (RTH) syndrome should be considered. *Case Presentation*: We present a case of a 30-year-old lady with underlying hyperthyroidism since July 2022 under health clinic follow up. She had initially presented with lethargy, tachycardia and goiter. Biochemistry revealed TSH: 1.77 mU/L with elevated free T4 (30.7 pmol/L) and was started with T.Carbimazole 10 mg OD since July 2022.She was referred to our hospital to rule out carbimazole resistant as her free T4 was persistently elevated despite increasing the dose. Assay interference has been ruled out as her thyroid function test showed similar pattern at the different analyser platform. A Thyrotropin Releasing Hormone (TRH) stimulation test showed blunted response and Ocreotide Suppression test showed both TSH and free T4 were suppressed by 75% after administration of IM Ocreotide Long Acting Release (LAR). Both results are suggestive of TSH-oma. MRI Pituitary showed no Pituitary Adenoma. CT Neck to look for ectopic TSH-secreting tumour at the nasopharynx is not consented by the patient yet. Discussion: In hyperthyroxinemia with non-suppressed thyrotropin case, once assay interference has been ruled out, it is crucial to differentiate between TSH-oma and Resistance to thyroid hormone (RTH) Syndrome by measuring alpha subunit, TRH Stimulation test and Ocreotide Suppression test. TSH-oma is a rare disease however ectopic Thyrotropin tumour are extremely rare. If CT Neck is negative patient will proceed with exploratory Trans Sphenoidal surgery. *Conclusion:* Finally, this extremely rare disease should be taken into consideration by endocrinologists when encountering cases of hyperthyroidism with normal or elevated TSH.

CP10. Challenges During Transition to a New Laboratory Information System: Experience in Hospital Sultan Ismail Petra, Kuala Krai

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Introduction: Laboratory Information Systems (LIS) represent the cornerstone of efficient modern clinical laboratories, which streamline workflows, efficient data management and accurate results interpretation. It can be challenging to fully understand the technical workflow and adequately prepare for a potentially protracted system implementation and the subsequent stabilisation. Our objective is to describe the top ten challenges that we encountered during the transition to the new LIS and offer suggestions on how to overcome these challenges. *Materials & Methods:* This study was performed at Hospital Sultan Ismail Petra, which recently changed to a new LIS. Challenges were recorded during LIS transition and we describe the top ten. *Results*: Our top ten challenges were configuration handled by LIS vendor staff who less familiar with the new system, high volume of dataset to be configured, harmonisation of test codes and laboratory barcode number, technical issues, limitation of the new system to meet particular laboratory requirements, no migration of existing data into the new system, workflow disruption, adaptation and resistance to the new workflows, training to non-lab users and limited financial and infrastructures resources. A few suggestions to overcome these challenges include regular discussion with LIS vendor, proper pre-implementation preparation, overall user acceptance testing, a change management plan in place, adequate training of laboratory and non-laboratory staff on new workflows and communication with top management. Conclusion: LIS transitions have many challenges requiring institutions to adapt and develop new infrastructures. This article should be helpful to other institutions facing or undergoing a similar endeavour.

CP11. Rare Cause of Remethylation Defect

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Introduction: Remethylation defect in neonates is rare. It is caused by a defective remethylation of homocysteine to methionine leading to hyperhomocysteinemia. One of the causes is 5,10 methylenetetrahydrofolate reductase (MTHFR) deficiency. The clinical manifestation is variable including encephalopathy, neurocognitive impairment, and epilepsy. Here we present an infantile onset of methylenetetrahydrofolate reductase (MTHFR) deficiency. *Case Report:* Baby L.R. presented on day 15 of life with a generalised tonic seizure associated with uprolling of the eyeball 1 day before admission. There is no history of fever or upper respiratory tract infection symptoms. She developed recurrent apnoea and fitting and required intubation. She was treated for presumed sepsis and an antibiotic was given. Cerebrospinal fluid findings are not suggestive of infection. Inborn errors of metabolism testing was sent because of early infantile epileptic encephalopathy (EIEE). Plasma amino acid shows low methionine with free homocysteine detected. Total homocysteine was elevated. The diagnosis of methylenetetrahydrofolate reductase (MTHFR) deficiency was further confirmed by mutation analysis. *Discussion and Conclusion:* MTHFR deficiency is a treatable metabolic condition. It should be considered in neonates presented with EIEE associated with elevated plasma homocysteine and low methionine levels.

CP12. From Friend to Foe: Chronic Digoxin Use Unmasked by Acute Kidney Injury, Leading to Bradycardic Crisis

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Introduction: Digoxin, a well-established medication for atrial fibrillation, has a narrow therapeutic window despite its safety profile. National Poison Centre data reveal that 15% of hospitalised patients on digoxin exhibit toxicity, with a mortality rate ranging from 3% to 25%. Cardiac arrhythmias are the leading cause of death in these cases. *Case Presentation:* We present a 57-year-old Malay female with chronic rheumatic heart disease, severe mitral regurgitation, and atrial fibrillation. She had been on digoxin 0.25 mcg OD for 6 months. The patient presented with decompensated heart failure and acute kidney injury, characterised by dyspnea, orthopnea, and bilateral lower limb swelling. Intravenous furosemide was administered for decongestion. However, worsening renal function, persistent hyperkalaemia, and dizziness raised suspicion of digoxin toxicity. An elevated digoxin level (4.9 ng/mL) confirmed the diagnosis. The patient exhibited bradycardia (heart rate 30 bpm), which responded to atropine. Digoxin was withheld, and continuous cardiac monitoring ensured safety. After 5 days of treatment with charcoal, symptoms resolved, and the heart rate improved to 52-99 bpm. Digoxin antibody was not administered, as the patient remained asymptomatic. *Discussion & Conclusion:* This case emphasises the critical role of laboratory tests in diagnosing and managing digoxin toxicity. Accurate and timely assessments of serum digoxin levels, renal function, and electrolytes are essential for detecting toxicity, guiding treatment decisions, and monitoring patient progress. Frequent serum monitoring is especially crucial for patients with prolonged digoxin use, electrolyte imbalances, advanced age, and declining renal function.

CP13. Diagnosis of Cobalamin C Deficiency in a Malaysian Cohort: A Single-Centre Study

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Introduction: Cobalamin C (cblC) deficiency (OMIM 277400) is the most common inborn error of intracellular cobalamin metabolism, leading to various systemic issues and has been described across diverse populations. This study aims to elucidate the demographic, clinical, biochemical, and molecular profiles of cblC deficiency in Malaysia. *Materials and Methods:* Data from high-risk screening of 131,914 samples received at the Institute for Medical Research from 2010 to 2023 were retrospectively reviewed and analysed. *Results:* 10 patients were identified (early-onset: n=5; late-onset: n=5) with their mean age of onset were 4.0 ± 3.1 months old and 4.0 ± 3.1 years old, respectively. Males and females were equally affected with the majority being Chinese (n=8). At presentation, seizures (50%), developmental delay (50%), and hypotonia (50%) were the most predominant features. Tandem mass spectrometry (MS/MS) detected elevated first-tier analytes— propionylcarnitine (C3), C3/acetylcarnitine ratio, and C3/palmitoylcarnitine ratio in all patients. Measurement of second-tier analytes—plasma total homocysteine by high performance liquid chromatography with fluorescence detection (HPLC-FLD) and urine methylmalonic acid (MMA) by gas chromatography-mass spectrometry (GC-MS) revealed marked elevations, with median concentrations of 137 µmol/L (normal range: 5-16 µmol/L) and 116 mmol/mol creatinine (cut-off ≤ 10 mmol/mol creatinine), respectively. DNA sequencing analysis of Methylmalonic aciduria and homocystinuria type C (*MMACHC*) gene found that the c.609G>A p.(Trp203*) mutation was the most prevalent (n=7). *Conclusion:* Our study cohort illustrates the clinically heterogeneous spectrum of cblC deficiency, which poses challenges for diagnosis. The implementation of high-risk screening involving first- and second-tier biomarkers is imperative for early detection and improved outcomes.

CP14. Analysis of Dried Blood Spot Sample Rejections For Inborn Errors Of Metabolism Screening- A National Reference Laboratory's Four Years Experience

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Introduction: Physicians rely on accurate and timely laboratory test results to make correct decisions. Inborn errors of metabolism (IEM) can present as life-threatening metabolic emergencies, and rejection of the sample could affect patient care and management. Therefore, providing results with high quality within turnaround time has become the major goal of clinical laboratories. This study aims to investigate the causes and patterns of rejections to provide insights for pre-analytical procedure improvement. *Method:* All dried blood spot (DBS) samples received at the Institute for Medical Research from 2020 to 2023 were retrospectively reviewed. Tests requested for IEM screening include DBS for Amino acids and Acylcarnitines, Biotinidase deficiency, Galactosemia, and Pompe screening. The causes of rejection and demographic data of samples rejected were reviewed and analysed. *Results:* From a total of 31,101 DBS samples received, 6,349 samples (20.4%) were identified as suboptimal. Out of 6,349 samples, 335 (5.3%) were rejected. The common causes of rejection were layering of blood (n=151, 45.1%), insufficient spot (n=63, 18.8%) and unsuitable filter paper (n=33, 9.9%). More than two-thirds of rejections were infants' sample (n=238; 71.0%) and half of the rejections were inpatients (n=168, 50.1%). *Conclusion:* This study highlights the importance of proper DBS sample collection to ensure accurate and timely results for IEM screening and patient care, particularly in vulnerable paediatric populations. To improve the quality of samples, quality control measures, such as standardized protocols for sample collection and regular training for healthcare professionals, are needed.

CP15. Unmasking the Culprit: Seizures Secondary to Hypocalcaemia - A Case Report

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Introduction: Severe hypocalcaemia defined as a serum calcium level below 1.9 mmol/L[1], can lead to serious complications like cardiac arrest and seizures2. In neonates, it is a critical condition that often presents with neuromuscular symptoms, including seizures. *Case presentation:* A 14-day-old infant admitted with a one-week history of tonic-clonic jerky movements, each lasting one minute and occurring more than ten times daily. On examination, the infant was in good health without abnormalities. During hospitalisation, he experienced three brief jerking episodes, which were successfully stopped with Phenobarbitone treatment. *Results:* Blood tests revealed hypocalcaemia, hyperphosphatemia and hypomagnesemia, with hypoparathyroidism and total 25-Hydroxy Vitamin D deficiency. The infant was diagnosed with hypoparathyroidism and vitamin D deficiency. A chromosomal study ruled out DiGeorge syndrome. *Discussion:* Hypoparathyroidism in neonates is a rare cause of hypocalcaemia.[3] The coexistence of hypomagnesemia and vitamin D deficiency further complicates the clinical presentation, as both conditions impair parathyroid hormone (PTH) secretion and function, exacerbating hypocalcaemia[3]. Hypomagnesemia blocks PTH release from the parathyroid glands, leading to hypoparathyroidism[3]. Additionally, hypomagnesemia impairs the sensitivity of target organs like the kidneys and bones to PTH[3]. This results in hypocalcaemia, hyperphosphatemia and increased neuromuscular irritability. Correcting the

hypomagnesemia is necessary to restore normal PTH levels and calcium homeostasis. The administration of calcium and magnesium, along with vitamin D supplementation, effectively stabilized this infant's condition. *Conclusion:* Managing neonatal hypocalcaemia necessitates a systemic approach to prevent life-threatening events. Accurately identifying the causes of hypocalcaemia is crucial for administering appropriate treatments, ensuring positive outcomes and reducing mortality rates.

CP16. A Peculiar Case of Male Ornithine Transcarbamylase Deficiency

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Introduction: Ornithine transcarbamylase (OTC) deficiency is an X-linked inborn error of metabolism of the urea cycle with variable phenotypic expression. Key biochemical markers for OTC deficiency are severe hyperammonemia, hypocitrullinemia and severe orotic aciduria. *Case Report:* A one-day-old boy with a strong family history of OTC deficiency presented with poor feeding and multiple hyperammonemic episodes. His older brother died on day 15 of life due to OTC deficiency and the mother is an OTC carrier. Biochemical analysis revealed persistent hyperammonemia ranged between 147 umol/L to 171 umol/L (normal range: 21-95 umol/L). Plasma amino acids revealed elevated glutamine with low citrulline. However, quantification of urinary orotic acid level was within normal range which is 1.42 umol/L/creatinine (normal level 1.3-5.3 umol/L/creatinine). Subsequent urinary orotic acid sent after started with protein restriction diet persistently showed normal level of 1.57 umol/L/creatinine (day 11 of life) and 1.12 umol/L/creatinine (day 28 of life) despite uptrending levels of ammonia and glutamine. Molecular testing for *OTC* gene revealed a hemizygous variant c.674C>T p.(Pro225Leu) classified as pathogenic using in silico prediction tools in accordance with American College of Medical Genetics guidelines. *Discussion:* This rare case suggests OTC deficiency should be considered in hyperammonemia with high glutamine and low citrulline, even with normal orotate levels, especially with a significant family history. However, orotic acid level still serve as a crucial biomarker in diagnosing, monitoring, and managing OTC deficiency worldwide due to fast and simple testing. Regular monitoring and early intervention are key to managing this metabolic disorder effectively.

CP17. From Hyper to Hypo: A Case of Neonatal Central Hypothyroidism in the Shadow of Maternal Autoimmune Hyperthyroidism

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Introduction: Central hypothyroidism (CH) involves low thyroid hormone (TH) due to insufficient thyroid-stimulating hormone (TSH). We report a CH case in a baby born to a mother with undertreated autoimmune hyperthyroidism (AIHT). *Case presentation:* A 26-year-old lady diagnosed with hyperthyroidism at 23 weeks gestation was inadequately treated with carbimazole resulting in severely raised free thyroxine (FT4), up to 70.3 pmol/L, and suppressed TSH, < 0.014 uIU/mL. TSH-receptor antibodies (TRAB) were 8 times the upper limit of normal. During delivery, the infant's cord TSH was suppressed (0.02 uIU/mL) with normal FT4 (16.8 pmol/L). Repeated TSH at day 5 of life was borderline low (0.903 uIU/mL). On day 23, TSH was mildly raised (12.40 uIU/mL) with very low FT4 (< 6.9 pmol/L). The infant was diagnosed with congenital hypothyroidism and started on Levothyroxine (LT4). By 2 months, his TSH and FT4 had normalised. *Discussion:* Intrauterine exposure of the fetal hypothalamic-pituitary-thyroid axis to high concentrations of TH due to transplacental transport of maternal TH and maternal TRAB stimulation of TH production by the fetal thyroid gland impairs foetal TSH production, causing CH. Decreased TRAB levels or shift of TRAB from predominantly thyroid-stimulating to thyroid-blocking in late pregnancy, likely resulted in the infant developing central hypothyroidism instead of hyperthyroidism. *Conclusion:* Neonatal CH from maternal AIHT is considered transient, but can persist in up to 30% of cases and may progress to primary hypothyroidism. Like other types of congenital hypothyroidism, this condition necessitates LT4 treatment and patient monitoring.

CP18. Surviving Severe hyperkalaemia Bypassing Cardiac Arrest: An Uncommon Instance

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Introduction: Hyperkalaemia is potentially lethal especially among those with underlying renal disease. Levels higher than 7 mmol/L can lead to significant haemodynamic and neurologic consequences whereas levels exceeding 8.5 mmol/L can cause cardiac arrest and can quickly be fatal.[1] *Case presentation:* We report a case of severe hyperkalaemia of > 10.0 mmol/L in a diabetic patient with underlying chronic kidney disease presenting with reduced consciousness level to our emergency department. To our knowledge, this is the highest described potassium value survived without cardiopulmonary resuscitation. During admission, the patient was hyperglycaemic (17 mmol/L) and further blood gas testing revealed a potassium level of >10 mmol/L. The patient was initially treated conservatively however subsequently dialysis was warranted. 36 hours later, the serum potassium concentration reduced to

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.

MM04. Carbapenem-Resistant Enterobacterales (CRE): Characterisation of CRE Genes and Susceptibility Testing of Novel B-Lactams against CRE Isolates.

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Introduction: There is a substantial knowledge gap on the activity of recently approved novel β-lactam against carbapenem-resistant Enterobacterales (CRE) isolates. This study aimed to genotypically characterise CRE isolates and to investigate novel β-lactam antibiotics (cefiderocol, ceftazidime-avibactam and imipenem-cilastatin-relebectam) susceptibility against the isolates. *Methods:* A total of 128 clinical CRE isolated from Hospital Kuala Lumpur from October 2023 to May 2024 were included. These isolates were subjected to conventional multiplex polymerase chain reaction for carbapenemase-producing genes detection. Disk diffusion test was done to determine the susceptibility of novel β-lactams according to CLSI M100 34th Edition. *Results:* Of the 128 CRE isolates, 76 (59.4%) were carbapenemase-producing carbapenem resistant Enterobacterales (CP-CRE) and 52 (40.6%) were non–carbapenemase producing. *Klebsiella pneumoniae* (50%) was the predominant isolate followed by *Enterobacter sp.* (25%), and *Escherichia coli* (12.5%). The bla_{NDM} (88.2%) and bla_{OXA-48} (19.7%) were prevalent among the CP-CRE isolates. Cefiderocol, *ceftazidime-avibactam* and imipenem-cilastatin-relebactam exhibited 87.5%, 46.1% and 29.7% sensitivity respectively, in all CRE isolates. Among 76 CP-CRE isolates, cefiderocol (78.3%) demonstrated superior activity compared to ceftazidime-avibactam (10%) and imipenem-cilastatin-relebactam (5%) in 60 bla_{NDM}-harboring isolates. Nine bla_{OXA-48}-harboring isolates had 100%, 88.9% and 22.2% susceptibility against cefiderocol, ceftazidime-avibactam, and imipenem-cilastatin-relebactam respectively. Remaining seven isolates which harboured two genes (6 bla_{NDM}+bla_{OXA-48}, 1 bla_{NDM}+bla_{VIM}), demonstrated 100% susceptibility to cefiderocol yet 100% resistance to other β-lactams. *Conclusion:* Cefiderocol has the highest activity compared to other investigated β-lactams against CRE isolates. Genotypic characterisation is crucial in determining the antibiotic susceptibility pattern. These findings provide insight into a tailored management of CRE infections.

MM05. Prevotella timonensis Infection of Urachal Cyst in a Young Adult Female: A Case Report

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Introduction: Infected urachal cysts are rare in adult age group and present diagnostic challenges. We report a case of *Prevotella timonensis* infection in an adult female with an urachal cyst, highlighting the need for comprehensive diagnostic and management strategies. *Case Presentation*: A 23-year-old female presented with pain and foul-smelling discharge from her navel for five days, without fever or systemic symptoms. Physical examination revealed tenderness and erythema localised to the supraumbilical region with purulent discharge. An infected urachal cyst was diagnosed, and surgical drainage was performed. Postoperatively, the patient was treated with Amoxicillin/clavulanic acid and responded well. Microscopic examination of the pus revealed numerous pus cells with gram-negative bacilli. The organism grew only on Schaedler blood agar, appearing as tiny colourless colonies. *Prevotella timonensis* was identified by matrix-assisted laser desorption ionisation time of flight (MALDI-TOF). *Discussion: Prevotella timonensis* is a gram-negative anaerobe part of the normal oral and gastrointestinal flora, rarely implicated in infections. Its identification in an infected urachal cyst is significant due to the rarity of both the pathogen and the infection site. Urachal cysts, remnants of the foetal urachus, can become infected, presenting with pain, erythema, and discharge. The unusual involvement of *P. timonensis* highlights the need to consider a broad spectrum of pathogens in atypical infections. *Conclusion:* This case underscores the importance of considering rare pathogens in infected urachal cysts. Comprehensive diagnostic approaches and appropriate antimicrobial therapy are essential for effective management and positive patient outcomes.

MM06. A Rare Case of Arcanobacterium haemolyticum In Chronic Osteomyelitis in Diabetic Foot Ulcer: A Case Report

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Introduction: Chronic osteomyelitis is a devastating sequelae of an acute infection resulting in bone destruction. Although the common causative pathogen in chronic osteomyelitis is *Staphylococcus aureus*, in immunodeficient patients, rare organisms such as *Arcanobacterium haemolyticum* can be the culprit. *Case Presentation:* A 64−year−old Malay gentleman with type 2 diabetes mellitus and hypertension presented with a painful non-traumatic ulcer at the right fourth toe since December 2023 which was progressively worsening. Clinically, there was an ulcer at the medial border of the fourth toe. Infective parameters were raised, and his right foot X−ray showed osteomyelitis changes at the distal phalanx of the fourth toe. He was treated with intravenous ampicillin/sulbactam 1.5 gm twice daily and emergency ray amputation of his right fourth toe was done. Intraoperatively, the distal phalanx was soft. All cultures from soft tissues and bone grew *A. heamolyticum* sensitive to penicillin, vancomycin and ceftriaxone.

Postoperatively, the wound was clean and patient remained well. *Discussion:* Most infections caused by *A. haemolyticum* are associated with head and neck conditions like acute pharyngitis and sinusitis. However, this organism can occasionally cause osteomyelitis in certain susceptible individuals. Patient factors such as extremes of age and comorbidities like diabetes mellitus can contribute to the occurrence of rare organisms present in common illnesses like chronic osteomyelitis. Treatment for chronic osteomyelitis aims to eliminate the causative pathogen. Amputation serves as a method of infection eradication. Hence the duration for targeted antibiotic treatment can be reduced with significant clinical improvement.

MM07. Beyond the Routine: Human Parechovirus Detection in Neonatal Meningoencephalitis Case

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Introduction: Human parechovirus, an emerging pathogen, is increasingly recognised as a serious cause of neonatal meningoencephalitis and sepsis, with its diagnostic importance growing in recent years. We present a case of a previously healthy 5-week-old baby boy referred from a private hospital due to seizures. He was diagnosed with human parechovirus meningitis using a rapid molecular test after other laboratory investigations yielded negative findings. *Case Presentation:* A five-week-old boy presented to the emergency department with a brief, self-resolving seizure and irritability. History-taking revealed a two-day history of fever, loose stools, inconsolable crying, lethargy, decreased oral intake, and contact with his brother, who had an upper respiratory tract infection. He was prescribed paracetamol as outpatient treatment for an uncomplicated URTI, but his fever persisted and symptoms worsened. Other systemic examinations were unremarkable. He was admitted for presumed sepsis. Due to upper motor neuron signs suggesting meningitis, he underwent brain contrast-enhanced computed tomography, which showed no focal lesions. Blood tests revealed mild anaemia, leukopenia, and elevated inflammatory markers, with normal renal and liver function. The cerebrospinal fluid (CSF) analysis was normal. Microbiological cultures were negative, but a CSF rapid molecular meningitis syndromic multiplex panel detected human parechovirus. The baby was treated with intravenous amoxicillin-clavulanic acid and gentamicin upon admission, later switched to cefotaxime and penicillin until test results were confirmed. He had fever spikes up to 38.9°C for the first three days but was afebrile thereafter. His condition improved under conservative management, and he was discharged on day 4 without residual neurological disturbance. *Discussion and Conclusion:* This case highlights the importance of human parechovirus in neonatal illness. Despite negative cultures, its detection via rapid molecular testing underscores its diagnostic relevance. The brief seizure in an otherwise healthy infant emphasises the need for vigilance in managing neonatal febrile episodes, especially with emerging pathogens.

MM08. Unmasking the Culprit: Overcoming Challenges in Diagnosing Cutibacterium acnes Endocarditis

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Introduction: Cutibacterium acnes, typically regarded as skin flora and a frequent blood culture contaminant. *Case Presentation:* A 21-year-old male with an underlying condition of truncus arteriosus underwent surgical repair in 2003, which included the replacement of a pulmonary prosthetic valve. He had a recent hospitalization due to arrhythmia. He presented with a persistent fever, cough with whitish sputum for one month, and petechiae on both lower limbs for two days. Initial physical examination showed cardiomegaly as the only abnormality. He was treated with empirical antibiotic therapy using intravenous cloxacillin and cefepime. However, his fever persisted, CRP level increase in trend, and raised white blood cell count. Subsequent echocardiograms revealed a significant vegetation on the pulmonary prosthetic valve, raising suspicion of infective endocarditis (IE). Blood cultures eventually grew *Cutibacterium acnes* sensitive to penicillin after an extended incubation period of total 6 days. The patient was then administered intravenous penicillin for a duration of 6 weeks. Ultimately, the antibiotic therapy proved effective, resulting in the resolution of fever and stabilization of his clinical condition. *Discussion & Conclusion:* This case underscores the significance of recognising *Cutibacterium acnes* as a potential pathogen, particularly in prosthetic valve endocarditis cases. Special attention to increase culture yield is mandated in IE; in which prolonged incubation periods in blood cultures can effectively isolate the organism. Furthermore, it emphasises the importance of tailored antibiotic therapy based on susceptibility testing to achieve favourable clinical outcomes in *Cutibacterium acnes* endocarditis.

MM09. Antimicrobial Susceptibility Patterns and Emerging Resistance in Burkholderia pseudomallei from a Tertiary Hospital in Pahang: A Three-Year Review (2021-2023)

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Introduction: Burkholderia pseudomallei is an environmental saprophyte which responsible for melioidosis. Malaysia is one of the melioidosis-endemic countries, and Pahang is having the highest average annual incidence rate of 11.3 per 100,000 based on NSAR data from 2014-2020. This study aims to describe the antimicrobial susceptibility profiles and resistance patterns of *B. pseudomallei* isolates from Hospital Tengku Ampuan Afzan (HTAA), Pahang, from 2021 to 2023 against six antibiotics. *Materials and Methods:* In this cross-sectional study, 423 clinical isolates of *B. pseudomallei* were obtained from routine laboratory cultures between 2021 and 2023. Susceptibility testing was conducted against six antibiotics: ceftazidime (CAZ), imipenem (IPM), meropenem (MEM), trimethoprim-sulfamethoxazole (TMP-SMX), amoxicillin-clavulanate (AMC), and doxycycline (DOX). Resistance patterns were analysed to determine trends over the three-year period. *Results:* Results showed an increasing trend in TMP-SMX-resistant over 3 years period, from 4.6% in 2021 to 12.7% in 2022 and 18.7% in 2023. Increasing resistance pattern was also observed in ceftazidime from 0.6% in 2022 to 7.3% in 2023. Blood samples accounted for 63.3% of TMP-SMX-resistant cases, with males showing higher incidence of 87.8%. Resistance was also noted in three relapse cases and two persistent cases. *Discussion/Conclusion:* TMP-SMX is crucial for eradicating *B. pseudomallei* infection, and it exhibits better efficacy when combined with β-lactams during intensive therapy. Our findings showed that the resistance rates for TMP- SMX were higher than those previously reported in Pahang, 9.6% in 2011-2015, and national data, 10% in 2013. The emergence of TMP-SMX-resistant strains could potentially lead to higher relapse rates, highlighting the need for ongoing surveillance and effective treatment strategies.

MM10. SARS-CoV-2 Infection in HIV Patients: Clinical Characteristics, Outcomes, and Duration of Positivity

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Introduction: The global pooled prevalence of HIV among COVID-19 cases was 2%[1]. HIV has been associated with prolonged shedding of SARS-CoV-2[2,3]. Evolution of the virus in immunocompromised individuals may lead to the emergence of new variants[4,5] or immune escape.[6] *Objective:* To determine duration of SARS-CoV-2 positivity (DOP) with HIV viral load and CD4 counts. *Materials and Methods:* Descriptive study from March 2020 until June 2023. A total of 149,191 tests were done at HCTM, comprising of 65,486 RT-PCR, 77,857 RTK-Ag and 5,848 rapid molecular tests. Out of 8,649 positive tests, 28 were HIV patients. *Results:* The study included 27 patients with median age of 36-years-old. In subgroup with measured CD4 within three months of hospitalization (n=22), patients with CD4 ≤200 cells/mm³ (n=17) had a longer median DOP of 12 days (IQR:6-34, P value 0.41) versus 5 days for patients with CD4 >200 cells/mm³ (n=5, IQR:3.5-19.5). In subgroup with measured viral load within three months of hospitalization (n=23), patients with viral load >400 copies/ml (n=17) had a longer median DOP of 12 days (IQR:4.5-24.5, P value=0.48) versus 6.5 days for patients with viral load ≤400 copies/ml (n=6, IQR:2.75-24.25). The longest positivity was 98 days. Most patients had mild COVID-19 with 63% CAT 1 and CAT 2. Three died during hospitalization where two deaths (7.1%) were attributed to COVID-19 pneumonia. Discussion/ Conclusion: DOP is prolonged in patients with CD4 ≤200 cells/mm³ and HIV Viral load >400 copies/ml. Although not statistically significant, cautious approach for de-isolation of severely immunocompromised patients may be considered.

MM11. Hospital Tengku Ampuan Afzan, Kuantan - Onsite Performance Evaluation of the COBAS 5800 System and Comparison to the Abbott M2000 Systems for Quantitative Measurement of HBV, HCV, and HIV-1 Viral Load

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Introduction: Quantitative viral load measurement of HBV, HCV, and HIV-1 is crucial for the patient's clinical management. This will help to establish the clinical stage of the disease, provide treatment guidance and monitor patient response. *Aim:* To evaluate the performance of the COBAS 5800 system in comparison with the in-use Abbott M2000 in quantitative measurement of HBV, HCV and HIV-1. *Methodology:* The evaluation consisted of correlation and precision assays using the tested platforms. 95 samples were subjected to HCV, HIV-1, and HBV PCR quantitative assays using both instruments. For the precision study, each biological replicate (low positive and high positive control) was continuously run for five days to determine reproducibility and reagent stability. *Results and discussion:* The correlation between viral load measurements was extremely high. The r^2 correlation coefficients were 0.978 for HBV, 0.973 for HCV, and 0.965 for HIV-1. Kappa agreement test showed 0.77 to 1.0 agreement. Variation in viral load measurement for each control was assessed based on repeated testing (5 replicates) for five days. The overall mean for the tested controls were 2.30 (Low Positive) and 6.31 (High Positive) for HBV, 2.26 (Low Positive) and 6.23 (High Positive) for HCV, 2.54 (Low Positive) and 5.28 (High Positive) for HIV assays. The calculated bias SD values passed (<0.20) the acceptable bias according to RCPA (SD = 0.25). Conclusion: This comparison study demonstrates the equivalent clinical performance of the new COBAS 5800 system compared with the Abbott M2000 system.

MM12. Ralstonia insidiosa Bacteremia Cases: A Pseudo-outbreak, What to do?

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Introduction: Ralstonia insidiosa pseudo-outbreak was declared in Hospital Tengku Anis, Kelantan. The aim of the study is to stop the outbreak in a month. *Materials and Methods:* The study was conducted in October 2023. Species identification was performed using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS). Environmental samples were obtained and culture according to standard procedure. Audits on infection prevention and control compliance were done every week. *Results:* Environmental materials were cultured on Mac Conkey agar and enhanced growth in Nutrient broth. All samples showed negative results, whilst audit's report showed 80% healthcare worker comply to IPC practice. There was no *R. insidiosa* reported in the following month and blood culture contamination rate reduced more than 50%. *Discussion:* Pseudo-outbreaks are managed similarly as true outbreaks as they may cause unnecessary treatment and costly. *R. insidiosa* is a gram-negative bacteria and it can be found in a water source. Hence pseudo-outbreak caused by *R. insidiosa* indicates serious action should be applied. The audit compliances were reducing the number of cases even though the pathogen was not found. As these pathogens cannot be totally eradicated from the hospital environments, infection control measures will be needed to prevent infections or outbreaks. *Conclusion:* We would like to emphasise the role of *R. insidiosa* in pseudo-outbreaks and the importance of compliance to infection control measures rather than unnecessary costly environmental sampling. The pseudo-outbreak should be prevented to provide better healthcare service and save the cost.

MM13. A Fatal Case of Mixta calida Septicaemia

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Introduction: Mixta calida was initially documented in 2010 after its discovery from powdered infant formula. This is the first reported fatal case of *Mixta calida* septicaemia in a premature infant. *Case presentation:* A premature infant, born at 24 weeks and weighing 685 g, was delivered via spontaneous vaginal delivery. The mother, a group B streptococcus carrier, received adequate antibiotics for prolonged leaking liquor. The infant, initially vigorous, required ventilation for respiratory distress syndrome and completed a course of penicillin and cefotaxime for presumed sepsis. A haemodynamically significant patent ductus arteriosus was treated with intravenous paracetamol. On day 8, the infant needed increased ventilation due to pulmonary haemorrhage and *Staphylococcus capitis* septicaemia, hence treated with cefepime. In the third week, *Mixta calida* was isolated from blood culture and treatment was escalated to meropenem. Despite blood culture clearance within 5 days, the infant remained critically ill and succumbed. Discussion: Identifying the definitive source of *Mixta calida* infection is challenging. *Staphylococcus epidermidis* was cultured from breast milk and blood cultures showed no evidence of catheter-related sepsis. Even though *Mixta calida* was isolated once in patient's blood culture sample, the organism is considered significant. The infant's extreme prematurity, underdeveloped immune system, prolonged NICU stay and use of central lines were significant risk factors predisposing to *Mixta calida* infection. Rapid identification using MALDI-TOF MS is useful to identify this organism especially in managing critically ill patients. *Conclusion: Mixta calida* should be recognised as a pathogen in premature infants. Further studies are needed to identify on its source, risk factors and pathogenicity.

MM14. A Case of Trichophyton Rubrum Presented as Scalp Carbuncle In A 12-Year-old Girl

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Introduction: Trichophyton is a form of dermatophytes and causes superficial infections such as onychomycosis and various types of tinea. *Trichophyton rubrum* is commonly associated with tinea cruris, tinea corporis and tinea pedis and rarely tinea capitis. It is not known to cause deep-seated infection such as carbuncle or skin abscess. *Case report*: A 12-year-old girl presented to ETD with a painful occipital swelling measuring 6 × 5 cm with multiple punctum discharges. She had the swelling for the past 2 weeks which was progressively increasing in size and was preceded by scalp itchiness for the past 2 months. She had no fever and no history of trauma. Investigation showed that she has neutrophilia, mild thrombocytosis with normal Hb level. She was then sent to OR and saucerization of occipital carbuncle done. She was empirically covered with IV Augmentin post-operation and was discharged with painkillers the next day. Tissue C&S grew Trichophyton Rubrum granular form on SDA on Day 2. *Discussion:* Carbuncle is an infection of the hair follicles that extends into the surrounding skin and deep underlying subcutaneous tissue. Most carbuncles are caused by gram-positive bacteria. In this case, tissue sample sent post-saucerization grew fungus on SDA after 2 days of incubation. Macroscopically, the media displayed slightly raised white colonies with pinkish-red reverse. Microscopically, numerous clavate to pyriform microconidia and moderate numbers of smooth, thin-walled multiseptated cylindrical macroconidia. *Conclusion:* This case illustrates a rare presentation of *Trichophyton Rubrum* infection in an immunocompetent 12-year-old girl.

MM15. Syndromic Diagnostic Testing for Aetiological Causes of Respiratory Infections and Meningitis: A Study in the HTAA Kuantan

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Introduction: Syndromic testing allows rapid identification of virulent pathogens, which is crucial in managing and providing efficient patient management. Qiastat-Dx respiratory SARS-COV2 and Qiastat-Dx Meningitis/Encephalitis Panel, a multiplex PCR, have been introduced to detect virulent pathogens within a short period of time. *Objective:* This study aims to determine the prevalence of isolated respiratory infection pathogens and meningitis using syndromic testing of Qiastat-Dx respiratory SARS-COV2 and the Meningitis/Encephalitis panel in HTAA Kuantan. *Method:* This study evaluated 155 nasopharyngeal swabs and 100 cerebrospinal fluids (CSF) using a Qiastat-Dx SARS-COV2 and Meningitis/Encephalitis panel at Hospital Tengku Ampuan Afzan, Kuantan, from November 2022 until June 2024. *Result:* From the analysis, the most common pathogen detected with the Qiastat-Dx SARS-COV2 panel are respiratory syncytial virus A+B (n=23) and rhinovirus/enterovirus (n=15), which had been found mostly in paediatric patients. In addition, about 17% of co-infection was also detected among the positive samples. Meanwhile, in the Qiastat-Dx Meningitis/Encephalitis panel, only 12 out of 100 samples were detected positive, which include Human Herpes Virus 6 (n=4) and *Cryptococcus neoformans/gattii* (n=3) in CSF samples. *Discussion and conclusion:* Syndromic testing has provided a vital link between rapid diagnosis and comprehensive epidemiological surveillance. In addition, the integration of rapid syndromic testing into clinical practice holds the promise of improving patient outcomes and facilitating informed decision-making.

MM16. Moulded Misery: Decoding the Threat of Pulmonary Mucormycosis in Post-TB Patient

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Introduction: Pulmonary mucormycosis, a rare lung fungal disease caused by Mucorales fungi, predominantly occurs in developing countries. *Case Presentation:* A woman with a history of tuberculosis (TB) presented with haemoptysis and fever for four days, progressing to respiratory distress. She was initially diagnosed with severe leptospirosis, with a rapid leptospirosis serological test positive and a leptospirosis microscopic agglutination test (1:800). She was treated with steroids; however, her condition worsened despite initial clinical improvement. A CT scan showed bilateral consolidation with cavitary lesions, necessitating intubation. Culture of bronchoalveolar lavage isolated *Rhizopus microsporus*, confirmed by molecular sequencing of the internal transcribed spacer (ITS) region. She was treated with amphotericin B for a week and then discharged on six months of oral isavuconazole, resulting in full recovery. *Discussion and Conclusion:* The patient's case presents diagnostic challenges with two hypotheses: co-infection of leptospirosis and pulmonary mucormycosis or steroid-induced mucormycosis following tuberculosis. Severe leptospirosis, a bacterial infection, and mucormycosis share symptoms like respiratory distress, pulmonary haemorrhage, and fever, complicating differentiation. Steroid therapy can impair bronchoalveolar macrophage function and induce hyperglycaemia, creating a vulnerable environment for the development of mucormycosis. Accurate diagnosis is critical and involves comprehensive laboratory investigations, including conventional cultures, morphological identification, molecular methods like PCR, and serological tests for leptospirosis. Post-tuberculosis patients are at increased risk for invasive pulmonary mucormycosis, underscoring the need for precise and timely laboratory approaches. A multidisciplinary approach is essential to distinguish mucormycosis-induced pulmonary haemorrhage from severe leptospirosis and to guide optimal treatment strategies.

MM17. Overlap of Limited Systemic Sclerosis and Primary Biliary Cholangitis Diagnosed in A Young Male Patient: A Case Report

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Introduction: Primary biliary cholangitis (PBC) is estimated to occur in two to three percent of patients with systemic sclerosis while about 1.4% to 12.3% of systemic sclerosis patients are associated with primary biliary cholangitis. *Case Presentation:* We reported a case of a 42-year-old male who presented with clinical symptoms strongly suggestive of limited systemic sclerosis with skin tightness over his hands and difficulty to flex his fingers. At the same time he also had signs such as telangiectasia observed on his face and chest, sclerodactyly and Raynaud's phenomena which were suggestive of limited variant of systemic sclerosis or CREST syndrome. Laboratory investigation showed positive anti-nuclear antibody at 1:640 with speckled pattern. At the same time his alkaline phosphatase (ALP) was also elevated at 269 IU/L that prompted further investigation to look for possible underlying primary biliary cholangitis. The diagnosis of PBC was supported by positive anti-mitochondria antibody and confirmed by the liver biopsy that showed florid duct reaction. Thus, the final diagnosis of overlap CREST and PBC was made. He was treated with azathioprine and ursodeoxycholic acid for CREST and PBC respectively. His symptoms were well-controlled with the medications and the ALP remained stable. *Discussion:* The overlap of both CREST and PBC occurs in a significant proportion of patients in both conditions. Thus, it is important to look for the diagnosis of another condition when one of these conditions is diagnosed. In this case, the presence of abnormal ALP triggered for further investigation of PBC which was confirmed by positive anti-mitochondria and liver biopsy. *Conclusion:* It is important to always aware the possibility of overlap syndrome that can occur in both systemic

sclerosis and primary biliary cholangitis as the treatment for both conditions is different.

MM18. Sudden Death Following COVID-19 Vaccines Administration: Is Mast Cell Responsible?

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Introduction: During the COVID-19 pandemic, administration of the vaccine was considered an effective measure to contain coronavirus. With limited safety data, continuous adverse event monitoring following vaccination is compulsory. We retrospectively analysed clinical information and serum tryptase level among postmortem cases from January 2021 to December 2022. *Material and Methods:* Request forms for postmortem tryptase investigation were reviewed. Cases with diagnosis of death within 30 days following COVID-19 vaccines administration of first/second/booster dose and their tryptase level were analysed. Tryptase was measured with Immunocap Phadia 250 (normal range <11.1ug/L). *Results:* All 239 cases presented with sudden death where 27.6% (n=66) were female and 72% (n=173) were male. Mean tryptase was 9.06ug/L. Following vaccination, 4.1% (n=10) cases died within 4 hours, 20% (n=48) cases died within 5 to 48 hours,62.7% (n= 150) died after 48 hours to 30 days while 13.4% (n=31) death cases have no time information. 25.5% (n=61) had elevated tryptase with mean tryptase of 18.79ug/L, where elevated level was observed; 73.8% (n=45) in 48hour-30days cases, 14.8% (n=9) within 4 hours' cases, 6.5% (n=4) in no information cases and 4.9%(n=3) in 5-48hours cases. *Discussion:* Sudden death required detailed postmortem investigation. Immediate vaccine hypersensitivity reactions usually occur within 4 hours after vaccine administration. Here, elevated tryptase was observed mostly among the 48-hour to 4-week cases, suggesting other causes of anaphylaxis and complex immune responses especially when using new vaccine technology. Further studies on non-Ig E mast cell degranulation and tissue examination need to be considered to determine the cause of death.

MEDICAL GENETIC

MG01. Leucine-Rich Repeat Kinase 2 (LRRK2) Knockout Leads to Senescence-Like Phenotypes in SH-SY5Y Neuroblastoma Cells

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Introduction: Autosomal dominant missense mutations within the *leucine-rich repeat kinase 2 (LRRK2)* gene are the most common genetic cause of Parkinson's disease (PD). An aberrant increase in LRRK2 activity contributes to the pathogenesis of PD. The present study was undertaken to generate LRRK2 knockout neuroblastoma SH-SY5Y (LKO) cells which can be leveraged to gain comprehensive insights into the impact of LRRK2 loss. *Materials and Methods:* LKO cells were generated using the CRISPR/Cas9 genome editing tool. DNA sequencing and Western blot were performed to confirm the LRRK2 knockout and protein ablation, respectively. Subsequently, cell morphological changes were examined under a cell imaging system, and cell size was measured using an automated cell counter. The cumulative population doubling of cells was calculated to plot the growth kinetics. Senescence-associated beta-galactosidase (SA-β-gal) staining was performed to determine the percentage of the positively stained population. Mitochondrial function was assessed using a real-time cell metabolic analyser. Results: CRISPR/Cas9-mediated the introduction of frameshift mutation and premature stop codon led to knockout of LRRK2. The LKO cells were significantly larger ($p<0.001$), exhibited loss of neurite-like processes, and proliferated slower than WT and mock cells. Besides that, in LKO cells, the percentage of the SA-β-gal positive population increased significantly ($p<0.001$) while mitochondrial respiration reduced markedly ($p<0.01$). *Discussion/ Conclusion:* Loss of LRRK2 led to senescence-like phenotypes in SH-SY5Y. A comprehensive assessment of phenotypic changes resulting from inhibition of LRRK2 is essential to ensure the safety of LRRK2 inhibitors.

MG02. A New Bioinformatic Method Uncovers Pathogenic Mutations Causing Incontinentia Pigmenti That Was Missed By The Standard Exome Analysis

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Introduction: The standard whole exome sequencing (WES) analysis can successfully identify pathogenic variants at unique regions of the genome but it fails when the target gene shares partly or completely, a very high sequence similarity to other genomic regions

(also called pseudogenes). The presence of pseudogenes reduces the read depth, decreases the mapping quality and causes poor read alignment for the real target gene, ultimately producing false negative results. Here, we aim to re-analyse the exomes of patients with negative diagnosis whose the target gene has known pseudogenes. *Materials and Methods:* We identified four patients with incontinentia pigmenti (IP) based on clinical presentations who received negative diagnosis using WES. IP is caused by mutation in the *IKBKG* gene which has a pseudogene, *IKBKGP1*, making this case suitable for re-analysis. Raw sequencing data was mapped to GRCh37 and the final BAM file was used as input for a recently published bioinformatics tool called Chameleolyser. The variants identified were viewed on IGV and interpreted using InterVar. *Results*: Chameleolyser found three variants in *IKBKG* gene; c.718G>T in exon 6 (p.E240X), c.518G>A in exon 4 (p.R173Q) and c.1020C>A in exon 8 (p.Y340X). All variants were predicted to be pathogenic and one of them was novel (c.1020C>A). Our re-analysis has increased the diagnostic yield from 0 to 75% for patients with IP. *Discussion/ Conclusion:* Re-analysis of patients' WES using specialised bioinformatic tools can reveal variants missed by the standard analysis and we have demonstrated one such example for cases involving pseudogenes.

MG03. Pluripotency Reprogramming Alters Cell Fate of OSCC-H103 and Reverses Tumorigenicity via TGF-ß Signalling Pathway

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Introduction: Pluripotent reprogramming and tumorigenesis are interconnected processes influenced by genetic and epigenetic factors. Reprogrammed cancer cells show reduced tumorigenicity, potential transformation from malignant to benign, and enhanced chemotherapy sensitivity. Also, transforming growth factor-beta (TGF-ß) has been implicated in promoting cancer plasticity and tumour development. In our previous study, induced pluripotent stem cells (iPSCs) were successfully derived from stage-1 (H103) human oral squamous cell carcinoma (OSCC) cells, referred to as Rep-H103. Hence, our current study aims to explore Rep-H103 cells to understand their origin and cancer properties, highlighting the potential of reprogrammed cells in OSCC pathophysiology. *Materials and Methods:* The study employed microarray profiling to compare gene and miRNA expression between H103 and Rep-H103 cells. Selected genes were validated using PCR arrays. Cell cycle and migration assays evaluated DNA content and migration potential in Rep-H103 cells, while drug sensitivity assays assessed Cisplatin potency in both H103 and Rep-H103 cells. *Results:* Our study reveals dysregulation of cancer-promoting genes (TGFßR2/SMAD3/THBS1) and associated miRNAs correlated to cellular plasticity in Rep-H103 cells. We observed decreased in S phase cell population, indicating reduced proliferation and migration potential. Additionally, Rep-H103 cells showed increased efficacy in response to Cisplatin treatment compared to parental H103 cells. *Discussion/Conclusion:* Pluripotency reprogramming mediates cellular plasticity via TGF-ß signalling pathway in Rep-H103 enables cancer cells to revert to a primitive stage with decreased tumorigenicity. TGFßR2/SMAD3/THBS1 and associated miRNAs provide insights into cancer plasticity mechanisms, suggesting their clinical utility as biomarkers for tracking malignant transformation and improving OSCC diagnosis, prognosis, and therapy.

MG04. Molecular Gene Profiling of Formalin-Fixed Paraffin-Embedded Tissue from Colorectal Cancer Using Next Generation Sequencing (NGS) Machine in Hospital USM

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Introduction: Mutation frequencies of pertinent genetic aberrant in colorectal cancer (CRC) are the focus of interest, especially using the Next Generation Sequencing (NGS) machine for CRC screening. *Method:* We carried out the first single-institution genomic profiling of CRC cases in our institution on 30 formalin-fixed paraffin-embedded tissues to detect the most mutated genes and patterns in CRC using an Illumina-specific panel that detects 50 genes using NGS machine. Result: Overall, 22/30(73.3%) samples completed the NGS run: 20 CRC and 2 non-CRC tissues. The average age mean is 53.5 years old. 552 mutations from 29 genes were identified. Most upregulated gene are KIT:68/552(12.3%)], EGFR:60/552(10.9%), FGFR4:61/552(11.1%), ALK: 53/552(9.6%), DCUND1:41/552(7.4%), PDGFRA:40/552(7.2%), KRAS:33/552(6.0%), CDK4: 27/552(4.9%), FGFR3:26/552(4.7%), MTOR:14/552(2.6%), PIK3CA, NRAS and CDK6; 13/552(2.4%) apiece respectively, BRAF, ERBB3, and JAK1:11/552(2.0%) apiece respectively. The least were IDH1, FGFR1, CCND1, HRAS, and AR at 2/552(0.4%) apiece respectively. The pattern of mutations revealed that the most involved chromosomes (chr) with gene mutation specificity are chr4:134/552(24.2%), chr7:84/552(15.2%), chr12:71/552(12.9%), chr5:64/552(11.6%), chr2:61/552(11.1%), chr1:43/552(7.8%), and chr17:10/552(1.8%).

The least involved is chr6 at 1/552(0.2%). The gene-chromosome-specific pattern showed chr3 for ALK, chr5 for FGFR4, chr6 for ESR1, and chr10 for REF. Multi-specific chromosome such as chr1 for NRAS, MTOR, JAK1 and DDR2, chr3 for DCUN1D1 and PIK3CA, chr11 for HRAS and CCND1, chr12 for KRAS, CDK4, and ERBB3. A significant association between the detected mutation and clinicopathological factors was revealed for tumour stage, tumour grade, and tumour stage level. *Conclusion:* Our genomic profiling revealed specific patterns and frequency of CRC mutation which could be a vital breakthrough toward early detection of CRC via non-invasive NGS approach.

MG05. Does Next Generation Sequencing (NGS) result have any unique and prognosticating correlation with colorectal cancer?

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Introduction: The prognosis of Colorectal Cancer (CRC) depends on clinical parameters and biomarkers but owing to suboptimal approaches to precision medicine, NG's reliable and effective use in clinical practices offers a breakthrough in comprehensive gene profiling. Method: We detected gene mutation using Illumina focus panel. Amplicon library from 22 formalin-fixed-paraffin-embedded (FFPE) tissues were sequenced using Next Generation Sequencing (NGS) machine, Fastq data generated and filter criteria for variants identification were treated on Illumina BaseSpace software. Variants detected were analysed on Illumina Variant-Interpreter. Prognostic possibility and association with clinicopathological details were investigated using correlation and regression analysis. *Results:* From 30 FFPE CRC samples, M: F ratio was 40% vs 60% with overall mean age of 53.5 years. Clinicopathology distribution revealed the highest data for "Duke Stages" at 19(63.3%) patients for "Duke-C" with M:F ratio of 7(23.3%) and 12(40%) patients, and Duke tumour Level" at 21(70.0%) patients for "Late stage" with M:F ratio of 7(23.3%) and 14(46.7%). 105 (15 genes) from 552 variants passed the filter criteria. The most occurring variants were ALK:53/105, FGFR4:19/105, NRAS:13/105, ERBB3:8/105, KIT, KRAS, and DDR2:5/105 apiece. Gene-chromosome correlations revealed a strong positive correlation with certain genes: e.g. chr1 correlated positively with DDR2 ($r=0.71$, $p<0.01$) and NRAS genes ($r=0.81$,$p<0.001$). Prognostic analysis using simple and multiple Cox regression analysis revealed the final model of the multiple regression analysis retained tumour stages, tumour level, and Duke staging. *Conclusion:* We report the first NGS analysis on CRC detection in our institution as promising tools for the prediction of CRC by revealing prognostic variants suspected in CRC propagation.

MG06. Whole Genome Sequencing Compared with Standard Genetic Tests for the Detection of Copy Number Alterations in Neuroblastoma

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Introduction: Neuroblastoma is a highly heterogeneous malignancy with outcomes ranging from >90% 5-year overall survival in low-risk disease to <50% in high-risk disease. Molecular markers are increasingly incorporated into its risk classification system, such as the detection of *MYCN* amplification and certain chromosomal copy number alterations (CNAs). This study aims to investigate the reliability of whole genome sequencing (WGS) for neuroblastoma prognostication to inform treatment strategies. *Materials and Methods:* We systematically compared neuroblastoma WGS data with standard genetic test results, e.g., single nucleotide polymorphism array (SNPa), to identify potential pitfalls and investigate the added value of WGS data. *Results:* A cohort of UK neuroblastoma patients (n=43) from three Genomic Laboratory Hubs were included. The mean WGS recall rate for SNPa-detected CNAs was 89.2%, with 23/37 (62.2%) samples showing perfect recall and 4/37 (10.8%) with <50% recall rate. Recall rates were significantly associated with agreement in ploidy estimations and was affected by low tumour cell content and the presence of subclonal CNAs. WGS clarified CNA calls for high copy number regions masked by SNPa allelic track complexities. Uneven coverage resulted in one false positive detection of *ATRX* intragenic deletion. WGS recalled 4/4 translocations and 2/3 hyper-rearrangements from optical genome mapping in one sample but made additional unvalidated calls. Mutational signature 18 was the most detected and was associated with 1p loss encompassing the *MUTYH* gene locus. Conclusion: Overall, WGS demonstrated good concordance with standard methods for CNA detection and provided additional information for tumour profiling, facilitating diagnosis and management.

MG07. Anti-Aging Effects of Umbilical Cord-derived Mesenchymal Stromal Cells Conditioned Medium on Oxidative Stress-induced Senescent Human Dermal Fibroblasts

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Introduction: Cellular senescence involves the deterioration in cellular function and lifespan, primarily due to telomere shortening. Telomeres are repetitive sequences (TTAGGG) at chromosome ends that protect chromosomes from damage. This can be compensated by telomerase, a ribonucleoprotein with reverse transcriptase activity. Mesenchymal stromal cells (MSCs) are multipotent cells found in various human tissues that can secrete therapeutic bioactive factors. This study explores the anti-aging effects of MSC-conditioned medium on senescent cells. *Materials and Methods:* Normal human dermal fibroblasts (NHDF) were treated with 200 µM hydrogen peroxide (H_2O_2) for 2 hours and cultured for 5 days to induce senescence. H_2O_2-treated NHDF was characterised by senescence gene expression (p16, p21, p53), telomere-related gene expression (TRF1, TINF2), senescence-associated beta-galactosidase (SA-β-gal) activity, telomere length, and cell proliferation. Senescent NHDF was then exposed to UC-MSC-conditioned medium (CM) for 48 hours, followed by similar assays and detection of telomerase activity. Results: H_2O_2-treated NHDF showed the presence of the senescence phenotype, but no significant changes were observed in telomere length and related genes. UC-MSC CM treatment downregulated senescence gene expression and SA-β-gal activity, increasing NHDF proliferation in senescent NHDF. Telomere length and related genes expression level showed no significant changes, and telomerase activity was undetected after UC-MSC CM treatment in senescent NHDF. *Discussion/Conclusion:* This study showed that UC-MSC CM mitigates the senescence phenotype in H_2O_2-treated NHDF, even without telomere length recovery. Further investigation is needed to determine the exact anti-ageing mechanisms of MSC CM.