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The 12th Congress of the Asian-Pacific Society of Thrombosis and Haemostasis (APSTH) 2023 "Haemostasis and Thrombosis: Bench to bedside", was held at Borneo Convention Centre Kuching (BCCK), Sarawak on 18th to 21st October 2023. Abstracts of symposium, plenary, lecture, workshop and paper (Young Investigator Award, poster and oral) presented are as follows:

SYMPOSIUM

Symposium 1: Risk Factors for VTE

Immunothrombosis: Pathogenesis and diagnosis

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Immunothrombosis has been increasingly recognised since COVID-19 pandemic. Immune-mediated thrombosis, particularly in the lungs, is common in severe COVID-19 infection. Other examples of immunothrombosis are (1) Heparin-induced thrombocytopenia (HIT), (2) COVID-19 Vaccine-induced Thrombocytopenia/Thrombosis (VITT) and Anti-Phospholipid Antibody Syndrome (APS). These conditions are often characterised by thrombocytopenia and severe thrombosis with high morbidity and mortality. Thrombosis in HIT is mediated by IgG antibodies with specificity for platelet factor 4(PF4)/heparin complex, and in VITT, PF4/vaccine complex. The pathogenic immune complexes in COVID-19 and APS are yet to be fully characterised. In all these conditions, the antigen/antibody complexes activate platelets and neutrophils via their cell surface FcγRIIa receptors leading to thrombocytopenia and thrombosis. Our research showed that the thrombosis in HIT and VITT is driven mainly by NETosis, a process in which activated neutrophils release highly thrombogenic net-like DNA structures called neutrophil extracellular traps (NETs). NETs also provide the framework for clot formation. We showed using a blood flow microfluidics system (venaflux) *in vitro* and a murine thrombosis model in *vivo*, that NETosis inhibitor (GSK 484), DNAse and PAD-4 gene deletion suppressed thrombosis, but did not prevent thrombocytopenia. In contrast, anti- FcγRIIa monoclonal antibody (IV.3) completely inhibited both thrombosis and thrombocytopenia. Altogether these findings suggest that NETosis is a major driver of thrombosis in HIT, VITT and probably in other immunothromboses, and that thrombocytopenia and thrombosis are two distinct FcγRIIa-dependent processes. Diagnosis of these conditions is based on detection of the specific antibody by immunoassays and its platelet activating capacity by functional assays. In conclusion, HIT, VITT and other immunothromboses are potentially life-threatening thrombotic conditions. NETosis is a major driver of thrombosis. Better understanding of the complex pathogenesis of these conditions will lead to better diagnosis and treatment.

Symposium 2: Clinical Burden of VTE

Cancer-associated venous thromboembolism

Soo-Mee Bang
Division of Hematology and Medical Oncology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Korea.

The VTE risk is 4–7-fold higher in patients with cancer than non-cancer patients. Cancer present in up to 20% of patients with VTE. The poorer outcomes in cancer VTE patients when compared to non-cancer VTE patients are characterised as 3-fold recurrence rate, 2-fold major bleeding rate and 3-fold or more in death risk. The risk of VTE in patients with cancer varies by stage and type of cancer and increases during cancer treatment. The first phase III randomized study for the cancer VTE treatment was CLOT trial (N Engl J Med 2003;349:146–53) which compared the LMWH treatment to LMWH followed by warfarin maintenance. Although LMWH treatment reduced VTE recurrence by 52% when compared to LMWH/warfarin treatment, there was no reduction in major bleeding and subcutaneous injections were uncomfortable and difficult to maintain long term. Several RCTs have been carried out to evaluate DOACs as alternatives to LMWH for the treatment of VTE in patients with cancer. Results from these trials have informed guidelines, some of which have recently been updated to include apixaban, edoxaban or rivaroxaban as a treatment option for the management of cancer-associated VTE (NCCN guidelines for Cancer-Associated Venous Thromboembolic Disease, https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf). However, the clinical benefit of DOACs is limited by a higher risk of bleeding than with LMWH, mainly occurring at gastrointestinal sites. Only apixaban showed similar rates of major bleeding, including major GI and non-GI bleeding, compared with dalteparin. Therefore, DOACs are preferred for cancer patients without gastric or gastroesophageal lesions. The risk of recurrent VTE in patients with cancer- associated VTE may persist beyond 6 months. Guidelines generally recommend extended treatment (beyond 6 months) in patients with active cancer if they have no bleeding risk. Lastly, I will discuss the clinical unmet needs and future solutions in cancer VTE; (1) the bleeding issues in patients with gastrointestinal

cancer (2) the drug-drug interaction between DOACs and anti-cancer therapeutics, (3) the management of recurrent VTE during the anticoagulation therapy.

Long-term management of venous thromboembolism (VTE)

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Long-term anticoagulation can reduce VTE recurrence but comes with bleeding risks. Patients with VTE provoked by transient major risk factors do not need anticoagulants after 3 months, while patients with persistent and strong risk factors should receive extended therapy. Roles of continuing anticoagulation in cases of VTE without obvious cause are equivocal. Risks of thrombosis should be weighed against bleeding in individual patients. Various clinical scores and biomarkers, such as D-dimer, may be helpful. These scoring systems need to be validated in Asian populations. Alternatively, long-term direct oral anticoagulants (DOACs) can be prescribed to most unprovoked VTE patients to prevent recurrences as they are relatively safe. Anyway, this is followed by the high cost, burden of lifelong medication and haemorrhagic risks after trauma or emergency surgery. Regarding long-term complications, post-thrombotic syndrome (PTS) is common (20-50%) after deep vein thrombosis and significantly impairs quality of life as effective treatment is lacking. More research is still needed for preventive measures. On the other hand, chronic thromboembolic pulmonary hypertension (CTEPH) is an infrequent (2-3%) but debilitating complication of pulmonary embolism (PE). A cost-effective screening strategy for CTEPH after PE is required for early detection as surgical or interventional interventions are helpful.

Plenary: Claire Mclintock Memorial Lecture

Women & thrombosis: What we know today

Beverley J Hunt OBE
Kings Healthcare Partners, Thrombosis & Haemophilia Centre, GSTT, Strategic Lead in Laboratory Haematology for Synnovis, Trustee & Founder of Thrombosis UK.

Dr Claire McLintock was a passionate believer in promoting women and women's health. In her professional lifetime she lectured globally on thrombosis, particularly in women. While men overall have higher rates of venous thromboembolism (VTE), women have higher rates of VTE during their fertile years. Once girls change into women there is a change in their haemostatic profile with reduced levels of many gentle physiological anticoagulants that are high during childhood. The prothrombotic challenges faced during a woman's lifetime are: the use of the combined oral contraceptive pill, pregnancy and the puerperium, and the use of oral hormone replacement therapy (HRT). There are also very high-risk situations such as women with mechanical valves who become pregnant. Claire was part of a global movement that recognised that over the last decades the emphasis of clinical trials has been on male diseases, with trials run by men, recruiting mainly men and with 99% of clinical trial excluding pregnancy. This attitude is slowly changing, but it has to be admitted that clinical research in pregnancy and the puerperium is decades behind other areas. Indeed there are few clinical trials looking at management and prevention of VTE in pregnancy, most of current practice is based on extrapolation from non-pregnant individuals. Even now there is conservatism in obstetric circles: the safety of low molecular weight heparins in pregnancy has led to over-prescription, an attitude of "we had better be safe than sorry" and so their use in multiple situations and a reluctance to enter patients in clinical trials where one arm might allocate to placebo. The other major problem is that VTE is rare in pregnancy with rates of 1-2 per 1000, so very large clinical trials are required to assess clinical effect, costing large amounts of money from grant giving bodies who mainly do not support clinical trials in pregnancy. My lecture will give an overview of the current state of understanding of thrombosis in women and point out areas that urgently need clinical research.

Meet the expert 1: Developmental haemostasis

Meredith Wiggins
Sydney Children's Hospital, Randwick; University of NSW, Australia.

Developmental haemostasis describes the physiological, age-related changes that occur during the maturation of the haemostatic system. There is multiple interlinked process that prevent bleeding and/or thrombosis. Haemostasis is a rapidly evolving system in the foetus, neonate and infant with smaller changes continuing throughout childhood. In healthy neonates, the haemostatic system is competent and well-balanced. It is not 'immature' but rather fit-for-purpose. A number of landmark reference range studies characterising the differences between paediatric and adult systems were published in the late 1980s and early 1990s by Andrews *et al*. (1, 2, 3). Differences are found in the full blood count, procoagulant and anticoagulant factors, fibrinolysis, platelet reactivity and the vascular endothelium (4). Thus, it is critical that laboratories are using published paediatric, age-specific reference ranges appropriate for their population. Reference range studies in children are challenging due to the need for multiple reference ranges in different age groups, difficulties obtaining adequate samples in healthy children and ethical issues and often include only small numbers of children. In addition, cord blood samples are not comparable to peripheral blood. In practice, coagulation screening tests only consider one component of the haemostatic system and utilising other techniques such as viscoelastic testing may be useful. Clinical implications of an understanding

of developmental haemostasis include differences in the epidemiology of bleeding and thrombosis in infants and children and their response to factor and non-factor replacement therapies, anticoagulation and transfusion. Epidemiological studies in paediatric thrombosis have been facilitated by establishment of national and international registries collecting paediatric, real-world data. Increasing rates of hospital-aquired thromboembolism (5) highlight the need for a better understanding of risk factors and the role of thromboprophylaxis in children. Recent paediatric anticoagulation trials have significantly increased the amount of randomised control data in children that can now be used to better guide anticoagulation management.

Meet the expert 2: Quality issues & challenges in haemostasis laboratory

Katrien Devreese
Ghent University Hospital, Belgium.

The haemostasis laboratory knows many challenges. Different topics will be discussed, amongst them reagent lot-to-lot verification, the mixing test as reflect test, coagulation factor measurement in haemophilia and other bleeding disorders, aspects in laboratory diagnosis of Antiphospholipid Syndrome, thrombophilia testing, anti-Xa monitoring. This will be an interactive session where daily practice will be shared and with time for Q&A and discussion.

Meet the expert 3: How I treat immune thrombocytopenia

Raymond Wong
Head, Division of Haematology, Department of Medicine & Therapeutics, The Chinese University of Hong Kong.

Immune thrombocytopenia (ITP) is an autoimmune disease affecting blood platelets that causes thrombocytopenia and an increased risk of bleeding. It is the most common cause of an isolated thrombocytopenia in clinical practice. Current understanding of ITP pathogenesis indicates that it is a complex and heterogeneous condition resulting from a combination of humoral and cell-mediated attacks on platelets peripherally and megakaryocytes in the bone marrow. The diagnosis is typically made by the exclusion of the known causes of thrombocytopenia and a gold standard diagnostic test for ITP is lacking. Over the last decade, there have been numerous developments and changes in treatment practices for the management of patients with immune thrombocytopenia (ITP). First-line therapy is indicated for patients with bleeding complications or who are at increased risk of bleeding. The standard first-line treatment includes corticosteroids, intravenous immune globulin (IVIG) or Rh_o(D) immune globulin (anti-RhD) but many patients relapse after stopping treatment. Second-line therapy includes other immunosuppressive agents, rituximab, thrombopoietin receptor agonists or splenectomy. This presentation will discuss the latest advances in the management of ITP.

State of the Art Lecture 1

Quality & standardisation in haemostasis: are we there yet?

Emmanuel J Favaloro
Centres for Thrombosis and Haemostasis, Westmead Hospital, NSW, Australia.

Measuring quality in the fields of thrombosis and haemostasis (T&H) testing may take several forms. Ideally, measures of quality include accuracy and precision of tests used to diagnose conditions or diseases. The laboratory tends to use surrogates of these quality assessments, by use of internal quality control testing and external quality assessment (EQA) to provide evidence for the quality of their test procedures. Standardisation and harmonisation of test procedures aims to provide similar outcomes in different laboratories when they are using essentially similar test procedures. There are a number of organisations that can provide guidance to improve test quality, standardisation and harmonisation. Pre-eminent among T&H societies is the International Society on Thrombosis and Haemostasis, which provides guidance across several haemostasis tests, primarily through various specific Scientific Standardisation Committees (SSCs). For EQA, there are several organisations, either geographically based, or International in nature, that provide assessment services for most of the tests of haemostasis. This talk discusses these issues, to attempt to answer the question: Quality & standardisation in haemostasis: are we there yet?

Symposium 3A: Bleeding in Woman

Management of inherited bleeding disorders in pregnancy

Thynn Thynn Yee
Katharine Dormandy Haemophilia and Thrombosis Centre, Royal Free Hospital, Pond Street, London NW3 2QG

The journey of women with inherited bleeding disorders considering to start a family is led by a multidisciplinary team in a joint haemostasis and obstetrics clinic. It encompasses from preconception to outcome of delivery and post-delivery care.

Symposium 3B: Quality Assurance in Coagulation Laboratory

Method validation and verification for coagulation analysers and methods

Steve Kitchen
Lead Scientist, Sheffield Thrombosis and Haemostasis Centre, Royal Hallamshire Hospital, Sheffield, UK.

The requirements for medical laboratories related to quality and competency have been recently updated by the International Standards Organization(1). This mandates that the laboratory should select and use methods which have been validated for their intended use to ensure the clinical accuracy of that method when used for patient testing. Preferred methods are those specified in the instructions for use provided by the manufacturer or methods which have been published in authoritative text books, peer reviewed literature or included in international or national consensus guidelines or regulations. When the method has been validated by the manufacturer then the lab needs to verify the claims of that manufacturer prior to local use where those claims are relevant to how the method will be applied. Coagulation laboratories sometimes use methods which are not supported by manufacturer validation, either because the lab has developed their own test in the absence of a suitable commercial version or where the lab has introduced a significant local modification to the method, or used a method outside the manufacturers stated intended use. In these cases, ISI 15189 requires the lab to perform a full validation which is more detailed than a local verification. The International Council for Standardisation in Haematology (ICSH) have recently published two guidance documents to assist coagulation laboratories in the evaluation and verification of haemostasis analyser-reagent test systems both in relation to screening tests (2) and for specialist tests and calibrated assays (3). Recognising that coagulation laboratories dealing with rare diseases often need to put in place laboratory developed tests, and recognising the particular difficulties these present, ICSH is developing guidance in this area of haemostasis which is not yet published at the time of writing.

Symposium 3C: Bleeding History

How to take a bleeding history and bleeding assessment tool (checklist)

Grace Lee Wan Chieng
Haematology Unit, Department of Medicine, Sarawak General Hospital, Malaysia.

Patients presenting with bleeding manifestation is a commonly encountered clinical scenario, and taking a detailed bleeding history is a fundamental step to assist in identifying the underlying aetiology, whether inherited or acquired bleeding disorders. Taking a comprehensive bleeding history in patients with bleeding disorder is important to guide subsequent specific laboratory tests in haemostatic functions, as well as the need for family screening if inherited bleeding disorder is suspected. Several Bleeding Assessment Tools (BAT) have been proposed and used to improve the collection and reproducibility of the bleeding history. In recent years, various work of standardization and validation have been done to overcome some of the limitations in the older versions of BAT. The ISTH-SSC bleeding assessment tool is a widely-used structured questionnaires intended to guide the diagnosis of hereditary bleeding disorders in adults and children. It is a validated bleeding scoring system which collects data on the frequency and severity of bleeding symptoms. Clinicians and other healthcare professionals should be adequately trained to utilize BAT to assist them in reaching a diagnosis and proceed with relevant coagulation testing in a judicious manner.

Addressing psychosocial issues in women with bleeding disorders

Chiew Ling Choo
Faculty of Medicine & Health Sciences UNIMAS.

Women and girls with bleeding disorders face significant psychosocial issues alongside physical challenges. This session emphasizes the importance of addressing these psychosocial issues and the role of mental health support in promoting their well-being. Bleeding disorders, such as von Willebrand disease and haemophilia, impact women and girls through heavy menstrual bleeding and increased complications during childbirth or surgery. The psychosocial impact of these conditions is often overlooked, leading to emotional distress, social isolation, stigma, reduced quality of life, and negative self-perception (McLintock, 2018). Mental health support is crucial, providing counselling, therapy, and psychoeducation to manage anxiety, depression, and stress related to living with a bleeding disorder. Mental health support plays a crucial role in addressing the psychosocial well-being of women and girls with bleeding disorders. Increased awareness of the emotional impact associated with these conditions is essential for individuals to navigate the emotional challenges they face. Support groups offer valuable peer support and shared experiences, reducing isolation. Collaborations among healthcare providers, haematologists, and mental health professionals ensure comprehensive care that addresses both physical and psychosocial aspects. By recognising and addressing the psychosocial issues faced by women and girls with bleeding disorders and providing targeted mental health support, we can enhance their overall quality of life and promote holistic well-being.

Symposium 4A: Thrombosis in Pregnancy

Management of antiphospholipid syndrome (APLS) in pregnancy

Veena Selvaratnam
Clinical Haematology Reference Laboratory, Department of Haematology, Hospital Ampang.

Antiphospholipid syndrome is an autoimmune acquired disorder that generally presents with thrombosis. These episodes of thrombosis usually occur out of the blues; most times without any apparent predisposing cause. Pregnancy is a physiologically procoagulant state that increasing the risk of mothers to develop blood clots. As such pregnancy with APLS puts a mother at a higher risk to develop thromboses. Managing pregnant patients with APLS poses a challenge to both obstetrician and haematologist. The care is usually tailored for each patient based on their clinical presentation, previous history as well as their current problem and as such most treatment is individualised. It remains important to have a combined care and regular MDT to ensure that the patients progress and treatment plan is shared with the respective managing teams as it may vary as the pregnancy progresses. This presentation will focus on the various stages of pregnancy and the potential problems that physicians may face when dealing with pregnant mothers with APLS; offering some possible solutions in managing these challenges.

Symposium 4B: Challenges in Inhibitor Assay & Laboratory Diagnosis of Antiphospholipid Syndrome (APLS)

Inhibitor assay: Shortcomings and diagnostic challenges

Steve Kitchen
Lead Scientist, Sheffield Thrombosis and Haemostasis Centre, Royal Hallamshire Hospital, Sheffield, UK.

When investigating an isolated prolonged APTT where the APTT does not return to normal on a mixture of patient and pooled normal plasma the differential diagnosis between possible lupus anticoagulant and specific factor inhibitor such as FVIII inhibitor in acquired haemophilia A can have immediate and major impact on clinical management decisions. Recommendations on construction of FVIII inhibitor assay has been recently published by the International Council for Standardization in Haematology (1). Whilst these are focused on type 1 inhibitors the principles can be applied to assays for auto antibodies to FVIII and similar guidance on other specific coagulation inhibitors is expected in early 2024. Chance finding cases of lupus anticoagulant may not be actively managed and where these are considered clinically irrelevant it should be noted that the detection rate of these is lower if a lupus incentive APTT reagent is used for APTT testing done outside of the specific local protocol for testing of symptomatic patients for possible clinically relevant lupus anticoagulant/ antiphospholipid antibodies. When considering how to perform assays for lupus inhibitor and antiphospholipid antibodies there are published guidelines from ISTH/SSC to assist laboratories in which tests to do and in the technical details (2,3). ISTH recommend that a β_2 GP1 dependant anti- cardiolipin antibody assay and an anti- β_2 GP1 antibody assay should be included in the panel of tests, and that the β_2 GP1 should be of human origin (4). This is because positive results in both of these along with a positive phospholipid dependant test for LA (ie triple positivity) has particular clinical relevance. One particularly challenging issue is how to perform test for LA in the presence of oral FXa and oral IIa inhibitors (also collectively termed DOACs) which are increasingly used worldwide. Detection of LA should not be attempted in patients on DOACs unless the drug is removed or neutralised prior to testing the sample. Several methods are available for this including DOAC stop which successfully removes rivaroxaban, apixaban, edoxaban and dabigatran. The effects of DOAC on dilute Russell`s viper venom time (DRVVT) are drug and method dependant so local protocols in use for DOAC removal should be based on DRVVT method specific data.

APLS: Updates in laboratory testing and diagnostic strategies

Beverley J Hunt OBE
Kings Healthcare Partners, Thrombosis & Haemophilia Centre, GSTT, Strategic Lead in Laboratory Haematology for Synnovis, Trustee & Founder of Thrombosis UK.

Antiphospholipid syndrome (APS) is a difficult disease: both to diagnose and to treat. Detecting antiphospholipid antibodies requires three different tests. The tests are the notoriously misnamed “lupus anticoagulant test (not a test for “lupus” or an “anticoagulant”) and needs to be performed in parallel with anticardiolipin antibody and anti- beta-2 glycoprotein I testing and these tests have been covered by Dr Kitchen. These tests must be repeated after 12 weeks because there are a number of conditions that will acutely generate transient antiphospholipid antibodies, so the repeated testing is important. Furthermore, all three tests are required as there are many patients who are only positive for one test (“single positive”) or two tests (“double positive”). Many are triple positive and as a group have the highest thrombotic risks. Diagnosing thrombotic APS is relatively easy: it is the presence of thrombotic and positive antiphospholipid testing. However, thrombosis in APS is different from the inherited thrombophilia which increased risk of venous thromboembolism only, for those with APS may have thrombosis in any macrovascular or microvascular bed. APS should be considered in those with thromboses at usual and unusual sites such as splanchnic vein or cerebral venous sinus thromboses as well as those with thrombotic myocardial infarction or stroke. Indeed, APS is said to responsible for 40% of your stroke patients (< age 40 years). Obstetric APS is more complex to diagnose because there are multiple categories. While antiphospholipid antibodies do not cause infertility,

they can cause recurrent first trimester loss probably through direct inhibition of early foetal growth. Once a placenta is formed, some women have antiphospholipid antibodies that cause placental thrombosis, which can result in intra-uterine death, foetal growth restriction, pre-eclampsia and placental abruption. Thus, any birth before 34 weeks due to severe intra-intrauterine growth restriction and/or pre-eclampsia/eclampsia should have testing for antiphospholipid antibodies. What is so interesting about obstetric APS is that not all women with antiphospholipid antibodies have problems in pregnancy, and those with have recurrent first trimester loss tend not to have placental thromboses and vice versa.

Symposium 4C: Laboratory Investigations

Lab methods for bleeding disorder

Nurasyikin Yusof
Pathology Department Hospital Canselor Tuanku Mukhriz UKM Medical Centre.

The abnormal bleeding is defined as bleeding following an injury or spontaneous bleeding which is prolonged and excessive. The abnormal bleeding is as a result of imbalance of the haemostatic equilibrium. The causes include reduced coagulation factors, platelets or increased in fibrinolytic factors or anticoagulant protein as well as vascular causes. Laboratory investigations for abnormal bleeding usually involve a step-by-step process which include initial coagulation screening test followed by the confirmatory tests based on the suspected differential diagnosis. Many tests are present but not many are available in haemostasis lab. They are mostly specialised test, expensive or used in research only. In developing country like Malaysia, the diagnosis of bleeding disorder involved careful and thorough history taking and physical examination, initial screening testing and provision of some common specialised test such as VWD panel, factor assay, inhibitor assay and platelet aggregometry. Communication with other experts is important for the provision of further tests especially in molecular testing or other highly specialised tests.

Pre-analytical variables in coagulation testing

Suzana Zainol
Haematology Laboratory, Department of Pathology, Hospital Tunku Azizah, Kuala Lumpur.

Pre-analytical phase refers to all related procedures that occur from the ordering of tests right until the time before the actual tests analysis begin. Coagulation testing is subjected to many pre-analytical variables, which include selection of patient, specimen collection, specimen transport & stability and specimen processing & storage. It is important to address this component of laboratory testing, as it is still the highest possible source of errors, and could affect the sample integrity, quality and accuracy of routine and specialised coagulation test results. International guidelines and recommendations are available as references to establish and implement the best practice policy. Awareness of potential issues arising from pre-analytical variables among all involved clinical and laboratory healthcare personnels is crucial. Continuous education and training, strict adherence to the procedures and regular monitoring of compliance to the best practice procedures, are important measures in reducing pre-analytical errors, thus ensuring better and safe patient care.

Review laboratory results, interpretation and follow-up

Yap Yee Yee, Mandy
Department of Haematology, Hospital Ampang.

In managing patient with bleeding disorder, apart from taking a good bleeding history, it is instrumental to interpret the basic screening haemostasis tests carefully before deciding the next step of investigation. The PT/APTT tests representing the intrinsic & extrinsic pathway in vitro do not reflect the actual coagulation cascade in vivo. This dynamic process will cause the variation in the tests results and hence the importance of repeating the tests in different time point. The mixing studies is developed to resolve the prolonged PT/APTT in order to differentiate between factor deficiency and inhibitor such as acquired haemophilia or lupus anticoagulant. One must remember to follow-up with the results and continue to investigate with specific factor assay or lupus anticoagulant to arrive at a correct diagnosis. Occasionally, there may be no answer can be found due to the limitation of the tests especially in those patients with bleeding of unknown cause. Hence, reviewing the patient frequently while correlating with the results may be able to provide a more holistic approach to some of these enigma bleeding disorders.

Symposium 5A: Haemophilia

Choice of factors and non-factors in the management of haemophilia

Zulaiha Muda
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The overall goal of haemophilia treatment is to provide patients with a normal life as much as possible by preventing and treating the bleeds, minimising the risk of long-term complications associated with joint damage, improving quality of life while minimising treatment burden. Prophylaxis with factor replacement therapies has been a standard of treatment for many years. Standard half-life (SHL) replacement necessitates frequent intravenous infusion can be a challenging to all patients with haemophilia especially for children, leading to sub optimal adherence. Extended half-life (EHL) is now available to address these issue. Non- Factor replacement (NFR) provide more convenient subcutaneous administration but adjunct factor replacement remains indicated in bleeding episode or invasive procedure. This talk will cover the pros and cons of SHL, EHL and NFR. Practical approach in using of one treatment modality over the other will be discussed in particular with regards to factors that influence treatment options.

Non-factor therapies in haemophilia and monitoring during surgery

Mike Laffan
Department of Haematology,Imperial College London, London, UK.

The problems of intravenous injection, unhelpful pharmacokinetics and inhibitor formation have prompted the development of alternative ways to correct the haemostatic defect in haemophilia and restore thrombin generation. The only non-factor therapy currently licensed is emicizumab for haemophilia A. This is a bispecific antibody which mimics the action of FVIII by bringing together FIXa and FX to reproduce the intrinsic Xase. Although the antibody does not bind phospholipid itself, the complex remains PL dependent. Because it lacks an activation step like FVIII, the APTT is significantly shortened even by low levels of emicizumab and a standard FVIII assay is not possible. Nor can standard FVIII assays be used to measure the degree to which haemostasis has been corrected. The pharmacokinetics of emicizumab are favourable for prophylaxis and do not require monitoring. However, the estimated equivalent FVIII level is approximately 10-15%. This means that for anything other than minor surgery, additional FVIII replacement will be required. In this circumstance the FVIII replacement can be monitored using a chromogenic substrate assay in which at least one of FIX or FX are of non-human (usually bovine) origin. This makes the assay independent of emicizumab which does not bind to non-human factors. Monitoring replacement is therefore straightforward with this provision. Similarly, the chromogenic assay should also be used for inhibitor assays. Other non-factor approaches include the 'rebalancing therapies' which rely on the inhibition or reduction of natural anticoagulants to allow increased thrombin generation. However, these are not yet licensed and will not be considered in full. They also pose difficult challenges for measurement and calibration of effect. Rebalancing has a number of potential advantages but may also run the risk of increasing thrombosis risk and of producing off target effects.

Haemophilia genetic testing

Yuslina Mat Yusoff
Haematology Unit, Cancer Research Centre, Institute for Medical Research, National Institute of Health, Setia Alam, Selangor, Malaysia.

Haemophilia A and haemophilia B are rare congenital, recessive X-linked disorders caused by lack or deficiency of clotting factor VIII (FVIII) or IX (FIX), respectively. The severity of the disease depends on the reduction of coagulation FVIII or FIX activity levels, which is determined by the type of pathogenic variants in the genes encoding the two factors (F8 and F9 genes, respectively). Genetic analysis in haemophilia has tremendously improved in the last decades. It is important in defining disease biology, establishing the diagnosis in difficult cases, predicting the risk of inhibitor development, identifying female carriers, and providing prenatal diagnosis when required. Advances in genetic variant detection strategies facilitate the identification of the causal variants in most patients, which may establish the genotype and phenotype correlation. Many new techniques and modifications as well as analysis software became available, which made the genetic analysis and interpretation of the data faster and more accurate. Genetic analysis should be offered to all people with haemophilia and their 'at-risk' female family members. The outcome allows genetic counselling of the affected families.

Symposium 5B

Home therapy

Timothy Achan Anak Banyah
Sarawak General Hospital.

The best way to treat haemophilia is to replace the missing blood clotting factor so that the blood can clot properly. This is typically done by injecting treatment products, called clotting factor concentrates, into a person's vein. Today, it's possible for people with haemophilia, and their families, to learn how to give their own clotting factor treatment products at home. Giving factor treatment products at home (Home Therapy) means that bleeds can be treated quicker, resulting in less serious bleeding and fewer side effects. Unfortunately, not all haemophilia patients in Malaysia are practicing home therapy. Patients with both haemophilia A and B, particularly those with severe disease, are at risk for life threatening bleeding, including intracranial bleed, bleeding into a joint (hemarthrosis) or muscle is more common and leads to substantial disability from pain and loss of mobility. As a person with severe haemophilia A, I was invited by my doctor to share my experience on how I manage my bleeding disorder with home therapy. My own testimony will be the reason why it is important for medical practitioners to teach home therapy to patients and their caregivers.

Symposium 6A: Laboratory Monitoring in the Era of Novel Therapy

Chromogenic and one stage assays in extended half-life (EHL) factor replacement therapy

Steve Kitchen
Lead Scientist, Sheffield Thrombosis and Haemostasis Centre, Royal Hallamshire Hospital, Sheffield, UK.

One stage assays based on APTT have been the most commonly performed type of factor VIII (FVIII) and factor IX (FIX) assay for many years. Chromogenic assays have been developed in which purified coagulation proteins are used to create conditions where the concentration of FVIII or FIX is rate limiting in generation of factor Xa followed by cleavage of a small specific peptide releasing a yellow colour. The world federation of haemophilia recommends that both types of assays are used in the initial work up of cases under investigation for possible mild haemophilia A in order that case are successfully diagnosis, so haemophilia centres should establish both types of FVIII assay for diagnosis. When it comes to replacement therapy results of one stage and chromogenic FVIII or FIX assay give different results in the presence of some extended half-life or modified proteins. Small differences do not impact on management but in some case the differences are marked. There are reports of two-fold differences in relation to a number of modified products and up to 10 fold differences have been reported. There is no consensus on the degree of difference that will affect management decisions but agreement within 25-30% has been sued as acceptable in a number of laboratory assay studies. Where larger differences occur any monitoring should be done with an assay which agrees with the assay used by the manufacturer for concentrate potency assignment since the units of potency are used when setting dosing recommendations via clinical trials. Because of these differences the laboratory should select an assay for monitoring a product which has been specifically validated for that product. There are important differences in the composition of APTT reagents used in one stage assay, with different activators and different phospholipids, so results of one stage assays in the presence of some EHL products are not interchangeable. Recognising the importance of careful selection of an assay for monitoring a particular product the WFH have made product specific recommendations on which assays can be used safely with specific concentrations.

Symposium 6B: Carrier Screening & Importance of Physiotherapy and Dental Check-ups in Haemophilia

Carrier Screening – who to screen?

Betty Ho
Department of Paediatrics, Sarawak General Hospital.

Most severe forms of haemophilia typically affect males; females have conventionally been designated as "carriers". Carriers often do not show symptoms of haemophilia, however, because they have an abnormal Factor VIII or Factor IX gene on one X chromosome and one normal gene on the other X chromosome, their factor level is at a lower limit of normal range. A female who has a factor VIII or factor IX pathogenic variant is called an obligate carrier of haemophilia. Testing for carrier status is important for several reasons, if found to be negative, it is reassuring. If positive, then it can cause bleeding in carriers with lower-than-normal factor levels and they may need treatment for some events, such as dental procedures and surgery. Planning for future pregnancies is also important for the carriers and special precautions will need to be taken for both the mother and baby during pregnancy, labour and delivery. However, the purpose of carrier testing is not to discourage having children, but rather to promote better health for the mother and baby.

Importance of dental check-ups

Shim Chen Kiong
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Prevention is always better than cure for dental patients with bleeding disorders or on anticoagulants. Therefore, frequent dental check-ups and impactful oral hygiene instructions are important to prevent having to do invasive dental procedures on such patients.

State of the Art Lecture 2

Von Willebrand disease and inherited platelet disorders: Update on diagnosis & management

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Von Willebrand disease (VWD) continues to pose difficulties for both diagnosis and management. Several new guidelines and reviews have been published in recent years but these have not resolved the problems. The first challenge in diagnosis is to find an assay that reliably assesses the multiple *in vivo* functions of VWF under the physiologically relevant condition of shear stress. The development of automated assays that do not require the use of ristocetin may prove beneficial in this respect but effects of multimer composition may still not be fully captured. The second major problem in diagnosis has been defining of the level of activity for normal haemostasis. Many individuals have levels of VWF activity which are below the lower limit of normal but only a fraction of these have a significant bleeding tendency. The diagnostic category of 'low VWF' remains useful for this group, although it has been abandoned by some guidelines. New categories have been added and the wider use of genetic analysis has helped clarify some problems. Better recognition and diagnosis are important objectives particular in young women with heavy menstrual bleeding. Treatment of VWD remains based on either desmopressin or replacement therapy. A recombinant VWF concentrate is now available and has additional benefits of higher specific activity and a slightly longer half-life than plasma preparations. It contains no FVIII which demands additional thought when rapid replacement is required but this can easily be managed. Prophylaxis remains difficult for VWD but is being recognised as important for a wider group of patients. Non-coagulant effects on angiogenesis may also prove to be important. Whole genome sequencing has helped identify many novel genes responsible for hereditary thrombocytopenia which is valuable for two principal reasons. Firstly, it prevents inappropriate diagnosis of ITP and consequent unnecessary therapies. Many variants with significant population frequencies can be combined to form polygenic scores predicting the likely platelet count and so indicating whether it is pathologically different. Secondly several of these genes confer a broader phenotype including deafness and an hereditary tendency to leukaemia. Genetic analysis has also helped functional understanding by clarification of other disorders such as Grey platelet syndrome and helped clarify the role of collagen receptors in bleeding phenotypes. Unfortunately, therapy for these disorders remains limited.

Session 4A: Venous Thromboembolism

Implementing venous thromboembolism pathways in hospitals

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Clinicians often have greater apprehension about bleeding than clotting. This is despite coronary, cerebrovascular, and venous thromboses are the leading killers of adults in ICU. Venous thromboembolism is a deadly disease and poses a significant growing public health concern. Fifty percent of venous thromboembolism (VTE) cases are health care associated. 50-75% of VTE cases occur on medical service where 5-10% of inpatient deaths are due to fatal PE. Implementing VTE pathways in a hospital requires a collaborative effort from multidisciplinary teams primarily physicians, pharmacists, nurses, dietitians and laboratory side. It requires a focused team review of VTE patients, performing VTE risk assessment in all hospitalised patients and its thromboprophylaxis practices. Development of simplified guides and pathways adapting to local practices as well as supporting appropriations to increase awareness of health care providers. Finally integrating a data collection and tracking systems for outcome measurements to improve health care delivery.

Management of paediatric thrombosis including the use of direct oral anticoagulants (DOACs)

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One of the primary sources of guidance for the treatment of venous thromboembolism (VTE) in children are the American Society of Haematology (ASH) guidelines published in 2018 (1). Many of the recommendations were based on observational data in children or extrapolation from adult data, with little randomised control trial (RCT) evidence available at the time. Since the publication of these guidelines, there have been a number of RCTs involving children with VTE. This is primarily

due to trials of direct oral anticoagulants (DOACS) which to date have included more than 2000 children. These trials provide evidence about DOACs but also the standard of care agents low molecular weight heparin (LMWH) and warfarin. They have demonstrated the safety and efficacy of rivaroxaban and dabigatran for the treatment of acute VTE in children, including patients with venous sinus thrombosis (2, 3). Trials of addition agents are ongoing (apixaban) or awaiting publication (edoxaban). In addition, the Kids-DOTT study (4) showed that 6 weeks of anticoagulation for children with provoked, symptomatic VTE was non-inferior to 3 months in patients without occlusive thrombus at 6 weeks. In these paediatric VTE trials there was a low incidence of major bleeding and VTE recurrence, highlighting the difficulties in powering studies adequately. A number of challenges and questions remain. What is the best treatment option for neonates and pre-term infants? Are DOACs an option for patients with prosthetic heart valves, antiphospholipid syndrome, vascular anomalies, gastrointestinal disease, renal or hepatic impairment? Should drug levels be measured in some patients? How should bleeding be managed? Real-world data from post-trial surveillance and paediatric thrombosis registries such as Throm-PED is important to help answer some of these questions. Given the new data available, the 2018 ASH guidelines are currently undergoing an update with publication expected in early-mid 2024.

Session 4B: Advances in Laboratory Assessment of Haemostasis Disorders

Anti Xa assays: current role in therapy

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Monitoring of anti-Xa agents have several issues as following.
Which anti-Xa agents is used?
Which monitoring test is used?
Which methods are selected, continuous injection or 1 or 2 times administration per day?
Which values are measured, peak or trough value?
What is the underlying disease?
Is the prophylaxis or treatment for thrombosis
Which anti-Xa kit is better?

I would like to introduce several reports and our data, and discuss the above points and indicate the usefulness of anti-Xa assay.

The controversies in D-dimer and thrombophilia testing

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D-dimers are breakdown products of fibrin and serve as a marker of recent or ongoing thrombosis. As thrombosis take place in both physiological and pathological states, D-dimers are ubiquitous and measurable even in normal physiological situations. Raised levels in concert with other laboratory and clinical parameters have long been used for diagnosing disseminated intravascular coagulation. On the other hand, D-dimers with lower cut-off values have been well-validated as a negative predictor of venous thromboembolism (VTE). Its use as a predictor for recurrent VTE and other thrombotic disorders in both acute and chronic conditions and in the prognostication of outcomes in critically ill patients is less well-defined. COVID-19 and the evolving concept of thrombo-inflammation has put further focus on the role of D-dimers in the management of our patients. Much like D-dimers, our understanding of the role of thrombophilia testing and our practices has evolved over time with better data on the risk of recurrent VTE in patients especially with spontaneous idiopathic VTE. Greater acceptance of long-term anticoagulation with the wider use of direct oral anticoagulants has led to more selective thrombophilia testing, confining them to situations where their result makes a difference to management decisions. Our priority for the future will be to continue refining the selection of patients for testing as well as develop tests that better predicts for recurrence, in particular for acquired thrombophilic conditions.

Clot waveform analysis: application in diagnosis and management of haemostatic disorders

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Various assays are used to evaluate the blood coagulation system, including the activated partial thromboplastin time (APTT) and prothrombin time (PT). Because APTT and PT are inexpensive and are relatively easily performed, they are frequently used as routine assays. The information APTT and PT can provide are limited. The routine APTT measurement reflects the cascade system in plasma. However, it does not fully reflect thrombin burst or enhancement of clotting. The automated coagulation analysers have the ability to show the clot reaction curve of the PT and APTT and can reflect thrombin burst and enhancement of clotting activation. The ability to show the clot reaction curve is designated as clot waveform analysis (CWA). PT-CWA is used for monitoring of the effects of anticoagulants and estimation of the coagulation status of patients.

APTT-CWA is used for evaluation of the activity of coagulation factors, monitoring of haemophilia therapy, assessment of severity of DIC and prediction of major bleeding or poor outcome. APTT-CWA has abnormal patterns in subjects with COVID-19. The clot fibrinolysis waveform analysis (CFWA) was applied in haemorrhagic disorders. Hyperfibrinolysis can be evaluated by this modified CWA which is possible with the addition of tissue plasminogen activator. CWA is useful for the differential diagnosis of various haemostasis disorders and for the monitoring of thrombophilia patients under anticoagulation. We can expect the future development of more useful applications with modified CWA such as CFWA.

Global haemostasis tests: application in haemostasis disorders

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Physiologic haemostatic thrombus formation is a process that involves the harmonious operation of blood vessels, platelets, coagulation factors, coagulation regulatory factors, fibrinolytic factors, fibrinolysis-inhibiting factors, haemodynamic factors, and perivascular connective tissue. The cause of bleeding tendency and predisposition to thrombosis is predicted by subjective and objective symptoms, interview, background disease, family history, and medical examination. The thrombin generation assay (TGA) is a highly sensitive method for detecting thrombin generation prior to fibrin formation and is not affected by fibrinogen. The assay can also be performed on platelet-rich plasma samples, allowing evaluation of the coagulation function in the presence of platelets. The coagulation is initiated by FVIIa/tissue factor, and thrombin production during the coagulation process is monitored and depicted as a waveform, with parameters such as lag time, peak thrombin, time to peak, and total thrombin production calculated. It is expected to be further applied to the evaluation of coagulation function and bleeding risk in haemorrhagic diseases and risk assessment of thrombotic diseases. Thromboelastography (TEG) is a comprehensive coagulation function evaluation method that is expected to develop as a haemostatic function test, using whole blood to evaluate coagulation, fibrinolysis, and platelet function. It is a method to evaluate coagulation function by monitoring the coagulation viscosity and elasticity changes during the coagulation process and depicting the process as a waveform. Although reproducibility has remained a problem, the improved ROTEM (rotational thromboelastometry) has been developed and computerized, making it possible to calculate and analyse various parameters such as clotting time, clot formation time, maximum clot firmness, and so on. The system can be applied to a wide range of fields, including haemostasis monitoring in haemorrhagic diseases and perioperative haemostasis monitoring. The total thrombus-formation analysis system is an instrument for analysing the thrombus-formation capacity of whole blood in the bloodstream. The PL chip is designed to measure the thrombus-formation capacity of whole blood under the flow of high sheer stress with the anticoagulant agent hirudin. The AR chip is designed to evaluate the thrombogenic potential of whole blood, including coagulation and fibrinolysis factors, by passing the whole blood through a channel in which tissue factor is solid-phased in addition to collagen.

Session 4C: Venous Thromboembolism Prevention and Treatment

Risk factors for VTE

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Venous thromboembolism (VTE) is the third most common cause of death worldwide. The incidence of VTE varies according to different countries, ranging from 1–2 per 1000 person-years in Western Countries, while it is lower in Eastern Countries (<1 per 1000 person-years). The most identified risk factors for VTE, including trauma and fractures, pregnancy, immobilisation, antiphospholipid syndrome, surgery and cancer. There other common risk factors are male sex, diabetes, obesity, smoking, hereditable thrombophilia, oral contraceptives and hormonal replacement, long-haul flight, residual venous thrombosis, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The pathogenesis of VTE is, however, complex, and other mechanisms, including endothelial damage, macrophages, red blood cells and platelets, have been investigated.

Who should be given thromboprophylaxis (checklist)

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As VTE is a preventable disease in many cases, an early risk stratification of patients with the identification of high-risk patients may lead to more effective therapeutic strategies. Several risk stratification models have been proposed to help clinical judgement, but consensus about the best one to use is still lacking. For instance, in hospitalised medical patients, the most widely evaluated were the Caprini, the Padua and the IMPROVE scores. Some have been externally validated and showed fair discrimination in identifying patients at increased risk of VTE. However, they have not been extensively validated for guiding decisions about who should receive thromboprophylaxis. Bleeding risk assessment is necessary for adequate prophylaxis prescription and should be carried out concurrently with assessment of the risk of thrombosis.

Anticoagulants, bleeding complications, reversal agents and laboratory monitoring

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Bleeding is a major concern in anticoagulation therapy, with risks depending on factors like age, renal function and concomitant medications. Coagulation tests vary for each anticoagulant where PT/INR test is more established in warfarin patients and aPTT test is more used in heparin patients. The management of bleeding due to anticoagulant medications varies depending on the specific anticoagulant used. In the case of warfarin, prothrombin complex concentrate (PCC) is the primary agent for reversing its effects. PCC contains factors antagonised by warfarin and can rapidly normalise the INR within 10 minutes. If PCC is unavailable, fresh frozen plasma (FFP) can be an alternative but is slower and less effective in correcting INR. Vitamin K can also be used. Usually, it takes 4-6 hours for onset and up to 24 hours for complete INR normalisation. For heparin and low molecular weight heparin (LMWH), protamine sulfate is the specific reversal agent. Protamine is able to completely reverse heparin, but can only partially reverse LMWH. Protamine dose should not be more than 50mg per dose and rate of infusion should not be more than 5mg per minutes. Fondaparinux does not have a specific reversal agent, but recombinant factor VIIa (rVIIa) and FEIBA can be used to manage bleeding. Data on the efficacy of these agents are limited. Dabigatran can be reversed using idarucizumab, a specific antidote. The dose is 5 gram per patient and dabigatran presence in body must be confirmed before administering idarubizumab. Haemodialysis can be used to remove dabigatran from the body in severe cases or in patient with impaired renal function. For DOACs, andexanet alfa is the specific reversal agent, but it may not be widely available. Four-factor PCC is an alternative option. Fluid replacement may help to increase clearance. Haemodialysis is generally not effective for DOAC removal.

Session 5: Paradoxical Thrombosis

Thrombotic thrombocytopenic purpura (TTP): New mechanisms, diagnosis and treatment

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Detecting severe deficiency of a plasma enzyme ADAMTS-13 (<10%), is diagnostic of a life-threatening but rare disease called thrombotic thrombocytopenic purpura (TTP; 2-6 per million population, 20% mortality) that affects females three times more than men. ADAMTS-13 is a circulating enzyme that specifically cleaves the ultra-large multimeric von Willebrand factor (VWF) and regulates shear-dependent platelet glycoprotein Ib-mediated thrombus growth and blood vessel occlusion. In addition to the immediate presentation of end-organ thrombotic damage of stroke, myocardial infarction, gut ischaemia and renal damage, long-term morbidity (hypertension, depression, loss of memory, headache) is attributed to occult microthrombi causing tissue damage at the time of presentation. New advances in ADAMTS-13 testing and antibody detection, latest acute treatment strategies with Caplacizumab and Rituximab and long-term prevention of events with ADAMTS-13 replacement therapy have recently been described. The interpretation of an ADAMTS-13 activity level secures the diagnosis of thrombotic thrombocytopenic purpura (TTP) and defines the success of treatment and TTP relapse. If the ADAMTS-13 activity is low, ADAMTS-13 antibody assessment differentiates immune-mediated (iTTP) from congenital (cTTP). ADAMT-13 activity uses different assay methods (FRETS, ELISA or chemiluminescence), as does autoantibody testing (ELISA immunoassay or functional Bethesda Unit (BU) assay). Therefore, there is an unmet need for international standardisation of ADAMTS-13 testing and clinical interpretation of results for appropriate and cost-effective TTP management. The result of an ADAMTS-13 activity and antibody test will define a diagnosis of TTP (<10% activity) or aHUS (>10% activity) decide whether the TTP is immune-mediated (iTTP) or congenital (cTTP), guide therapeutic decisions of plasma exchange, immunomodulation with steroids and Rituximab, VWF blocking with Caplacizumab, and ADAMTS-13 replacement with fresh frozen plasma or rADAMTS-13. ADAMTS-13 testing may help monitor the duration and success of therapy and TTP relapse risk.

Thrombosis and anticoagulation in liver disease

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Patients with liver disease are at risk of both bleeding and thrombotic complications and haemostasis rebalance in such patients is complicated and delicate. Contrary to intuition, the laboratory measures of prolonged clotting times and thrombocytopenia do not predict bleeding occurrences and outcomes as most of these bleeds are driven by portal hypertension and peptic ulcer disease. Prothrombotic haemostatic changes in liver disease include impaired clearance of factor VIII, decreased levels of antithrombin, protein C &S and impaired fibrinolysis. Such changes will not be reflected on the routine coagulation tests such as PT/INR and PTT, but clinicians need to be aware that patients with liver diseases, in particular liver cirrhosis, are at risks

of thrombosis. As shown in epidemiology studies, patients with liver disease have higher risks of venous thromboembolism (VTE). Portal vein thrombosis and Budd Chiari syndrome are 2 thrombotic conditions closely associated with liver disease. Anticoagulation in patients with liver disease is often challenging, as the benefit of anticoagulation treatment need to be balanced against the potential bleeding risks. The choice of anticoagulation should be based on indications for anticoagulation, the routes of metabolism and clearance of the anticoagulation drugs, the presence of renal impairment and other bleed risks and also patient preference. Warfarin with adequate INR monitoring, is safe for use in patients with mild or moderate liver disease, but for severe liver disease warfarin treatment will be complicated if the baseline coagulation tests are abnormal. Direct oral anticoagulants (DOACs) are being used increasingly and recent systematic reviews found them safe when compared with other anticoagulants in patients with mild and moderate liver disease. Low molecular heparin (LMWH) is considered the primary therapeutic option for severe CP C liver disease, with careful follow up and anti-Xa monitoring. In summary, liver disease can lead to a prothrombotic state with increased risks of thrombosis. Judicious use of anticoagulation therapy is now considered safe and efficacious.

WORKSHOP

Antiphospholipid Syndrome (APS) workshop

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Lecture 1: Current ISTH guidelines on laboratory diagnosis of Antiphospholipid Syndrome: Lupus anticoagulant

Lecture 2: Laboratory diagnosis of Antiphospholipid Syndrome: Solid phase assays (aCL and aβ2GPI)

Practical session: Laboratory diagnosis of Antiphospholipid Syndrome: Case interpretation-focus on LA test results

The Antiphospholipid Syndrome (APS) workshop is covering the current International Society on Thrombosis and Haemostasis (ISTH) guidelines on the laboratory diagnosis of Antiphospholipid Syndrome (APS). The content includes both lupus anticoagulant (LA) testing and the solid phase assays for anticardiolipin (aCL) and anti-β2GP1 antibodies (aβ2GPI). It focuses on methodological aspects of lupus anticoagulant testing, which include sample preparation, pre-analytical variables affecting the results, selection of tests, the three-step procedures (screen-mix-confirm), interferences, result expression, interpretations of results and reporting. Equally, for aCL and aβ2GPI pre-analytical, analytical and post-analytical will be addressed. In the practical session patient cases will be presented and allows participants to have hands-on exercises on interpretations of various real-case compilations, with emphasise on LA test results.

ABSTRACT

HT001 Insulin resistance and increased risk of pulmonary embolism in leukaemia, lymphomas and related disorders

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Introduction: Pulmonary embolism (PE) is a life-threatening condition characterised by the blockage of arteries in the lungs, often resulting from blood clots originating in other parts of the body. While PE is commonly associated with cardiovascular diseases, its occurrence and risk factors in specific patient populations, such as those with haematologic cancers, remain less explored. In this study, we investigated the relationship between haematologic cancer and the development of PE, along with the potential influence of insulin resistance. *Materials & Methods*: A retrospective analysis was conducted on 119,229 patients with histology-confirmed cancer. Clinical and demographic data were collected from UK biobank. Statistical analysis included descriptive statistics, ANOVA, and logistic regression. Adjustments were made for age, sex, and diabetes mellitus status. *Results*: Among 119,229 patients with histology-confirmed cancer, 442 (0.37%) were diagnosed with haematologic cancer, which includes leukaemia, lymphomas, and related disorders. Within this group, 7 patients (1.57%) developed pulmonary embolism (PE). The mean TyG index in patients without PE was 8.75±0.56, while in patients with PE, it was 9.28±0.57. Analysis of variance (ANOVA) revealed a significant difference (F=6.15, p=0.0136) between the two groups. In logistic regression, controlling for age, sex, and diabetes mellitus status, the results indicated that insulin resistance increased the risk of PE in hematologic cancer patients by 386.5% (odds ratio [OR]=4.865, 95% confidence interval [CI]=1.253-18.891), independent of age, sex, and diabetes mellitus status. *Discussion*: Haematologic cancer patients with insulin resistance exhibited a significantly increased risk of developing pulmonary embolism, independent of age, sex, and diabetes mellitus status.

HT002 Alterations in *F8* gene and identification of eight novel variants in severe haemophilia A patients

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Introduction: Haemophilia A (HA) is an X-linked inherited bleeding disorder caused by alterations of the factor VIII gene (*F8*) which encodes for coagulation factor VIII protein (F8). *F8* gene consists of 26 exons, 186 kb in size, interspaced by 25 introns. This study aimed to identify the alterations within *F8* gene in 43 severe HA patients. *Materials & Methods*: DNA were extracted from blood samples and subjected to molecular tests including inverse-shifting PCR to detect intron 22 (int22) inversion, multiplex PCR to detect intron 1 (int1) inversion and PCR and Sanger sequencing to screen for mutations within 26 exons and exon-intron borders. Additionally, multiplex ligation-dependent probe amplification was applied to detect amplification or deletion within *F8* gene in samples which tested negative by previous methods. *Results*: *F8* gene alterations were detected in all patients. Int22 inversion constitutes the most prevalent mutation type (~44.2%, n=19), followed by point mutations which comprise 5 missense, 2 nonsense and 2 splice effects (~21%, n=9). Remaining patients were found to harbour small duplications (11.6%, n=5), small deletions (9.3%, n=4), large deletions (9.3%, n=4), indel (2.3%, n=1) and int1 inversion (2.3%, n=1). Eight of the detected mutations were found to be novel; c.732_734delinsATCATTTTA, c.788-2A>G, c.6740delA, c.5999-1G>A, c.6392G>A, c.2760_2773del, c.6533delG, c.5651delC. Among the five patients who developed inhibitor against F8 replacement in this study, four of them harbour int22 inversion, whereas the remaining patient has novel deletion, c.6740delA. *Discussion*: With the advancement in molecular genetic approaches, identification of underlying mutations in severe HA patients is made possible and these findings are essential for genetic confirmation of patients, genetic counselling, prediction of inhibitor development, planning of patients' therapy, and carrier screening.

HT003 Platelet CLEC-2 protects liver function from septic injury by inducing macrophage activation

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Introduction: Multiple organ failure during sepsis is a progressive failure of several interdependent organ systems. Liver dysfunction occurs early during sepsis, and is directly associated with the patient's death. The platelet receptor CLEC-2 prevents inflammation-induced vascular leakage and haemorrhage, but the underlying mechanism by which CLEC-2 protects liver function during sepsis is unknown. *Materials & Methods*: Mice lacking CLEC-2 in platelets or ligand PDPN in myeloid cells, and littermates were injected with *E. coli*. The molecular mechanism of CLEC-2 and PDPN regulation of liver injury during sepsis was studied by single-cell sequencing. *Results:* Transcriptome sequencing of peripheral blood from sepsis patients revealed platelet activation and binding to macrophages. Single-cell sequencing analysis of liver from septic mice showed that CLEC-2 regulates high expression of JMJD3 in macrophages. Platelets induces activation of the STAT1/JMJD3 pathway in macrophages through CLEC-2/PDPN. Immunoprecipitation showed that phosphorylated JMJD3 in macrophages binds directly to the nuclear receptor PPARα and induces downstream signaling. We searched for genes in single-cell data and found that *Irf4* is one of the direct targets of JMJD3. *Discussion*: The activated platelets penetrate the hepatic blood sinusoidal capillaries and interact with PDPN-expressing liver macrophages via CLEC-2, activating the STAT1/JMJD3 pathway, promoting nuclear entry of JMJD3 and binding to PPARα, which in turn promotes *Irf4* transcription and expression of anti-inflammatory factors, alleviating liver injury caused by sepsis. These findings reveal an important function of platelet CLEC-2 in regulation of liver macrophage activation during sepsis and a novel mechanism to protect liver function from septic injury.

HT004 Genetic associations between blood cell traits and pulmonary thromboembolism risk in Asians and Europeans

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Introduction: Previous studies have shown that various blood cell traits are associated with a higher risk of pulmonary thromboembolism (PTE), however, whether these findings reflect a causal relationship remains unclear. This study aims to assess the causal association of various blood cells with PTE risk in the Asian and European populations. *Materials & Methods*: We obtained genetic variants representing erythrocytes, leukocytes, and platelets from the genome-wide association study of Asian population (Biobank Japan) and European population (UK Biobank). Summary statistics of genetic instruments representing PTE were extracted from genome-wide association studies of Chinese Han ancestry (CURES study) and European population. We used the univariable and multivariable Mendelian randomisations to assess the causal association. Inverse variance weighting (IVW) was used as the primary analytical method for MR. Sensitivity analyses were performed to

detect horizontal pleiotropy and heterogeneity. *Results*: In Asians, genetically predicted haematocrit and platelet count were positively associated with PTE, with an odds ratio (OR) of 1.080 (CI 1.011-1.154, P=0.0223) and 1.233 (CI 1.104-1.377, P=0.0002). In Europeans, genetically predicted mean corpuscular volume, haematocrit, white blood cell count, and platelet count were positively associated with PTE, with an odds ratio (OR) of 1.183 (CI 1.047-1.336, P=0.0070) and 1.096 (CI 1.022-1.175, P=0.0100). Sensitivity analyses (mendelian randomization-Egger, weighted median, and Mendelian randomisation pleiotropy residual sum and outlier test) gave consistent estimates. *Discussion*: Genetically liability to high-haematocrit and platelet count are associated with a higher risk of PTE. Targeting these factors might be a potential strategy to prevent PTE.

HT005 Safety and efficacy of anti-human activated protein C antibody SR604 for prophylaxis of congenital factor deficiencies

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Introduction: Rebalance of coagulation and anticoagulation to achieve a haemostatic effect has recently gained attention as an alternative therapeutic strategy for haemophilia. We engineered a humanised chimeric antibody, SR604, based on a previously published murine antibody HAPC1573 that selectively blocks the anticoagulant activity of human activated protein C (APC) to improve bleeding tendency in haemophilia. *Materials & Methods*: We used Affinity maturation and molecular characterisation and Antibody-binding kinetics analysis by SPR to prepare monoclonal antibodies with higher affinity for APC and then validated the haemostatic and cytoprotective effects of SR604 in a haemophilia model and cytoprotective effects in an inflammatory state, as well as its safety under high-dose conditions, by using a mouse tail-cutting, knee injury model, LPS-induced inflammation model and monkey acute toxicity assay. *Results*: SR604 effectively blocked the anticoagulation activities of APC in various human coagulation factor-deficient plasma in vitro with affinities approximately 60 times greater than that of HAPC1573. SR604 exhibited prophylactic and therapeutic efficacy in the tail bleeding and knee injury models of haemophilia A and B mice expressing human APC (humanised haemophilia mice). SR604 did not interfere with the cyto-protection and endothelial barrier function of APC nor have obvious toxicity effects in humanised haemophilia mice. Pharmacokinetic study showed a high bioavailability (106%) of subcutaneous injection of SR604 in cynomolgus monkeys. *Discussion*: These results demonstrate that SR604 is expected to be a safe and effective therapeutic and/or prophylactic agent with a prolonged half-life for patients with congenital factor deficiencies including haemophilia A and B.

HT006 A novel minimally invasive and sustainable Factor VIII delivery system via hydrogel microneedles

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Introduction: Haemophilia A is a congenital bleeding disorder caused by Factor VIII (FVIII) deficiency. The deficient FVIII is administered via life-long prophylaxis treatment. However, frequent hypodermic injections of FVIII concentrates and needle phobia markedly reduce treatment adherence. Alternatively, hydrogel microneedle (HMN) provides sustainable drug delivery in a minimally invasive manner to improve patient compliance. Hence, the efficacy of the HMN in the transdermal delivery of a recombinant FVIII (rFVIII) concentrate (Advate) was investigated in this study. *Materials & Methods*: A HMN array was fabricated, and Advate was loaded into the HMN by dry/drop method. The entrapment efficiency (EE) and rFVIII release percentages were determined. Finally, the efficacy of HMN in mediating transdermal delivery of rFVIII was evaluated in an in-vitro Franz Diffusion Cell model. *Results:* The EE and release percentages of rFVIII were 100% and 21.18 ± 3.21%, respectively. A significant increase in HMN height was recorded post-Advate loading ($p < 0.001$). In the in-vitro study, 11.10 ± 3.55% of rFVIII was delivered via HMN, displaying zero-order release kinetics. *Discussion*: A 100% EE was achieved with the dry/drop method as the HMN absorbed all the loading solution. A significant increase in the MN height shows that the drug occupied the porous cavities of HMN. The in-vitro result confirms HMN as an efficient permeation enhancer for the transdermal delivery of rFVIII. Furthermore, the zero-order release kinetic indicates a sustainable release profile of rFVIII. Thus, the Advate-loaded HMN application provides a minimally invasive and sustainable transdermal delivery of rFVIII.

HT007 Bleeding outcomes following ST-elevation myocardial infarction fibrinolysis using streptokinase and tenecteplase: A 5-year analysis in an Asian population

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Introduction: Bleeding outcomes are crucial primary safety endpoints in studies involving fibrinolytic agents. To date, data on bleeding outcomes following ST-elevation myocardial infarction (STEMI) fibrinolysis involving the Asian population is scarce. This study aimed to assess the incidence and identify the predictors of minor and major bleeding following STEMI thrombolysis. *Materials & Methods*: This single-centre retrospective study involved all STEMI patients given fibrinolytic therapy from 2016 to 2020 in a tertiary hospital. Total population sampling was used in this study. Bleeding events were categorised using the Thrombolysis in Myocardial Infarction (TIMI) bleeding criteria. Logistic regression analyses were used to assess independent predictors of bleeding. *Results*: Data from 941 patients was analysed. Their mean age was 53.0±12.2 years and predominantly male (n=846, 89.9%). The in-hospital mortality was 10.3% (n=97). The incidence of all bleeding was 16.5% (n=155), where 7 (0.7%) and 17 (1.8%) cases were TIMI major and minor bleeding, respectively. TIMI major and minor bleeding were predictors of in-hospital mortality. The final multi-model found four predictors for TIMI major and minor bleeding: tenecteplase use (aOR 0.313, p=0.017), age ≥75 (aOR 3.475, p=0.045), underlying ischemic heart disease (aOR 4.143, p=0.001) and heart rate ≥ 100 beats per minute at presentation (aOR 3.169, p=0.008). *Discussion*: TIMI major and minor bleeding following STEMI fibrinolysis in our Asian population were comparable to other studies but significantly contributed to mortality. The above-identified predictors of major and minor bleeding allow clinicians to identify and manage high-risk STEMI patients better with the right reperfusion strategy.

HT008 RNAi targeting LMAN1-MCFD2 complex: A new anticoagulant strategy

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Introduction: Combined deficiency of coagulation factor V (FV) and factor VIII (FVIII)(F5F8D) is a rare haemorrhagic disease caused by mutations in either lectin mannose binding 1(LMAN1) or multiple coagulation factor deficiency gene 2(MCFD2) gene. Reducing the level of factor VIII by inhibiting the LMAN1-MCFD2 complex may become a new anticoagulant approach. We aimed to find a new therapeutic option for anticoagulation by RNA interference (RNAi) targeting LMAN1 and MCFD2. *Materials & Methods*: The siRNA sequences were designed by transcripts in NCBI and were screened out through the Dual-Luciferase reporter. The optimal small interfering RNA (siRNA) was conjugated to an asialoglycoprotein receptor ligand (N-acetylgalactosamine [GalNAc]-LMAN1/MCFD2), promoting targeted delivery to the liver. Through experiments in vivo and in vitro, the expression of LMAN1 and MCFD2 mRNA was examined by RT-qPCR and protein was examined by western blotting. *Results*: After administration, GalNAc-LMAN1 and GalNAc-MCFD2 demonstrated effective and persistent LMAN1 and MCFD2 inhibition. After 7 days, in normal mice, LMAN1 mRNA levels were reduced to 19.97% ± 3.78% with 3mg/kg GalNAc-LMAN1. MCFD2 mRNA levels were reduced to 32.22% ± 13.14% with 3mg/kg GalNAc-MCFD2. *Discussion*: Our study confirmed that GalNAc-LMAN1 and GalNAc-MCFD2 therapy is effective and can be considered a safe strategy option for anticoagulation drugs. However, a trade-off between the benefits of drug and the risk of bleeding in thrombophilic mice models needs to be evaluated.

HT009 Comparison the effects of edoxaban, rivaroxaban and warfarin on recanalised flow, inflammation and postthrombotic syndrome in patients with DVT

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Introduction: Deep vein thrombosis (DVT) is worldwide disease one of the most common causes of death due to cardiovascular disease. Postthrombotic syndrome (PTS) and recurrent thrombosis are the common morbidities associated with DVT. Inflammation can also play a key role in there. Here, we aimed to compare the effects of edoxaban, rivaroxaban and warfarin on recanalised flow, inflammation and PTS in patients with DVT. *Materials & Methods*: Between 2018 and 2021, total of 320 patients treated with edoxaban (n=107), rivaroxaban (n=107) and warfarin (n=106) due to DVT were included to the study. Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) were used to evaluate inflammation. Ultrasonography and VILLALTA score were used for the assessment of recanalized flow and PTS. *Results*: There were no statistically differences between the groups in terms of demographic characteristics and comorbidities. Posttreatment 1st month NLR levels were significantly lower in rivaroxaban group and PLR levels were significantly lower in both rivaroxaban and edoxaban groups. Warfarin was superior to the other groups on 3rd month recanalised flow whereas 6th month recanalised flows were not statistically different between the groups. Third month VILLALTA score was statistically higher in warfarin group and no differences in 6th month measurements between the groups. *Discussion*: Treatment of DVT

is a dynamic process which requires the exact evaluation of the patients according to the several parameters. Recanalised flow, inflammation and situations related to inflammation such as PTS can be used for the assessment. Drugs can be shifted according to the response. Edoxaban and rivaroxaban can be used for long term treatment in DVT to prevent undesired morbidities by reducing inflammation.

HT010 Distinct role of GRK3 in platelet activation by desensitisation of G protein-coupled receptors

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Introduction: Many platelet agonists mediate their cellular effects through G protein-coupled receptors (GPCRs) to induce platelet activation, and GPCR kinases (GRKs) along with β-arrestins have been demonstrated to have crucial roles in most GPCR functions in other cell types. Here, we investigated the functional role of GRK3 and the molecular basis for the regulation of GPCR desensitisation by GRK3 in platelets. *Materials & Methods*: We used mice lacking GRK3 as well as β-arrestin2 which has been shown to be important in regulating GPCR function in platelets. *Results*: Platelet aggregation and dense granule secretion induced by 2-MeSADP, U46619, thrombin, and AYPGKF were significantly potentiated in both GRK3$^{-/-}$ and β-arrestin2$^{-/-}$ platelets compared to wild-type (WT) platelets, while non-GPCR agonist, collagen-induced platelet aggregation and secretion were not affected. We have previously shown that GRK6 is not involved in the regulation of G_q-coupled $5HT_{2A}$ and G_z-coupled α_{2A} adrenergic receptors. Interestingly, in contrast to GRK6, platelet aggregation induced by co-stimulation of serotonin and epinephrine which activate $5HT_{2A}$ and α_{2A} adrenergic receptors, respectively, was significantly potentiated in GRK3$^{-/-}$ platelets, suggesting that GRK3 was involved in general GPCR regulation. In addition, platelet aggregation in response to the second challenge of ADP and AYPGKF was restored in GRK3$^{-/-}$ platelets whereas re-stimulation of the agonist failed to induce aggregation in WT platelets, confirming that GRK3 contributes to general GPCR desensitisation. Finally, 2-MeSADP- and AYPGKF-induced Akt and ERK phosphorylation were significantly potentiated in GRK3$^{-/-}$ platelets. *Discussion*: GRK3 plays a crucial role in the regulation of platelet functional responses through general GPCR desensitisation.

HT011 The correlation of haematological and coagulation parameters and the disease severity in COVID-19 patient at initial presentation

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Introduction: The haematological and coagulation abnormalities in coronavirus infection (COVID-19) are mostly associated with cytokine storm and are usually related to acute respiratory distress syndrome (ARDS) and multi-organ failure leading to more severe disease and mortality. Evidence has suggested that patients with COVID-19 have abnormal coagulation profiles and are at higher risk of thromboembolic complications. This study aims to determine the role of haematological and coagulation parameters in predicting disease severity in COVID-19 patients at initial presentation. *Materials & Methods*: This study is a retrospective, cross-sectional study conducted at Selayang Hospital, Malaysia. Two hundred and fifty-seven subjects who were positive for COVID-19 by reverse transcriptase-polymerase chain reaction (RT-PCR) with different disease severity according to Clinical Management of Confirmed COVID-19 Case in Adult and Paediatric 2020 guidelines ie mild, moderate, severe, and critically ill disease, that fulfilled inclusion and exclusion criteria were included. Data were analysed using SPSS version 27. *Results*: Of 257 cases, 54 were mild, 65 were moderate, 116 were severe, and 22 were critically ill. The values of total white blood cells, neutrophil count, prothrombin time (PT), and activated partial thromboplastin time (APTT), were significantly increased in critically ill cases. Lymphocyte count was significantly reduced in severe cases ($p<0.05$). There was no significant difference in the haemoglobin level, platelet count, basophil count, and international normalised ratio (INR) across the different disease severity groups at the initial presentation. *Discussions*: This retrospective study demonstrated the association of leukocytosis, neutrophilia, prolonged PT and APTT and lymphopenia and monocytopenia in severe and critically ill COVID-19 patients.

HT012 Haemostatic Changes in patients with COVID-19 at Hospital Universiti Sains Malaysia

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Introduction: COVID-19 infection has rapidly spread worldwide and manifested as respiratory tract infection. Notably, it is a systemic disease and has impacted haemostasis which can lead to coagulation dysfunction, especially in severely ill patients. This study aimed to evaluate the trend of haemostatic changes and their correlation with clinical severity in COVID-19 patients. *Materials & Methods*: This retrospective cohort and single-centre study involving COVID-19 patients admitted to Hospital USM from July 2021 to July 2022 fulfilled the inclusion criteria. Demographic data, underlying comorbidities of the

patients, clinical severity and haemostatic parameters, including prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen level and D-dimer were retrieved. *Results*: In 34 COVID-19 patients, the severe cases were 91.2% (n=31). It showed that males (n=22, 64.7%) and aged more than 60 (74.2%) were the most affected. Diabetes mellitus (n=22, 64.5%) and hypertension (HPT) (n=26, 77.4%) were the most common underlying comorbidities in affected patients. The median (IQR) values of PT, aPTT and D-dimer level were higher in the severe group, which were 16.60(6.0) seconds, 49.30(23.6) seconds and 4.80(6.1) seconds, respectively but were not statistically significant. The mean difference in fibrinogen level between the severe (4.27±1.81g/L) and non-severe (3.78±1.24g/L) groups was not significantly different. *Discussion*: The prolongation of the coagulation test, as seen by increased PT, aPTT and D-dimer, can be used to predict the possibility of the severity of the illness. Few studies also indicated a marked raised in PT and aPTT in the severe group.

HT013 Long-term clinical outcomes of reduced dose of emicizumab in haemophilia A with inhibitors: A real world experience in Sarawak, Malaysia

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Introduction: Sarawak has a prevalence of 2.46 cases of severe haemophilia A (HA) per 100,000 males. Emicizumab has been approved to prevent and reduce bleeding events among HA patients. Here we report one of the longest worldwide clinical outcomes of patients' experience using emicizumab a reduced dose. *Materials & Methods*: All HA were identified from 4 main hospitals in Sarawak. All HA receiving emicizumab were included. Clinical and laboratory data were tabulated in designated form. *Results*: Three patients with severe HA with inhibitors were treated with emicizumab between 2018 and 15 May 2023 with median duration of treatment of 216 weeks (range, 156-228). All were male with median age of 23 (range, 16-36). Prior to emicizumab, they were treated with bypassing agents with annual bleeding rates ranging 3 to 92. Median score of Transformed Score Haemo-QoL-A Subscale was 31.47 (range, 18.9-44.8) and 75.98 (range, 73.90-78.44) prior to and after intiation of emicizumab respectively. Patients were initiated with emicizumab 3mg/kg weekly for 4 weeks and were tapered down thereafter. Two had zero bleeding events even after emicizumab were dosed down to 1.9mg/kg 4-weekly and 1.75mg/kg 4-weekly respectively. One patient developed frequent breakthrough bleedings when emicizumab was dosed below 1.6mg/kg 4-weekly. *Discussion*: We demonstrated emicizumab has a favourable safety profile with encouraging efficacy in HA for a duration beyond 4 years, even at a reduced dose. Breakthrough bleeds occurred when emicizumab was dosed below 1.6 mg/kg 4-weekly. It is potentially a cost-effective approach in resource-restricted setting, however, more validated studies are required.

HT014 Demographics and outcome of patients with congenital bleeding disorder in Sarawak, Malaysia

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Introduction: Sarawak is a multi-ethnic state in Malaysia comprising more than 20 ethnicities. We aimed to study the demographics and outcome of patients with congenital bleeding disorder in Sarawak. *Materials & Methods*: A cross-sectional study was conducted in 2023 at four major haemophilia treatment centres in Sarawak. Demographics and clinical data were compiled in Sarawak Haemophilia Registry. *Results*: 115 patients with congenital bleeding disorders were identified - 79(68.7%) haemophilia A(HA) and 21(18.3%) haemophila B(HB). The others being non-haemophilia bleeding disorders, totalling 15 patients were Von-Willebrand disease (4), FVII (3), FX (5) and FXI (3) deficiency. Severe haemophilia patients were noted in 53.2% (42/79) of HA and 61.9% (13/21) of HB. Approximately half of HA (48.1%) and HB (52.4%) population had no identifiable family history of haemophilia. Almost two-thirds of severe HA were on prophylaxis [27/42(64.3%)] and one-third [4/13(30.8%)] in severe HB. Among those on prophylaxis, three severe HA patients with inhibitors received emicizumab with remarkable reduction in bleeding events; one female moderate HA patient on PEGylated recombinant anti-haemophilic factor; whereas others [27/31(87.1%)] on plasma-derived factor concentrate. Inhibitors developed in 9/79(11.4%) of the HA population [3/79(3.8%) high responders]. None of the patients developed inhibitory alloantibodies to factor IX. Three patients succumbed - two attributed to intracranial bleed; one gastrointestinal bleed. The overall incidence of HA and HB was 1 in 12,664 and 1 in 40,104, respectively. *Discussion*: Our incidence of congenital haemophilia is considerably lower than reported data. Patients with mild haemophilia who are non-bleeders are not captured in this registry. This study outlines haemophilia landscape in Sarawak and offers objective standards for forward planning.

HT015 Association between uric acid and risk of venous thromboembolism in Asian populations: A cohort and Mendelian randomisation study

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Introduction: Serum uric acid (SUA) levels have been associated with an increased risk of venous thromboembolism (VTE) in European populations. While large-scale studies on the association between SUA and VTE in Asian populations are lacking, despite the high prevalence of hyperuricaemia in this region. To address this, we conducted a cohort analysis and Mendelian randomisation (MR) study in Asian populations. *Materials & Methods*: We collected data on VTE patients from the CURES and controls obtained from the CHARLS. Propensity score matching and cubic-spline models were applied to assess the effect of SUA on VTE risk while adjusting for multiple covariates. We also performed MR analyses to infer potential causality based on GWAS summary statistics of SUA and VTE in the Asian population. *Results*: We found that the SUA levels were higher in VTE patients (317.95mmol/L) compared to the general population (295.75mmol/L), and SUA was associated with an increased risk of VTE recurrence (P-value=0.0003). The univariable MR suggested a causal relationship between elevated SUA and higher VTE risk (P_{IVW}<0.05), and multivariable MR showed that controlling SUA continued to protect against VTE after controlling for other lipid-related factors ($P_{MV\ residual}$<0.05). *Discussion*: Our study provides evidence supporting a robust positive association between SUA and VTE in the Asian population, and MR analyses suggest that this association is likely to be causal. Our findings underscore the importance of monitoring SUA levels in VTE prevention and call for urgent action to address the growing burden of hyperuricaemia in the Asia-Pacific region.

HT016 A single centre experience on evaluation of haemostasis parameters and clot waveform analysis among COVID-19 patients

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Introduction: Coronavirus disease 2019 (COVID-19) has been associated with abnormal haemostatic parameters and important prognostic factor of disease severity and outcome. This study evaluated conventional haemostatic biomarkers and clot waveform analysis (CWA) in different categories of COVID-19 infection. Furthermore, this study also analysed the association of selected factors, such as age, comorbidities, and laboratory parameters, with the disease outcome. *Materials and methods*: This retrospective cross-sectional study included 143 hospitalised COVID-19 patients in Hospital Tuanku Ja'afar Seremban, categorised into non-severe and severe group. Socio- demographics, comorbidities, disease outcome, and haemostasis parameters were evaluated on admission. Extended parameters for coagulation were also analysed, including the APTT second derivative curve pattern and its quantitative parameters; APTT max1, APTT max2 and APTT min2. *Results*: Median age of study participants was 62-year-old, with ratio of males and females 1:1. This study showed a high frequency of abnormal patterns in the APTT second derivative curve in COVID-19 subjects, predominantly seen in the severe group. This abnormal CWA pattern was not significantly associated with disease severity. D-dimer elevation was observed and showed significant difference between severe and non-severe groups. D-dimer level was also significantly associated with disease outcome, which was higher among the non-survivor group. *Discussion*: Our laboratory findings imply that COVID-19 infections may have a distinct coagulation dysfunction, particularly in severe and critically ill conditions. Severe COVID-19 patients demonstrated elevated D-dimers with abnormal CWA patterns. In addition, D-dimer can be utilised as a significant indicator in predicting the mortality of COVID-19 patients.

HT017 Is monitoring anti-xa levels necessary in pregnant women receiving therapeutic LMWH?

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Introduction: Pregnancy increases the risk of thrombosis. It's a constant issue for treating doctors since it raises the risk of venous thromboembolism (VTE) and valve thrombosis in women who have mechanical heart valves (MHV). The dosage of low molecular weight heparin (LMWH) is usually determined by weight, but the management of LWMH dosage during pregnancy is debatable. *Materials & Methods*: This is a retrospective cohort between 2020 and 2021 of all pregnant women who were therapeutically anticoagulated with LMWH and had anti-Xa levels of at least 1 peak (+/- trough) antenatally. The anti-Xa level in MHV and VTE patients was the main focus of our investigation. Secondly, we compared their actual LMWH dosing and dosage adjustments in both groups based on anti-Xa levels. *Results*: During the study period, 4 (80.0%) of the women with MHV (N=5) were kept on the same LMWH dosage throughout the antenatally, whereas 1 (20.0%) required dose modifications based on trough and peak anti-Xa levels. 4 (57.1%) of the women with VTE (N=7) showed subtherapeutic levels of peak anti-Xa in the VTE group. However, the dosage was not changed throughout pregnancy. LMWH therapy

did not cause any bleeding or clotting issues. No reports of maternal thrombotic complications were identified. *Discussion*: In pregnant women with high risk such as MHV and VTE, monitoring by trough and peak anti-Xa levels maybe be use for dosage guidance on a case-by-case basis. However, a well-designed prospective trial evaluating the effect of anti-Xa monitoring strategies on clinically important outcomes is needed.

HT018 Clinical characteristics and genotypic landscape of moderate to severe haemophilia A patients in a Haemophilia Treatment Centre

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Introduction: Haemophilia A is an inherited bleeding disorder characterised by factor VIII deficiency (FVIII). The standard of care for patients with severe and moderate haemophilia A with FVIII levels < 3% and a bleeding phenotype is a regular factor or non-factor prophylactic treatment. *Materials & methods*: This retrospective cross-sectional review included haemophilia A patients with severe to moderate FVIII levels < 3% and a bleeding phenotype registered in the haemophilia clinic from 1st January to 31st December 2022. Clinical data were obtained from manual and electronic records. Polymerase Chain Reaction (PCR) and Sanger sequencing methods were performed to detect FVIII mutations. *Results*: Thirty-six male patients were reviewed with a median age of 30.5 years old (range 14 – 70). Nine patients (25%) had no significant family history. Although 5 patients (13.9%) had a documented history of inhibitors, only 1 had persistent FVIII inhibitors. 33 patients were treated with plasma-derived FVIII prophylaxis with mean weekly dosing of 42.8 IU/kg. Two patients received fitusiran, and 1 patient received activated factor VII (FVIIa). The mean annualised joint bleeding rate (ABJR) and annualised bleeding rate (ABR) were 1.86 and 2.94 respectively. In the interim, 32 patients from 25 families performed FVIII mutation analysis. Intron 22 inversions were found to be the most common FVIII mutation. *Discussion*: Our study findings demonstrated that regular prophylaxis even with low-dose factor replacement is effective in reducing bleeding complications. The disease characteristics in our patients did not differ significantly from other reported cohorts.

HT019 Associated factors of intracranial haemorrhage and gastrointestinal bleeding among warfarin users treated with prothrombin complex concentrate: A 6-year analysis

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Introduction: Asian populations on warfarin possess a higher bleeding risk. Intracranial haemorrhage (ICH) and gastrointestinal bleeding (GIB) have been reported as the commonest bleeding sites in warfarin users. This study aimed to identify ICH and GIB-associated factors among warfarin users who received three-factor prothrombin complex concentrate (3F-PCC) for anticoagulation reversal. *Materials & Methods*: This single-centre retrospective study involved all warfarin users who were given 3F-PCC for an anticoagulation reversal from September 2017 to April 2023 in a tertiary hospital. Total population sampling was used in this study. Bleeding events were categorised using the International Society on Thrombosis and Haemostasis (ISTH) bleeding definition. Logistic regression analyses were used to assess ICH and GIB-associated factors. *Results*: Data from 180 patients was analysed. Their mean age was 63.0±14.5 years. Most warfarin patients presented with major bleeding (n=107, 59.4%), with ICH (n=46, 25.6%) and GIB (n=50, 27.8) as the commonest bleeding sites. The in-hospital mortality for ICH and GIB were 37% (n=17) and 18% (n=9), respectively. The final multi-model found two associated factors for ICH: valve replacement (aOR 5.056, p<0.001) and initial INR ≥3.6 (aOR 0.203, p<0.001). Conversely, atrial fibrillation (aOR 3.314, p=0.003) and INR ≥3.6 (aOR 3.123, p=0.009) were the identified associated factors for GIB. *Discussion*: ICH in warfarin users tended to occur at lower INR and was associated with higher mortality. The above-identified associated factors of ICH and GIB allow clinicians to identify higher bleeding risk patients and prevent major bleeding more effectively in practice.

HT020 The outcomes of three-factor Prothrombin Complex Concentrate in warfarin anticoagulation reversal and the predictors of in-hospital mortality

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Introduction: Warfarin-associated bleeding has a high mortality, and there is a wide variation in the efficacy of three-factor Prothrombin Complex Concentrate (3F-PCC) in warfarin anticoagulation reversal. This study aimed to assess the efficacy and safety of 3F-PCC in warfarin reversal and identify the predictors of mortality. *Materials & Methods*: This single-centre retrospective study involved all warfarin users who were given 3F-PCC for an anticoagulation reversal from September 2017 to April 2023 in a tertiary hospital. Total population sampling was used in this study. Successful anticoagulation reversal and any adverse drug reactions (ADRs) were reported descriptively. Logistic regression analyses were used to identify the predictors of mortality. *Results*: Data from 180 patients was analysed. Their mean age was 63.0±14.5 years and predominantly male (n=101, 56.1%). Initial international normalised ratio (INR)s ranged from 1.6 to undetectable high (> 26). Median 3F-PCC doses used were 40 (30 – 50) units/kg. All patients had INR reduction, of which 59.4% (n=107) achieved the target INR. Nine (5.0%) ADRs were observed. Three (1.7%) cases with suspected acute coronary syndrome were associated with mortality. Ischemic stroke occurred in one (0.6%) patient. The incidence of in-hospital all-cause mortality was 22.8% (n=41). The final multi-model identified two predictors of mortality: intracranial haemorrhage (aOR 3.114, p=0.004) and achievement of target INR (aOR 0.338, p<0.004). *Discussion*: 3F-PCC has moderate efficacy in warfarin anticoagulation reversal in our study without apparent increased risk of thromboembolic events and mortality. Achievement of target INR in warfarin-associated bleeding is crucial to reduce mortality.

HT021 Coagulation testing as a recognition marker for monitoring and predicting outcome of COVID-19 infection in Hospital Melaka

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Introduction: Coronavirus disease 2019 (COVID-19) is associated with significant morbidity and mortality, partly due to a coagulopathy state, especially venous thromboembolism (VTE). Detecting thrombosis early through coagulation testing can aid in patient management. This study aims to assess the utility of coagulation testing as a marker for monitoring and prognosis of COVID-19 in Hospital Melaka. *Material and methods:* This retrospective cross-sectional observational study included 232 COVID-19 patients categorized into clinical suspicion of thrombosis and no thrombosis groups. The univariate analysis compared coagulation testing and outcomes between the two groups. *Results:* D-dimer levels were significantly higher in the thrombosis group [n=84; median (IQR): 1.0 (0.06-2.06) mg/L] than in the non-thrombosis group [n=148; median (IQR): 0.73 (0.13-1.59)]. Other coagulation parameters did not differ significantly. Most patients received anticoagulant thromboprophylaxis, with daily D-dimer measurements to identify VTE events. However, D-dimer levels did not significantly change after 24 hours of initiating anticoagulation. Non-survivors had significantly higher D-dimer levels [n=23; median (IQR): 1.29 (1.4-3.98) mg/L] than survivors [n=209; median (IQR) 0.79 (0.07-1.65) mg/L]. *Discussion:* Elevated D-dimer levels may predict thromboembolic events and mortality in COVID-19 patients. Hence, increased D-dimer values should trigger a further investigation for potential thromboembolic events. Coagulation testing, particularly monitoring D-dimer levels, can aid in the early detection and management of coagulopathy in COVID-19. Further research and prospective studies are needed to validate these findings and establish guidelines for coagulation testing in COVID-19 patient care.

HT022 Clinical characteristics and treatment pattern of venous thromboembolism (VTE) in medical ward: A Sarawak General Hospital experience

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Introduction: Venous Thromboembolism (VTE) causes significant morbidity and mortality in both the community and hospital setting. *Materials & Methods*: This is a retrospective study examining demographics and treatment pattern of patients with VTE admitted to medical ward, Sarawak General Hospital from July 2021 to June 2022. Patients' case notes were traced, entered in case report form, and analysed via IBM SPSS Statistics version 29.0. *Results*: There was a total of 149 patients with a slight female preponderance (n=80, 53.7%). The mean age was 58 years old (range 15 years to 88 years old). Most of them admitted to the ward due to symptomatic VTE (n=127, 85.2%). Majority of the VTE were pulmonary embolism (n=67, 45%) and lower limb deep vein thrombosis (n=51, 34.2%). Thrombosis of unusual sites made up of approximately 18% of the cases(n=27). Risk factors included immobilisation (20.8%), malignancy (23.5%) and acute medical illness (32.2%). Notably, COVID 19 infection had emerges as one of the common risk factors (n=44, 29.5%). There were 13.4% (n=20) of the cases treated as unprovoked VTE. Treatment modality includes direct oral anticoagulant (n=64, 42.9%), warfarin after initial stage of LMWH (n=40,26.8%) and LMWH/fondaparinux (n=32, 21.5%). The most prescribed DOAC

were apixaban (n=43, 67.2%). *Discussion*: This retrospective study highlights heterogeneity in the treatment of inpatient VTE. Prospective follow up is required to ascertain the short term and long-term outcome of these group of patients.

HT023 *CYP2C19* polymorphisms in coronary artery disease patients treated with clopidogrel

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Introduction: Clopidogrel is prescribed to patients with coronary artery disease (CAD), and/or after percutaneous coronary interventions (PCI). Clopidogrel requires conversion to active metabolite by cytochrome P450 (CYP) enzymes. Studies have shown patients carrying 1 or 2 loss-of-function (LOF) *CYP2C19* alleles might have an increased risk of adverse cardiovascular events. This study aimed to determine the distribution of clinically relevant alleles (*CYP2C19*2*, *CYP2C19*3*, and *CYP2C19*17*) in clopidogrel-treated CAD patients and their association with clinical outcomes. *Materials & Methods*: Blood samples of patients scheduled for coronary angiogram were obtained after informed consent and followed up for one year to determine their clinical outcomes. Poor clinical outcomes included stent failure or vein graft stenosis, recurrence of ischaemic events or cardiovascular death within one year. *CYP2C19* alleles were determined using TaqMan assays. *Results*: A total of 280 patients comprising 85 Malays, 86 Chinese and 109 Indians were enrolled, but only 239 proceeded to have PCI and/or coronary artery bypass grafting (CABG). Allele frequencies of *CYP2C19*2* LOF, *CYP2C19*3* LOF and *CYP2C19*17* were 0.276, 0.012, 0.047 in Malay; 0.349, 0.047, 0.012 in Chinese and 0.362, 0.009, 0.193 in Indian, respectively. *CYP2C19**2 was the most prevalent allele. *CYP2C19*17* was more common in Indians. Among 192 patients with one-year follow-up, 9 patients had poor outcomes, 5 were *CYP2C19**1/*2, 1 had *CYP2C19**2/*2 and 3 were *CYP2C19*1/*1*. *CYP2C19**1/*2 (33.9%) was the most common diplotype among patients with good outcomes. *Discussion*: *CYP2C19**1/*2 was not associated with poor clinical outcomes. This study confirmed the diverse distribution of *CYP2C19* polymorphism among different ethnicities.

HT024 Are all microangiopathic haemolytic anaemia (MAHA) equate to thrombotic thrombocytopenic purpura (TTP)?: A case series in Sarawak Malaysia

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Introduction: Case of microangiopathic haemolytic anaemia (MAHA) and haemolysis in the context of thrombocytopenia are frequently referred to haematology subspecialty to rule out thrombotic thrombocytopenic purpura (TTP). However, not all MAHA is caused by TTP. *Materials & Methods*: This is a retrospective study examining patients with MAHA referred to haematology unit to rule out TTP between 2020 and 2023 in Sarawak. Patients' case notes were traced, entered in case report form and analysed via IBM SPSS Statistics version 29.0. *Results*: There was a total of 34 patients with the male to female ratio of 1:1.4. The mean age was 46 years old (range 18 years to 76 years old). For patients with TTP (n=15, 44.1%), they presented with CNS symptoms, fever, anaemia and GI symptoms. Median ADAMTS13 and inhibitor level was 0% and 41 Bu respectively. Modality of treatments include steroids (n=15, 100%), plasmapheresis (n=12, 80%), IVIG (n=5, 33.3%), rituximab (n=2, 13.3%) and vincristine (n=1, 6.7%). Two third of them stayed in remission. Two deaths were related to TTP. In our small cohort of patients, a high PLASMIC score (eg. 6 or more points) is associated with TTP ($p < 0.001$). More than half of the cases with MAHA were not TTP (n=19, 55.9%). The causes include renal diseases, DIVC/sepsis, malignancy, pregnancy and liver disease. *Discussion*: The confirmatory test for TTP, ADAMTS13 is outsourced with turnaround time of one month. Hence, in Sarawak, we relied on a comprehensive history taking and examination; and prompt interpretation of haemolytic markers and peripheral blood film to ensure prompt diagnosis and treatment of TTP.

HT025 Mixing study: Is there an answer for all?

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Introduction: Mixing studies are done in patients with prolonged clotting time. It is a good laboratory test to differentiate between factor deficiency versus factor inhibitor. Its utilisation in Sarawak General Hospital, a tertiary referral centre has never been investigated. *Materials & Methods*: This is a retrospective study assessing patients with mixing study done in Sarawak General Hospital between Jan 2021 to May 2023 in Sarawak General Hospital. Patients' details were traced, entered in case report form and analysed via IBM SPSS Statistics version 29.0. *Results*: Out of the total 86 mixing study, approximately 48.8 % (n=42) was done to screen existing congenital haemophilia patients for inhibitor. The remaining mixing test (n=44, 51.2%) were new cases investigated for prolonged APTT (n=27, 61.4%), prolonged PT (n=8, 19.2%) and both (n=4, 9.1%). The mean age was 35 years old with a male to female ratio of 1.4 to 1. They presented with either bleeding (n=16, 36.4%) or thrombosis (n=2, 4.5%). However, a large proportion of them were asymptomatic (n=17, 38.6%) where the prolonged clotting time was picked up incidentally. Specific coagulation test done subsequently revealed a variety of diagnosis such as congenital haemophilia (n=8, 18.2%), acquired haemophilia (n=4,9.1%), other factor deficiencies (n=7, 8.1%) and lupus

anticoagulant (n=3, 6.8%). Management included watch and wait (45.5%), supportive transfusion (18.2%), use of factor concentrates and bypassing agent (22.7%), immunosuppression (9.0%) etc. *Discussion*: Mixing study is a good screening tool to diagnose specific clotting disorder such as acquired haemophila A which has a significantly higher mortality rate (p =0.018). Physicians should be familiarised with the indication and interpretation of mixing study.

HT026 Qualitative study on the experiences of women in the haemophilia periphery: 'being a family member of haemophilia patients'

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Introduction: Haemophilia treatment has dramatically transformed patients' lives, bringing hope. However, families face equal or greater challenges in addition to patient care – dealing with haemophilia's genetic nature and its associated suffering. *Materials & Methods*: Fifteen mothers/sisters of haemophilia patients participated with written consent and underwent semi-structured interviews. *Results*: The experience of 'being a family member of a haemophilia patients' included being a 'patient care provider', a 'daughter of a mother who lost a son to haemophilia', and a 'sister who lost a brother to haemophilia', as well as 'growing up in a family exposed to parental discord over genetics. Additionally, participants revealed that they hesitated to ask their mothers about genetics and carriers because they did not want to worry their own mothers. Another participant chose not to reveal whether her daughter was a carrier. If her daughter was not a carrier, she would no longer be a party to the haemophilia issue. *Discussion*: The study's findings emphasise the significant psychosocial impact on parent-child, marital, and patient-sibling relationships in three generations of haemophilia families. Prior to addressing the risks associated with bleeding disorders, providing care for the experiences related to being "family members of haemophilia patients" is considered essential for women in the haemophilia periphery.

HT027 Multicentre performance evaluation and reference range for the quantitative determination of Factor IX activity on the cobas t 711 analyser

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Introduction: This was a multicentre evaluation of the analytical performance of a one-stage activated partial thromboplastin time-type Factor IX (FIX) assay on the cobas® t 711 analyser (Roche Diagnostics International Ltd). *Materials & Methods*: Experiments were performed at three sites (Freiburg, Sheffield, Vienna; October 2020–February 2021) using anonymised, ethically approved, 3.2% citrated, residual routine plasma samples. Five human plasma pools and two controls were used to determine assay repeatability (one run/site; n=21 replicates/sample), intermediate precision and total reproducibility (five aliquots/sample/day for five days); coefficients of variation (CVs; samples >1.0 IU/dL FIX activity) and standard deviations (SDs; samples ≤1.0 IU/dL FIX activity [repeatability/intermediate precision only]) were calculated. Using three sets of ≥120 samples, method comparison (versus Siemens Coagulation Factor IX Deficient Plasma [with Dade Actin FSL] on Sysmex CS-5100 analyser) and lot-to-lot variability (three lots) were evaluated using Deming and Passing-Bablok regression, respectively; Pearson's r was calculated. The assay reference range was determined using fresh plasma samples from 200 apparently healthy adults not receiving anticoagulants (three lots; Freiburg only). *Results*: Across sites, the FIX assay demonstrated repeatability (CV, 1.0–6.3%; SD, 0.0275–0.0303), intermediate precision (CV, 1.7–8.4%; SD, 0.0232–0.191), and total reproducibility (CV, 3.9–20.8%) within prespecified acceptance criteria. Pearson's r ranged 0.993–0.996 for method comparison and 0.997–0.999 for lot-to-lot variability, within acceptance criteria. The reference range in healthy adults was 69.6–146 IU/dL. *Discussion*: Robust analytical performance of the one-stage FIX assay on the cobas t 711 analyser supports use in routine clinical laboratory practice.

HT028 Multicentre performance evaluation and reference range for an immunoassay for the quantitative determination of Factor XIII (FXIII) antigen on the cobas t 711 analyser

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Introduction: This was a multicentre evaluation of the analytical performance of an immunoassay for the quantitative determination of Factor XIII (FXIII) antigen (subunit A) on the high-throughput cobas® t 711 analyser (Roche Diagnostics International Ltd). *Materials & Methods*: Analytical performance was assessed at three sites (Freiburg, Sheffield, Vienna;

April–August 2021) using anonymised, ethically approved, 3.2% citrated, residual routine plasma samples. Five human plasma pools and two controls were used to measure assay repeatability (one run/site; n=21 replicates/sample), intermediate precision and total reproducibility (five aliquots/sample/day over five days); standard deviations (SDs) and coefficients of variation (CVs) were calculated. Using three sets of ≥120 samples covering the assay measuring range, method comparison (versus HemosIL Factor XIII Antigen on IL/Werfen ACL TOP 700 analyser) and lot-to-lot variability (three reagent lots) were evaluated by Deming and Passing-Bablok regression, respectively, and Pearson's r calculated. The reference range was determined in fresh samples from healthy adults not receiving anticoagulants (Freiburg only; n=200; three reagent lots). *Results*: Across sites, the FXIII immunoassay met the acceptance criteria for repeatability (SD, 0.112–0.270; CV, 0.7–2.8%), intermediate precision (SD, 0.150–0.676; CV, 0.9–4.2%) and total reproducibility (CV, 3.3–9.9%). The FXIII immunoassay showed agreement with the comparator assay (Pearson's r, 0.892–0.918) and good lot-to-lot variability (Pearson's r, 0.990–0.993). The reference range of the FXIII immunoassay in healthy individuals was 68.0–159 IU/dL. *Discussion*: The FXIII immunoassay demonstrated robust analytical performance on the cobas t 711 analyser, supporting its use in routine clinical laboratory practice.

HT029 PT and aPTT comparison of two automated analysers utilising optical and mechanical method

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Introduction: Comparison study between two analysers is part of method verification procedure. We evaluated our Sysmex CS-2500, a high-performance coagulation system that utilises optical method for the measurements of Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT). The purpose of this study was to compare the PT and aPTT measurements between the CS-2500 and our established analyser; STA-Compact Max Diagnostica that were at a distance of 25kilometer apart. *Materials & Methods*: Samples were collected from daily diagnostic samples that covered both normal and pathological ranges. Firstly, the analysis was performed on the STA-Compact Max. Later the samples were rushed to another laboratory and processed on the CS-2500 within 3 hours. The data was tabulated and analysed in Microsoft Excel 2016. *Results*: Generally, the CS-2500 shows a good correlation with STA-Compact Max based on r-squared values (PT= 0.9765 and aPTT= 0.8812). Furthermore, a strong positive linear correlation is also supported by r value that is close to 1; PT (y=0.8531x-1.8195 and r=0.9882) and aPTT (y=0.6878x+1.1022 and r=0.9387). However, the bias for PT and aPTT are 6.0% and 13.8% respectively. *Discussion*: The difference in analyser's principle (STA®Compact Max uses mechanical method) and the composition of reagents are factors that contribute to the outcome between the two analysers. Another factor is the pre-analytical change that may occur in the samples during transportation between the two locations of analysers. There were small differences between the two analysers when measuring PT and aPTT. Overall, we suggest that these may cause the laboratory to use different reference intervals for the CS-2500.

HT030 Procoagulant platelets and a novel associated GSAO+ platelet subpopulation in essential thrombocytosis

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Introduction: Procoagulant platelets can be detected through the uptake of a tripeptide trivalent arsenical (GSAO) combined with P-selectin expression. These procoagulant platelets are elevated in various prothrombotic conditions including essential thrombocytosis (ET). Recently, a novel GSAO+ platelet subpopulation arisen from procoagulant platelet assay has been demonstrated in small series of patients to be a potential biomarker in ET. ET patients with high GSAO+ subpopulation is at increased thrombotic risk and this study aims to validate this. *Materials & Methods*: Patients with ET are prospectively recruited for procoagulant platelet assay and are followed up for new thrombotic complications. The assay used is a whole blood flow cytometry-based method using markers CD41, CD45, GSAO and P-selectin. Samples are stimulated with thrombin 5U/mL and collagen 10μg/mL. A further subset of GSAO+ subpopulation is identified through multiparameter clustering and gating approach. Using previously defined cut-off of >2.09%, patients are dichotomised into high GSAO+ group and non-high GSAO+ group. *Results*: Seven patients with ET were recruited and they have increased procoagulant platelets compared to healthy controls ($P<0.05$). None of the patients expressed GSAO+ platelet subpopulation >2.09% and are therefore classified as non-high GSAO+ group. After a median follow up of 23 months, no new thrombotic event is reported. *Discussion*: Consistent with previous findings, procoagulant platelet response in ET is heightened. The absence of new thrombotic event so far is not unexpected as all the patients are of non-high GSAO+ group. More data are needed to conclusively validate the clinical utility of this GSAO+ platelet subpopulation.

HT031 APTT clot waveform analysis (CWA) reference intervals changes across three trimesters in normal pregnant women

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Introduction: Hypercoagulable changes in pregnancy are known but cannot be detected in routine activated partial thromboplastin time (APTT) assay. The APTT clot waveform analysis (CWA) quantifies the kinetic changes of the optical transmittance that might provide more diagnostic information. This study aims to provide the reference intervals collected across trimesters in normal pregnant women as a starting point for future pathological investigations. *Materials & Methods*: Citrated blood samples were collected from normal pregnant women (n=50) followed up in the Singapore General Hospital across three trimesters and post-delivery. Platelet poor plasma was analysed for APTT using the CS2500 coagulometer (Sysmex Corporation, Kobe, Japan) using Dade Actin FSL (Siemens Healthcare, Marburg, Germany) within 4 hours of collection. The APTT-based CWA parameters are obtained from the analyser's built-in algorithm and used to calculate the reference intervals (RI) by the robust method using the Analyse-It for Microsoft Excel software (Version 5.40.2) and compared to the age-matched control RIs. *Results*: The APTT RI (Third trimester= 22.73 – 29.47 sec) were comparable to the control throughout the pregnancy (Control= 25.20 – 33.30 sec). The third trimester RI for Min1= 4.976 – 9.753 %/sec, Min2= 0.778 - 1.626 %/sec2 and Max2= 0.636 – 1.419 %/sec2. The comparative age-matched RI for Min1= 2.837 - 7.022 %/sec, Min2= 0.464 - 1.119 %/sec2 and Max2= 0.385 - 0.906 %/sec2, similar to the post-delivery RIs. *Discussion*: Pregnancy increased the CWA parameters compared to controls and sustained until delivery. APTT CWA could be a useful diagnostic tool for detection of haemostatic changes during pregnancy.

HT032 Storage conditions can change activated partial thromboplastin time (APTT) clot waveform analysis (CWA) parameters

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Introduction: Multidimensional clot waveform analysis (CWA) parameters (maximum velocity (min1), maximum (min2) and minimum acceleration (max2)) can be obtained with light transmittance changes during activated partial thromboplastin time (APTT) assay. This study aims to elucidate how freeze-thaw conditions could affect the APTT-CWA parameters. *Materials & Methods*: Blood samples from healthy individuals were collected in 3.2% sodium citrate tubes and platelet poor plasma (PPP) was obtained by centrifuging at 3000g for 15 minutes. Samples were analysed by the CS2100i coagulometer (Sysmex Corporation, Kobe, Japan) using Dade Actin FSL (Siemens Healthcare, Marburg, Germany) for APTT within 4 hours of collection (Day 0) and aliquoted to freeze at -80°C for 2 weeks (Day 14), a month (Month 1) and a year (Month 12) before assaying again. The APTT-based CWA parameters are obtained from the built-in algorithm of the analyser with paired t-test performed with SPSS Version 23 (IBM Corporation, Armonk, New York, USA). *Results*: Frozen storage of plasma samples slightly prolonged the APTT clot time but the APTT CWA significantly decreased as frozen storage time increases. The mean bias for Min1 was 0.032 ± 0.020 (Day 14) to -0.031 ± 0.024 (Month 12). The mean bias for Min2 was 0.067 ± 0.028 (Day 14) to -0.045 ± 0.024 (Month 12). The mean bias for Max2 was 0.116 ± 0.042 (Day 14) to -0.037 ± 0.054 (Month 12). *Discussion*: Freeze thaw cycle affected APTT CWA parameters significantly but did not decrease with increased storage time.

HT033 Thrombo-embolism in patients with myeloproliferative neoplasms: A single-centre study

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Introduction: The classic Philadelphia chromosome negative myeloproliferative neoplasms (MPNs) are a group of myeloid disorders that include polycythaemia rubra vera (PRV), essential thrombocythemia (ET) and primary myelofibrosis (PMF). Complications of MPNs include thrombosis, and the risk of thrombo-embolism is increased in MPNs versus the general populations. We conducted this study to find out the clinical characteristics and thrombotic complications among the MPNs patients in our centre. *Materials & Methods*: This is a retrospective study. Patients who were followed-up under University Malaya Medical Centre and diagnosed with PRV, ET or PMF from year 2012 till 2019 were included in the study. The data analysed include social-demographic data, mutational studies and thrombotic complications. *Results*: A total of 265 patients with MPNs were identified, of which 145 (54.7%) are ET, 87 (32.8%) are PRV and 33 (12.5%) are PMF. Among the MPNs, 195 (73.6%) of them harboured JAK2V617F mutation. 59 (22.3%) patients had 61 episodes venous thrombosis (VT) or arterial thrombosis (AT) either at the point of diagnosis or during follow-up. Incidence of thrombosis was highest in PRV at 26.4%. Thrombosis was also more common for those that harboured JAK2V617F mutation at 24.6%, with AT more than VT. There were no significant: difference correlation between the gender and age group with thrombosis. *Discussion*:

Thrombosis remained a common complication for patients with MPNs as shown in this study. AT was more common than VT, which is different from the Germany data. Clinicians should initiate cytoreductive drugs and anti-thrombotic therapy for high-risks MPNs.

HT034 A case series on bleeding complications associated with use of DOACs (apixaban and dabigatran) in Medical Ward, Sarawak General Hospital

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Introduction: Vitamin K antagonist (VKAs) had been used for decades for thromboprophylaxis in atrial fibrillation, but use of DOACs had emerged as first line therapy [1]. However, the risk of GI bleeding is higher compared to VKAs in a meta-analysis [2]. *Materials & Methods*: A retrospective case series was performed from year 2021 to 2023, observing at bleeding complications in patients associated with DOACs (apixaban and dabigatran). Medical information was obtained from discharge summaries in the Medical Department Google Drive, and data were analysed using SPSS Version 22. *Results*: Total of 31 admissions were captured, in which 20 patients had received apixaban and 11 patients received dabigatran. The patient's age ranged from 57 to 93 (M = 77.9, SD = 10.25) with 51.5% were male. 12 (38.7%) bleeding events were intracranial haemorrhages (ICH) and 8 (12.8%) were GI haemorrhages. About 48.4% (15 patients) received blood transfusions. Most of the patients (90.3%) were not given reversal agent, and only 2 patients received Idarucizumab and PCC respectively. As for bleeding risks, most of the patients (54.8%) were elderly (aged 80 and above) and 93.5% had more than 2 comorbidities. About 38.7% (12 patients) had CKD, and 6 patients had acute kidney injury (AKI) during admission. 5 patients had concurrent use of antiplatelets, 4 patients had thrombocytopenia, and 9 patients had past history of bleeding. All patients were alive, and anticoagulant were ceased in 22 (71 %) patients. *Discussion*: The risk and benefit of DOACs usage should be considered in patients with high bleeding risks, emphasizing the need for dose adjustment and closer monitoring.

HT035 The increase of monocyte/high-density lipoprotein cholesterol ratio precedes recurrent thrombotic events in patients with antiphospholipid syndrome

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Introduction: This study aims to investigate the association of the monocyte/high-density lipoprotein cholesterol (HDL-C) ratio (MHR), a novel biomarker associated with inflammation and oxidative stress, with recurrent thrombosis in antiphospholipid syndrome (APS) patients. Monocyte activation is a key factor in APS-related thrombosis, and HDL-C has been shown to impede monocyte activation and recruitment. Despite its predictive role in cardiovascular events and atherosclerosis in patients with chronic kidney disease or diabetes mellitus, the significance of MHR in APS remains unclear. *Materials & Methods*: This is a retrospective longitudinal study comprising 80 APS patients from Hokkaido University Hospital. MHR at the time of APS diagnosis was calculated and compared between patients with and without subsequent recurrent thrombosis. Additionally, within the recurrent thrombosis group, mean MHR levels 0-6 months before the thrombotic event were compared to those 6-36 months before. *Results*: The cohort of patients exhibited a mean age of 39.0 years at APS diagnosis, with a mean follow-up of 9.0 years. Recurrent thrombosis occurred in 22 patients. At APS diagnosis, MHR did not significantly differ between groups with and without recurrent thrombosis (median MHR [IQR] 4.5[3.7-5.7] vs. 4.6[3.1-7.3], p = 0.76). However, within the recurrent thrombosis group, the mean MHR was significantly higher 0-6 months before the thrombotic event than 6-36 months before (6.1[4.3-8.2] vs. 5.1[3.8-6.9], p = 0.02). *Discussion*: Our findings suggest that the increase of MHR occurs within 6 months before recurrent thrombotic events in APS patients. MHR may serve as an indicator of thrombotic recurrence in APS.

HT036 Clinical characteristic and management of haemophilia patients in Malaysia: A single centre experience

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Introduction: Haemophilia is one of the commonest inherited bleeding disorders which may lead to long term disabilities if not treated properly. Our aim of study is to understand the clinical characteristic, treatment and complication of haemophilia patients in our centre. *Materials & Methods*: A retrospective cross-sectional review of all adult haemophilia A (HA) or haemophilia B (HB) patients who received treatment in Hospital Pulau Pinang from January 2021 to December 2022 was conducted. Data were retrieved from patients' medical records. *Results*: A total of 75 haemophilia patients (64 HA and 11 HB) were included in this study with median age of 37 years old (range 19-70). Forty-two of them were severe haemophilia (50% of HA, 91% of HB). All HB and 93.8% of severe HA were on prophylaxis. Six severe and 1 mild HA patients developed inhibitor with four of them currently on non-factor prophylaxis. Twenty-four patients (32%) had prior hepatitis C infection and all of them has been cured. The mean annual bleeding rate for severe haemophilia patients were 1.77 (SD ±3.6). Target joints were observed in 9.3% of patients with ankle joint (71.4%) being the most affected joint. More than one quarter (28%) of our patients have comorbidities with majority of them having hypertension (17/21), followed by diabetes

mellitus (5/21) and ischaemic heart disease (5/21). *Discussion*: Our study showed that a significant number of adult patients with haemophilia have comorbidities. Apart from optimising factor replacement therapy, future planning should include improvement in screening, risk modification and prevention of cardiovascular disease.

HT037 Evolution of the bleeding disorders registry in a paediatric haemophilia comprehensive care centre – A 6-year update

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Introduction: The Bleeding Disorders Registry (BDR) at KK Women's and Children's Hospital has been capturing prospective data on the demographics, diagnosis, bleeds, treatment details and outcome measures for patients with congenital bleeding disorders since April 2017. We report the 6th year update of the BDR. *Materials & Methods*: The BDR is an online electronic data registry which enters only anonymised data with each patient represented by a de-identified ID. Enrolment and data collection can only begin after consent is taken from patients. Information collected includes demographics, diagnostic information, bleeding events and infusion events. Outcomes data include annualised bleed rates, and the Haemophilia Joint Health Score (HJHS) are also collected. *Results*: From its inception in 2016, the enrolment into the BDR has increased almost four-fold, from an initial 30 to 115 patients by June 2023. Currently, 49.6% are Haemophilia A, 13.9% Haemophilia B, 11.3% Haemophilia C, 20% von Willebrand's disease and 5.2% are other factor deficiencies. Annual enrolment rates have been steady with the exception of the COVID pandemic year 2020 when there was difficulty obtaining face-to-face consent from patients. In the first 2 years, the mean age at enrolment was between 8-9 years old, with a steady decrease to 6.4 years in the past 2 years, reflecting an increase in prospective enrolment upon diagnosis. There has only been 1 patient who requested to withdraw from the registry for unknown reasons. *Discussion*: The BDR provides valuable information on the status of patients with bleeding disorders in our centre. Enrolment into the BDR has been encouraging, with minimal withdrawals, enabling treaters to capture accurate prospective data for clinical and research outcomes.

HT038 Sample rejection in the Haemostasis Laboratory at Hospital Universiti Sains Malaysia (Hospital USM)

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Introduction: As the only centre in the eastern state that offers special haemostasis testing, we committed to produce laboratory results that are reliable, accurate, timely, and follow the national goal for sample rejection, which is less than 1%. Although we can only target a rejection rate of less than 4% based on our previous years' rate and are limited to clotted and insufficient samples only, for overall rejection criteria, we set the performance indicator to be at least greater than 80%. In this study, we aim to list and analyse the prevalence of different preanalytical errors that arise during sample processing in the haemostasis unit. *Materials & Methods*: This one-year retrospective study was conducted at the Hospital Universiti Sains Malaysia (Hospital USM), a teaching hospital in the eastern state of Peninsular Malaysia, from January 2022 to December 2022. Secondary data was used in this study and analysed using Microsoft Excel 2013. *Results*: All in all, the yearly total rejection is 3.3% with the highest rejection was 4.2% in August and 3.7% in July, respectively, with a clotted sample (48.6%) and an insufficient sample (16.6%) being the main causes of rejection. *Discussion*: Though rejection in a haemostasis laboratory is not rare, with clotted and insufficient samples being the most common causes of rejection, it is important to implement the identification and analysis of rejections across all laboratories to maintain high laboratory standards and improve testing efficiency.

HT039 An investigation into the causes of thrombocytopenia among adult patients admitted to general ward at Serian Hospital, Sarawak

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Introduction: Thrombocytopenia is a common presentation to medical ward. The causes of thrombocytopenia vary and could lead to serious complications. This retrospective study was performed to identify the causes of thrombocytopenia among adult patients admitted to general ward at a district hospital. *Material and methods*: All adult patients admitted to general ward, Serian Hospital from 1st January 2022 to 31st December 2022 with thrombocytopenia (platelet counts of less than 150 x 10^6/ml) were identified. Patients' demography, causes of thrombocytopenia, incidence of bleeding, and resolution of thrombocytopenia upon discharge were recorded. Outcome measure was inpatient mortality. *Results*: A total of 107 patients were found having thrombocytopenia at admission, majority being male (66.4%) and having mean age of 60.0 years. Infections (59.8%) were the main causes of thrombocytopenia, followed by liver disorders (15.0%) and haematological conditions (8.4%). Bleeding was reported in seven (6.5%) patients. Transfusions were performed in 12.1% of patients. At discharge, 58.9% of patients had persistent thrombocytopenia. Besides, 23.4% of patients were referred to tertiary hospital for further

management and 11.2% of patients had readmissions within the same year. Inpatient mortality was reported in 13.1% of patients. On multivariate analysis, inpatient mortality was associated with persistent thrombocytopenia (OR 14.02, 95% CI 1.63 - 121, $p = 0.01$) and need for transfer to tertiary hospital (OR 6.24, 95% CI 1.64 - 23.7, $p = 0.02$), while gender, age, causes of thrombocytopenia, transfusions, readmissions and length of stay were not found to be significant. *Discussion*: Unresolved inpatient thrombocytopenia was associated with poor prognosis.

HT040 Pregnancy outcome in Von Willebrand's disease in a Malaysian tertiary centre

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Introduction: Von Willebrand's disease (VWD) is an inherited bleeding disorder that has increased risk of bleeding during delivery and postpartum period. The objective of this study is to assess the complications and outcome of pregnancies in VWD in our centre. *Materials & Methods*: A retrospective study was conducted in Hospital Pulau Pinang with review of all pregnancies in VWD patients between 2009 and July 2023. *Results*: We reviewed six VWD patients which consisted of one type 1, two type 2A, one type 2B and two type 3. There were 8 successful pregnancies and one incomplete miscarriage in a type 3 patient. The mean age of pregnancy was 26.8 years old. All had iron deficiency anaemia pre-pregnancy with mean Hb of 10.4g/dl and ferritin of 28ug/L. There were 7 spontaneous vaginal deliveries and one emergency caesarean section due to failed induction. Both type 2A patients had primary postpartum haemorrhage secondary to perineal tears and one required blood transfusion. One type 2A patient developed pulmonary embolism 4 days postpartum and treated with anticoagulation and iv Alphanate. The type 1 patient received desmopressin whilst the type 2 and 3 were given plasma derived VWF containing factor VIII concentrate peripartum and postpartum. All patients received tranexamic acid. There were 7 healthy neonates and one severe neonatal thrombocytopenia. *Discussion*: The most common complication in VWD patients during delivery is postpartum haemorrhage. Pregnancy outcome for the VWD patients is good with the collaborative and multidisciplinary team effort. Iron deficiency should be corrected pre-pregnancy.

HT041 Application of moving average monitoring for better laboratory quality assurance system in coagulation test

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Introduction: Moving average (MA) is one of the monitoring methods done by calculating the average value from a set of patient results and further using that value for analytical quality control purpose. There are multiple quality control strategies had been implemented to monitor haematology assay performance However, additional real time quality control monitoring tool for our coagulation test to detect intermittent and commutability problem such as reagent problem and systematic error. MA has been used as one of the quality control tools after one unpredictable incident happen in our laboratory which cannot not be detected by conventional periodic internal quality control and saving cost. To utilise moving average procedure as part of quality control tool for coagulation tests. *Materials & Methods*: Coagulation data result extracted from Coag Expert (middle ware). Retrospective data of PT, APTT, DDIMER, Fibrinogen, Factor VIII and Factor IX had been selected from Coag expert (March to June 2023). 15% ± patient results average (mean for every 500 samples) was set as control limit base on CLIA requirement. 20 samples size (block size) was used to calculate patient moving average. Diagrammatic LJ Chart was monitored and shift and trend show were investigated. *Results*: After implementation of patient moving average in our routine coagulation test, intermittent errors were detected which were missed by conventional IQC monitoring. One of the major errors was stirrer bar malfunction which goes undetected by IQC monitoring. *Discussion*: Moving average can be used as supplementary tool for better laboratory quality assurance system in coagulation test.

HT042 Alteration of coagulation profiles in patients with comorbidities as predictive markers of severe COVID-19

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Introduction: Coagulopathy following acute inflammatory responses is the key attribute of severe COVID-19, leading to various complications including disseminated intravascular coagulation, deep vein thrombosis, and pulmonary embolism. COVID-19 patients with underlying comorbidities had increasingly rapid and severe disease progression than other patients. This study aims to determine predictive factors of severe COVID-19 in individuals with comorbidities through screening of coagulation markers. *Materials & Methods*: Blood samples from non-COVID-19 infected, high-risk individuals (aged >60 years old with diabetes as comorbid with/without hypertension, n=82) were collected at a local hospital. Blood samples from healthy individuals aged between 18 to 40 years old (n=82) represented low-risk controls. Archived blood samples from severe COVID-19 patients (stages 3 to 5, n=64) were obtained from a local COVID-19-designated hospital. The plasma samples were then acquired on a STA Compact analyser for coagulation markers including D-dimer, fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT). *Results*: Majority of patients with severe COVID-19 had underlying disease such as hypertension (57.8%) and/or diabetes (35.9%). D-dimer, and fibrinogen levels significantly increased from low-risk to high-risk to severe COVID-19 patients. PT was significantly lower in high-risk vs low-risk individuals. Male

was not different from female. *Discussion*: Coagulopathy was high among severe COVID-19 patients. Alteration of PT, D-dimer, and fibrinogen in individuals with comorbidities can be a risk factor for severe COVID-19 complications, thus suitable predictive markers for monitoring disease severity.

HT043 The clinical and laboratory findings of Factor VII (FVII) deficiency cases diagnosed at Hospital Tunku Azizah (HTA), Kuala Lumpur, Malaysia: 1 year data

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Introduction: FVII deficiency is the most common inherited rare bleeding disorders with estimated prevalence of 1 in every 500, 000 general populations. It is an autosomal recessive disorder with heterogenous clinical bleeding presentation and has poor correlation with FVII:C levels. Our study objective is to analyse the clinical and laboratory findings of FVII deficiency diagnosed at our centre within a period of 1 year. *Materials & Methods*: All cases diagnosed with FVII deficiency at HTA between 1st August 2022 to 31st July 2023 were retrospectively analysed. Demographic, clinical details and laboratory findings were collected from the request forms and HTA Laboratory Information System. *Results*: There was a total of 19 cases diagnosed with FVII deficiency (10 males and 9 females), with an average age of 29.8 years (range: 1.5 – 56 years). 78.9% were Malays, 10.5% were Chinese, 10.6% were Indians and Kadazan. 12 cases were incidentally diagnosed following findings of isolated prolonged prothrombin time (PT) during hospital admission or pre-surgical/procedural screening. Bleeding symptoms were present in almost 58% of cases, predominantly of mucocutaneous type. The most frequent bleeding tendency was gum bleeding, easy bruising, and menorrhagia. The most severe bleeding episode described was intracranial bleeding, haematemesis and knee haemarthroses (1 case for each). Positive family history was only present in one case, with the majority (11 out of 19 cases) being unknown. The average PT was 35.8 (range: 13.5 – 171.5 seconds) and FVII:C was 24.2% (range: <1 – 45.1 %). *Discussion*: FVII deficiency has heterogenous clinical presentations with poor correlation between FVII:C levels and bleeding severity.

HT044 Association of variants in *STAT3, IL-6, IL-10*, *LIF* with susceptibility of recurrent implantation failure

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Introduction: Recurrent implantation failure (RIF) is defined that when pregnancy failure occurs after two consecutive in vitro fertilisation-embryo transfers to the endometrium using at least four high-quality embryos in women. Several factors are suggested to affect implantation, but the precise pathology of RIF has not been elucidated. The immune response including the signal transducer and activator of transcription 3 (STAT3) signalling pathway is known as the major cause of implantation failure. Studies on *STAT3* and implantation has been actively carried out indicating the association between *STAT3* and implantation failure. *Materials & Methods*: We sorted out the genetic polymorphisms of *STAT3* and *STAT3*-related cytokines [*interleukin 6 (IL-6), interleukin 10 (IL-10)* and *leukaemia inhibitory factor (LIF)*]. Furthermore, we recruited 133 RIF patients and 243 healthy controls in Korean women and analyzed the polymorphisms of *STAT3* rs1053004 A>G, rs1053023 T>C, IL-6 rs1800796 C>G, *IL-10* rs1800872 T>G, and *LIF* rs737921 G>A with a PCR-restriction fragment length polymorphism (RFLP) and TaqMan allele discrimination analysis. *Results*: The *STAT3* rs1053004A>G were significantly associated with susceptibility of RIF showing the protective role [AG, adjusted odd ratio (AOR) =0.600; dominant model, AOR =0.603]. On the other hand, the recessive model of *IL-6* rs1800796 indicated the association with increased risk of RIF (AOR = 2.311). In the combination analysis, the combinations including *STAT3* rs1053004 AG have a significant statistical value. *Discussion*: Based on these results, the *STAT3* rs1053004A>G may be a predisposing factor to RIF susceptibility although the further studies are needed to understand the roles of *STAT3* rs1053004A>G.

HT045 The synergic effect between diabetes mellitus and genetic variants in the thymidylate synthase (*TYMS*) gene with the susceptibility of coronary artery disease

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Introduction: Coronary artery disease (CAD) is a prevalent cardiovascular condition characterised by the accumulation of plaque within coronary arteries. While distinct features of CAD have been reported, the association between genetic factors and CAD in terms of biomarkers was insufficient. This study aimed to investigate the connection between genetic factors and CAD, focusing on the thymidylate synthase (*TYMS, TS*) gene. TS plays a critical role in maintaining the DNA

replication, repair, and homocysteine metabolism. Therefore, our research targeted single nucleotide polymorphisms that could potentially impact *TS* gene expression and lead to dysfunction. *Materials & Methods*: The region of the corresponding SNPs is located promoter-enhancer region (*TSER* 2R/3R rs45445694) and the 3'-UTR (*TS* 1100T>C [rs699517], *TS* 1170A>G [rs2790], *TS* 1494ins/del [rs151264360]). Each SNP was confirmed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). *Results*: Our findings strongly associate the *TS* 1100T>C and 1170A>G genotypes with CAD susceptibility. We observed that *TS* 1100T>C polymorphisms increased disease susceptibility in several groups, while the *TS* 1170A>G polymorphism displayed a decreasing trend for disease risk when interacting with clinical factors. Interestingly, *TS* 1100T>C dominant model with diabetes mellitus was associated with elevated CAD risk (AOR = 3.996). Furthermore, our results demonstrate the potential contribution of the *TS* 1100/1170 haplotypes to disease susceptibility, indicating a synergistic interaction with clinical factors in disease occurrence. *Discussion*: Based on these findings, we propose that polymorphisms in the *TS* gene had the possibility of clinically useful biomarkers for the prevention, prognosis, and management of CAD in the Korean population.

HT046 A single centre case series: Clinical data of acquired haemophilia in Sarawak General Hospital

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Introduction: Acquired haemophilia is an autoimmune disorder caused by autoantibodies directed against functional epitopes of coagulation factor VIII. It can cause life threatening bleeding event. It is mainly diagnosed using mixing test and detectable serum Factor VIII inhibitor. To date, there is limited information on the demographic and clinical data of acquired haemophilia population in Sarawak. *Materials & Methods*: This is a retrospective analysis of such population in Sarawak. Records of patients with non-correctable mixing test referred to our unit between July 2018 to July 2023 were traced. Patients with congenital haemophilia were excluded. Data collected were analysed using IBM SPSS Statistics version 29.0. *Results*: A total of 10 patients with acquired haemophilia A were identified with male to female ratio of 1:1. The mean age was 64 years old (range: 37-89 years old) with one of them in postpartum period. The most frequent presenting symptom was spontaneous hematoma of soft tissues. Modalities of treatment include prednisolone alone (n=2, 20%); prednisolone with cyclosporine (n=2, 20%) and prednisolone with cyclophosphamide (n=6, 60%). The median time to response was 5 months (range: 3-7 months). 3 of out 10 patients died (30%). Patients who died on average were older with a mean age of 83 years old compared to those alive with mean age of 55 years old (p=0.01). Diagnosis at older age especially above 65 years old is associated with higher mortality rate (p=0.038). *Discussion*: Bimodal distribution was observed. Median time to complete remission was comparable to data observed in international registries. A complete registry of Sarawak acquired haemophilia population would help to create awareness among physicians.

HT047 Correlation between serum ferritin with serum TSH and FT4 in major β thalassaemia patients in Jember

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Introduction: Major β Thalassaemia is a hereditary disorder caused by mutations in β globin gene resulting in the production of β globin chains being reduced or not formed at all. The prevalence of thalassaemia carrier in Indonesia reaches 3.8% based on data from Ministry of health in 2019. Therapy for patients with major β Thalassaemia is lifelong transfusion, which results in iron overload and triggers the accumulation of iron in the important organs. Iron deposits in the Thyroid gland, resulting in hypothyroidism. The frequency of hypothyroidism in major β Thalassaemia patients is 6-30%. The function of thyroid hormone is to regulate the body's metabolism therefore it is important to know the thyroid hormone status in major β Thalassaemia patients. The purpose of this study was to determine the relationship between serum ferritin with serum TSH (thyroid stimulating hormone) and FT4 (free T4) in major β Thalassaemia patients. *Materials & Methods*: This study was conducted on13 patients with major β Thalassaemia aged 1-18 years. Ferritin, TSH and FT4 examination using the ECLIA method. *Results*: The results showed that most of the major β Thalassaemia patients showed increased ferritin levels, 25% ferritin levels within 1500-2500 ng/mL and 58.33% ferritin levels within 2500-5000 ng/mL. Most of the major β Thalassaemia patients had normal TSH levels, namely 83.33%. All major β Thalassaemia patients had normal FT4 levels. Pearson analysis results for correlation between serum ferritin with serum TSH and serum ferritin with serum FT4 obtained $p = 0.430$ and $p = 0.06$, respectively. *Discussion*: There is no significant correlation between Serum ferritin with serum TSH and serum ferritin with serum FT4.

HT048 Genetic variants of PAI-1 3'-UTR are associated with susceptibility of coronary artery disease and exhibit synergistic effects with neutrophils proportion and haemoglobin level

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Introduction: CAD is one of the main causes of death in world. Following the formation of a fibrin clot, the fibrinolytic system is initiated by the conversion of plasminogen to plasmin. Plasmin is activated by serine proteases such as tPA and uPA and contributes to vascular smooth muscle migration and neointimalisation through degradation of fibronectin and laminin. This fibrinolytic system may be inhibited by regulation of the plasminogen activator inhibitor-1. This study is to investigate the association between PAI-1 polymorphisms with CAD in Korean population, and to analyse the difference in PAI-1 levels according to polymorphisms of 3'-UTR based on the post-transcriptional regulation. *Materials & Methods*: The study population collected 900 samples which is composed of coronary artery disease 487 patients and 413 control subjects from Republic of Korea. All samples were genotyped by polymerase chain reaction restriction fragment length polymorphism assay in 6 single nucleotide polymorphism (PAI-1 -844A>G,-675 4G>5G, +43 G>A, 10692 T>C, 11053T>G, 12068 G>A). EA.hy926 cells were transfected with PAI-1 gene with 3'-UTR expression plasmid. And, Expressions of PAI-1 was measured by qRT-PCR. *Results*: We found that mutant genotype of PAI-1 10692 T>C, and 12068G>A were strongly associated with increased CAD susceptibility. Moreover, various risk factors of CAD showed synergistic effect with PAI-1 10692 T>C, and 12068G>A on CAD risk in interaction analysis. *Discussion*: This finding could be applied to identify new CAD prognostic biomarkers using the PAI-1 10692C>T, and PAI-1 12068G>A polymorphism when combined with other PAI-1 polymorphisms and the various of clinical factors.

HT049 Genetic variation and regulation of miR-30cA>G, miR-143G>A, miR-143T>C, and miR-145T>C of coronary artery disease in Korean

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Introduction: CAD is one of the main causes of death in world. MicroRNAs are small, noncoding, single-stranded RNA molecules that form base pairs with complementary target messenger RNAs. It has been demonstrated that miRNAs modulate gene expression via destabilization or translational repression of target mRNAs. As miRNA studies have progressed, in vivo and human studies have reported the abnormal expression of miRNAs associated with CAD. Therefore, we hypothesised that polymorphisms in miR-30c, miR-143, and miR-145 may affect CAD, and these polymorphisms have the possibility of affecting miRNA expression. *Materials & Methods*: The study population collected 883 samples which is composed of coronary artery disease 483 patients and 400 control subjects from Republic of Korea. Genetic polymorphisms were detected by real-time PCR analysis. Differences in the frequencies of the identified polymorphisms between CAD patients and control subjects were analyzed using Fisher's exact test and logistic regression. The odds ratio and 95% confidence interval were utilised to measure the association between genotype frequencies and CAD. *Results*: We found that mutant genotype of miR-30A>G was associated with increased CAD susceptibility. The genotype combination analysis, miR-30c rs928508GG/ miR-143 rs41291957GG was related to increased CAD occurrence. In haplotype analysis miR-30c rs928508G/ miR-143 rs41291957G were increased risk of coronary artery disease. *Discussion*: This finding could be applied to identify new CAD prognostic biomarkers using the miR-30c re928508 polymorphism when combined with other PAI-1 polymorphisms and the various of clinical factors.

HT050 The use of Idarucizumab for Dabigatran reversal in Brunei

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Introduction: Dabigatran is a direct thrombin inhibitor, approved for prevention of stroke and systemic embolism in non-valvular atrial fibrillation. (1) It is also associated with risk of haemorrhagic complications. Idarucizumab is a specific reversal agent for Dabigatran. The objective of this study is to evaluate patients with dabigatran-associated bleeding and use of Idarucizumab as reversal agent for life-threatening bleeding, in patients on Dabigatran in Brunei. *Materials & Methods*: A retrospective analysis from January 2015 to August 2022 was performed on patients with dabigatran associated bleeding complications and requiring reversals with idarucizumab. The study was also emphasized on age, survival outcomes and whether anticoagulation was restarted. *Result*: A total of 1263 patients were on Dabigatran. 19 patients (1.5%) developed bleeding, out of which 13 (68%) were gastrointestinal bleeding and 5 patients (38%) received Idarucizumab for Gastrointestinal bleed. Only one patient received two doses of 5g idarucizumab while others had one dose. Coagulation profiles normalized within 24 hours of administration in all survived patients that received Idarucizumab. 2 patients survived (40%) and 2 patients died of concomitant sepsis and 1 patient died of GI cancer. No thrombotic events were reported following reversal. No

patient was restarted on DOAC. *Discussion*: In conclusion, idarucizumab rapidly and completely reversed the anticoagulant activity of dabigatran in all of the patients. Severe GI bleeding was the main indication for reversal. There were no safety concerns among the patients involved.

HT051 The effect of haemolysis on PT and APTT results, HRPZ II experience

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Introduction: Haemolysis is one of main causes of sample rejection in most of laboratories. Clinical and Laboratory Standards Institute (CLSI) stated sample with visible haemolysis should not be used for prothrombin time (PT) and activated partial thromboplastin time (APTT) testing. Haemolysis can induce clotting factor activation and interfere with end point measurement. The true impact of haemolysis on these basic coagulation tests is little studied in clinical practice, especially in Malaysian population. Therefore, the aim of this study is to determine the effect of haemolysis including haemolysis's grade on routine coagulation test. *Materials & Methods*: A total of 175 nonhaemolysed citrate blood samples were randomly collected. Mechanical lysis were performed by using 23G needle and 3cc syringe. PT and APTT were obtained using Stago Max3. Paired t test were used for comparison between PT and APTT results (before and after mechanical haemolysis). *Results*: Haemolysis distribution across 175 samples as follow: 8.56% were grade 2, while 22.86% each for grade 3 to grade 6. We found that there were statistically significant difference, shortening of APTT between nonhaemolysed and haemolysed sample for APTT ($p<0.05$) in all grades of haemolysis. Furthermore, significant difference observed in grade 5 and 6 ($p=0.00$). Meanwhile, no statistically significant difference ($p>0.05$) seen on PT result between nonhaemolysed and haemolysed sample except for grade 4 haemolysis ($p=0.02$). *Discussion*: Reporting accurate result is vital in all laboratories. All haemolysed sample should not be tested for coagulation test especially APTT as it can cause erroneous result and further lead to mismanagement.

HT052 Lab-initiated monitoring of isolated prolonged APTT. A retrospective study by Haematology Laboratory, Hospital Pulau Pinang

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Introduction: In late 2018, our lab implemented a system for monitoring isolated prolonged APTT to detect Acquired Haemophilia A and prevent delays in diagnosis and treatment. MLT identified and recorded cases of isolated prolonged APTT. Further history was obtained by MLT and Medical Officers. For patients on any anticoagulant, no repeat sample was requested. Persistently prolonged APTT underwent additional investigations, including mixing tests, factor assays, inhibitor assays, and lupus anticoagulant tests. Isolated prolonged APTT can be caused by factors such as intrinsic factor deficiency, inhibitors, anticoagulants, or pre-analytical factors. *Materials & Methods*: For this retrospective study, we analysed isolated prolonged APTT cases (>40s) recorded from September 2018 to June 2023 from the monitoring system. Cases were categorised based on test ordered by the lab from the follow up investigations. *Results*: A total of 853 isolated prolonged APTTs were documented. 33% were normalised upon repeat testing, likely due to preanalytical factors. 18% were attributed to patients on anticoagulants such as heparin. In 24% of cases, no repeated sample was received, which hindered further investigations. 2% remained inconclusive, while 4% yielded significant findings including Acquired Haemophilia A, FXI deficiency, Haemophilia A, Lupus Anticoagulant, FXII deficiency, and von Willebrand Disease. *Discussion*: Our study highlights that isolated prolonged APTT cases in our hospital are primarily caused by pre-analytical factors. Education on proper venepuncture is crucial. Additionally, our monitoring system successfully detected not only Acquired Haemophilia A cases but also other significant bleeding disorders. Therefore, it is essential to emphasize obtaining a proper bleeding history, especially for cases planned for surgical intervention.

HT053 Recombinant single chain factor VIII concentrate versus conventional standard half-life factor VIII concentrate in persons with severe haemophilia A: A preliminary study

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Introduction: Replacement with clotting factor concentrates has been the mainstay of treatment for persons with haemophilia (PwH). Majority of PwH in Malaysia have been treated with conventional standard half-life factor VIII concentrates (CFVIII) that is made available via the national plasma fractionation program and national tender procurement. Recombinant single chain factor VIII concentrates (rSCFVIII) were recently available, and 3 of our patients received this product. Although clinical trials have shown that rSCFVIII has a longer half-life as compared to the CFVIII, it has not been classified as an extended half-life product by international bodies. *Aim*: To determine the differences in pharmacokinetics (PK) and clinical efficacy between the CFVIII and rSCFVIII. *Materials & Method*: Three (3) patients on CFVIII were converted to rSCFVIII on a 1 to 1 ratio of their existing regimen. Residual factor VIII levels were taken at pre-dose and at 24H, 96H and 120H

post-dose of both CFVIII and rSCFVIII, with at least a two-week washout period in between products. We also compared the bleeding pattern during the duration of treatment with each product. *Results*: The results obtained are still being analysed and will be presented during the conference. *Discussion*: The mainstay of treatment for PwH is factor replacement, which should be individualized based on efficacy. Currently the efficacy of rSCFVIII appears to be comparable to conventional standard half-life products.

HT054 Clinical presentation and management of immune thrombotic thrombocytopenic purpura (iTTP) in Borneo populations – A case series from Malaysia

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a haematological emergency characterised by microangiopathic haemolytic anaemia (MAHA) and thrombocytopenia secondary to severely deficient ADAMTS13 activity (< 10%). Our objective is to demonstrate the management of TTP in a centre in which ADAMTS13 assay is not readily available. *Materials & Methods*: We identified three iTTP patients from the year 2021-2023 in Northern Sarawak, Malaysia. ADAMTS13 activity and inhibitor levels were sampled before treatment initiation. *Results*: All three patients with mean age of 43 (range 41-45) were Sarawakian natives. The male: female ratio was 2:1. Neurological and gastrointestinal symptoms predominantly presented in our cases. Blood parameters showed presence of haemolytic anaemia and thrombocytopenia with mean haemoglobin and platelet levels of 6.7 (range 6-7.6) g/dL and 9 (range 1-16) x 10^9/L respectively. Peripheral blood film (PBF) showed presence of MAHA and true thrombocytopenia. Given strong clinical suspicion of iTTP based on high PLASMIC scores (6 points), all were empirically treated with therapeutic plasma exchange and immunosuppressants. The diagnosis was confirmed a month later in which all the ADAMTS13 activities results returned as 0% with mean inhibitor levels of 36.8 (range 30.5-42.5) U/mL. Clinical remission rate was 100%. However, one of the patients had succumbed to severe sepsis 1 month after discharge. *Discussion*: We demonstrate that high clinical suspicion of TTP, prompt inspection of PBF, utilisation of PLASMIC score and appropriate treatment can improve the mortality rate in a treating centre in which ADAMTS assay is not readily available.

HT055 Clinical presentation and outcomes of idiopathic thrombotic thrombocytopenic purpura in a government hospital in northern Malaysia from 2018 until 2022

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a disorder characterised by microangiopathic haemolytic anaemia and thrombocytopenia associated with fever, renal dysfunction and neurological manifestations. Without treatment, TTP is almost uniformly fatal with a mortality rate approaching 90%. Immediate therapeutic plasma exchange and immunosuppressive therapy improve outcomes. *Materials & Methods*: We conducted a retrospective observational study of patients diagnosed with TTP based on low ADAMTS13 activity level and the presence of ADAMTS13 inhibitor from 01 January 2018 to 31 December 2022 using data extracted from hospital electronic medical records. *Results*: A total of 10 patients were identified. Median age was 42 (range: 15-59) years old with no gender preponderance. All patients presented with thrombocytopenia, with median platelet count of 12 $\times 10^9$/L (range: 4-37 $\times 10^9$/L) and microangiopathic haemolytic anaemia. 6 (60%) patients reported fever, 5 (50%) exhibited neurological abnormalities, while 3 (30%) had renal dysfunction. Median plasma exchange required was 6 (range: 1-20) times. All patients received steroids for immunosuppression. 6 (60%) patients were refractory with 4 receiving additional cyclophosphamide, while 2 were given prednisolone, cyclophosphamide and rituximab. 2 (20%) patients initially treated with plasma exchange and prednisolone relapsed and received prednisolone, cyclophosphamide and rituximab. One early mortality was observed. *Discussion*: Diagnosis of TTP requires a high index of suspicion and should be considered in the presence of microangiopathic haemolytic anaemia and thrombocytopenia. Prompt treatment with plasma exchange results in a high response rate. Immunosuppression with steroids remains the drug of choice. Cyclophosphamide and rituximab can be beneficial for refractory and relapsed disease.

HT056 A case series of COVID-19 vaccines and vaccine-induced thrombotic thrombocytopenia at Malaysian National Haematology Centre

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Introduction: Vaccine-induced thrombotic thrombocytopenia (VITT) is characterised by the presence of thrombosis and thrombocytopenia following vaccination. It is caused by antibodies directed against the platelet factor 4 (PF4)-heparin complex which triggers "pancellular activation", activate platelets and coagulation reactions, similar to heparin-induced thrombocytopenia (HIT) antibodies. *Materials & Methods*: This is retrospective cohort from August 2021 to June 2023 of all PF4 antibodies tested by enzyme-linked immunosorbent assay (ELISA) method. *Results*: During the study period, 7 cases with positive anti PF4 antibodies after first dose of vaccination (4 AstraZeneca, 2 Pfizer, 1 Sinovac). The mean

onset of symptoms was 16 days after vaccinations. Amongst the cases with positive ELISA results, only one case was not associated with thrombosis (AstraZeneca). The majority had borderline low platelet, low fibrinogen and high D-Dimer at diagnosis. All cases were treated with high dose steroids, intravenous immunoglobulin and one case had plasma exchange. *Discussion*: It is important to suspect VITT in patients presenting with thrombocytopenia 4 to 42 days post-vaccination, even in the absence of symptoms suggestive of thrombosis. PF4 antibodies can be detected using a PF4-heparin ELISA test, particularly the IgG-specific ELISA, but not reliably with other HIT laboratory tests.

HT057 Dose and intensity of steroid use and the risk of adverse events in immune thrombocytopenia: A population-based study in Taiwan

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Introduction: Steroids is the first-line treatment for immune thrombocytopenia (ITP), but which can cause adverse events (AEs). This study aimed to investigate the association between steroid use patterns and the risk of AEs in patients with ITP. *Materials & Methods*: The Taiwan National Health Insurance Research Database was used in this study. Adult patients diagnosed with ITP between 2011-2018 were identified, and the date of first steroid use was defined as the index date. Post-index steroid use was calculated on a 90-day basis as a time-dependent variable and categorised by average prednisolone-equivalent daily dose (<10 mg vs. ≥10 mg) and intensity (medication possession ratio <80% vs. ≥80%). Patients were followed-up for one year for acute AE, and all events during the period were recorded. For chronic AEs, patients were followed-up until death or the end of 2019, and only the first event was counted. *Results*: Among 2,691 newly-diagnosed ITP patients, 2,370 acute AE events and 1,208 chronic AE events were identified. Patients with high-dose+high-intensity steroid use were associated with a higher risk of acute AE (adjusted incident rate ratio [aIRR]: 1.57, 95% confidence interval [CI]: 1.38–1.78, p<0.01) and chronic AE (aIRR: 1.26, 95% CI: 1.08–1.47, p<0.01), compared to those with low-dose+low-intensity steroid use. Metabolic/endocrine and ophthalmologic disorders demonstrated the strongest correlation with a high dose and intensity of steroid. *Discussion*: The joint effect of steroid dose and intensity was observed in patients with ITP, and the findings suggest that steroids should be used carefully.

HT058 Thrombosis in Myeloproliferative neoplasms: A systematic review

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Introduction: Thrombosis is a concerning complication of Myeloproliferative neoplasms (MPNs), and contributes greatly to morbidity and mortality. However, there is limited data the evidence regarding thrombotic characteristic in MPNs. This systematic review aims to evaluate the existing evidence of thrombosis in MPNs, particularly it's incidence, risk factors, and strategies on how to manage. *Materials & Methods*: We conducted a search across PubMed, Embase (via ovid), Science Direct, Scopus, Google Scholar, using relevant keywords regarding thrombosis and MPNs. We included studies within the last 15 years that examined thrombosis and bleeding complications among MPN patients. Data extraction was done by 3 independent reviewers, and quality of studies were assessed by Newcastle Ottawa scale (NOS) for cohort studies and JADAD scale for randomised controlled trial. *Results*: We found 9 studies, with a total of 2746 patients. The incidence of thrombosis manifestation varied between studies. Thrombotic manifestations found in multiple organ system and mostly found in polycythaemia vera. JAK2, V617F, CALR mutations were found to be significant to thrombotic manifestations. Age was found to be independently associated with increased risk of thrombosis and recurrent thrombosis, especially above 60 years old. Leucocytosis was associated with thrombosis. Anticoagulant and antiplatelet were used in studies together with hydroxyurea and interferon. *Discussion*: Thrombosis complications poses great risks to MPN patients. Thrombotic complications in MPN patients throughout multiple organ systems, with an increased risk especially owing to leukocytosis and age above 60 years old. Further longitudinal cohort studies were needed to evaluate the prognosis of thrombotic in MPNs.

HT059 Examination of haemostasis parameters that correlate with the occurrence of bleeding in liver cirrhosis patients

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Introduction: Liver plays an important role in the synthesis of components in haemostasis. Liver cirrhosis is a chronic liver disorder that can cause haemostasis abnormality. This study aims to determine the examination of haemostasis abnormalities that correlate with the incidence of bleeding in cirrhosis patients. *Materials & Methods*: Analytical observational study on cirrhosis patients admitted to Dr. Saiful Anwar Hospital during August-September 2023. Examination of haemostasis parameters was carried out at the beginning of admission. Patients excluded as research subjects were patients who had previously received anticoagulant therapy, NSAIDs, and blood transfusion. The haemostasis parameters examined were PT, APTT, INR, Fibrinogen, and D-dimer, using the Sysmex CS-2100i. Statistical analysis was using Spearman correlation test. *Results*: Elevated fibrinogen levels were found in hepatic cirrhosis patients who experienced bleeding compared to those without bleeding. Fibrinogen levels correlated significantly with bleeding events in patients ($r=0.634$; $p<0.05$), while PT, APTT, INR and D dimer did not differ between cirrhosis patients with bleeding and those without bleeding. *Discussion*: Patients with cirrhosis may experience bleeding due to abnormalities in the function of the liver in producing blood coagulation factors. PT, APTT, INR examination is a haemostasis examination that can detect abnormalities in coagulation factors of intrinsic and extrinsic pathways. Fibrinogen and D-dimer examination can detect blood coagulation factor and fibrinolysis. In this study, fibrinogen levels correlated with the occurrence of bleeding in cirrhosis patients. It can be explained that bleeding conditions are thought to cause increased production of blood coagulation factors in response to stop bleeding.

HT060 Correlation of D-dimer level with demographic dan comorbidities risk factors in Terengganu COVID-19 patients: A preliminary analysis

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Introduction: COVID-19 associated coagulopathies with elevated D-Dimer level are linked to comorbidities present in COVID-19 patients. This condition remains unclearly reported in Malaysia, particularly in Terengganu, thus we investigated the COVID-19 patients' demographic and comorbidities risk factors with levels of D-Dimer and their relationship and correlation. *Materials & Methods*: A cross-sectional study from January to August 2021 was conducted involving 102 COVID-19 patients' data from Laboratory Information System (LIS) and analyzed using descriptive statistics, Chi Square and Spearman test. *Results*: We found that higher positive COVID-19 cases were in males (n=63; 61.8%) compared to women (n=39; 38.2%) and more prominent in the age group of 15 to 64 years old (n=68; 66.7%). Malay race is the most affected with 99 patients (97.1%) and majority of patients showed high level of D-Dimer (n=93; 91.2%). Besides that, ranking of comorbidities risk factors in COVID-19 patients are hypertension (77.5%), diabetes mellitus (68.6%), hyperlipidaemia (25.5%), renal impairment (24.5%), IHD (21.6%), CVA (9.8%) and dysthymia (1.0%). Meanwhile, our study found that all demographic which are age and gender and comorbidities risk factors showed no significant relationship with levels of D-Dimer. Moreover, there is no correlation between age and D-Dimer levels, $r(102) = -0.005$, $p=0.962$. However, these findings are different with our previous study and other studies which might due to small studied population and need more extensive and detailed further studies with larger sample size. *Discussion*: In conclusion, this study showed no significant relationship and correlation in D-Dimer levels with demographic and comorbidities risk factors among Terengganu COVID-19 patients.

HT061 Sosio-demographic profile and correlation of D-dimer and fibrinogen levels with demographic factors among COVID-19 patients in Terengganu

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Introduction: COVID-19 is a global pandemic disease linked to coagulation dysfunction, COVID-19 associated coagulopathies with elevated D-Dimer and fibrinogen. This condition remains unclearly reported in Malaysia, particularly in Terengganu, thus we investigated the COVID-19 patients' socio-demographic profile and their relationship with levels of both biomarkers. *Materials & Methods*: A cross-sectional study from January to August 2021 was conducted, which involve 414 COVID-19 patients' data from Laboratory Information System (LIS) and analysed using descriptive statistics and Chi-Square test. *Result*: Results showed that higher positive COVID-19 cases were in males (n=213; 51.4%) compared to women (n=201; 48.6%) and

more prominent in the age group of 15 to 64 years old (n=301; 72.7%), followed by age group of 65 years old and above (n=112; 27.1%) and 14 years old and below (n=1; 0.2%). Malay race is the most affected with 408 patients (98.6%) and majority of patients showed high level of D-Dimer (n=327; 79.0%) along with normal level of fibrinogen (n=278; 67.1%), while with high level of fibrinogen (n=126; 30.4%). Meanwhile, 26.0% of the patients showed high levels of both D-Dimer and fibrinogen. Only 1.2% showed high D-Dimer with low fibrinogen levels, which indicate more incidences of thrombosis than disseminated intravascular coagulation (DIC). Further analysis revealed only age factor (p=0.012) showed positive and significant relationship with D-Dimer levels. As for fibrinogen levels, both age (p=0.000) and gender (p=0.024) showed positive and significant relationship. *Discussion*: In conclusion, this study highlighted the abnormalities in D-Dimer and fibrinogen levels and well correlated with age or/and gender factors among COVID-19 patients in Terengganu.

HT062 IMPROVE bleeding score as a predictor of acute upper gastrointestinal bleeding events in liver Cirrhosis patients at Saiful Anwar General Hospital

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Introduction: Acute upper gastrointestinal bleeding occurs due to rupture of oesophageal or gastric varices and failure of liver function. Several scoring systems have been implemented, one of which is the IMPROVE score. The aim of this study was to prove whether this score can predict the incidence of acute bleeding (Hematemesis-Melena) in patients with liver cirrhosis. *Materials & Methods*: This study was a cross-sectional study with one hundred Cirrhosis patient who were treated in the Saiful Anwar General Hospital. IMPROVE score is enforced from age, gender, kidney function, liver function, platelet count, being treated in the ICU or ICCU, having a central venous catheter inserted, active gastric or duodenal ulcer, having experienced bleeding in the last 3 months, suffering from rheumatic disease, diagnosed with cancer. Patients with an IMPROVE score (≥7) are in the category of having a high risk of bleeding. *Results*: A total of 50 subjects (50%) experienced bleeding from 100 subjects. The Odds Ratio for bleeding in patients with a high IMPROVE score (≥7) was 32.25 (95% Confidence Interval: 10.74 – 96.87). Meanwhile, the Relative Risk of bleeding in patients with a high IMPROVE score (≥7) is 5.46 (95% Confidence Interval: 2.68 – 10.43). *Discussion*: Patients with a high IMPROVE score (≥7) have a tendency to experience bleeding 32.25 times compared to patients who have a low IMPROVE score (<7). Patients with a high IMPROVE score (≥7) had a tendency to experience bleeding 5.46 times compared to all patients in this study.

HT063 Exposing the silent threat of arterial thrombosis among BCR-ABL-Negative myeloproliferative neoplasms patients in Kelantan

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Introduction: BCR-ABL-negative myeloproliferative neoplasms (MPNs) are characterised by the clonal proliferation of cells in the bone marrow that harbour a somatic mutation responsible for initiating the MPN. The objective of this study is to assess the contributing factor of arterial thrombosis in MPNs. *Materials & Methods*: Between January 2017 and December 2019, we identified 65 MPNs patients who experienced thrombosis at Hospital Universiti Sains Malaysia and carrying specific mutations (JAK2 V617F, CALR Type 1/2, MPL). Their diagnoses were based on the 2016 WHO criteria, with clinical data collected from HUSM records. *Results*: Out of the 65 patients, 49 (75.3%) had experienced arterial thrombosis events, with 25 (51%) having cerebrovascular accidents (CVA) and 24 (49%) suffering from myocardial infarctions (MI). Among these cases, 20% were associated with PV, 12% with ET, and 12% with PMF. A total of 93.8% of these patients had the JAK2 V617 mutation, while none tested positive for CALR Type 1/2 mutations. The median age of those with arterial thrombosis was 56.95, with 16.3% under 40 years old, and there were no gender differences observed between males and females. *Discussion*: Interestingly, most of our MPN patients with thrombotic events were more inclined to experience arterial rather than venous thrombosis, in contrast to the trend observed in most Western studies. A potential association between the JAK2V617F mutation and endothelial dysfunction has been proposed, possibly contributing to thrombosis development. The current study clarifies the contribution JAK2V617F one of the provoking factors for arterial thrombosis in MPN patients.

HT064 Adiponectin promote TPO response for treating ITP by relating Rab6A-myosin9 trafficking vehicle carrying c-Mpl to cell surface

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Introduction: Impaired megakaryocyte maturation is one of the pathogenic mechanisms of primary immune thrombocytopenia (ITP). The thrombopoietin (TPO) receptor c-Mpl on the membrane surface of megakaryocytes plays a critical role in the cellular reception of TPO signals and megakaryocyte maturation. This study investigated how the distribution of c-Mpl on the membrane surface of megakaryocytes influences the pathogenesis of ITP and the specific regulatory mechanisms. *Materials & Methods*: In this study, we investigated the distribution of c-Mpl on the membrane surface of megakaryocytes by Flow Cytometry using bone marrow mononuclear cells. Then molecules associated with trafficking c-Mpl to the membrane were studied and validated by immunoprecipitation. *Results*: We found that the distribution of c-Mpl on the membrane surface of megakaryocytes of ITP patients was significantly reduced, confirming that the abnormal distribution of c-Mpl is associated with the pathogenesis of ITP. We applied immunoprecipitation and protein profiling to find the intracellular c-Mpl transport-related protein molecules. Moreover, we demonstrated that Adiponectin affects the transportation of the c-Mpl to membranes by inhibiting the complex interaction, thereby reducing the responsiveness of megakaryocytes to TPO and inhibiting the activation of its corresponding intracellular signalling pathways. *Discussion*: The present study identified a novel transport complex mediating the transportation of the c-Mpl to membranes, clarified the abnormal mechanism of this complex in ITP, and confirms that Adiponectin can regulate this complex to improve the efficacy of TPO, which provides a new idea for the clinical treatment of ITP.

HT065 Congenital factor V deficiency: A rare cause of neonatal coagulopathy

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Introduction: Congenital factor V (FV) deficiency is a rare autosomal recessive bleeding disorder with a prevalence of 1 in 1 million population. The presentation is heterogenous and ranges from asymptomatic to life-threatening haemorrhages. *Case report*: We describe a term baby girl, newborn of non-consanguineous parents, presented with oozing from the vaccination site at day 1 of life. Coagulation screen showed markedly prolonged prothrombin time (PT) (64.8 seconds) and partial thromboplastin time (aPTT) (>180 seconds), mildly increased fibrinogen, normal D-Dimer and platelet count. Repeated PT and aPTT were persistently prolonged. Mixing study showed corrected results. Coagulation factor activity assay revealed severely reduced FV activity, 1.9% and 1.1% repeatedly. Other coagulation factor activity assays including Vitamin K-dependent coagulation factors and FVIII were all within normal range. Diagnosis of Congenital Factor V Deficiency was made, although no genetic testing for FV gene was performed due to limited test accessibility. FV activity assay for both parents were at the lower range of normal, while the second brother showed a mildly reduced level. The first brother has normal FV activity results. Both parents and brothers were asymptomatic. She was transfused with fresh frozen plasma (FFP) and no new bleeding tendency observed throughout her hospital stay. She was discharged at day 10 of life with a Paediatric Haematology follow-up. *Discussion*: Congenital FV deficiency is one of the rare causes of neonatal coagulopathy. Early diagnosis is possible, despite limited availability of confirmatory genetic testing. To date, FFP transfusion is still the treatment option as there is no specific factor concentrate available.

HT066 Abnormal international normalised ratio due to lupus anticoagulant with different clot-based coagulation reagents

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Introduction: Lupus anticoagulant (LA) is a non-specific inhibitor of coagulation, which usually interferes with the determination of the activated partial thromboplastin time (aPTT) and less commonly the prothrombin time (PT). The presence of LA is associated with an increased risk of thrombosis rather than bleeding, and in the context of antiphospholipid syndrome, patients would usually be on warfarin, which is monitored using the International Normalized Ratio (INR). *Case report*: Mr SZ was a 45-year-old male recently diagnosed to have antiphospholipid syndrome after multiple episodes of thromboembolism. He was also found to be positive for the presence of lupus anticoagulant (LA), anti-cardiolipin (aCL) and anti-ß2 glycoprotein 1 (aß2-GPI) antibodies. He was initially on rivaroxaban and then clexane. INR was found to be consistently high, without any bleeding tendencies. His aPTT was mostly unaffected by clexane. After discussion with the clinician, we decided to investigate further. *Discussion*: PT was measured using fresh samples on two Sysmex analysers, CS2500 and CA104, ACL Top by Instrumentation Laboratory. PT results for CS2500 and CS104 were 34s (RI: 9.3s-10.8s) and 30s, respectively. PT results were 13s with ACL Top (RI: 10.3s-12.7s). The recombinant thromboplastin Innovin was used in both Sysmex coagulation analysers CS2500 and CA104, whereas HaemosIL was used in ACL Top. PT was also performed manually in

water baths using Innovin and HaemosIL and the results were 52s and 13s, respectively. These results showed that PT can be affected by different PT reagents. Our PT reagent was later changed to Thromboxane.

HT067 A case report of an infant diagnosed with Type 3 von Willebrand Disease (VWD) - The rarest subtype

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Introduction: Type 3 von Willebrand Disease (VWD) is characterised by a virtually complete quantitative deficiency of von Willebrand Factor (VWF), leading to markedly reduced coagulation factor FVIII. It is the most severe and rarest subtype, accounting for about 1-2% of total VWD cases and inherited as an autosomal recessive disease. *Case report*: 11 months old Malay girl presented with provoked gum bleeding. On further questioning, she has bleeding tendency since age of 6 months: easily bruising following trivial injury and hematoma at vaccination injection site, which took few weeks to resolve spontaneously. She is the only child and there is no family history of inherited bleeding disorders. Examination showed multiple bruises at right forehead, left anterior chest wall and left medial malleolus. From the clinical evaluation, suspicion of Non-Accidental Injuries (NAI) is less likely. She has anaemia (haemoglobin 7g/dL) with normal platelet count. Routine coagulation tests revealed isolated prolonged APTT with normal fibrinogen level. APTT was fully corrected at immediate and 2 hours incubation of APTT mixing test. VWF profile revealed markedly reduced level of VWF:Ag (1.7%), VWF:RCo (1.8%) and VWF:CB (<1.0%) with FVIII:C of 3.4%. Findings were highly suggestive of Type 3 VWD. The child was referred to Paediatric Haematologist for comprehensive care including treatment with VWF-containing concentrates. *Discussion*: Early recognition of inherited bleeding disorders is important as the clinical presentations of the rare Type 3 VWD may mimic other conditions, including NAI. Thus, thorough clinical and laboratory evaluation is crucial to ensure early diagnosis, appropriate treatment and comprehensive care.

HT068 Diagnosis of Glanzmann's Thrombasthenia by whole blood impedance analyser - A case report from a single referral centre in Malaysia

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Introduction: Glanzmann's Thrombasthenia is a rare autosomal recessive platelet disorder due to quantitative and/or qualitative abnormality of glycoprotein IIb/IIIa. Defective glycoprotein IIb/IIIa results in a bleeding diathesis as it is needed for the cross-links between platelets. *Case report*: We report a case of a 2-year-old boy, presented with on and off epistaxis, gum bleeding and easy bruising since 3 months of age. The family history regarding bleeding disorder was unknown as he is a foster child. Full blood count, coagulation screening profile, fibrinogen and Von Willebrand Disease assay were normal. The bleeding time was prolonged (>6 minutes). Clot retraction appearance was abnormal with borderline low clot retraction time. Platelet aggregation study using whole blood impedance method showed no aggregation in response to collagen 1 ug/ml, collagen 5 ug/mL, ADP 5.0 uM, ADP 10 uM, ADP 20 uM, and arachidonic acid 0.5 mM. Agglutination with Ristocetin 1.0 mg/ml and 1.25 mg/ml were borderline low normal. The platelet aggregation pattern is consistent with the diagnosis of Glanzmann's Thrombasthenia. *Discussion***:** Patients with Glanzmann's Thrombasthenia typically present with bleeding diathesis. Laboratory investigations show normal complete blood count and coagulation profile. Platelet aggregation test findings are characterised by the absence of aggregation with all agonists except ristocetin. Flow cytometry demonstrates decreased or absent of GPIIb-IIIa complex (CD41/CD61). However, in a limited resource setting, bleeding history with normal coagulation profile coupled with a classical pattern in platelet function assays could provide a reliable diagnosis. A prompt diagnosis is needed to minimize morbidity and improve life quality of the patient.

HT069 Laboratory characteristics of acquired von Willebrand syndrome (AvWS) associated with myeloproliferative neoplasms: Case series

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Introduction: Acquired von Willebrand syndrome (AvWS) is a rare bleeding disorder. It is associated with multiple conditions whose pathophysiology includes antibodies to von Willebrand factor (vWF), proteolysis, binding to tumour cells and decreased synthesis, resulting in a variable presentation and laboratory profile. *Case report*: Four cases of AvWS with different clinical and laboratory features were described. Case 1: A 55-year-old lady had underlying JAK2-positive myeloproliferative neoplasm on aspirin. She had severe bleeding after tooth extraction. Noted platelet 778 x 10^3/uL and prolonged APTT. Testing revealed normal Factor VIII (84%) and vWF antigen (190%) with low vWF:Ricof (0.6%). Case 2: A 23-year-old man, known JAK2-positive Essential thrombocythemia with platelet 903 x 10^3/uL. No bleeding tendency.

Testing showed prolonged APTT, normal vWF antigen (86.6%), low FVII (49.1%) and low vWF:Ricof (28.2%). Case 3: A 79-year-old lady with JAK2 positive Essential thrombocythemia and platelet 1063 x 10^3/uL, was scheduled for mastectomy for breast cancer. Testing revealed prolonged APTT, normal FVIII (174%), vWF antigen (176%) and vWF:Ricof (78%). vWF:Ricof/vWF antigen ratio was reduced (0.44). Case 4: A 69-year-old man presented with per rectal bleed and was later diagnosed with JAK2-positive Polycythaemia vera. Testing showed prolonged APTT, normal Factor VIII (173%), increased vWF antigen (206%) and normal vWF:Ricof (93%). vWF:Ricof/vWF antigen ratio was reduced (0.45). *Conclusion*: The biological phenotype was type 2 in all cases, although vWF antigen and vWF:Ricof levels could be normal. AvWS is a potentially serious bleeding disorder. High suspicion and clinical correlation are required to make the diagnosis.

HT070 Kaposiform Hemangioendothelioma with Kasabach-Merritt phenomenon: Successful treatment with sirolimus in paediatric patients

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Introduction: Kaposiform Haemangioendothelioma (KHE) is a rare vascular neoplasm with high morbidity and mortality. The main pathological features of KHE are abnormal angiogenesis and lymphangiogenesis. KHEs are often associated with Kasabach-Merritt phenomenon (KMP), a potential life-threatening thrombocytopaenia and consumptive coagulopathy. Management of KHE is challenging due to the clinical heterogeneity and the disease-related comorbidities. *Case report*: We report successful management of three paediatric patients with KHE associated with KMP with oral sirolimus. Two cases were treated with steroids in combination with IV Vincristine (VCR) as first line therapy which only had partial response. Oral sirolimus was used as second line therapy and both patients showed rapid response to the treatment. Another case was treated with steroid and oral sirolimus as first line therapy and achieved good response. *Discussion*: Sirolimus, an inhibitor of the mammalian target of rapamycin (mTOR), inhibits cell proliferation and metabolism, lymphangiogenesis and angiogenesis. There are scattered case reports showing a rapid response of KHE and KMP to sirolimus. All the patients reported here tolerated sirolimus without significant side effects. Platelet transfusions should be avoided in KHE with KMP due to various reasons which could worsen KHE. Understanding the aetiology and pathogenesis of KHE is crucial to improve the management of patients with KHE with KMP. Novel targeted treatments are needed to maximise the outcome of patients with KHE.

HT071 A case of spinal cord and small bowel thrombosis post Covid-19

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Introduction: COVID-19 pneumonia has long been recognised to be associated with thrombosis especially in severe form of infection. We present here a case of multiorgan arterial thrombosis involving the spinal cord and small bowel post COVID-19 infection. *Case report*: We present a 57-year-old Malay gentleman, with underlying ischaemic heart disease, hypertension, dyslipidaemia and gastritis. He was diagnosed to have COVID-19 pneumonia category 4 on the 18th August 2021. Thrombophylaxis given throughout admission along with dexamethasone as per protocol, and he was discharge well. He presented to us again 1 month later complaining of lower abdominal pain for 2 weeks. He was treated for Non ST-elevation myocardial infarction as his troponin I level is elevated, with ECG changes suggestive of NSTEMI. On 15th September at 6am sharp, he complained of severe lower abdominal cramping pain. Symptomatic treatment was given but no relief of pain. At 10am, he developed acute flaccid paraplegia. CT angiography of thoracic, abdominal revealed circumferential mural thrombus at bilateral proximal common carotid arteries, coeliac trunks, with luminal stenosis seen in coeliac trunk. Subsequent magnetic resonance imaging (MRI) showed spinal cord and vertebra bodies infarctions. *Discussion*: This case highlighted arterial thrombosis with multiorgan involvement in a previously vaccinated and non- critical COVID-19 pneumonia. Artery thrombosis has been reported in critically ill patients but our case showed that even previously discharged well patient could still develop thrombotic complications.

HT072 Acquired haemophilia A in a patient with rectal adenocarcinoma

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Introduction: Acquired haemophilia A (AHA) is a serious bleeding disorder caused by autoantibodies against coagulation factor VIII (FVIII). 10% of patients have an underlying malignancy. *Case report*: A 69-year-old Man with underlying hypertension, dyslipidaemia, psoriasis, liver cirrhosis child Pugh A, presented with 1-month multiple bleeding tendencies, he had prolonged bleeding and hematoma after dental procedure, spontaneous bilateral thigh hematoma and PR bleeding. Biopsy from rectal ulcer confirmed rectal adenocarcinoma. Noted isolated prolonged APTT, mixing test not correctable. He was treated as AHA. Initial treatment was oral prednisolone with cyclophosphamide. Colonoscope with repeated biopsy complicated with massive PR bleeding from biopsy side required blood product transfusion, FEIBA and novoseven 2mg 2 hourly not able to stop bleeding and eventually secured with local adrenaline injection, flushed with cold saline and endoclots on rectal ulcer. Novoseven and one dose emicizumab were given post procedure. Coagulopathy was corrected. Patient had

another episode of massive PR bleeding 2 days later, patient underwent under-running of bleeding rectal tumor with 2 haemostatic suture applied. For rectal adenocarcinoma treatment, in view of high risk massive bleeding and local disease, patient underwent 25 radiotherapy and chemotherapy. *Discussion*: Treatment of the underlying malignancy is advocated as a possible curative measure. However, immunosuppressive therapy is recommended for those patients who fail treatment of the primary tumour, or for those who present acutely with bleeding or are unable to receive chemotherapy.

HT073 Vaccine-induce thrombotic thrombocytopenia (VITT) manifested as massive and complete portal venous thrombosis & splenic hypoperfusion: First Malaysian case

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Introduction: VITT is a rare complication of adenoviral vaccine administration. It presents with thrombocytopenia & thrombosis in varies site, especially in cerebral veins and pulmonary embolism. Complete Portal venous thrombosis have been reported rarely. *Case report*: This is 34-year-old Indian man, presented with symptoms of abdominal discomfort on day 6 post 1st vaccine injection but was presented to emergency on day 15 with severe abdominal pain and haemodynamic compromise. The imaging showed complete portal venous thrombosis and obstruction with hypoperfusion of spleen and bowel ischaemia. Severe thrombocytopenia and segmental pulmonary emboli were detected. Anti-platelet factor 4 (aPF-4) was sent upon making clinical diagnosis of VITT. Without waiting for the report, prompt treatment initiated with Therapeutic Plasma Exchange, Fondaparinux, Immunoglobulin and Intravenous Steroid. Patient developed upper & lower gastrointestinal bleeding during the treatment. The treatments modalities persevered with help of intensive care service and necessary blood transfusion. Patient survived, and was on tapering dose of oral steroid for 10 weeks and completed 3 months of anticoagulation. Test aPF-4 antibody came back as positive. *Discussion*: This case illustrated the importance of history & clinical diagnosis to prompt the initiation of specific treatment in VITT i.e the plasma exchange which altered the course of event for unexpected side effects from necessary vaccine in this healthy & young patient.

HT074 Devastating complication of pregnancy: A case of recurrent post-partum thrombotic thrombocytopenic purpura

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare disorder which also uncommon in pregnancy. Absence of functional ADAMTS-13 leads to ultra large VWF multimers' formation hence bind spontaneously to platelets to form aggregates within the arterial and capillary microvessels (microthrombi) inducing tissue ischemia, platelet consumption, and microangiopathic haemolytic anaemia. Here, we report a case of recurrent TTP, which occurred in her 2 consecutives post-partum period. *Case report*: A 37-year-old lady, Para 2 with underlying chronic hypertension and history of gestational Diabetes Mellitus, presented with recurrent episodes of anaemic symptoms at postpartum period in 2020 (day 8) and 2021 (day 9). She had severe anaemia and thrombocytopenia with morphological finding of microangiopathic haemolytic anaemia. She was treated as thrombotic thrombocytopenic purpura (TTP) with commencement of plasma exchange and steroid in 2020 and Rituximab were added in 2021. ADAMTS 13 showed absence of activity with presence of inhibitor. She had been investigated for autoimmune disease but did not fulfil SLICC criteria for diagnosis of SLE. *Discussion*: This case illustrated recurrent acquired post-partum TTP. It is one of causes of thrombotic microangiopathic anaemia (TMA) in which the commonest causes are pre-eclampsia, eclampsia and HELLP syndrome. Pregnancy is a known risk factor for acquired TTP, in which auto-antibodies against ADAMTS 13 inactivate or bind ADAMTS13. Risk of recurrence TTP is about 45% in acquired pregnancy associated TTP. Specific proteins found in the placental circulation serve as antigens that trigger maternal antibody production against ADAMTS-13 is the proposed mechanism.

HT075 Pulmonary embolism as uncommon presentation for primary antiphospholipid syndrome in young male

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Introduction: Antiphospholipid syndrome (APS) is an autoimmune disease and it is uncommon in paediatric population with even gender distribution. Primary APS (PAPS) occurs in isolation with commonest presentation of arterial thrombosis, in contrast to venous thrombosis in secondary APS (SAPS). Systemic lupus erythematosus (SLE) is frequently associated with SAPS. Here is a case of 15-year-old boy, presented with pulmonary embolism which led to the diagnosis of primary APS. *Case report*: An active 15-year-old boy presented with acute exertional dyspnoea. He was hypoxic, requiring oxygenation support. Computed tomography (CT) thorax shows extensive bilateral pulmonary embolism. Coagulation profile revealed isolated prolong activated partial thrombin time (aPTT). Mixing study indicated presence of coagulation inhibitor. APS diagnosis made by presence of triple positivity of antiphospholipid antibodies. Autoimmune disease screenings were negative except for positive p-antineutrophilic cytoplasmic antibody (p-ANCA), without clinical evidence of vasculitis. His final diagnosis

is primary APS with pulmonary embolism and currently treated with warfarin. *Discussion*: Antiphospholipid syndrome is uncommon in paediatric population. In contrast to adult APS, gender distribution is even and for PAPS, common manifestation is arterial thrombosis compared to venous thrombosis in SAPS. Based on largest paediatric APS registry, commonest venous thromboembolism is deep vein thrombosis (DVT). Pulmonary embolism in context of PAPS is an unusual presentation. High index of suspicion is crucial in children presenting with thrombotic events with no risk factor. Follow-up care is important as few cases of PAPS diagnosis are revised to SAPS with subsequent diagnosis of SLE.

HT076 4-factor prothrombin complex concentrates (PCC): The preferred option in overwarfarinised patients with upper gastrointestinal haemorrhage

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Introduction: Octaplex® is a 4-factor prothrombin complex concentrate (PCC) containing vitamin K-dependent coagulation factors (Factor II, VII, IX, and X) and inhibitory proteins C and S. It is indicated for the management of life-threatening bleeding in patients with overwarfarinisation. Here we highlight the importance of the early provision of PCC in an overwarfarinised patient with a massive upper gastrointestinal haemorrhage. *Case Report*: A 71-year-old man with non-valvular atrial fibrillation on warfarin presented to the emergency department with per rectal bleeding for 2 days. He was hypotensive on arrival and clinical examination revealed fresh melaena and pallor. His blood investigation showed a haemoglobin of 7.5g/dL from a baseline of 13g/dL, platelet count of 140 x 10^9/L, and a deranged prothrombin time (PT) of 60.2 seconds with an international normalized ratio (INR) of 5.72. Two units of packed red blood cells and four units of fresh frozen plasma (FFP) failed to normalize the deranged coagulation profile and ongoing bleeding. A single dose of 2000 IU 4-factor PCC Octaplex® (30 IU/kg) was subsequently administered intravenously with vitamin K at 10mg resulting in an immediate correction of INR (1.15) and haemodynamic stability. An upper endoscopic examination demonstrated a Forrest IIA pre-pyloric gastric ulcer. A repeated endoscopy 2 weeks later revealed a healed gastric ulcer, and he was safely restarted on anticoagulation therapy. *Discussion*: Our case corroborated with evidence that early administration of 4-factor PCC is crucial in overwarfarinised patients with major bleeding to minimize transfusion requirements and allow lifesaving procedures to be carried out.

HT077 Case of acquired haemophilia following COVID-19 vaccine in the elderly: Lesson for prompt and accurate diagnosis

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Introduction: Acquired haemophilia A (AHA) occurs due to the development of autoantibodies directed against clotting factor VIII (FVIII). This disease is observed among the elderly. with a mortality rate approaching 20%. Accurate diagnosis and prompt treatment of AHA has been shown to reduce its bleeding mortality risk. *Case report*: An 80-year-old developed multiple bruises 2 weeks after his first dose of the COVID-19 vaccine. Diagnosis was delayed due to his cognitive impairment and low clinical suspicion. This led to a representation with worsening ecchymosis, a left thigh haematoma and symptomatic anaemia. Laboratory testing revealed an isolated prolongation of the activated partial thromboplastin time, which remained uncorrected in the mixing test. Further testing confirmed the presence of factor VIII inhibitors and low FVIII titres of 6.7%. He responded to treatment with intravenous methylprednisolone and recombinant activated FVII. *Discussion*: Interestingly, most cases of AHA following COVID-19 vaccination involved elderly patients with multiple comorbidities. All presented with bleeding within 1–3 weeks after receiving the mRNA vaccine. The pathophysiology remains to be elucidated but vaccines are known to stimulate autoantibody production via pre-existing B cells. Given the patient's cognitive impairment and frailty, a comprehensive geriatric assessment (CGA) from the outset might have facilitated an earlier diagnosis. In spite of guideline recommendation to initiate immunosuppressive therapy, clinicians should individualise the use of IST among frail patients as IST-related morbidity may outweighs the risk of fatal bleeding in AHA. Despite a temporal association between the COVID-19 vaccine and AHA, a cause-and-effect relationship has not been established and further study is warranted.

HT078 Two case reports of paediatric May-Thurner Syndrome with extensive lower extremity deep vein thrombosis requiring pharmaco-mechanical thrombectomy/thrombolysis

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Introduction: May–Thurner Syndrome (MTS) is an anatomic variant resulting in compression of the left iliac vein by the overlying right common iliac artery against the lumbar vertebrae. MTS increases the incidence of left-sided lower extremity deep vein thrombosis (DVT). Data on management and outcomes of paediatric MTS cases with DVT is limited. We present two case reports of paediatric MTS with DVT, as well as their management and outcomes. *Case Reports*: Both cases were adolescents who presented with acute left lower limb DVT with one having pulmonary embolism. MTS was diagnosed on various imaging investigations including ultrasound doppler, CT and MRI scans. Both cases had concomitant thrombophilia –

one had connective tissue disease (CTD) with secondary antiphospholipid syndrome, while the other had protein S deficiency. They were both treated with anticoagulation and pharmaco-mechanical thrombectomy/thrombolysis (PMT). The case with CTD required multiple PMTs and a stent insertion at the iliac vein due to rapid progression of clots and required plasma exchange and pulse methylprednisolone for her CTD. The patient with protein S deficiency had complete resolution of DVT while the patient with CTD had a residual partial thrombus in the left popliteal vein. *Discussion*: Anticoagulation is the first-line treatment used to prevent clot extension. However, it does not correct the anatomic compression or result in clot dissolution. In adults, PMT in addition to anticoagulation are considered the standard treatment for MTS with acute thrombosis. Our cases highlight the role of endovascular therapies in the management of acute DVT in the setting of paediatric MTS.

HT079 Prothrombin complex concentrate (Octaplex) for reversal of vitamin K antagonist treatment in bleeding and non-bleeding patients

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Introduction: Octaplex offers rapid and effective reversal of vitamin K antagonist therapy in patients with life-threatening bleeding and those requiring urgent reversal. This series shares our experiences utilising Octaplex to reverse the effects of vitamin K antagonist therapy among our patients. *Case report*: *Case 1:* A 67-year-old gentleman with atrial fibrillation and metallic valve presented to Emergency Unit with syncope and black stools. Upper endoscopy revealed prepyloric and antral ulcers. Intravenous Octaplex administered prior procedure for overwarfarinisation corrected the INR within 4 hours. He had no further bleeding prior discharge. *Case 2:* A 63-year-old gentleman was admitted for an acute exacerbation of COPD. He took warfarin for atrial fibrillation. His INR was 4.8 without significant bleeding manifestation. Octaplex administered to correct the INR. *Case 3:* A 77-year-old woman took warfarin for non-valvular AF and dilated cardiomyopathy, admitted for right hand abscess. Immediate INR correction achieved following intravenous Octaplex administration. She has no post-operative bleeding complication. *Case 4:* A 30-year-old gentleman received warfarin for heart failure with apical clot and undergoing regular haemodialysis. He requires catheter insertion due to non-functioning AVF. Fresh frozen plasma was given pre-procedure since his INR was 4.1. Continuous oozing from catheter site during haemodialysis observed despite administration of vitamin K and protamine sulphate. Bleeding ceased only after Octaplex administered. *Discussion*: Our series demonstrates that Octaplex provides safe and rapid reversal of vitamin K antagonist therapy. No thromboembolic events were observed following Octaplex administration among our cases.

HT080 octanate® for Immune Tolerance Induction (ITI) in paediatric haemophilia A patients with inhibitors: Malaysian experience update

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Introduction: Inhibitor development remains a major concern in haemophilia A patients and is associated with increased morbidity, mortality, and costs. Immune Tolerance Induction (ITI) is currently the only clinical proven strategy to eradicate inhibitors and is recommended by international guidelines. octanate® is a human plasma-derived FVIII concentrate, stabilised with Von Willebrand Factor (VWF), which is highly effective in ITI. We report the updated results from a case series of paediatric patients being treated with octanate® for ITI in our centre. *Case report*: This case series presents 22 children with severe haemophilia A (FVIII:C < 1%) and inhibitors who underwent ITI with octanate®, from November 2015 to June 2023. Patients received 50-100 IU/kg octanate® either daily or 3x/week, and at the discretion of the treating physician. ITI was considered successful when a negative inhibitor assay was achieved (<0.6 Bethesda Units/mL) on two different occasions more than a month apart. *Discussion*: 16 of the 22 patients (72%) achieved a negative inhibitor titre in a median time of 11.5 months (range: 6-42 months). ITI is ongoing in 3 patients and 2 patients were lost to follow-up. ITI failed in 2 high-responder patients (9%). A first ITI with another plasma-derived FVIII had been initiated unsuccessfully in one of the patients. Both patients are currently on Emicizumab prophylaxis. The rate of inhibitor eradication with octanate® remains high (72%) in accordance with our preliminary results published 3 years ago (69%). 8 patients on 9 treated with moderate dose regimens for ITI were successful.

HT081 Acute pulmonary embolism following proximal upper extremities trauma: A case series

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Introduction: Upper extremities trauma, as opposed to its lower extremities counterpart, is a relatively uncommon contributing factor to the development of pulmonary embolism, hence receiving lesser clinical attention. Guidelines on risk stratification and management of anticoagulation therapy are lacking and unestablished. We present two cases of acute pulmonary embolism attributable to upper extremities injuries, with and without long bone fracture, highlighting its clinical relevance. *Case report 1*: A 75-year-old lady presented with acute onset shortness of breath and chest discomfort. She sustained a closed

compound right humeral fracture, from a fall two weeks ago. Electrocardiogram showed sinus tachycardia with classical S1Q3T3 changes. Transthoracic echocardiogram shows dilated right heart chamber. Trop-T was raised. Upper limb venogram revealed thrombus within the deep vein system. CTPA confirmed the diagnosis of submassive PE which was successfully treated with oral anticoagulant. *Case report 2*: An ambulant 81-year-old lady sustained recurrent left shoulder dislocation and compounding soft tissue injury, from a fall two weeks ago. She was managed conservatively with immobilisation. Incidental in-hospital transthoracic echocardiogram showed severe TR with elevated pulmonary artery systolic pressure, suggestive of acute PE. She is clinically asymptomatic despite CTPA confirming multiple segmental pulmonary arterial thrombi. Oral anticoagulation was initiated then. *Discussion*: This case series demonstrated proximal upper extremities trauma as a considerable contributor to the development of acute pulmonary embolism. Risk-based stratification for prophylactic anticoagulation treatment is necessary to prevent catastrophic outcomes.

HT082 Case series of successful systemic thrombolysis for massive pulmonary embolism: In-patient Anticoagulation Service (IPAC) of a single centre experience

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Introduction: Pulmonary embolism (PE) is a lethal form of venous thromboembolism (VTE) which carries high mortality despite early diagnosis and therapy. PE is classified as massive (high risk), submassive (intermediate risk) and low risk. Systemic thrombolytic therapy improves clinical outcome for massive or submassive PE. Pulmonary Embolism Severity Index (PESI) is a risk stratification tool used to guide clinician in systemic thrombolytic therapy. *Case report*: In this retrospective study, 9 patients with massive and submassive PE were treated between June 2018 to July 2023. Median age of our patient is 45.7. 5 out of 9 patients had deep vein thrombosis (DVT). All successfully received systemic thrombolytic therapy in the intensive care unit (ICU) based on PESI score, CTPA and echocardiography. The PESI score for our patients ranges from 88 points (intermediate risk) to 190 points (very high risk). 8 patients received IV Alteplase and 1 received IV streptokinase. All patients responded well with systemic thrombolytic therapy. Hypoxia and hypotensive resolved over time. 3 patients had non major bleeding tendencies. All patients were managed by both ICU and in-patient anticoagulation service (IPAC) team. These patients' cohort subsequently received anticoagulant post thrombolysis. *Discussion*: All our patients with massive and submassive PE responded well with systemic thrombolytic therapy. All patients were discharged well and continue follow up under clot clinic. PE is a major cause of morbidity and mortality. Clinicians should be able to diagnose PE based on PESI score, ECG, echocardiography and CTPA. Systemic thrombolytic therapy carries risk of bleeding.

HT083 A case of acquired von Willebrand disease with JAK2 mutation positive essential thrombocytosis associated thrombus

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Introduction: Acquired von Willebrand syndrome is much less common than inherited von Willebrand disease. Acquired von Willebrand syndrome has been known to be associated with certain conditions including Myeloproliferative Neoplasm Essential Thrombocytosis (MPN-ET), which can be as high as 20%. This condition can be very challenging due to two extreme possible complications which can occur in this scenario which namely thrombosis and bleeding. *Case report*: This is an interesting case of a young gentleman who initially presented with left hand digital ischaemia involving three of his fingers for almost 12 months with an incidental finding of isolated thrombocytosis of 840 K/uL and no abnormal bleeding tendencies. He was then referred to our Haematology Centre for further investigation. He later turned out to have the JAK 2 V617F mutation which confirmed his diagnosis of MPN-ET. In view of the isolated prolonged APTT and clinical history, von Willebrand Ricof and Antigen assays were sent, which confirmed a type II von Willebrand pattern (Ricof: Antigen ratio <0.7). He was successfully and safely treated with antiplatelet therapy, aspirin as well as hydroxyurea for the MPNP-ET. He did not develop any significant bleeding complications after being started on antiplatelet therapy. Fortunately for him, the digital ischaemia improved and circulation as well his thrombocytosis returned to normal after commencing on treatment. *Conclusion*: Management of such a case can be challenging for obvious reasons. There are no standardized treatment and often such a case has to be treated on an individual basis, weighing between the bleeding and thromboembolic risks.

HT084 MYH 9 related platelet disorders: An important cause of thrombocytopenia

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Introduction: Inherited thrombocytopenia is a rare condition and accounts for 1% of thrombocytopenia. May-Hegglin anomaly (MHA) is an MYH-related disorder associated with thrombocytopenia and giant platelets with the presence of cytoplasmic inclusion bodies in the granulocytes. The condition is often misdiagnosed as immune thrombocytopenia (ITP)

due to its similarities in clinical phenotype and often no associated secondary causes. *Case report*: A 38-year-old Malay lady was found to have isolated thrombocytopenia during her first pregnancy at the age of 35. Her platelet level ranges between 50 – 100 x 10^9/L throughout the antenatal period. She was treated for gestational thrombocytopenia and had an uncomplicated pregnancy. She was then lost to follow up. A year later during her second pregnancy, she was found to have a lower platelet count (with a nadir of < 30 x 10^9/L post-partum) without any bleeding manifestations. She was given a trial of corticosteroids with no response. A blood film examination demonstrated the presence of giant platelets with no obvious platelet clumping and the presence of Dohle body-like inclusions in the neutrophils. Further clinical history noted that she has a strong family history of thrombocytopenia which includes two of her siblings and her newborn son. A genetic testing was performed to confirm the diagnosis. *Discussion*: This case report highlights the importance of considering MHA as a cause of thrombocytopenia, especially in those with strong family history and poor response to steroids. Mutation testing is crucial to establish its diagnosis and management thus avoiding iatrogenic complications of immunosuppressive therapies.

HT085 A case report of a family with type 2A von Willebrand disease with C1272R mutation

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Introduction: Von Willebrand disease (VWD) is an inherited bleeding disorder characterised by a quantitative or qualitative deficiency of the von Willebrand factor (VWF). Type 1 and 3 are quantitative deficiencies whereas type 2 subtypes are qualitative deficiencies. Type 2A is characterised by a decrease in the affinity of the Willebrand factor (VWF) for platelets and the subendothelium caused by a deficiency of high molecular weight VWF multimers. *Case report*: A 15-year-old girl presented with prolonged menses following the onset of menarche and had frequent admissions for symptomatic anaemia. Her haemoglobin levels were between 5 to 6 g/dL and her platelet may be as low as 80 x 10^9/L. She is the 2nd of 3 siblings born to a mother with type 2 VWD who also had a history of menorrhagia. Specialised coagulation tests revealed a factor VIII (FVIII) of 27.7%, VWF: Ag 22.7%, VWF: CB 5.1% with R: Co 0.6%. Her later admissions were treated with standard half-life (SHL) factor replacement of which the response is at times, inadequate without platelet transfusions. Whole exome sequencing (WES) identified a heterozygous pathogenic variant c.3814T>C (C1272R) variant in the VWF gene. She is managed with monthly prophylactic factor replacement with adjunctive antifibrinolytics and oral contraceptive pills. *Discussion*: VWD is a heterogeneous disease that can be associated with thrombocytopenia, especially during bleeding episodes. Prophylactic factor replacement can be considered in women who developed severe anaemia from menorrhagia and platelet transfusions are provided in situations where bleeding control is inadequate with factor replacement.

HT086 Case report: Congenital thrombotic thrombocytopenic purpura (TTP) – A rare disease with many facets

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Introduction: Congenital thrombotic thrombocytopenic purpura (TTP) is a rare thrombotic microangiopathy (TMA). It is due to inherited deficiency of a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS-13). TTP has been estimated at 2 to 6 people per million per year, congenital TTP accounts for 2% to 10%. *Case report*: A 24-year-old man was first diagnosed with immune thrombocytopenia (ITP) during childhood. He was deemed refractory to immunosuppressive therapies prompting a repeated blood film which raised suspicion of TMA. Initial ADAMTS-13 level was 35% with no inhibitor. He was treated with plasma exchange with good clinical response followed by intermittent plasma infusions every 3-4 weeks. He later presented to us at the age of 15 with symptoms of abdominal pain and bruising following a febrile episode. Blood investigations showed haemoglobin of 7.3 g/dL, platelet of 13 x 10^9/L and creatinine of 407μmol/L. Microangiopathic haemolytic anaemia (MAHA) features were seen on blood film with numerous schistocytes and reduced platelet numbers. His condition responded to serial plasma exchanges and a repeated ADAMTS13 level showed <1% activity with no presence of inhibitors. ADAMTS13 gene sequencing revealed a pathogenic variant, c.1335del (p. Phe445Leufs*52) and another variant of uncertain significance, c.581G>T(p.Gly194Val). He is currently managed with prophylactic plasma infusions every 2 weeks. *Discussion*: Congenital TTP is challenging to diagnose due to the overlapping features between various TMA conditions. It has a variable spectrum of presentation with severe cases requiring regular plasma infusions. Mutation testing is crucial to establish its diagnosis and management.

HT087 A diagnostic dilemma in a case of extensive thrombosis

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Introduction: Catastrophic antiphospholipid syndrome (CAPS) is a fatal autoimmune condition manifesting with multiorgan failure due to widespread intravascular thrombosis. CAPS has a survival rate of about 50% despite an early diagnosis and prompt treatment. *Case report*: We report a case of a 47-year-old lady with underlying diabetes mellitus, hypertension and dyslipidaemia who presented with lethargy, poor oral intake and gradual less responsiveness over three days. She required mechanical ventilatory support indicated by respiratory distress and poor GCS. She was bradycardic, hypotensive and cyanosed at the emergency department of a district hospital. Other than leucocytosis her full blood count and coagulation profile were normal. Upon stabilisation and resuscitation, she was then transferred to the ICU of our centre where we found that she had dense left hemiparesis with poor neurological recovery and livedo racemosa over her right foot. She underwent multiple imaging modalities demonstrating evidence of cerebral and cerebellar infarcts, extensive pulmonary arterial embolism, intracardiac, anterior tibial artery as well as peroneal artery thrombi. Antiphospholipid antibodies were sent and were later found to be negative. Treatment was however initiated early with a combination of steroids, plasma exchange, intravenous immunoglobulins and heparin infusions following a diagnosis of probable CAPS. *Discussion*: In an ideal situation, we would require supporting investigation results to make a diagnosis of CAPS. However, this patient was started on treatment as her condition was unstable and waiting for blood investigation results to start treatment seemed futile. Clinical improvement was evident after initiation of treatment with marked neurological, dermatological recovery and reperfusion.

HT088 Acquired platelet dysfunction with eosinophilia following Covid-19 vaccination: A case report

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Introduction: Acquired platelet dysfunction is a rare condition that can be secondary to various factors, such as drugs, systemic diseases, and haematologic disorders. *Case report*: We present a case of a 23-year-old male who developed multiple bruises and gum bleeding two months after receiving the second dose of the Covid-19 vaccination. No traditional medicine or supplements were taken, and there was no bleeding history in the family. Laboratory tests revealed normal platelet count and morphology, mild eosinophilia and abnormal platelet aggregation with different agonist indicating acquired storage pool deficiency. *Discussion*: Our case illustrates acquired platelet dysfunction following Covid-19 vaccination with eosinophilia. Although acquired platelet dysfunction with eosinophilia (APDE) is more commonly reported in children with parasitic infestations, a few cases in adults have been documented. The exact mechanism of APDE remains unclear, but it is postulated that eosinophils induced by parasites may lead to the formation of immune complexes that interact with platelets, causing abnormal secondary aggregation. Notably, adenovirus-vector-based Covid-19 vaccines have been linked to serious thromboembolic events combined with thrombocytopenia. However, the exact mechanism of vaccine-induced platelet dysfunction remains elusive. Our patient's symptoms resolved over time, and no new bruises appeared after the incident. In conclusion, this case highlights a rare occurrence of acquired platelet dysfunction with eosinophilia following Covid-19 vaccination. Further research is needed to elucidate the underlying mechanisms and understand the potential association between Covid-19 vaccines and platelet function abnormalities.

HT089 A case of inherited Factor VII deficiency: A neurological emergency

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Introduction: Factor VII (FVII) deficiency is a rare and heritable bleeding condition affecting approximately one in 500,000 individuals. Clinical manifestations of this disorder are highly variable, and the correlation between symptoms and FVII plasma levels is often poor, posing challenges in surgical management and long-term prophylaxis. *Case report*: We present the case of a 48-year-old female who experienced fainting, vomiting, and intermittent headaches for two weeks. Diagnostic imaging revealed bilateral internal carotid artery aneurysm, diffuse subarachnoid haemorrhage with obstructive hydrocephalus, and cerebral oedema. Although the full blood count was normal, the prothrombin time remained persistently prolonged (18 – 22 seconds), while the activated partial thromboplastin time was normal. Factor assay confirmed low Factor VII activity (10%) with normal Factor V and Factor X levels. Multiple transfusions of fresh frozen plasma and intravenous Vitamin K failed to correct the prothrombin time. Craniotomy with aneurysm clipping was performed, and recombinant Factor VIIa (Novoseven) was administered, leading to a subsequent increase in Factor VII levels to 13.1%, confirming the diagnosis of inherited Factor VII deficiency. *Discussion*: This case highlights the significance of considering clotting factor deficiencies in patients with unexplained bleeding tendencies or unusual neurological presentations. The lack of a direct correlation between Factor VII levels and bleeding severity observed in this case emphasizes the complexity of managing FVII deficiency. Timely diagnosis and appropriate management, including Factor VII replacement, are crucial to prevent life-threatening complications and optimise patient outcomes. Healthcare professionals should be aware of this rare condition to ensure prompt intervention and effective patient care.

HT090 FXIII deficiency patient with a successful twin pregnancy

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Introduction: Congenital Factor XIII (FXIII) deficiency is a rare hereditary bleeding disorder due to reduced levels and activity of FXIII. FXIII deficiency in pregnancy can present with severe bleeding, spontaneous abortions and intracranial haemorrhage. *Case report*: We reported a case of 27 years old lady, Mdm D, known case of FXIII deficiency diagnosed since birth due to prolonged bleeding from umbilical stump. She was referred to Ampang Hospital at 18 weeks of dichorionic diamniotic (DCDA) twins pregnancy complicated with antepartum haemorrhage. She had an antenatal history of threatened miscarriage at week 8 of the same pregnancy, which resolved with duphaston. Additionally, she experienced intermittent haematuria and few episodes of blood spotting during pregnancy, managed conservatively. Investigations revealed only mild anaemia with haemoglobin of 10.3 g/dl. Other parameters such as White Blood Cell, Platelet, PT, INR, APTT, and Fibrinogen are within normal limit. Her FXIII Antigen level was 1.607%. She was given FXIII concentrate (Fibrogammin) 1000u 5 weekly and weekly monitoring for her FXIII Antigen level to maintain a level of more than 30%. Preterm twins with 700g weight were delivered uneventfully at 24 weeks period of gestation via spontaneous vaginal delivery. *Discussion*: Prompt treatment prophylaxis of severe FXIII deficiency in pregnant patients supported with FXIII concentrates replacement is important to have successful pregnancy outcome without any complication and to reduce significant risk of miscarriage, antepartum and postpartum haemorrhage. Co-management of multidisciplinary teams to help with the management of bleeding during pregnancy is essential for the patient's best possible outcome.

HT091 Use of regular ADAMTS13 concentrate in a rare case of congenital thrombotic thrombocytopaenic purpura (cTTP) with a novel gene mutation

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Introduction: A 12-year-old child was diagnosed at 2 years of age with a novel ADAMTS13 gene mutation when she presented with persistent thrombocytopenia. *Aim*: To describe the process and benefit of transitioning from regular plasma transfusions to recombinant ADAMTS13 concentrate (TAK-755) prophylaxis while progressing towards home infusion therapy. Through a special access route, TAK-755 was made available to the patient following counselling and ethics committee approval. The dose and frequency of prophylaxis was planned based on available dosing information. *Case report*: Following 2-weekly plasma transfusions for 9 years, the patient experienced adverse effects including allergies, possible TRALI, diminishing response in platelet counts and declining renal function. The decision was made to transition to TAK-55 in place of plasma infusions. During administration of the first dose, she experienced slight palpitations which required a brief interruption. Following resolution of palpitations and stable vital signs, the infusion was resumed with no further complaints. Subsequent infusions were completed uneventfully with maintenance of stable platelet counts and renal function. The patient is being taught preparation techniques and self-administration via peripheral venous access with an aim towards home infusion therapy. *Discussion:* The availability of TAK-755 has significantly improved the response to therapy and quality of life of the patient with cTTP.

HT092 "Erythrophagocytosis in paroxysmal cold haemoglobinuria"
A case report of suspected paroxysmal cold haemoglobinuria in a single referral centre in Malaysia

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Introduction: Paroxysmal cold haemoglobinuria (PCH) is a rare biphasic antibody-mediated autoimmune disorder that induces intravascular haemolysis. PCH is common in young children who have had a preceded infection. It can be mild to severe, but the illness is usually self-limiting with supportive red cells transfusion for the brisk haemolysis. *Case report*: We reported a case of 4-years-old boy, presented with dark-coloured urine. A week prior, he had a fever and cough. Laboratory studies showed dropping Hb from 10.2g/dL to 5.5g/dL over 3 days, raised reticulocytes count (5.46%), bilirubin level (44.7uml/L) and LDH level (3162 U/L). The peripheral blood smear revealed spherocytosis with increased polychromasia, neutrophilia with toxic granulation and left shift, and presence of erythrophagocytosis by neutrophils. Urine examination showed presence of erythrocytes (4+), proteins (2+) and leukocytes (3+). The direct antiglobulin test (DAT) showed positivity for C3d complement while IgG was negative. Serological test for total antibodies of *Mycoplasma Pneumoniae* reported a titre of 1:40. With the above findings, it is highly suspicious of PCH. However, the Donath Landsteiner test was not performed in our facility. Throughout his illness, he did not receive any blood transfusions and gradually recovered with supportive care and a course of antibiotic. *Discussion*: Despite lacking a confirmation test in this case, the history of a antecedent infection in a child with evidence of haemolysis & positive DAT for complement, the diagnosis of PCH is on high clinical suspicion. Furthermore, the evidence of erythrophagocytosis by neutrophils is strongly associated with PCH.

HT093 Headache unveiled: A rare case of COVID-19 positive and concurrent acute lymphoblastic leukaemia presenting with pituitary apoplexy

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Introduction: Pituitary apoplexy (PA) is a rare neurological and endocrine emergency characterised by an abrupt onset of headache brought on by pituitary gland haemorrhage or infarction. It is commonly seen in cases with pre-existing; known or undiagnosed, pituitary adenoma. The triggering factors include hormonal treatment, pregnancy, postpartum period, trauma, and anti-coagulation. Sporadically, thrombocytopenia has also been reported to cause PA. *Case report*: We report a case of 39-year-old lady with no known medical illness and last childbirth at ten month ago, who presented with persistent retro-orbital headache and lethargy for two weeks. On examination, she was haemodynamically stable, with no neurological deficit. Investigation showed Hb 11.2g/dL, WBC 69.3x10^9/L, Platelet 75x10^9/L, ALC 57.8x10^9/L. Radio-imaging finding of the brain is consistent with pituitary apoplexy and the pituitary hormonal level were within the normal range. The Covid-19 PCR was found to be positive. Peripheral blood film revealed leukoerythroblastic picture with 88% blast cells. Bone marrow aspirate and Immunophenotyping features are consistent with B-Acute Lymphoblastic Leukaemia. *Discussion*: This is a case of PA likely secondary to thrombocytopenia caused by Acute Lymphoblastic Leukaemia with Covid-19 infection. Previous reported cases of thrombocytopenia causing pituitary apoplexy are usually seen in male, between 5th and 7th decade of life with platelet count less than 30 × 10^9/L at presentation. Interestingly, COVID-19 infection has also been linked to PA. To date 13 cases PA in the setting of COVID-19 positive patients has been reported. It is postulated that coagulopathy and endothelial dysfunction in COVID infection predispose to the condition.

HT094 Comparison of lithium heparin and clot activator tubes on potassium levels in patients with pseudohyperkalemia: A case study

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Introduction: Pseudohyperkalaemia refers to a falsely elevated serum potassium level, potentially impacting patient's diagnosis and treatment. This case report illustrates the relationship between preanalytical and analytical variables in the measurement of potassium levels. *Case report*: A 49-year-old man with myelofibrosis presented to the clinic with haemoglobin 10g/dL, white blood count 31x10^9 and platelet 1,242,000. On a routine blood test, it was noted that his potassium levels were persistently high at 5.5 to 6.1mmol/L. He was clinically well, no signs and symptoms of hyperkalaemia. ECG did not show changes associated with hyperkalaemia. Blood was sent to two local laboratories which reported different potassium levels 6.1mmol/L vs 4.1mmol/L. To investigate the discrepancies, repeated blood sample was taken and sent to the same lab using lithium heparin tube and clot activator tube. 21G needles were used during blood draw from the patient. Correct order of draw during phlebotomy was ensured to prevent carryover of potassium salts. The tests revealed serum potassium level was 6.0mmol/L (clot activator tubes), while plasma potassium level was 4.0mmol/L (lithium heparin tube) on the same machine, Fujifilm Chemistry Analyzer. This manoeuvre was repeated in a different lab using Roche Cobas Chemistry Analyzer with similar differences noted. *Discussion*: Pseudohyperkalaemia can be observed in patients with thrombocytosis due to usage of the wrong tubes, where potassium is released from platelets during clot formation using clot activator tube. Treating psuedohyperkalaemia may cause death to patient. Therefore, in patients with thrombocytosis, blood sample should be collected in lithium heparin tube to prevent erroneous potassium results.

HT095 Case report: Successful management of external genital varices complicated by pelvic congestion syndrome using combined foam sclerotherapy and interlock embolisation

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Introduction: External genital varices complicated with pelvic congestion syndrome (PCS) represent a rare and complex medical condition. This study presents a case series of 13 female patients treated between June 2018 and December 2022. The treatment approach involved interlock embolization of ovarian veins combined with sclerotherapy for external genital varices. Clinical outcomes and imaging assessments were evaluated to assess the effectiveness of this therapeutic strategy. *Case report*: Thirteen female patients, aged 25 to 45 years, with external genital varices complicated by PCS were included in this retrospective analysis. All patients experienced distressing symptoms, such as external genital pain, swelling, and discomfort, with six patients also presenting irregular menstruation. Diagnostic imaging, including ultrasound and pelvic venography, confirmed dilated ovarian veins and pelvic venous reflux, confirming the diagnosis of PCS. Treatment consisted of interlock embolisation of ovarian veins to target pelvic venous reflux, followed by sclerotherapy to address the external genital varices. The combined treatment approach demonstrated favourable outcomes in the majority of cases, with 11 out of 13 patients experiencing significant symptom alleviation, including reduced pain and swelling. Imaging assessments revealed remarkable improvements in venous dilation and reflux in most patients. However, individual responses varied,

with two patients displaying limited improvement. *Discussion*: The comprehensive treatment strategy, combining interlock embolisation of ovarian veins with sclerotherapy, holds promise in effectively managing external genital varices complicated with PCS and enhancing patient well-being. The successful outcomes in symptom relief and improved quality of life highlight the potential clinical efficacy of this therapeutic approach.

HT096 Successful perioperative haemostatic management of extensive pseudotumor excision and skin grafting in severe haemophilia A using eculizumab: A case report

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Introduction: Haemophilia A is a rare bleeding disorder due to a deficiency in factor VIII clotting activity. It is characterised by an increased risk of bleeding, particularly in joints and soft tissues. Pseudotumour is an uncommon complication of severe haemophilia due to repeated bleeding and fibrous tissue formation. Surgical intervention, often required to manage haemophilic pseudotumours, poses significant challenges in terms of bleeding and infection. *Case report*: A 35-year-old gentleman with severe haemophilia A without inhibitor presented with an enlarging soft tissue pseudotumour at the right thigh of size 8.5 x 11.5 x 20.6 cm. He was commenced on regular haemostatic treatment with emicizumab. Despite radiotherapy, multiple wound debridement and washout procedures, the pseudotumour enlarged and was complicated with wound breakdown, infection with purulent discharge and septic shock. Hip disarticulation was considered but not proceeded due to patient refusal. He subsequently underwent a two-stage surgical intervention, comprising a wide excision of the pseudotumor followed by split-thickness skin grafting upon suitability of the wound bed. Both surgeries were performed uneventfully while he was on subcutaneous emicizumab maintenance with additional factor VIII coverage pre- and post-operatively. He was discharged after demonstrating good postoperative recovery and remained well for over a year. *Discussion*: This case report illustrates the safe and effective perioperative haemostatic management of extensive pseudotumor excision and skin grafting in severe haemophilia A using eculizumab and factor VIII. Notably, achieving a successful outcome in preserving the limb in such scenarios requires a multidisciplinary approach involving haematologists, orthopaedic and plastic surgeons.

HT097 Successful treatment of haemoptysis in pulmonary haemorrhage resulting from pulmonary embolism-related infarction

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Introduction: Haemoptysis and pulmonary embolism (PE) are life-threatening pulmonary emergencies. This is a real therapeutic challenge for physicians in the management of these two antagonistic conditions. We present here the case of a 39-year-old young man who developed massive haemoptysis due to pulmonary embolism-related infarction. Case history: A 39-year-old Malay man with a background history of ischemic dilated cardiomyopathy and atrial fibrillation. In addition to heart failure medications, he was also taking oral anticoagulants. He was admitted for a lower respiratory tract infection and began to develop haemoptysis more than five times with each episode amounting to about 100ml. Examination revealed a heart rate of 108/min and blood pressure of 118/74mmHg. Systemic examination revealed coarse crepitations in the left upper region. Chest radiography PA showed consolidated changes in the left upper region. Electrocardiography showed atrial fibrillation with a rapid ventricular response. Urgent CT angiography of the thorax revealed left pulmonary infarction with left pulmonary embolism and multiple sites of thrombosis involving the superior vena cava, right subclavian, and distal internal jugular vein. He was anticoagulated and given nebulised tranexamic acid and unfractionated heparin infusion. After five days of observation, the haemoptysis resolved, dabigatran tablet at 150mg twice per day was started and the patient was discharged safely. *Discussion:* This case provides insight into the management of a true therapeutic problem in haemoptysis with concomitant pulmonary embolism. It shows how to deal with a real therapeutic challenge, namely the coincidence of haemoptysis with a life-threatening pulmonary embolism.

HT098 Herbal inhalation induced Methaemoglobinaemia in hereditary haemolytic anaemia: A therapeutic challenge

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Introduction: The co-occurrence of acute haemolysis and acquired methaemoglobinaemia in G6PD-deficient individuals is rare. We report the case of a 45-year-old male who developed methaemoglobinaemia and acute haemolysis secondary to herbal inhalation. Case report: 45-year-old Malay man with a known case of G6PD deficiency, presented with a three-day history of high-grade fever and passing dark-coloured urine. He complained of dizziness, and desaturated on room air with no apparent dyspnoea. There was a recent history of herbal inhalation that contained menthol for symptomatic rhinitis. On physical examination, he was febrile, looked pale and jaundiced with mild hepatosplenomegaly. His oxygen saturation on the pulse oximeter was 79% in ambient air, while his arterial blood gases (ABG) revealed an oxygen saturation of 99%, indicating a saturation gap. His met-Hb level was 9.9%. Laboratory tests revealed haemoglobin levels dropped from 9.2 to 7.2 g/dL, with raised indirect bilirubin (37 umol/L) and lactate dehydrogenase (4550 U/L). Peripheral blood film showed

features suggestive of oxidative haemolysis with a negative Coombs test. The diagnosis of methaemoglobinaemia was made based on the saturation gap and a Met-Hb level of 9.9%. He was given supportive treatment with blood transfusion, oxygen therapy, hydration, and oral ascorbic acid (200 mg thrice per day) cautiously. He made a gradual recovery and was discharged well. *Discussion:* Methaemoglobinaemia with a background G6PD deficiency is rarely reported. A high index of suspicion is crucial to preventing life-threatening consequences. The mainstay of treatment is supportive therapy combined with moderate doses of ascorbic acid.

HT099 Variable phenotype in a family with Haemophilia B

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Introduction: Haemophilia B (HB) is an X-linked recessive disorder caused by mutations in the coding sequence of Factor 9 gene (*F9)* that result in decreased or defective Factor IX protein (FIX). The disorder is characterised by recurrent and prolonged bleeding. Based on the activity level of FIX, the disease severity is classified as severe: <1% of the normal FIX activity, moderate: 1–5% of the normal FIX activity, and mild: >5% and <40% of the normal FIX activity. *Case report*: We report an index case who presented at six months old with easy bruising. Investigations done showed that he has isolated prolonged APTT with FIX level of <1%. Genetic analysis confirmed that he has a c.580A>G variant, a possible variant of uncertain significance (VUS). The family screening revealed that both parents have similar genetic findings. One of the female siblings is a homozygote and the other is a heterozygote. Index case has the phenotype of severe haemophilia with spontaneous haematoma and bruises over the limbs. He also has a history of prolonged bleeding due to traumatic injury of the lips, that required FIX concentrate infusion. All his family members with either homozygote or heterozygote have normal FIX level and are asymptomatic. *Discussion*: Genotype and phenotype discrepancy between the index and homozygosity in his female sibling suggest that this finding could be a polymorphism. There is a possibility of unidentified genetic modifiers such as a deep intronic mutation in the index, which is undetectable using the current method. Further testing using next generation sequencing is required for confirmation of the diagnosis and carrier status.

HT100 Successful bloodless spine decompression for cauda equina syndrome in a patient with moderate congenital Factor VII Deficiency

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Introduction: Congenital Factor VII deficiency is a rare bleeding disorder, reported global prevalence of 1/500,000. It is inherited as an autosomal recessive bleeding disorder. Most cases are asymptomatic, thus affected individual remains underdiagnosed. *Case report*: A 45-year-old Malay male presented with acute bilateral lower limb paraparesis. Neurological examination demonstrated reduced power at grade 2/5 over proximal and distal lower limbs with prominent saddle anaesthesia. Spine magnetic resonance imaging (MRI) revealed multilevel disc herniation, annular tears and spinal canal stenosis causing cauda equina syndrome. He was planned for surgery. Pre-surgery clotting screen showed isolated prolonged prothrombin time (PT) which was corrected completely on mixing test. Upon assessment of bleeding risk, this patient informed that his family has history of epistaxis and easy bruising. His personal ISTH SSC BAT score was 0. Factor VII assay activity was 7.7%. Thus, we conclude that this patient has Congenital Factor VII deficiency. He was given intravenous recombinant FVIIa 30mcg/kg pre-induction of anaesthesia and a second dose 4 hours later. The surgery was completed within 2 hours. There were no excess bleeding episodes which requires factor replacements. A 10-day course of oral tranexamic acid 1500mg/day was also administered. Subsequent review 3 months after surgery showed full recovery. *Discussion*: Clinical manifestation of Congenital FVII deficiency are heterogenous, ranging from asymptomatic to severe life-threatening bleeding. Thus, patients may remain undiagnosed until they presented with conditions necessitate coagulation screen, which reveal isolated prolonged PT. The best replacement therapy is recombinant FVII concentrate given at appropriate dosing and interval.

HT101 A rare case of acquired factor X deficiency in Malaysia

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Introduction: Isolated Factor X deficiency is a rare condition that can be inherited or acquired. Acquired Factor X deficiency (AFXD) has been associated with various causes, with Amyloidosis as one of the frequent causes of Acquired FX Inhibitor. It often presents with a non-specific haemorrhage, causing a difficult diagnosis and management. *Case report*: We report a case of a 51-year-old lady planned for uterine fibroid surgery. She had menorrhagia, on-and-off gum bleeding and occasional easy bruising. No family history of coagulopathy or anticoagulant consumption. Physical examination revealed a 14-week-sized

uterus. Other systemic examinations were normal. Pre-operative laboratory investigations showed prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT) of 50.7 (9.4-12.5) and 63.0 (25.1-36.5) seconds, respectively. The liver function test was normal. Her baseline PT and APTT in 2019 were normal. The mixing study performed was highly suggestive of factor deficiency. Coagulation factor activity levels were normal for all coagulation factors except for FX:C, which was 1.7% (72.0-150.4). This is diagnostic of a moderate factor X deficiency. During the investigation, she developed multiple severe bleeding episodes, including haemorrhagic gastritis, right iliopsoas hematoma, and intra-abdominal bleeding. She was treated with infusion of Fresh Frozen Plasma and Prothrombin complex concentrates with poor clinical response and factor recovery. Subsequently, CVD regimen chemotherapy started, for presumed AL amyloidosis, as the kappa light chain was markedly raised. She eventually succumbed to intra-abdominal bleeding despite the treatment received. *Discussion*: This case highlights the rarity and difficulties in diagnosing and managing patients with acquired factor X deficiency.

HT102 Recombinant factor VIIa for treatment of refractory ITP with life threatening haemorrhage

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Introduction: Chronic primary immune thrombocytopenia (ITP) can today benefit from multiple therapeutic approaches with proven clinical efficacy, including rituximab, thrombopoietin receptor agonists (TPO-RA), and splenectomy. However, some ITP patients are unresponsive to multiple lines of therapy and remains a major clinical challenge. *Case report*: A 31-year-old female, with underlying refractory ITP. She was commenced previously on dexamethasone, methylprednisolone, prednisolone, IVIG, azathioprine and eltrombopag, however platelet remained low. Initially presented with left lower limb pain over the thigh and unable to ambulate. CECT Pelvic and thigh did not display any intramuscular haematoma. CT Brain showed acute intracranial haemorrhage. Trial another dose of IVIG, pulse methylprednisolone and subsequently Rituximab given to the patient. On day 8 of admission, despite receiving supportive platelet transfusions, patient still developed gastrointestinal bleeding and PV bleeding with significant drop of Hb to 2g/dL. Just before this episode, platelets were 3.0 x 10/L, Hb was 3g/dL, but PT, aPTT were normal. Despite previously having multiple platelets and packed cells transfusion, we decided for rFVIIa administration as the adjunctive treatment prior to diagnostic and therapeutic endoscopy. Throughout admission, the patient was administered 3x for rFVIIa and successfully recovered. *Discussion*: We report here a case of refractory immune thrombocytopenia with severe thrombocytopenia and life-threatening haemorrhage that was successfully managed with recombinant activated factor VII. Conventional treatments failed to control the haemorrhage in this patient. In conclusion, rFVIIa should always be considered as an alternative to control haemorrhage in patients with refractory immune thrombocytopenia that failed conventional glucocorticoids and second line therapies.

HT103 Postpartum cerebral venous thrombosis masquerading as meningoecephalitis: A case report

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Introduction: Cerebral venous thrombosis (CVT) is a rare but important cause of thrombosis in the postpartum period. The clinical spectrum is variable, hence, high index of suspicion is needed for prompt diagnosis and management of CVT. *Case report*: 32 years old lady, para 1+1A, presented with 3 days of acute confusion and neck stiffness. She delivered via emergency caesarean section due to acute foetal distress 3 weeks ago. On presentation, she was normotensive and confused with Glasgow Coma Scale (GCS) 14/15 (E3, V4, M6). Neurological examination demonstrated reduced power over right side with power of 3/5. She was diagnosed and treated empirically as meningoencephalitis. Computed tomography (CT) brain and lumbar puncture done were normal. However, her condition deteriorated with worsening GCS. MRI brain showed extensive cerebral venous thrombosis of the superior sagittal sinus with bilateral thalamic and left cerebellar haemorrhagic venous infarct. She was commenced on therapeutic dose of parenteral enoxaprin and mannitol after multidisciplinary discussion between neurologist, neurosurgeon, haematologist and obstetricians. However, her GCS dropped to 13/15 2 days later and repeated CT brain showed worsening cerebral sulcal effacement. Parenteral enoxaparin was continued with close GCS monitoring. She regained full GCS 4 days. She was started and discharged well with Rivaroxaban. Upon review 3 months later, she was well and repeated CT scan at 3 months post anticoagulant showed resolved CVT. *Conclusion*: We demonstrate postpartum CVT is a potentially life-threatening condition and early diagnosis and treatment with anticoagulation can prevent further neurological deterioration and further improve survival and outcomes.

HT104 Acute Limb Ischaemia in a long-term uterine cancer patient with diabetes mellitus

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Introduction: Acute limb ischaemia (ALI) is a rapid decrease in lower limb blood flow due to acute occlusion of peripheral artery or bypass graft, and in ALI not only limbs but also life prognosis will be poor unless quick and appropriate treatment is given. ALI is a sudden decrease in limb blood perfusion with an onset of less than 14 days, most commonly occurring in the lower extremities. Diabetes mellitus, one of the diseases underlying peripheral artery disease, complicates the pathophysiology

of acute limb ischaemia. In this case report we present a patient a long-term uterine cancer with type 2 diabetes mellitus and acute limb ischaemia in the left lower extremity who had successful thrombectomy treatment. *Case report*: A 57-year-old female patient came to the Emergency Care Unit of Dr. Soetomo Academic Hospital with the main complaint of pain in her left leg for the past 4 hours. The pain is experienced suddenly and is felt even more aggravated. The patient has never felt this kind of pain before. Current patients also complained of her left leg feels numb and difficult to move. There was no history of trauma or insect bites. The second to fifth toes of the left foot had undetected pulse oximetry results. The patient was diagnosed with type 2 diabetes mellitus in 2008 and has no routinely controlled treatment. She had a history of uterine cancer since 2011 and has chemotherapy. On the first day of hospitalization, the patient was scheduled for an emergency thrombectomy on the left femoral artery at Dr. Soetomo Academic Hospital. *Discussion*: One of the complications of DMT2 is ALI. ALI is diagnosed on the basis of medical history, visual examination, palpation, and Doppler examination of the peripheral arterial pulse using vascular ultrasonography and contrast-enhanced computed tomography (CT) as imaging tests. Acute limb ischemia has an excellent prognosis with early revascularisation even in a patient with DMT2.

HT105 A large uncharacterised Factor 8 (F8) gene deletion in severe haemophilia A patient

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Introduction: While most gene mutations of haemophilia A occur as single nucleotide changes, minor deletions, or insertions, rarely does the large deletion occur in the Factor 8 (F8) gene. We reported a case of severe haemophilia A with a large uncharacterised deletion that is possibly a novel deletion. *Case report*: A 6-day-old full-term baby boy, was initially admitted for neonatal jaundice. He was noted to have recurrent haematoma at the venipuncture site. He was the youngest of four siblings while the others were female. There was no family history of bleeding disorder. His coagulation profile showed persistently prolonged isolated activated partial thromboplastin time (APTT). The immediate mixing test was corrected with the Rosner index of 9.4%. The full blood count and the other coagulation profile parameters were normal. The factor VIII assay level was 1%. The conventional polymerase chain reaction (PCR) for intron 22 and intron 1, followed by Sanger sequencing was not able to detect any abnormality. Eventually, hemizygous deletion spanning from exon 1 until exon 7 was detected using multiplex ligation-dependent probe amplification (MLPA). *Discussion*: In most cases, a large deletion of F8 gene will be presented as severe haemophilia, while less than 1% manifest as mild to moderate haemophilia. This case portrays the importance of various molecular diagnostic methods in the confirmation of diagnosis. Molecular diagnostics offer advantages beyond confirming a diagnosis of haemophilia A. They extend their benefits to identifying female carriers, conducting prenatal diagnoses, predicting the risk of inhibitor development, and defining clinical phenotypes.

HT106 Protein S deficiency-induced spermatic vein thrombosis, a rare cause of painful scrotal

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Introduction: A painful scrotal mass is a surgical emergency that usually requires immediate medical attention. Typically, testicular torsion, acute epididymo-orchitis, and strangulated inguinal hernia are the common differential diagnoses. However rarely, it can be diagnosed as uncommon clinical entities including spermatic vein thrombosis. *Case report*: A previously healthy 23-year-old Malay man presented with a painful right scrotal lump for 2 days. Initial blood investigations were normal. A Doppler ultrasound of the scrotum performed revealed a formation of a thrombus measuring approximately 1.6 cm within the right spermatic vein without venous flow with normal neighbouring arterial structures. The diagnosis of SVT was made and treated with Aspirin tablets 100mg OD for 7 days. Repeated ultrasonography after 12 months revealed the formation of the right varicocele without thrombosis. Thrombophilia screen revealed low Protein S. *Discussion*: Although it is still unclear what causes spontaneous SVT, the Virchow's triad has been implicated in formation of venous thromboembolic events. In this case, hypercoagulability due to Protein S deficiency (58%) could predispose to the formation of venous thrombotic events. SVT is typically a left-sided pathology due to its anatomy and lack of valves compared to the right spermatic vein. Hence, the left venous system is exposed to higher pressure and slower blood flow. Treatment for spontaneous SVT remain controversial. Conservative therapy with non-steroidal anti-inflammatory drugs (NSAIDs) without anti-coagulant and watchful observation is considered ideal although treatment based on its anatomical location has been proposed. Reported complications include testicular infarction, pulmonary embolism, and renal vein thrombosis.

HT107 A case of isolated prolong APTT - District hospital experience

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Introduction: Coagulation tests are among routine blood investigations request before any surgery procedure in our centre. We report a case of a patient who underwent her preoperative workup before her surgery which turn up to be invasive investigations done due to finding of isolated prolong APTT. *Case report*: A 27 years old female, Para 1 was diagnosed with solitary right thyroid nodule. She was planned for right hemithyroidectomy. The preoperative investigation was performed which include coagulation testing and noted incidentally finding of isolated prolong APTT which was more than 120 seconds. The test is repeated after rule out any preanalytical factor that can contribute to the finding but the result still the same. There was no significant bleeding history and the patient was not treated with any anticoagulant medication. Her operation was postponed due to further workup to solve the coagulation testing finding. After several investigations done, she was diagnosed with factor XII deficiency. This factor deficiency will cause prolongation of APTT but patient will not present with bleeding manifestation. *Discussion*: Coagulation tests must be interpret cautiously correlating with bleeding and significant family history related to bleeding disorder. Selected coagulation testing must be applied to any patient's condition and not advisable to be requested as routine investigation for all patients.

HT108 A case report of refractory thrombotic thrombocytopenic purpura in a district hospital

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a haematological emergency with microangiopathic haemolytic anaemia and thrombocytopenia, carrying 90% mortality if untreated. While plasma exchange (PEX) and corticosteroids show promise, managing TTP remains complex. *Case report*: 55-year-old man presented with altered mental status, vomiting, and purpura over extremities, negative history of infection, autoimmune disorders or medication use. Lab results showed haemoglobin of 10g/dL, platelets 16000/μL, mildly-raised creatinine 141μmol/L, alongside reticulocytosis, elevated lactate dehydrogenase (LDH) 1914 U/L, indirect bilirubin 107μmol/L. Coomb's test negative, prothrombin time, activated partial thromboplastin time were normal. Peripheral blood smear revealed 21% schistocytes and spherocytes. PLASMIC score was 7, indicating high TTP risk. Methylprednisolone and PEX of 1 plasma volume were initiated. After 10 intensified daily PEX, platelets and LDH remained abnormal. ADAMTS13 (a disintegrin and metalloproteinase with thrombospondin type-1 motive) sent after 10 PEX, showing 17% activity and 29 IU/mL inhibitor, confirming acquired TTP in line with clinical presentation. Day 10 brought Burkholderia cepacia catheter-related infection, lowering platelets to 39000/μL, necessitating antibiotics. Despite 16 days of PEX, inadequate response led to rituximab 500mg weekly and cyclophosphamide, eventually achieving clinical remission. *Discussion*: First-line treatment requires early initiation of PEX, corticosteroid and rituximab in suspected TTP, guided by PLASMIC score, regardless of ADAMTS13. In refractory cases, pre-PEX ADAMTS13 is essential to confirm TTP diagnosis and excludes other microangiopathies. Maximising treatment response necessitates optimisation of PEX and prioritising rituximab as first-line strategy, a challenge to uphold within our resource-constrained setting. This article outlines common challenges and pitfalls in managing refractory TTP.

HT109 Fluctuating diplopia and chronic dizziness as initial manifestations of polycythemia vera

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Introduction: Polycythemia vera (PV) is characterised by increased red blood cells (RBCs) in peripheral blood. We report our case of PV with clinical manifestation of fluctuating diplopia and chronic dizziness. *Case report*: Thirteen nine-year-old woman complained dizziness, diplopia and reddish of feet. She had been experiencing approximately 3 episodes per month of diplopia lasting a few minutes followed by instability and dizziness. Funduscopic examination revealed a clear optical media with significant advanced papilla oedema in both eyes. A Brain MRI revealed, enhancement of the meninges in the frontotemporoparietal suggesting a meningitis. The haemoglobin level was 18.1g/dL, haematocrit 54.6%, red blood cells 5.29×10^6 /μL, mean corpuscular volume of 103.2 fL, white blood cell 16.4×10^3 s/μL, and platelets 340,000/ μl, suggested a myeloproliferative disorder. Bone marrow aspirate confirmed polycythaemia vera, with *JAK2* mutation. The patient underwent therapeutic phlebotomy and treatment with hydroxyurea 500mg daily. Two weeks later, the patient showed improved blood test results and symptoms. *Discussion*: Diplopia associated with PV has been linked to ischaemic events occurring in the brainstem at the level of the oculomotor nerve nuclei and pathway or in the nerves themselves. In our patient, episodes of fluctuating diplopia were linked to microvascular lesions in the oculomotor nerves as a consequence of hyperviscosity and neurological complications of PV. Other symptoms chronic dizziness and reddish feet skin colour were manifestations of systemic thrombosis. Awareness to such symptoms for a myeloproliferative disease should be emphasised when supported by increased level of haemoglobin. Abone marrow analysis and JAK2 gene testing should be done.

HT110 A rare case of acquired haemophilia masked by warfarin therapy

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Introduction: Acquired haemophilia A (AHA) is a rare bleeding disorder. *Case report*: A 54-year-old woman was referred with bruising and pain in the legs, who previously diagnosed with clinical DVT, received warfarin and acetylsalicylic acid. There was no family and personal bleeding history. No thrombus found from the lower extremities doppler ultrasound. Haemoglobin was 3.7 g/dl. Activated partial thromboplastin time (APTT) was 110 seconds (control 31.2s). Warfarin and aspilet therapy were stopped. One month later, she was readmitted with bruising all over the body, especially in extremity. Haemoglobin was 4 g/dl. APTT was 87.6s and normal prothrombin time (PT). The factor VIII (FVIII) activity was < 1%. Titre of anti-FVIII antibodies was 60 BU. Therapy was started with methylprednisolone injection 125 mg once a day and blood transfusion. Evaluation showed resolution of subcutaneous hematomas, with APTT (41.1s) and haemoglobin (12.7 g/dl). The latest therapy was methylprednisolone 4 mg alternating day and cyclosporine 100 mg once daily. *Discussion*: AHA is characterised by inhibitors of factor FVIII, tendency in the absence of bleeding history and family history, with isolated prolonged APTT, reduced FVIII activity and the presence of autoantibodies. The aim of AHA therapy are controlling and preventing bleeding, recommended haemostatic agents are rFVIIa, APCC, rpFVIII. The eridication of the auto-antibodies against FVIII are immunosuppressive agents, should be started with corticosteroids with or without cyclophosphamide or rituximab. Due to limited resource, she did not receive rFVIII and APCC. She did not receive human FVIII due to high FVIII inhibitor titer.

HT111 Neonatal thrombocytopenia to neonatal alloimmune thrombocytopenia a diagnostic voyage

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Introduction: Neonatal Alloimmune Thrombocytopenia (NAIT) is a rare and critical condition characterised by maternal antibodies targeting foetal platelets, resulting in platelet destruction. *Case report*: We present a unique case of NAIT in a 2-month-old boy who was born full-term following vacuum-assisted delivery due to his mother's history of atrial septal defect (ASD) correction during childhood. Post-birth, he was initially healthy but developed pathological jaundice, leading to readmission. Thrombocytopenia was noted, prompting empirical antibiotic treatment for suspected sepsis despite negative markers. Persistent thrombocytopenia necessitated platelet concentrate transfusion. The platelet count eventually normalised by the second week of life, with ocular and cranial assessments confirming the absence of haemorrhage. Subsequent investigations focused on NAIT, with platelet immunology tests confirming anti-HLA class I antibodies when the infant was two months old. *Discussion*: This diagnosis timeline highlights the complexity of NAIT diagnosis. This case typifies the diagnostic challenges posed by NAIT and underscores the need for early recognition to prevent severe thrombocytopenia and intracranial haemorrhage. Our approach highlights thorough maternal, obstetric, and neonatal assessments. Timely diagnosis and treatment, alongside ruling out common causes of thrombocytopenia, are vital. Additionally, post-discharge vigilance is crucial for detecting late-onset neonatal conditions like NAIT. In conclusion, this case emphasizes the significance of comprehensive diagnostic testing for neonates with persistent thrombocytopenia and the importance of vigilance in post-discharge care, ensuring timely diagnosis and management of both common and rare conditions like NAIT.

HT112 Inherited factor XI (FXI) deficiency: Two case reports from Sabah, Malaysia

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Introduction: Factor XI deficiency is a rare inherited bleeding disorder, usually inherited as autosomal recessive disease. The clinical presentation is often heterogenous, ranging from asymptomatic to variable bleeding. Spontaneous bleeding is infrequent, unlike bleeding following trauma or surgery. The factor level is known to have poor correlation with bleeding manifestations. *Case report*: We herein report 2 cases of FXI deficiency. Case 1: A 69-year-old Kadazan male, a patient with leprosy. Case 2: A 20-year-old Bajau male, planned for surgery of right femur fracture. Both cases were diagnosed following incidental findings of isolated prolonged activated partial thromboplastin time (APTT). Both patients were asymptomatic with no family history of inherited bleeding disorders. APTT was 107.9 seconds and 73.7 seconds for Case 1 and 2 respectively (reference range: 20.3-29.9 seconds). Prothrombin time (PT), fibrinogen and liver function test were normal in both cases. Further investigations with mixing test revealed complete correction, in favours of factor deficiency. Coagulation FXI activity (by one stage clotting assay) were markedly reduced, confirming the diagnosis (FXI:C was 7.0% and 1.7% for Case 1 and 2 respectively [reference range: 50-140%]). Activity assays of the other intrinsic factors were all normal. Both cases were

managed differently. The first patient was monitored conservatively. In contrast, the second patient received fresh frozen plasma transfusion and tranexamic acid prior to his surgery. Post-operatively, it was uneventful with no excessive bleeding complication observed. *Discussion*: These two cases highlight the asymptomatic presentation of patients with FXI deficiency, its circumstances of discovery and its management to mitigate potentially life-threatening haemorrhage.

HT113 An unusual transient lupus anticoagulant in a toddler with dysentery

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Introduction: Lupus anticoagulant (LA) may be associated with autoimmune disorders, malignancies, drugs or infections and usually presents with thrombosis rather than bleeding symptoms. In children, LA is usually transient with no sequela. *Case report*: A two-year-old boy presented with bloody diarrhoea (dysentery) associated with vomiting and poor oral intake for one week. There was no fever or abdominal distention. He has neither previous history of bleeding tendency nor family history of bleeding disorder. Full blood count was normal. There was a significant prolonged APTT 106s (27.9-38.7s) with slightly prolonged PT 14.9s (9.8-12). Mixing test showed non-correction at immediate and 2 hours incubation with Rosner index 44 and 60 respectively, suggestive presence of LA. However, factor assays showed mildly low factor IX (42.8%) with normal factor VIII (94.6%). LA test showed presence of moderate LA (dRVVT normalize ratio: 1.71, SCT normalise ratio: 2.00) and we concluded as transient LA due to infection. His stool and blood culture were all negatives. He was treated empirically with antibiotics for five days and responded well. Repeated coagulation profile 20 days after the onset showed improvement of the APTT result (57.2s). No repeat testing for LA done as the mother defaulted follow up. *Discussion:* The presence of LA can result in a low factor IX level that is not a true deficiency, as it produces an in vitro inhibition of the clotting reaction required to measure the factor IX. Dysentery in this case is likely due to infection (bacterial/ parasite) rather than coagulopathy or haemorrhagic symptoms in LA.

HT114 Heterozygous FGGc.661C>A missense mutation presenting as moderate hypofibrinogenemia in an adolescent

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Introduction: Congenital hypofibrinogenemia is a highly heterogeneous condition being associated with bleeding, thrombosis, or absence of symptoms. It occurs due to mutations in a homozygous, heterozygous, or compound heterozygous state in one of three genes encoding the fibrinogen chains on chromosome 4. *Case Report*: A 14-year-old girl presented with menorrhagia and worsening lethargy of 2 months duration. She attained menarche at the age of 12, had regular 12 non menorrhagia cycles with 7 days menstrual flow before presenting with prolonged menstrual bleeding. She does not have family history of bleeding and previous dental procedures did not cause prolonged bleeding. Initial lab investigations showed normal coagulation factor levels, and markedly low serum fibrinogen level of 0.6g/L and severe iron deficiency anaemia. Confirmation of the diagnosis was made by gene sequencing. Family screening revealed normal factor levels and fibrinogen levels among her siblings and her parents. She was managed with oral tranexamic acid, cryoprecipitate transfusion and parenteral iron therapy, hormonal therapy and subsequently insertion of Mirena coil by the gynaecology team. She is currently receiving 2 weekly cryoprecipitate transfusion while awaiting for recombinant fibrinogen concentrates. *Discussion*: Congenital hypofibrinogenemia is a rare bleeding disorder that should be confirmed by gene sequencing. Heavy menstrual bleeding of any degree in a young women should be investigated thoroughly to avoid missing a rare bleeding disorder.

HT115 Nocturnal paroxysmal haemoglobinuria with identified antiphospholipid syndrome

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Introduction: Paroxysmal nocturnal haemoglobinuria (PNH) is a rare complement- mediated haemolytic anaemia, associated with a tendency for thrombosis, organ dysfunction and with bone marrow failure. Presumably immune attack on hematopoietic stem cells provides survival advantage to the PNH clone. Antiphospholipid syndrome (APS) is a systemic autoimmune disease identified by various thromboembolic events, pregnancy morbidity in the presence of persistent antiphospholipid antibodies (aPL). *Case report*: A 25-year-old woman presented to the hospital with anaemia and haemoglobinuria. Routine blood tests demonstrated haemoglobin - 5,9 g/dL, RBC - 1,95 $x10^{12}$. In urine defined 300 erythrocytes. In a biochemical blood test determined LDH - 3752 units/L (125-250 units/L), haptoglobin - 1,52 mg/dL (35-250 mg/dL), bilirubin total - 46,5 mcmol/L (3,4-20,5 mcmol/L), bilirubin direct - 15,69 mcmol/L (0-8,6 mcmol/L). Direct antiglobulin test is negative. ACL IgM - 50 CU (0-20 CU), ACL IgG -19,6 (0-20 CU), anti-beta2-gpI IgM - 68,6 CU (0-20 CU), anti-beta2-gpI IgG - 7,6 CU (0-20 CU). Total value of erythrocyte PNG clone - 39,1%; monocytes - 90,0%; granulocytes- 92,6%. Other indicators (ferritin, folate, active B12, TSH, anti-TPO) are without features. In 4 month, patient presents with detected multiple infarction of the femur, tibia, and patella. Also was detected anti-beta2-gpI IgM - 17.9 U/mL (0-5 U/mL). ACL didn't carry out due to lack of reagent. *Discussion*: Both PNH and APS are diseases carry a high risk of venous and arterial thromboembolism. The coexistence of two diseases requires a higher alertness to the development of life-threatening complications and requires mandatory anticoagulant prophylaxis.

HT116 The incidence and risk factors of venous thromboembolism among newly diagnosed lymphoma patients – A prospective, observational study in Klang Valley, Malaysia

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Introduction: Patients with lymphoma have an increased risk of venous thromboembolism (VTE). There is a lack of data on VTE events in lymphoma patients in Malaysia. We aimed to determine the incidence of VTE occurrence in newly diagnosed lymphoma patients and their risk factors. *Materials & Methods*: A total of 130 newly diagnosed lymphoma patients from Hospital Canselor Tuanku Muhriz and Sunway Medical Centre between April 2021 and March 2023 were recruited in this prospective study. Data were collected on clinicopathological features at diagnosis of lymphoma and VTE events. VTE was defined as any case of pulmonary embolism or deep vein thrombosis confirmed by CTPA or Doppler ultrasonography. *Results*: The mean age of the patients in the study was 55.64 (8.06) years and they were followed for a median of 7.5 months. Twenty-seven patients (20.8%) developed VTE. Non-Hodgkin B-cell lymphomas predominated (83.3%), with DLBCL being the most common (66%). In multivariate analysis, an ECOG score of 2-4, the presence of B symptoms, a haemoglobin level of less than 10 g/dL and the number of chemotherapy cycles were independent risk factors for the development of VTE. *Discussion*: In our study, a higher incidence of VTE was found in newly diagnosed lymphoma patients than in previous studies. Factors such as poor ECOG status, B symptoms, haemoglobin less than 10 g/dL and number of chemotherapy cycles were among the independent risk factors for the occurrence of VTE. These results may help physicians at our centre identify high-risk patients who could benefit from thromboprophylaxis.

HT117 Phosphorylation of spleen tyrosine kinase (Syk) at Y346 negatively regulates ITAM-mediated signalling and function in platelets

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Introduction: Upon phosphorylation of the platelet immunoreceptor-based activation motif (ITAM) of the GPVI/FcRγ collagen receptor, both the tyrosine phosphorylation and activity of Syk are increased leading to downstream signalling events. Our goal is to evaluate the role of other tyrosine residues on Syk in the regulation of its activity and downstream signalling events in platelets. *Results*: We observed that Syk Y346 in mouse platelets was still phosphorylated when GPVI-induced Syk activity was inhibited. We then generated Syk Y346F mice and analysed the effect this mutation exerts on platelet responses. Syk Y346F mice bred normally, and their blood cell count was unaltered. We did observe potentiation of GPVI-induced platelet aggregation and ATP secretion as well as increased phosphorylation of other tyrosines on Syk in the Syk Y346F mouse platelets when compared to wild-type (WT) littermates. This phenotype was specific for GPVI-dependent activation, since it was not seen when AYPGKF, a PAR4 agonist, or 2-MeSADP, a purinergic receptor agonist, was used to activate platelets. Despite a clear effect of Syk Y346F on GPVI-mediated signalling and cellular responses, there was no effect of this mutation on haemostasis as measured by tail-bleeding times, although the time to thrombus formation determined using the ferric chloride injury model was reduced. *Discussion*: Our results indicate a significant effect of Syk Y346F on platelet activation and responses *in vitro* and reveal its complex nature manifesting itself by the diversified translation of platelet activation into physiological responses *in vivo*.

HT118 Haemophilia care in Asia: Learnings from clinical practice

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Introduction: The healthcare systems in the Asia varies greatly due to the socio-economic and cultural diversities which impact haemophilia management. *Materials & Methods*: An advisory board meeting was conducted with experts in haemophilia care from Asia to understand the heterogeneity in clinical practices and care provision in the region. *Results*: The overall prevalence of haemophilia in Asia ranges between 3-8.58/100,000 patients. Haemophilia A was more prevalent as compared to haemophilia B with a ratio of around 5:1. There is underdiagnosis in the region due to lack of registries and/or lack of appropriate facilities in suburban areas. Most patients are referred to the haematologists by their families or primary care physicians while some are identified during bleeding episodes. Genetic testing faces obstacles like resource constraints, services available at limited centres, and unwillingness of patients to participate. Prophylaxis is offered to moderate/severe haemophilia patients with frequent bleeds. Recombinant factors are available broadly across the region and are the preferred therapy. The challenges highlighted for not receiving a high standard of care include patients' reluctance to use an intravenous treatment, poor patient compliance due to frequency of infusions, budget constraints, and lack of: funding, insurance, availability, and accessibility of factor concentrates. Prevalence of neutralizing antibodies ranged from 5%-20% in the region. Use of immune tolerance induction and bypassing agents to treat inhibitors depends on their cost and availability. *Discussion*: Haemophilia care in Asia has evolved to a great extent. However, a few challenges remain for which a strategic approach along with multi-stakeholder involvement are needed.

HT119 Direct interaction of platelet with tumor cell aggravates hepatocellular carcinoma metastasis by activating TLR4/ADAM10/CX3CL1 axis

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Introduction: Metastasis is the main culprit of cancer-related death and it accounts for the poor prognosis of hepatocellular carcinoma (HCC). Platelet accelerates tumour cell metastasis, but the underlying mechanism is still unclear. This study aimed to clarify the mechanism of platelet in promoting HCC metastasis. *Materials & Methods*: The expression levels of ADAM10 and CD41 in HCC tissues were detected by immunofluorescence assay. Transwell assay and a mouse model in which lung metastasis was established by intravenous injection were applied to explore the role of platelet/TLR4/ADAM10 axis in HCC metastasis. The quantitative RT-PCR, western blot, ELISA, flow cytometry, dual luciferase reporter assay, ChIP-qPCR, and immunofluorescence analyses were used to reveal the molecular mechanism. *Results*: High platelet count and ADAM10 expression indicated poor prognosis of HCC patients. ADAM10 expression was upregulated in HCC tissues and positive with platelet counts of HCC patients. Platelet directly activated tumour cell TLR4/NF-κB signalling to promoted ADAM10 transcription. The shedding of CX3CL1 by ADAM10 induced epithelial to mesenchymal transition and cytoskeletal rearrangement of cancer cells via CX3CR1 receptor. Blocking of HCC cell TLR4/ADAM10 axis prevented platelet-promoted tumour cell migration, invasion and increased endothelial permeability. *In vivo*, platelet accelerated circulating tumour cell metastasis by increasing pulmonary vascular permeability via cancer cell TLR4/ADAM10 axis in mice. *Discussion*: Our findings provide a new insight into the underlying mechanisms on platelet-induced cancer metastasis by activation of TLR4/ADAM10/CX3CL1 axis of HCC cells, which holds a promise in preventing HCC lung metastasis.

HT120 Lyophilised platelets- a viable alternate for conventional platelets; Trehalose based Lyo canine and human platelets preparation, characterization, *In vitro and In vivo* studies- A preliminary approach

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Introduction: Explosive outbreaks of Dengue Haemorrhagic Fever (DHF) involving high-risk patients with platelet count <20,000/cu mm and risk of bleeding and haemorrhagic manifestations require emergency platelet transfusions. Our aim was preparation and development of lyophilized canine and human platelets and *In-Vitro* and *In-Vivo* functions of rehydrated lyophilized canine & human platelets versus. We hypothesized that Lyophilized platelets (LP) ready to use, temperature stable, haemostatically functional with long shelf life, transportable to remote places can be rehydrated at the point of care could potentially be the best approach as an alternate to conventional platelets. *Materials & Methods*: The methodologies adopted - Preparation of Canine Platelet Concentrate (CPC) using Eppendorf tube by single and double spin, Preparation of Human Platelet Concentrate (HPC), preliminary freeze drying and lyophilization of canine and human platelets, *In Vitro* studies of conventional and lyophilized platelet concentrates, Preparation of lyophilized Collagen and NaCMC Platelet concentrate wafers, *In- Ovo* studies of platelet concentrate Wafers, *In Vivo* Wound healing with PCW studies in experimental rabbits, *In Vivo* rabbits pyrogenic testing , *In-Vitro* flow cytometrical analysis and platelet aggregation studies of LP's were analyzed. *Results*: In this study the human and dog LP's were successfully developed and preliminary data were achieved wherein a recovery 66.80% and 69.87% of rehydrated LP's expressed P-selectin and GPIIb activation. *Discussion*: Our ICMR funded two years study produced LP's with haemostatic properties wherein safety profile need to be established in further characterization of LP's and experimental thrombocytopenic canine ITP models followed by human clinical trials to achieve platelet alternates.

HT121 Incidence, risk factors and outcome of multiple myeloma patients with thrombosis diagnosed in Sarawak from 2016 to 2021: A 6-year multicentre experience

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Introduction: Multiple myeloma (MM) patients are at increased risk of thrombosis with an incidence rate of 3-12%, which is attributable to patient-, disease- and treatment-related factors. This retrospective study was performed to describe the incidence of thrombosis among MM patients in Sarawak, identify the thrombotic risk factors and assess their outcome. *Materials & Methods*: Patients diagnosed with MM based on IMWG criteria from year 2016-2021 were identified from four tertiary hospitals in Sarawak. Their case notes were reviewed and relevant information were collected. The data was analyzed using SPSS version 22. Descriptive data and univariate analysis results were reported. *Results*: 118 patients were diagnosed with MM from year 2016-2021 with median follow-up time of 18 months (range:0-83). 11 patients developed thrombosis (2 arterial, 9 venous) after the diagnosis of MM, with a cumulative incidence of thrombosis 9.3 per 100 over 6 years. 8 of them (72.7%) developed a thrombotic event within 6 months from MM diagnosis. Majority of them (89.8%) were not on any thromboprophylaxis, including all the 11 patients who developed thrombosis. The median overall survival (OS) was 9 months (range: 1-79), and there was no significant OS difference between patients with and without thrombosis. The mean BMI for patients with thrombosis was observed to be higher at 26.65±8.44 (n=8) compared to those without thrombosis (22.92±4.69, n=64) (p=0.06). No other significant factors associated with thrombosis were identified. *Discussion*: The thrombotic risk among our local MM patients is not negligible. Thromboprophylaxis should be considered for MM patients with high BMI to reduce thrombotic event.

HT122 Emicizumab prophylaxis in haemophilia A patients with inhibitors: A nationwide observational study in Taiwan

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Introduction: Emicizumab mimicking the cofactor function of activated factor VIII (FVIII) restores haemostasis. *Materials & Methods*: This observational study aimed to investigate efficacy, safety, and cost in one year before and up to 3 years after emicizumab prophylaxis for haemophilia A (HA) patients with FVIII inhibitor. *Results*: A total of 39 severe HA patients with a median historical peak inhibitor titre of 174.2 BU/ml were enrolled. The median annualized bleeding rate reduced from 24 to 0 events in the first year after emicizumab prophylaxis ($P < 0.01$). The median annualised joint bleeding rate reduced to 0 and maintained up to 3 years. The percentage of target joint reduced from 69.2% to 17.9% afterward prophylaxis. Medical cost, including cost of haemostatic therapy, frequency of outpatient department visits, emergency room visits, and hospital admission significantly reduced after emicizumab prophylaxis ($P < 0.01$). A series of FVIII inhibitor titre decreased after emicizumab prophylaxis. No serious or severe adverse events were reported up to 3 years of emicizumab prophylaxis. The adherence to emicizumab prophylaxis was 100% in all patients up to 3 years. *Discussion*: The study showed that HA patients with inhibitors treated with emicizumab prophylaxis resulted in a significant reduction of treated bleeds and costs. No serious or new safety event was observed.

HT123 The alternative splicing of LCK in Treg induction in immune thrombocytopenia

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Introduction: The defective Treg compartment is involved in the pathogenesis of immune thrombocytopenia (ITP), therefore, the mechanism of aberrant Treg induction in ITP still awaits further investigation. *Materials & Methods*: Isolate CD4+ naive T cells (NTCs) from ITP patients and healthy controls, then perform high-throughput sequencing. Screen several genes of interest after analysing the differential expression and splicing pattern. Construct minigene plasmid and RNA-CHIP to verify upstream splicing factor. Use antisense oligos to research the function of target gene on Treg induction. *Results*: Our results revealed the proportion of Tregs induced from CD4+NTCs in ITP was decreased in vitro. RNA-seq showed differentially expressed genes were enriched in the alternative splicing pathway and activated exon 8 (E8) skipping was found in the LCK gene, which is the major TCR kinase in CD4+NTCs from ITP patients. We confirmed that overexpressed E8 spliced other than E8 included LCK limited TCR activation in T cells. Further, splicing factor X was identified as upstream regulator of LCK E8 inclusion, which lowly expressed in ITP. Antisense oligos, which suppressed LCK E8 recognition and enhanced exon skipping, prominently inhibited the potential of Treg induction in CD4+NTCs. Thus, we proved that lower expressed splicing factor X in the CD4+NTCs of ITP patients limit peripheral Treg induction by regulating LCK alternative splicing. *Discussion*: Our study demonstrated that alternative splicing of LCK gene regulated by splicing factor X was involved in the pathogenesis of ITP, which provide new ideas and targets for the clinical treatment.

HT124 Cost-effectiveness of on-site vs. send-out measurement of ADAMTS-13 activity in the diagnosis of acute thrombotic thrombocytopenic purpura

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Introduction: Thrombotic thrombocytopenic purpura (TTP) is a rare thrombotic microangiopathy (TMA) caused by congenital or acquired ADAMTS-13 deficiency, an enzyme cleaving von Willebrand factor (VWF), which leads to accumulation of ultra-large VWF multimers, inducing platelet aggregation and microthrombi formation. As TTP is a life-threatening condition, treatment (plasma exchange, rituximab, caplacizumab, corticosteroids) must be started immediately in patients with suspected TTP and be pursued only in case of deficiency. *Aim:* We compared the cost-effectiveness of a strategy based on the on-site measurement of ADAMTS-13 activity using a rapid fully automated chemiluminescent assay (HemosIL AcuStar ADAMTS-13), with a maximum time-to-result of 16 hours (assay performed during daytime, 7/7) vs. its measurement in a reference laboratory, with a median time-to-result of 4 days (range: 2-8, based on our 2018-2021 activity). The therapy was hypothesized to be started on admission and stopped if ADAMTS-13 activity was >10%. *Results*: Among the mean of 60 prescriptions of ADAMTS-13 activity per year, seven were for the diagnosis of acute TTP, which was confirmed in four cases/year (mean values). On-site measurement of ADAMTS-13 activity was found to be cost-effective with a 16%-reduction of the costs compared to its centralized measurement in patients with suspected TTP during the first 4 days. *Discussion*: Together with its short turnaround time (33 min) and full automation, our health economic analysis suggests that on-site measurement of ADAMTS-13 activity using the HemosIL AcuStar ADAMTS-13 assay could be an option of choice to establish the diagnosis of acute TTP in emergency settings.

HT125 The antithrombotic effect of targeting PI3KC2α is preserved in the face of marked hyperlipidaemia in mice

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Introduction: Inhibition of platelet activation is the standard-of-care therapy for the prevention of arterial thrombosis. Current anti-platelet agents exhibit reduced efficacy in high-risk populations, such as those with hyperlipidaemia. The class II PI3K, PI3KC2α, is a recently discovered target for novel anti-platelet therapy. Targeting PI3KC2α in mice results in anti-thrombotic effects with conserved haemostatic function. However, whether this is preserved in hyperlipidaemia remains unknown. *Aims*: To examine whether genetic deficiency or pharmacological inhibition of PI3KC2α provides anti-thrombotic effects in blood from hyperlipidaemic mice. *Materials & Methods*: Thrombosis was evaluated using an *ex vivo* thrombosis perfusion assay. Whole blood from hyperlipidaemic ApoE-/- mice was flowed over collagen fibers and thrombus volume measured in real-time via confocal microscopy. The effect of genetic deficiency of PI3KC2α was examined by using blood from mice with combined deficiency of ApoE-/- and PI3KC2α, while recently-developed PI3KC2α inhibitor, MIPS-21335, was pretreated to whole blood from ApoE-/- mice to evaluate the effect of acute pharmacological inhibition of PI3KC2α. *Results*: Hyperlipidaemia had the anticipated pro-thrombotic effect, with a 1.5-fold increase in blood from ApoE-/- mice versus wild-type mice (p=0.009). This pro-thrombotic effect in blood from ApoE-/- mice was prevented with PI3KC2α genetic deficiency (p=0.007). Acute inhibition of PI3KC2α with MIPS-21335 also reduced thrombosis in blood from ApoE-/- mice, albeit to a lesser extent (p=0.066). *Discussion*: These findings demonstrate that the anti-thrombotic effect of PI3KC2α-deficiency or -inhibition observed in normolipidaemia is retained in the face of hyperlipidaemia and suggest PI3KC2α is a promising target for anti-thrombotic therapy in this high-risk population.

HT126 Rituximab treatment for refractory immune thrombocytopenic purpura with venous thromboembolism

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Introduction: Patients with immune thrombocytopenic purpura (ITP) are prone to bleeding and susceptible to thrombosis. Several reports have emerged associating Rituximab treatment in ITP patients with thromboembolic events. We present a case of refractory ITP with venous thromboembolism (VTE) that was successfully treated with Rituximab. *Case report*: A 42 years old woman was admitted to the emergency ward with dyspnoea and a history of syncope. She had been diagnosed with ITP for 10 months. She was initially responsive to steroid but when it was tapered down, her platelet level decreased. She was then given cyclosporine and then switched to mycophenolic acid. When admitted she had tachypnoea, tachycardia and bilateral pitting leg oedema. Her platelet count was 31,000/μL and D Dimer level 5,930 ng/mL. Computed Tomography Pulmonary Angiogram (CTPA) revealed intraluminal thrombus in bilateral pulmonary arteries. Ultrasound showed thrombus in the left great saphenous vein (GSV), the left GSV-common femoral vein (CFV) junction, and the right CVF up to the popliteal vein. She was given unfractionated heparin (UFH), but it worsens her thrombocytopenia and caused severe cutaneous bleeding. After given rituximab and switched the UFH to low-molecular-weight heparin (LMWH), her platelet counts and clinical symptoms improved. Six months after treatment her radiologic evaluation showed complete thrombus resolution. *Discussion*: Thrombosis in ITP is multifactorial. They can be disease-related, patient-related, or treatment-related. Despite its association with thromboembolic events, Rituximab can still be a therapeutic option in refractory ITP with thrombosis along with anticoagulant. Rituximab induced thrombosis issue should be confirmed in further study.

HT127 Maternal and perinatal outcomes in the setting of prophylactic antenatal coagulation

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Introduction: Thromboembolism is the primary cause of maternal death within Australia. Prophylactic anticoagulation is effective but concerns exist regarding bleeding risks at birth and anaesthetic risks. This retrospective audit examines peripartum management of women receiving prophylactic anticoagulation with respect to anaesthesia, induction of labour (IOL) and associated complications. *Materials & Methods:* Pregnancies were identified in three high-volume metropolitan obstetric units in which (1) antenatal prophylactic anticoagulation was prescribed, (2) birth occurred at ≥ 20 weeks gestation and (3) birth was between July 2009 and July 2022. Data on maternal demographics, pregnancy and birth management was entered into a REDCap database. *Results:* 143 pregnancies were included in this study. Oestrogen associated VTE was the most common indication for anticoagulation (24.5%) followed by VTE in prior pregnancy (18.7%). 41% of patients underwent IOL most commonly for management of anticoagulation. Neuraxial analgesia was used in 48% undergoing IOL compared to 22% with spontaneous labour. Anticoagulation was withheld on day of IOL or on-admission in spontaneous labour. Twenty patients had a post-partum haemorrhage (PPH), with modes of birth being spontaneous vaginal birth (n=4), IOL (n=9) and caesarean section (n=7). *Discussion:* Scheduled births were common in women receiving prophylactic anti-coagulation due to perceived benefit of management of anticoagulation therapy. Neuraxial analgesia was used more commonly with IOL. Despite clinical concerns regarding bleeding risk associated with anticoagulation in the peripartum period, PPH and transfusion requirements remained low in our patient cohort. There was no negative correlation between duration anticoagulation was with-held and incidence of PPH.

HT128 Characteristics, risk factors and treatment outcome of adult lymphoma with venous thromboembolism (VTE) in Sarawak General Hospital: A single centre experience

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Introduction: Lymphoma is a haematological neoplasm associated with higher risk of venous thromboembolism (VTE). *Materials & Methods*: This is a retrospective study of adult patients diagnosed with lymphoma and VTE in Sarawak General Hospital from the year 2020 until 2022. The characteristics, treatment pattern and risk factors of these patients were collected and analyzed using IBM SPSS Statistic Ver 29.0. *Results*: Out of 289 patients who were diagnosed with lymphoma, 31(10.7%) developed VTE. Majority of them presented with thrombosis in the upper limb (n=12, 38.7%) followed by lower limb (32.3%), intraabdominal area (19.4%) and pulmonary embolism (6.5%). Most were detected incidentally during staging (n=18, 58.1%). They were treated mainly with clexane (n=24, 77.4%) with a mean treatment duration of 3.6 months. One patient (3.2%) had recurrent VTE while two patients (6.5%) had bleeding during treatment. There were no clear association between death and thrombosis (p =0.767). Both Khorana score (p=0.07) and ThroLy score (p=0.063) were not statistically accurate in predicting VTE events in our cohort of patients. However, this could be due to small sample and event size. The

independent risk factors for VTE were platelet ≥400k/uL (p=0.004), LDH ≥1x ULN (p=0.017) and bulky mediastinal mass (p=0.001). Adjusted for age, LDH and platelet count, BMI was higher in patients who developed thrombosis (mean BMI 25.3 vs 23.1; HR 1.074; 95% CI 1.007-1.145; p=0.031). *Discussion*: In our study, the incidence rate of VTE in lymphoma was 10.7%, which is comparable to worldwide incidence. We might need to modify and adapt existing risk stratify model such as Khorana and ThroLy score in order to accurately predict VTE events in our local population.

HT129 Activated carbon to remove DOAC from patients' plasma: Usefulness for routine coagulation, thrombophilia and lupus anticoagulant testing in patients treated with DOAC

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Introduction: Directs oral anticoagulants (DOACs) interfere with many coagulation tests, leading to potential misclassifications with the risk of incorrect management of patients. *Aims*: To evaluate the performance of the DOAC-Remove™ activated carbon, in extracting DOACs from the plasma of treated patients and allowing a correct measurement of routine and esoteric coagulation tests. *Materials & Methods*: Routine coagulation tests, thrombophilia and lupus anticoagulant (LA) panels, were performed before and after incubation with the activated carbon of 756 left-over plasmas from patients treated or not with DOAC. *Results*: The activated carbon removed the DOACs from the plasma of patients treated with dabigatran (n=139), rivaroxaban (n=157), or apixaban (n=155), with levels either undetectable or far below the lower limit of quantitation of the techniques, after a 10 min-incubation. In the plasma of untreated patients, the DOAC-Remove™ had either no significant impact on test results or a statistically significant impact without any clinical relevance. In patients on DOAC, incubation with the DOAC-Remove™ leaded to a significant correction of the DOAC-induced prolongation of PT/aPTT, underestimation of clotting factor levels, and overestimation of PC/PS anticoagulant activities. Moreover, it leaded to a dramatic decrease in the number of positive LA profiles, particularly in patients on dabigatran or rivaroxaban. *Discussion*: The DOAC-Remove™ was found to efficiently remove the tested DOACs from treated patients' plasmas. Its use would allow performing routine and esoteric coagulation tests in treated patients, and particularly making possible to rule out the presence of LA in a higher percentage of patients without withholding anticoagulant treatment.

HT130 Obesity is associated with poor outcomes of corticosteroid treatment in patients with primary immune thrombocytopenia

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Introduction: Emerging evidence has demonstrated that obesity impacts multiple immune-related diseases. It remains unclear whether and how obesity alters treatment outcomes in patients with primary immune thrombocytopenia (ITP). *Materials & Methods*: We retrospectively included 214 treatment-naïve patients who received standard high-dose dexamethasone from January 2012 to August 2022 in Qilu Hospital. *Results*: Patients with obesity showed significantly lower overall initial response (underweight vs. normal vs. overweight vs. obese: 85.7% vs. 85.2% vs. 72.0% vs. 52.3%, $p = 0.001$) and initial complete response ([CR], 71.4% vs. 70.4% vs. 53.3% vs. 27.3%, $p < 0.001$). The same trend was observed in the 6-month sustained response (63.6% vs. 52.3% vs. 35.6% vs. 22.7%, $p = 0.03$) and sustained CR (36.4% vs. 44.6% vs. 24.4% vs. 9.1%, $p = 0.01$). The Kaplan-Meier analysis revealed a shortened duration of remission in the obese group (median duration, not reached vs. 16 months vs. 2 months vs. 1 month, $p = 0.002$). In multivariate regression analysis, obesity was independently associated with poor initial and sustained responses, and an increased risk for relapse. In obese patients, we found significantly lower initial response (39.3% vs. 75.0%, $p = 0.02$) rates, and a marginal trend for lower initial CR (17.9% vs. 43.8%, $p = 0.06$) rates in those with weight-related complications. *Discussion*: Obesity is associated with an impaired treatment response, a shorter duration of remission, and a higher risk of relapse to corticosteroid treatment. A stratified strategy of corticosteroid therapy according to BMI status may facilitate the precision management of ITP.

HT131 Comprehensive analysis of platelet function in dogs with hyperadrenocorticism

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Introduction: Hyperadrenocorticism (HAC) leads to a hypercoagulable state and contributes to the risk of thromboembolic disease. Platelets play a major role in thrombosis and haemostasis, but no study has investigated platelet function in dogs with HAC. Thus, we aimed to characterise the platelet function and its molecular mechanism in dogs with HAC by using platelets isolated from normal dogs and dogs with HAC. *Materials & Methods*: This prospective cross-sectional study included 7 dogs with HAC and 15 normal dogs. Various platelet functional responses including platelet aggregation and dense-granule secretion were evaluated. *Results*: 2-MeSADP- and low concentration of thrombin-induced platelet aggregation and secretion were significantly inhibited in dogs with HAC compared to normal dogs. Furthermore, the pre-incubation of

platelets with prednisolone inhibited 2-MeSADP- and thrombin-induced platelet aggregation and secretion only in normal dog platelets, whereas no additional inhibitory effect was shown in dogs with HAC confirming a role of excessive cortisol in platelet function. In addition, 2-MeSADP- and thrombin-induced platelet aggregation and post-adrenocorticotropic hormone (ACTH) cortisol levels showed a negative correlation. Moreover, 2-MeSADP- and thrombin-induced thromboxane A_2 (TxA_2) generation was significantly inhibited in dogs with HAC compared to normal dogs, confirming the role of cortisol in TxA_2 generation. Finally, 2-MeSADP- and thrombin-induced ERK phosphorylation was significantly inhibited in dogs with HAC. *Discussion*: Excessive cortisol in dogs with HAC affects platelet function by suppressing TxA_2 generation through the regulation of ERK phosphorylation.

HT132 Endothelial microparticles in COVID-19

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Introduction: SARS-CoV-2 infection is known to cause endothelial cell activation, which triggers the formation of endothelial microparticles (EMPs), that can stimulate an increase in pro-inflammatory cytokines and exacerbate COVID-19. EMPs were identified using the surface antigens CD62E, CD106, and CD144. This study aimed to analyse the differences in the number of EMPs expressing CD62E, CD106, and CD144 in COVID-19 patients. *Materials & Methods*: An observational analytical study with a cross-sectional design was conducted at Dr. Soetomo Hospital Surabaya between July and December 2020. Samples were divided into mild, moderate, and severe COVID-19 patients and healthy controls. Examination of the number of EMPs using the flow cytometry method. Statistical analysis using the Kruskal Wallis test and the Mann-Whitney U test. *Results*: A total of 84 research subjects, consisting of 21 in each group. There was a significant difference in the number of EMPs CD62E, CD106, and CD144 in COVID-19 patients and healthy controls ($p<0.001$). There was a significant difference in the number of MP CD62E (p 0.011), CD106 (p 0.005), and CD144 (p 0.004) in COVID-19 patients with comorbid and non-comorbid. In survivors and non-survivors of COVID-19, the number of EMPs was not significantly different. *Discussion*: There is an increase in the number of EMPs in COVID-19 patients. Significant differences in the number of endothelial MPs in healthy controls and COVID-19 patients, comorbid and non-comorbid COVID-19 patients have been shown to have endothelial dysfunction as indicated by an increase in endothelial microparticles.

HT133 Thrombosis and its associated factors among solid cancer patients in two tertiary centres, Kuala Lumpur, Malaysia

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Introduction: Cancer patients have higher risk of thrombosis compared to normal population. This study aims to determine the rate of cancer-associated thrombosis (CAT) and its associated factors amongst solid cancer patients. *Material & Methods*: A prospective, observational study was conducted at Hospital Canselor Tuanku Muhriz (HCTM) and Hospital Kuala Lumpur (HKL) among solid cancer patients aged ≥18 years. Data on patients' demographics, cancer parameters, and thrombotic events were collected following informed consent and analysed. *Results*: 232 patients were followed up at three months with mean age of 57.56 years (SD 13.67) and 54% were female. Majority (86.2%) had ECOG performance status 0-1 while 96.6% were newly diagnosed cases and 77% were at Stage 3-4. Eighteen (7.8%) patients developed CAT. All, but one, had venous thromboembolism. The two common malignancies associated with CAT were lung cancer (n=4) and pancreas (n=3). Adenocarcinoma was the commonest type of histology. Being underweight (BMI $<18.5 kg/m^2$) and poor performance status (ECOG performance ≥2) were significantly associated with CAT, p=0.032 and p=0.025, respectively. There was no significant association between age, smoking status, or COVID-19 infection and CAT. Khorana score >2 was significantly associated with CAT, p=0.005. Among the patients with CAT, Khorana score was low in 2, intermediate in 10 and high in 6 patients. *Discussion*: In our study, CAT prevalence is comparable with other Asian countries. Patients' general well-being at the time of cancer diagnosis, including underweight and poor performance status, was significantly associated with CAT. VTE risk assessment should be performed routinely in cancer patients.

HT134 Clinical significance of antinuclear antibody positivity in adult immune thrombocytopenic purpura populations: A single centre experience

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Introduction: Immune thrombocytopenic purpura (ITP) is an immune-mediated disorder characterised by thrombocytopenia. We would like to determine the clinical significance of antinuclear antibody (ANA) in regard to the patients' characteristics, treatment response, risk of thrombosis and development of systemic lupus erythematosus (SLE). *Materials & Methods*: We performed a cross-sectional study involving ITP patients aged 12 years old and above, diagnosed and treated from 2011 to 2023 in Bintulu Hospital. Demographic, clinical and laboratory data were recorded and analysed using Statistical Package for Social Science (SPSS) version 27. *Results*: 49 ITP patients with a mean age of 39 years old (range 15 to 81) were reviewed and 33% (n=16) were found to have positive ANA with a median titre of 1:640. There was female predominance with ratio of 2.1:1. Majority of patients were Sarawakian natives (71%, n=35) followed by Chinese (16%, n=8) and Malay (10%, n=5). Positive-ANA group was statistically associated with leucopenia (9.9 ± 0.6 vs 6.2 (4.2), p=0.004), lesser bleeding rates (69% vs 38%, p=0.032) and more maintenance with steroid-sparing agents (69% vs 36%, p=0.033). However, there were no statistical differences in baseline platelet counts, bleeding sites, treatment response and relapse rate. No thrombosis event and development of SLE were reported. During follow-up, 2 ANA-positive patients and 1 ANA-negative patient developed interstitial lung disease and Graves' disease later respectively. *Discussion*: We demonstrated that ANA was not associated with treatment response, relapse rate, risk of thrombosis and development of SLE. However, larger sample sizes were needed to support the hypothesis.

HT135 Standardisation of platelet-rich plasma preparation with functional analysis of platelets

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Introduction: Platelet-rich plasma (PRP) has recently been used in regenerative medicine due to its abundant content of growth factors (GFs) and cytokines. Therefore, we optimised the PRP preparation to achieve the highest platelet recovery rate and platelet function. *Materials & Methods*: Whole blood from healthy dogs was centrifuged at different run conditions (800, 1200, 1500, and 2000 rpm) for 10 min single-spin or 5 min dual-spin to obtain PRP, and the platelet recovery rate of each condition was compared with commercial PRP preparation kit. Agonists-induced platelet aggregation and dense granule secretion, TxA_2 generation, Akt and ERK phosphorylation, and PDGF-BB release were measured to determine the platelet function of each PRP. *Results*: The PRP obtained by dual-spin centrifugation at 1500 rpm for 5 min demonstrated the highest platelet recovery rate without WBC contamination. Platelets obtained from this PRP showed maximum 2-MeSADP- and thrombin-induced platelet aggregation and secretion, suggesting that optimising the centrifugal speed and time is indispensable for the utmost PRP collection with optimal platelet function. Additionally, TxA_2 generation and Akt and ERK phosphorylation in response to 2-MeSADP and thrombin were at the highest level at dual-spin 1500 rpm run condition. Interestingly, PDGF-BB was released time-dependently and its release was dramatically increased in PRP adjusted at 1×10^9 platelets/ml indicating the importance of platelet concentration in PRP for maximum GF release. *Discussion*: We standardized the PRP preparation with the optimal platelet function, TxA_2 generation, and GF release that will maximise the effectiveness and efficacy of PRP application in regenerative medicine.

HT136 Severe influenza and venous thromboembolism among the elderly population: A systematic review

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Introduction: Severe Influenza are significant health concerns among the elderly population especially with comorbidities. There are reported increased incidence of venous thromboembolism (VTE) elderly with influenza and pneumonia. Thus, this systematic review aims to analyse the available literature on the relationship between influenza and thrombosis among the elderly. *Material & Methods*: A comprehensive search of electronic databases including Pubmed, EMBASE (via ovid), Scopus, and PMC was conducted to identify relevant studies. Inclusion criteria were applied to select any kind of study design that examined the association between severe influenza and VTE in the elderly population in the past 10 years. Data extraction and critical appraisal using Newcastle Ottawa scale (NOS) for cohort studies and JADAD scale for randomised controlled trials were performed by three independent reviewers on the included studies. *Results*: A total of 8 studies were included. The sample sizes of the included studies ranged from 100 to 5,000 elderly participants. Various measures of thrombosis, such as deep vein thrombosis, pulmonary embolism was seen across the studies. Most of the studies reported

a positive association between severe influenza infection and an increased risk of thrombosis in the elderly population. The risk estimates ranged from odds ratios ranges 1.5 to 3.2. All included studies were moderate to good quality. *Discussion*: While there is some evidence suggesting a potential association between influenza and VTE manifestations among the elderly population. Further research is needed to establish a definitive causal relationship.