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Instructions to authors *are available on the AIMS website: www.aims.org.au*

Evolution of viscoelastic haemostatic assays

Cathie Gore

AIMS Fellowship Dissertation

Abstract

Standard coagulation tests (SCT) such as prothrombin time (PT), activated partial thromboplastin time (aPTT), plasma fibrinogen levels and platelet counts are often used to assess coagulopathy and to guide haemostatic interventions with blood components. There are major limitations in the use of these laboratory-based tests in critical bleeding as they are time-consuming and the PT and aPTT were not designed to accurately reflect thrombin generation or to guide coagulation therapy in massive transfusion and critical bleeding.

Viscoelastic haemostatic assays (VHA) provide a holistic view of cell-based haemostasis, from clot initiation and formation to a measure of clot stability and fibrinolysis. The results are based on whole blood coagulation with some results being available within 5-10 minutes of the commencement of the test. VHA can provide a summary of overall haemostasis, platelet function, coagulation inhibitors and proteases and the fibrinolytic system thereby providing a good base for assessing the need for component therapy and allowing for earlier blood component replacement.

VHA have been utilised to optimise acute bleeding management in high blood loss procedures including liver transplantation and cardiac surgery. More recently there has been increased interest from other clinical areas including trauma, obstetrics and paediatrics.

Currently VHA have low sensitivity to GPIIb/IIIa antagonists, aspirin and low molecular weight heparin (LMWH) and have no detection of von Willebrand Factor (vWF) function defects. Future and emerging directions of viscoelastic testing are being investigated including their use in preoperative screening as well as in the monitoring of direct oral anticoagulants (DOACS).

This dissertation reviews the history, current technologies and utilisation of VHA, as well as exploring areas of future prospective and novel applications.

Haemostatis and standard coagulation tests

Haemostasis is the body's physiological mechanism that leads to the prevention and cessation of bleeding from a blood vessel. Haemostasis involves multiple interlinked steps resulting in blood fluidity and blood vessel integrity (LaPelusa and Dave 2023).

Primary haemostasis is divided into two stages. The first stage results in localised contraction of the blood vessel (reducing blood flow to the injured site) followed by the formation of a temporary 'platelet plug'.

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Secondary haemostasis involves activation of the coagulation cascade, a series of chemical reactions involving numerous plasma components which leads to the formation of a fibrin polymer which with the addition of platelets results in the final blood clot.

Once the injury begins to heal and blood vessel integrity is restored, the clot begins to remodel and dissolve in a process known as fibrinolysis. There are a range of clinical scenarios where the ability to manage the clot can become disrupted, leading to acquired hyperfibrinolysis. This can result in development of severe coagulopathy and potentially fatal bleeding.

SCT are often used to assess bleeding and clotting risks in patients; however such tests were initially developed to assess patients with isolated clotting factor deficiencies or those being treated with anticoagulants and are not sensitive to coagulopathy (Haas *et al* 2015).

The laboratory-based model of the coagulation cascade provides framework for the understanding of how different plasma proteins are activated and interact with each other. This model is used to understand and interpret SCT such as PT and aPTT.

In conjunction with PT and aPTT, plasma fibrinogen levels and platelet counts are often used to assess coagulopathy and to guide haemostatic interventions with blood components (Haas *et al* 2015). Research suggests that the traditional cascade model does not fully explain the clinical presentations of many coagulation disorders and SCT such as INR and aPTT have not shown to be reliable in predicting bleeding or thrombosis (Ho and Pavey 2017).

The cell-based model of coagulation highlights the importance of cellular control involving three overlapping stages; initiation, amplification and propagation (Hoffman and Monroe 2001). This model represents a more thorough and accurate representation of *in vivo* haemostasis (Hoffman 2003) and proposes that coagulation is regulated by interactions on the cell surface of platelets, rather than a cascade of protein activations.

The significance of the platelet surface in acting as a catalyst for further activation of other coagulation factors in both the amplification and propagation stages is of interest in the cell-based model and is not well described in the cascade model (Ho and Pavey 2017). This model also importantly demonstrates that platelet activation and subsequent activation of GPIIb/IIIa receptors, allows cross-linkage of platelets by fibrinogen, which is necessary for clot development (Ho and Pavey 2017).

Standard coagulation tests

Prothrombin time

Most coagulation factors are produced in the liver with FII, FVII, FIX and FX dependent on Vitamin K for the conversion into a functional form. Prothrombin time is a screening test used to measure how well the extrinsic and common pathways are working and can detect abnormalities or deficiencies (Perry 2023). Most commonly the PT is expressed as an International Normalised Ratio (INR) which is used to monitor anticoagulation therapy, in particular warfarin treatment. Warfarin is a commonly used anticoagulant which inhibits Vitamin K dependent clotting factors, thereby inhibiting the extrinsic pathway (Yang and Moosavi 2022).

Activated partial thromboplastin time

The aPTT is used as a screening test to identify any abnormalities in the intrinsic and common pathway of the coagulation cascade (Perry 2023) and is commonly used to monitor patients receiving heparin (which inhibits FX and thrombin) for anticoagulation therapy. It is also used to investigate bleeding disorders due to common factor deficiencies such as FVIII or FIX leading to Haemophilia A or B (Roshal and Reyes Gil 2019).

Neither the PT nor aPTT provide sufficient information on overall thrombin generation and there is limited evidence these tests are useful for diagnosis of coagulopathy or to guide coagulation therapy (Haas *et al* 2015).

Fibrinogen

The major function of fibrinogen is the formation of fibrin that then binds together with platelets and other plasma proteins to form a blood clot. If plasma fibrinogen levels are low, a clot with sufficient firmness and quality cannot be formed (Hayakawa 2017). Fibrinogen also acts as a ligand to GPIIb/IIIa receptors on the platelet surface and plays an important role in platelet aggregation. Fibrinogen assays can be used as part of an investigation into a bleeding tendency or to investigate a prolonged PT or aPTT. The fibrinogen level is quantitative though, not qualitative, and has no ability to account for functional versus non-functional protein (Brill *et al* 2021). In severe trauma patients, fibrinogen levels decrease earlier and faster than other coagulation factors and have been shown to be independent predicters for massive transfusion (Hayakawa 2017).

Platelet count

A platelet count is used to determine the number of circulating platelets. A decreased platelet count ($< 150x10^9$/L) may indicate an increased risk of bleeding after an injury to a blood vessel or tissue. Prophylactic and inappropriate platelet transfusion does not necessarily prevent bleeding and/or blood transfusions. A low platelet count has been associated with worse outcomes in critically bleeding patients (Görlinger *et al* 2019).

Viscoelastic haemostatic assays

History

VHA were first introduced and described by Helmut Hartert in 1948 as a 'Thrombus stressography' (Hartert 1948). Viscoelasticity refers to the ability of a material to exhibit both viscous and elastic characteristics. Under normal conditions blood is considered viscous and during the process of coagulation changes occur that cause it to lose viscosity and become more elastic in nature. The primary measurement in VHA is the observation of the transition from a viscous to elastic state and the measurement of the shear elastic modulus (amount of force required to shear a material) (Hartmann *et al* 2020).

VHA provide a holistic view of cell-based haemostasis from clot initiation and formation to the measure of clot stability and fibrinolysis. VHA measure clotting in whole blood, unlike aPTT and INR which use platelet-poor plasma (Ho and Pavey 2017). In terms of thrombin generation, SCT assess only the initial 10% of thrombin generation, whereas VHA can assess the whole clot formation and dissolution (Saner and Kirchner 2016). VHA provide a summary of overall haemostasis including platelet function, coagulation inhibitors and proteases as well as the fibrinolytic system, thereby providing a good base for assessing the need for component therapy and allowing for earlier blood component replacement in critical bleeding and massive transfusion.

The first reported clinical application of VHA was during the Vietnam War in an attempt to guide transfusion of blood components in injured soldiers (Hardaway and Bredenberg 1988). The adoption of VHA grew slowly and was limited primarily to research laboratories but gained momentum in the 1980s in high blood loss procedures such as liver transplantation and cardiac surgery (Hartmann *et al* 2020). More recently, VHA have become widely accepted and used in trauma settings involving haemorrhagic shock and in guiding the management of obstetric haemorrhage.

Technology

Two similar technologies were initially developed and have defined the first 30 years of clinical application of VHA. Thromboelastography (Thromboelastograph [TEG®] Haemostasis analyser) by Haemoscope was the first device available (Figure 1), followed by Thromboelastometry (ROTEM®) by Tem International GmbH (Hartmann *et al* 2020).

***Figure 1**. TEG® 5000.*

The first-generation point of care (POC) devices, TEG® 5000 and ROTEM® Delta (Figure 2), have been used extensively over the past two decades. These devices have established the clinical relevance of VHA but have been limited in growth by the manual nature of performing the tests, in particular the need to pipette blood samples and reagents manually with correct technique by appropriately trained staff (Hartmann *et al* 2020).

***Figure 2**. ROTEM® Delta.*

Both TEG® 5000 and ROTEM® delta are based on the same principle of mechanical viscoelastic testing. Whole blood is manually pipetted into a cup for each assay, specific test activators are added as required and when the test is started, a pin is placed in the middle of the cup. Clot formation/dissolution kinetics and strength are assessed by measuring and displaying the amount of a continuously applied rotational force that is transmitted to an electromechanical transduction system by the developing clot (Whiting and DiNardo 2014).

The resistance to movement as the fluid in the cup transitions from a viscous to elastic state is translated into a graphical trace resulting in measurement of the speed and strength of clot formation (Curry *et al* 2018).

TEG® 5000 operates by moving the cup filled with whole blood in a limited arc every five seconds, with a pin on a torsion wire suspended in the blood. As the clot develops, changes in the measurement are directly transmitted to the torsion wire and detected by an electromechanical transducer (Whiting and DiNardo 2014).

ROTEM® delta has an immobile cup in a heating block with a sensor pin fixed on a steel axis and stabilised by a ball bearing which slowly oscillates every six seconds. The mechanical resistance of the forming clot is detected

optically using a charge coupled device image sensor system (Hartmann *et al* 2020; Whiting and DiNardo 2014).

The next generation of devices have been developed to target key concerns such as inter- and intra- variability of results between hospitals and operators (Rossaint *et al* 2023).

Cartridge-based TEG® 6s and ROTEM® Sigma devices have been developed in part to reduce the risk of user errors, making the analysers more user-friendly and more resilient to vibrations, or jolting of the analysers (Gill 2017; Dias *et al* 2017). Cartridge based technology has also allowed for automation of sample aliquoting, reagent mixing and testing of different channels simultaneously (Hartmann *et al* 2020). The results from these second-generation instruments show good correlation with those from the previous versions of the devices along with increased device stability and enhanced portability to the bedside (Faraoni and DiNardo 2021).

The TEG® 6s (Figure 3) uses a different mechanism to measure clot strength known as the resonance method (Gill 2017). This method measures the resonance frequency of a whole blood sample that is exposed to a fixed vibration frequency. The resultant up/down motion of the blood meniscus is then measured by a detector and LED illumination. The frequency leading to resonance is then identified and converted to a readout. As the TEG® 5000 and the TEG® 6s use different mechanisms to assess the clot, the absolute values produced are not interchangeable and new algorithms need to be developed (Volod *et al* 2022).

***Figure 3**. TEG® 6s system.*

***Figure 4**. ROTEM® sigma.*

The ROTEM® Sigma (Figure 4) is a fully automated system with closed tube direct sampling, replacing the practice of pipetting. The ROTEM® Sigma device continues to utilise the proven cup and pin technique used in ROTEM® delta, allowing for the use of same algorithms that are already established for ROTEM® delta device (Volod *et al* 2022).

There are several other newer variants of VHA instruments including Clotpro and Quantra with limited market penetration within Australia.

The ClotPro (Figure 5) is a six-channel analyser that utilises elastic motion thromboelastography employing established cup and pin technology (GmbH 2020). TheClotPro has a simplified reagent dispersal mechanism, with reagents being preloaded into the pipette and dispersed upon contact with the whole blood sample (Infanger *et al* 2021). The clot firmness (CF) parameter in ClotPro strongly correlates with ROTEM® and other SCT, but substantial variability was found in the clotting time (CT) parameter as well as the FIBTEM CF (Yoshii *et al* 2022).

***Figure 5**. ClotPro.*

Quantra (Figure 6) uses patented SEER (sonic estimation of elasticity via resonance) sonorheometry that uses novel ultrasound technology to measure the viscoelasticity using ultrasound-induced resonance (Hemosonics 2023). Quantra has been designed for ease of use, complete automation, and rapid turnaround time. At this stage, unlike other VHA, Quantra has shown to provide insight into platelet dysfunction, but does not appear to accurately indicate when blood component therapy is required or what products should be administered (Zghaibe *et al* 2020).

***Figure 6**. Quantra.*

Emerging technologies

There are various new and emerging technologies in POC haemostatic assays that are currently under investigation as well as research into their clinical applications. Some of these technologies include speckle rheometry, mechanical resonant frequency, ultrasonic deformation, and parallel plate viscometry. The latter has potential to be adapted for prehospital areas for early POC-guided resuscitation (Volod *et al* 2022).

Limitations

Although some of the technical limitations (e.g. manual pipetting and resistance to vibrations) have been addressed in the development of second-generation devices, there are still limitations of which users need to be aware.

There continues to be a lack of standardisation with no published consensus on reference ranges across institutions and devices (Curry *et al* 2018). Reference ranges need to be developed locally and re-established when a new device is introduced. The frequency of internal quality control also varies, with report frequencies ranging from eight hourly to weekly (Curry *et al* 2018).

VHA are relatively insensitive to some coagulation abnormalities such as von Willebrand Disease and deficiencies in antithrombin-III, protein C, protein S or factor V Leiden. Standard VHA cannot detect specific platelet receptor abnormalities, due to the overwhelming effect of thrombin, without the use of specialist assays (Volod *et al* 2022).

The evidence available to support full implementation in clinical care settings is limited due to availability of mainly observational data and small-scale studies. Acceptance and use in clinical areas could be increased with further research providing level 1 evidence from high quality randomized control trials (Hartmann *et al* 2023b).

Assays

A wide range of assays have been developed to allow visualisation of the different aspects of clot formation, including the contribution of platelets and fibrinogen clot strength as well as the effect of clot lysis through various coagulation pathways (Hartmann *et al* 2020). Details of the various assays can be seen in Table 1 (TEG®) and Table 2 (ROTEM®). TEG® and ROTEM® utilise different reagents, activators and inhibitors which limits direct comparability of the tests when interpreting the results (Sankarankutty *et al* 2012).

***Table 1**. Details of specialised TEG® assays.*

TEG® assays	Activators and additives	Description
Kaolin TEG®	Kaolin	Intrinsic pathway test
Kaolin TEG® with heparinase	Kaolin + heparinase	Intrinsic pathway test with heparinase to neutralise effect of heparin
Rapid TEG®	Kaolin + tissue factor +	Extrinsic & intrinsic pathway test to speed coagulation allowing rapid assessment
TEG® with functional fibrinogen	Kaolin + tissue factor + Abciximab	Extrinsic pathway test with platelet receptor (GPIIb/IIIa) inhibitor. Allows quantification of fibrinogen contribution to clot strength

***Table 2**. Details of specialised ROTEM® assays.*

ROTEM® assays	Activators and additives	Description
INTEM	Ellagic acid	Intrinsic pathway test with contact activation
EXTEM	Recombinant tissue factor + polybrene	Extrinsic pathway test with tissue factor activation
FIBTEM	Recombinant tissue factor + polybrene + cytochalasin D	Analysis without platelet contribution, Quantification of fibrinogen contribution to clot strength
HEPTEM	Ellagic acid + heparinase	Analysis without heparin influence, used in conjunction with INTEM to assess heparin effect
APTEM	Recombinant tissue factor + polybrene + aprotinin/tranexamic acid	Inhibits fibrinolysis: fast detection of lysis when compared to EXTEM

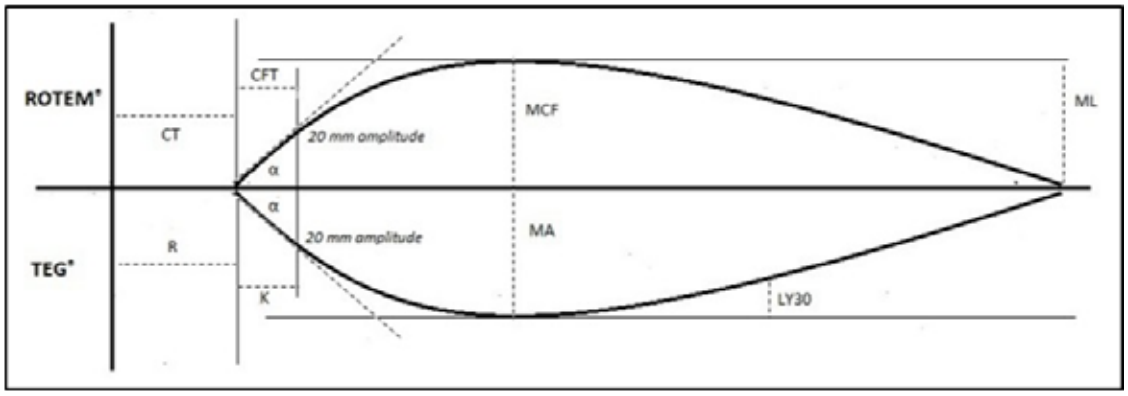


***Figure 7**. Illustration of thromboelastometry (ROTEM®) and thromboelastography (TEG®) and the accompanying parameters (Cannata* et al *2021). Reproduced with permission (CC BY 4.0).*

Parameters

The results from VHA are reported as a live trace reflecting the different haemostatic contributors to a blood clot (Carll and Wool 2020). As seen in Figure 7, the trace is a representation of the viscoelastic changes associated with fibrin clot formation. Several parameters are recorded throughout the different stages of clot formation and dissolution and these reflect the strength and stability of the clot. The trace and parameters that are produced by TEG® and ROTEM® are visually very similar but (as mentioned previously) due to the use of different reagents in the assays, they are not considered fully equivalent and interchangeable (Sankarankutty *et al* 2012).

The parameters that are measured and the stage during the clotting process, initiation, kinetics, strength, and stability that this occurs, are outlined in Table 3.

The reaction time (R) and clotting time (CT) is the time in seconds from the start of the measurement until initiation of clotting, thrombin generation and start of clot polymerisation. Prolongation may represent coagulation factor deficiencies, fibrinogen deficiency or heparin presence and shortening indicates hypercoagulability.

Clot formation/kinetics (K) and clot formation time (CFT) measures the time it takes from the onset of clotting time to when the clot reaches an amplitude of 20 mm, representing the clot amplification stage. Prolongation can be caused by poor platelet function, low platelet count, fibrin polymerisation disorders or fibrinogen deficiency and shortening may represent hypercoagulability.

The α-angle is the angle of the tangent between 0 mm and the curve when the clot reaches an amplitude of 20 mm.

A more acute angle could be caused by poor platelet function, low platelet count, fibrin polymerisation

***Table 3**. TEG®/ROTEM® parameters.*

	TEG®	ROTEM®
Clot initiation	Reaction time (R)	Clotting time (CT)
Clot kinetics	Clot formation/Kinetics (K) Angle (α) in degrees	Clot formation time (CFT) Angle (α) in degrees
Clot strength	Maximum amplitude (MA)	Amplitude 5 (A5) & Amplitude 10 (A10) Maximum clot firmness (MCF)
Clot stability	Lysis 30mins after MA (LY30)	Lysis index 60mins (LI60) after CT in % of MCF Maximum lysis (ML) in % of MCF

***Table 4**. ROTEM® parameters, interpretation, determinants and corrective components.*

Parameter	ROTEM®	Interpretation	Main Determinants	Corrective Components
Clotting time	CT	Initiation of clot	Activity of coagulation factors	FFP
Clot formation time	CFT	Clot amplification	Platelets & fibrinogen	Platelets/fibrinogen
Rate of clot polymerisation	α-angle	Thrombin burst	Platelets & fibrinogen	Platelets/fibrinogen
Amplitude	Ax	Clot strength	Platelets & fibrinogen	Platelets/fibrinogen
Maximum clot firmness	MCF	Ultimate clot strength	Platelets, fibrinogen & FXIII	Platelets/fibrinogen/FXIII
Maximum lysis	ML	Degree of fibrinolysis	Activity of fibrinolytic factors	Antifibrinolytic drugs
Clot lysis at 30 & 60 minutes	LI30, LI60	Degree of fibrinolysis	Activity of fibrinolytic factors	Antifibrinolytic drugs

disorders or fibrinogen deficiency and a high α-angle may represent hypercoagulability.

The strength of the clot can be assessed using the amplitude measurement, with the ROTEM® assay measuring amplitude at both 5 and 10 minutes after the clot begins to form. The amplitude can provide early assessment of clot firmness, increased stabilisation of the clot by polymerised fibrin and platelets as well as FXIII.

Low amplitude suggests a problem with fibrinogen or platelet function.

Ultimate clot strength is a measurement of the greatest vertical amplitude of the trace and is reported by maximum amplitude (MA) in TEG® and maximum clot firmness (MCF) in ROTEM®.

A low MCF indicates decreased platelet number or function, decreased fibrinogen level or fibrin polymerisation disorders, or a low activity of FXIII.

The degree of fibrinolysis is expressed as lysis at a fixed time (LY30 and LY60) in TEG®, but in ROTEM® is a calculated lysis index (LI30 and LI60) and is a measure of residual clot. This provides information about the stability of the clot and is measured at both 30 and 60 minutes by both devices.

If clot stability is lost rapidly by hyperfibrinolysis, bleeding complications may arise.

Interpretation of VHA traces and correlation with blood product use

The following section pertains to interpretation of thromboelastometry traces produced by ROTEM®.

There are three main areas to consider when interpreting a trace and considering which product might be required, including:

1) How long will the clot last?
2) How strong is the clot?
3) How long does it take for the clot to form?

The different parameters, the main determinants and the blood component that could be transfused to correct these parameters are outlined in Table 4.

As well as using the measured parameters to apply algorithms to guide blood component transfusion, familiarity with the shape of a normal trace (Figure 8) compared with an abnormal clot, can provide early information on coagulopathy.

When looking at how long a clot lasts and the degree of fibrinolysis, the ML parameter can be assessed with a value ≥ 15% in the EXTEM and INTEM indicating fibrinolysis. A prolonged CT may also be observed in the FIBTEM. The APTEM assay can be used to confirm hyperfibrinolysis if the maximum lysis is corrected in comparison to the EXTEM (Figure 9).

***Figure 8**. An example of normal coagulation as represented by the EXTEM and FIBTEM. The EXTEM show a normal coagulation activation (CT), normal clot formation (CFT and MCF) and a stable clot with minimal lysis. The FIBTEM shows a normal fibrin clot (A5 FIB 5-20mm) (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

If there is no correction, this could indicate hyper clot retraction associated with high platelet numbers.

The strength of the clot is determined by the interaction of platelets, fibrinogen and FXIII. An example of a fibrin polymerisation disorder e.g. low fibrinogen or low FXIII, with decreased amplitude and MCF in both the EXTEM (reference range {RR} MCF EX 50-72s) and the FIBTEM (RR MCF FIB 9-25s) is shown in Figure 10.

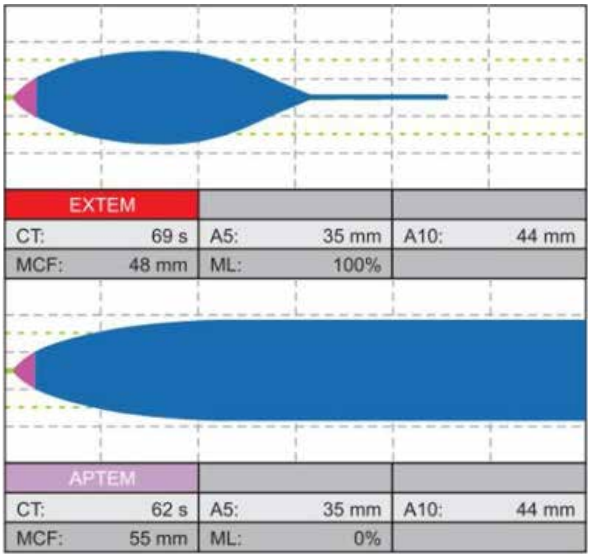


***Figure 9**. An example of hyperfibrinolysis where the maximum lysis (ML) in the EXTEM is ≥ 15% which is corrected in the APTEM (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

The amplitude of the FIBTEM can be used to differentiate between a platelet problem or a fibrin polymerisation problem. If the FIBTEM A5 is ≥ 9mm (Figure 11), thrombocytopenia or severe platelet dysfunction is suggested whereas an increased A5/A10 or MCF is associated with hypercoagulability (Figure 12).

The speed of clot formation can be assessed by looking at the CT and can provide information as to whether there are adequate or excessive clotting factors present in the plasma. A prolonged CT EXTEM (RR CT EX 38-79s) can indicate deficiency of vitamin K-dependent factors including warfarin therapy or significant fibrinogen deficiency.

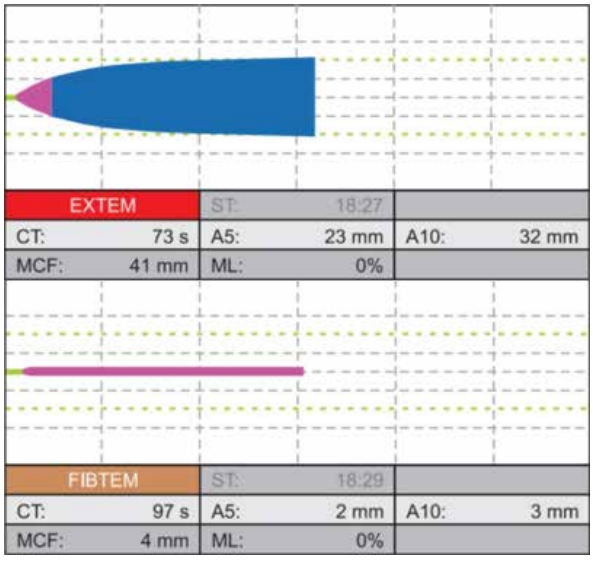


***Figure 10**. An example of a fibrin polymerisation disorder where a decreased amplitude (A) is observed in both the EXTEM and FIBTEM (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

The CT compared before and after administration of prothrombin complex concentrate is shown in Figure 13.

A prolonged INTEM CT (RR CT IN 100-240s) that is then corrected when comparing with the HEPTEM assay indicates heparin interference. Low dose heparin in Figure 14a and high dose heparin such as in cardiopulmonary bypass in Figure 14b. Non correction of the CT HEPTEM suggests either a clotting factor deficiency, excess protamine sulphate during heparin reversal or a clotting factor inhibitor i.e. FVIII inhibitor.

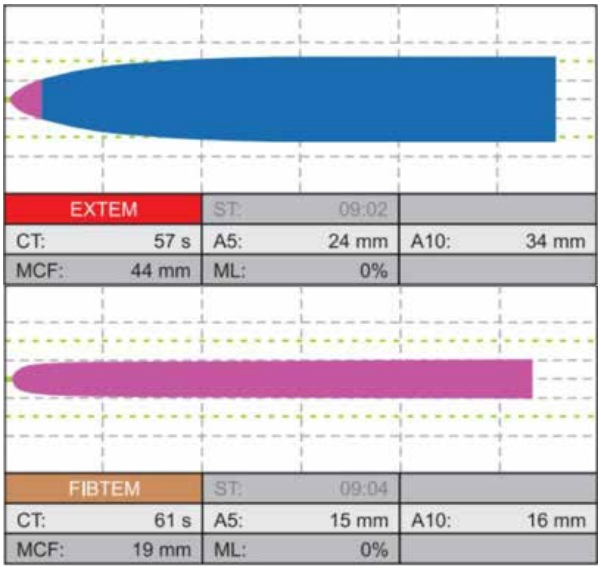


***Figure 11**. This is an example of thrombocytopenia or a severe platelet dysfunction which can be differentiated from a fibrin problem (Figure 14) by observing an amplitude (A5) ≥ 9mm in the FIBTEM. Reproduced with permission (CC BY 4.0).*

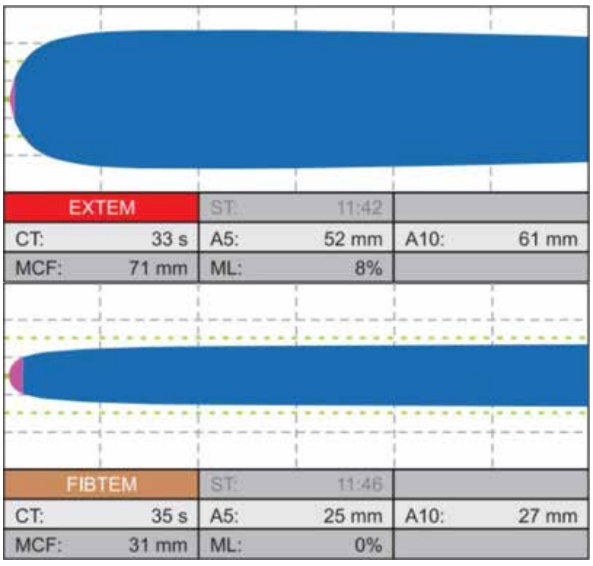


***Figure 12**. This is an example of hypercoagulability with an observable increase in amplitude and maximum clot firmness (MCF) in both the EXTEM and FIBTEM. This can be indicative the patient is at a high thrombotic risk (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

VHA based algorithms

There is enough evidence available to support the use of VHA based algorithms to guide blood component transfusion in a variety of different clinical situations including trauma, cardiac, obstetric, and liver transplantation. Further evidence is accruing to support the implementation of VHA guided transfusion algorithms not only reduces the use of blood products and haemostatic medication, but also results in reduction of overall hospital stay, costs and complication rates (Kuiper *et al* 2019; Görlinger *et al* 2019). Significant reduction in transfusion requirements and improved management of bleeding is apparent in not only the adult population, but also in the paediatric cohort (Haas and Faraoni 2020).

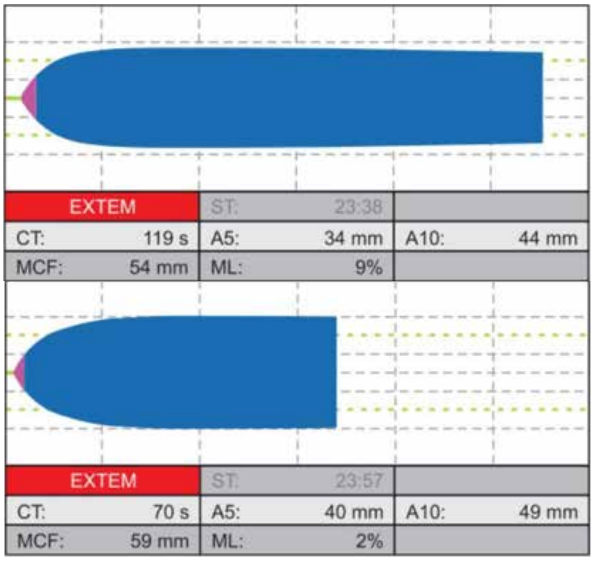


***Figure 13**. An example of an extended clotting time in the first EXTEM (CT 119secs) which was corrected to 70 secs post administration of four factor prothrombin complex concentration (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

The aim of VHA guided algorithms is to assist in selection of the appropriate blood component, in the right dose, at the right time and in the right sequence. The elements of the trace produced in different assays, whether it is ROTEM®, or TEG®, can be dissected and analysed to assess the need for blood component therapy. For example, a slower reaction (K)/clotting time (CT) can indicate clinically significant levels of DOACS, reduced clot formation can indicate fibrinogen deficiency and/or platelet number and function, and a decreased clot strength can be indicative of platelet or fibrinogen deficiency requiring product transfusion (Brill *et al* 2021).

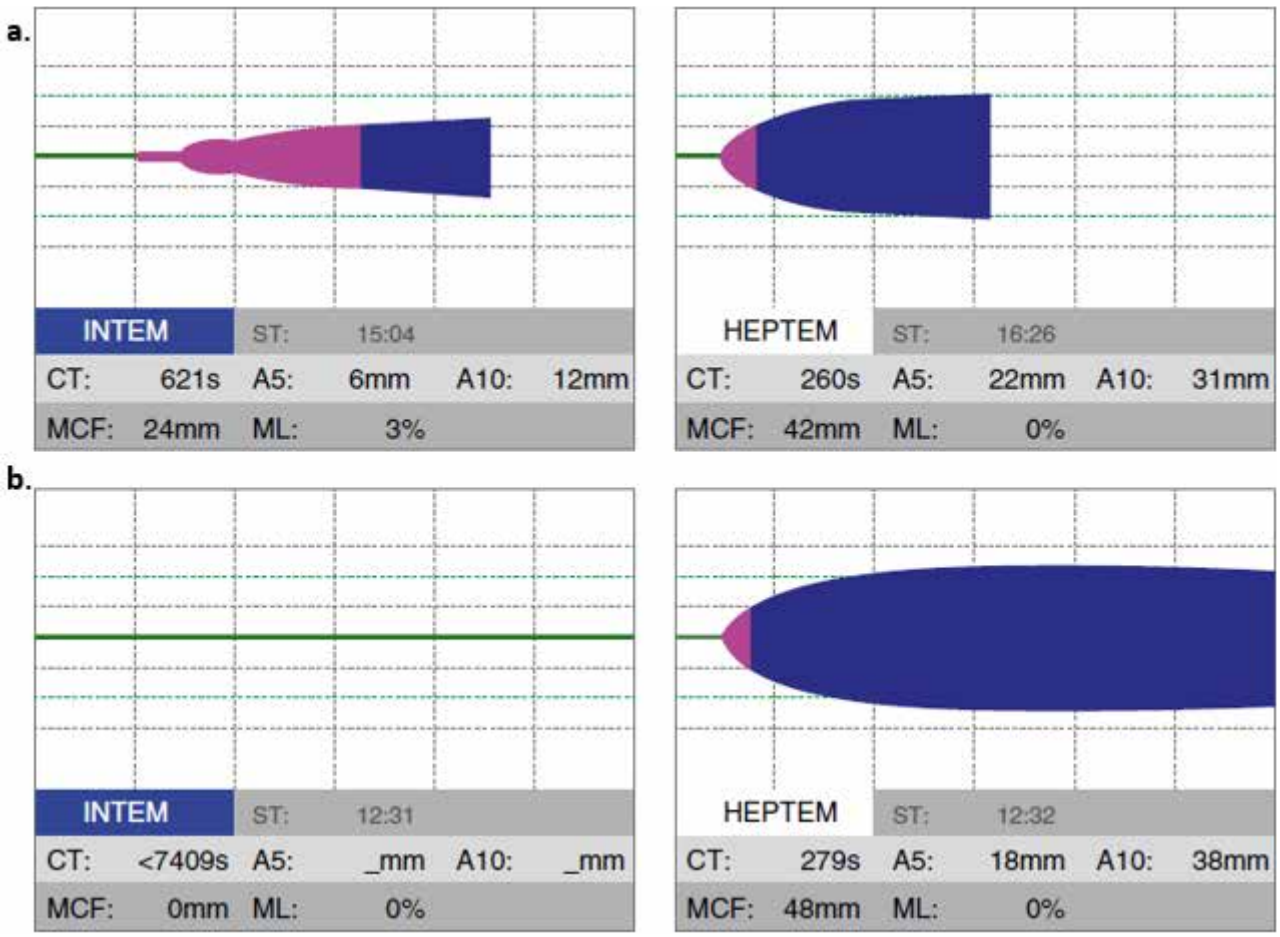


***Figure 14**. Heparin effect in INTEM a) low dose due to endogenous heparin e.g. liver transplant, sepsis or shock b) high dose such as during cardiopulmonary bypass (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

For algorithms to be developed, optimum threshold parameters need to be determined with these being based on practical data rather than theoretical considerations (Baksaas-Aasen *et al* 2019). Algorithms will differ for various clinical settings, with the focus being slightly different depending on the setting. Trigger values used in algorithms have been determined in setting-specific observational studies by receiver operating characteristics (ROC) curve analysis or multivariate regression analysis (Görlinger *et al* 2019). ROTEM® based algorithms for cardiovascular, trauma, obstetric and liver transplantation in which the target values for therapeutic interventions have been validated by setting specific interventional trials are shown in Figure 15 (Görlinger *et al* 2019).

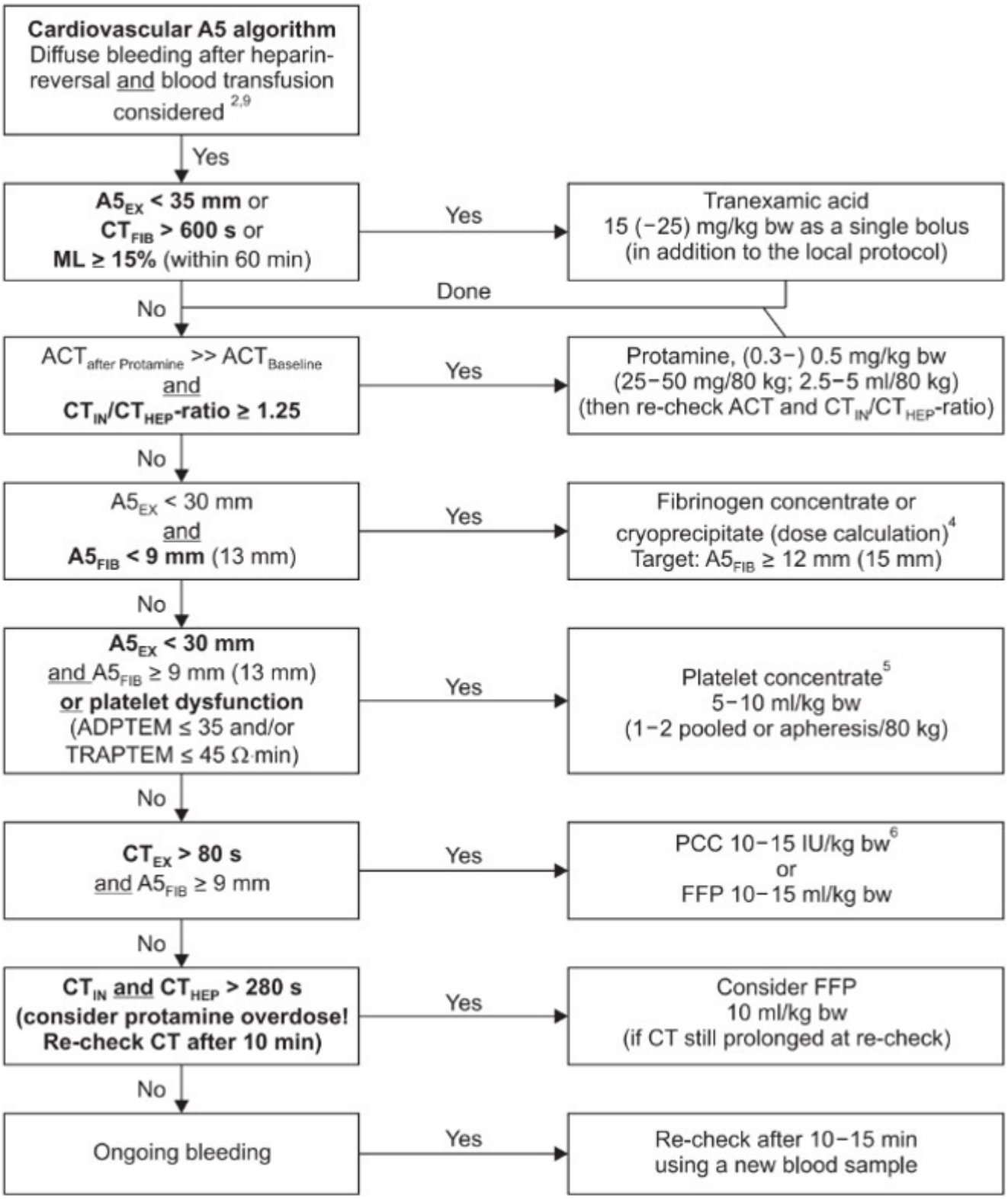
VHA are now often utilised in single site developed algorithms to guide administration of blood components with several international guidelines published that favour the use of VHA based transfusion algorithms for patients at risk of bleeding (Faraoni and DiNardo 2021). The most recent European Guideline on management of major bleeding and coagulopathy following trauma recommends VHA can be used for early and frequent monitoring of haemostasis (Rossaint *et al* 2023).

Critical bleeding

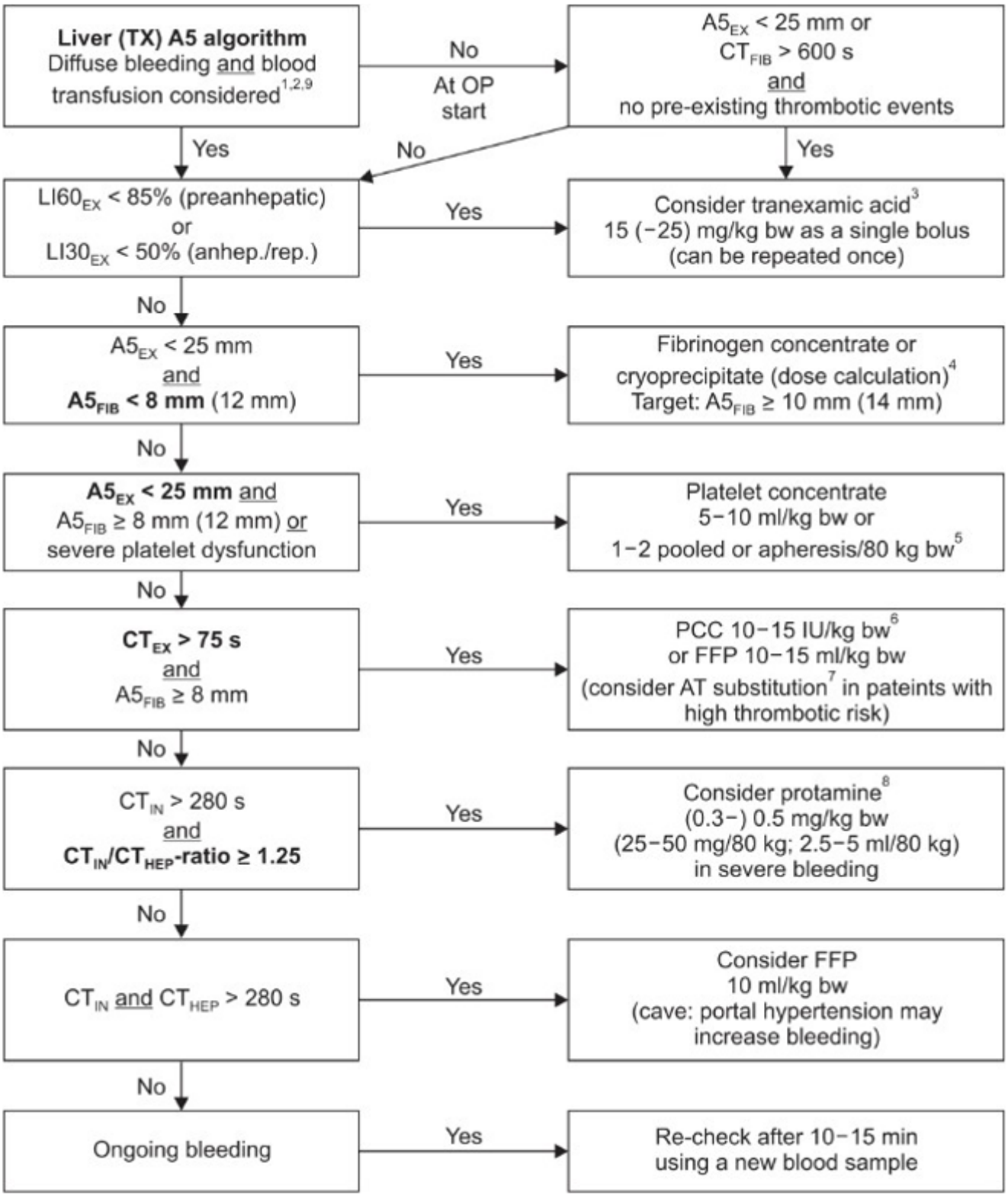
VHA allow the prompt diagnosis of coagulopathy and are used extensively in critical bleeding scenarios, particularly associated with cardiac, liver transplant and trauma patients. VHA have now become standard practice in critical bleeding with the particular advantage of providing early parameters to detect coagulopathies and to identify therapeutic treatment options (Faraoni and DiNardo 2021). There have been multiple publications reporting a reduction in the transfusion of both red blood cells (RBC) and fresh frozen plasma (FFP) when VHA guided transfusion management is in place in comparison with SCT (Santos *et al* 2020; Saner and Kirchner 2016; Fahrendorff *et al* 2017; Snegovskikh *et al* 2018; Kuiper *et al* 2019; Tangcheewinsirikul *et al* 2022; Gonzalez *et al* 2016).

Although results from VHA do not directly guide the use of RBCs, it is hypothesised that the reduction of RBC transfusion volume may be due to more patient specific

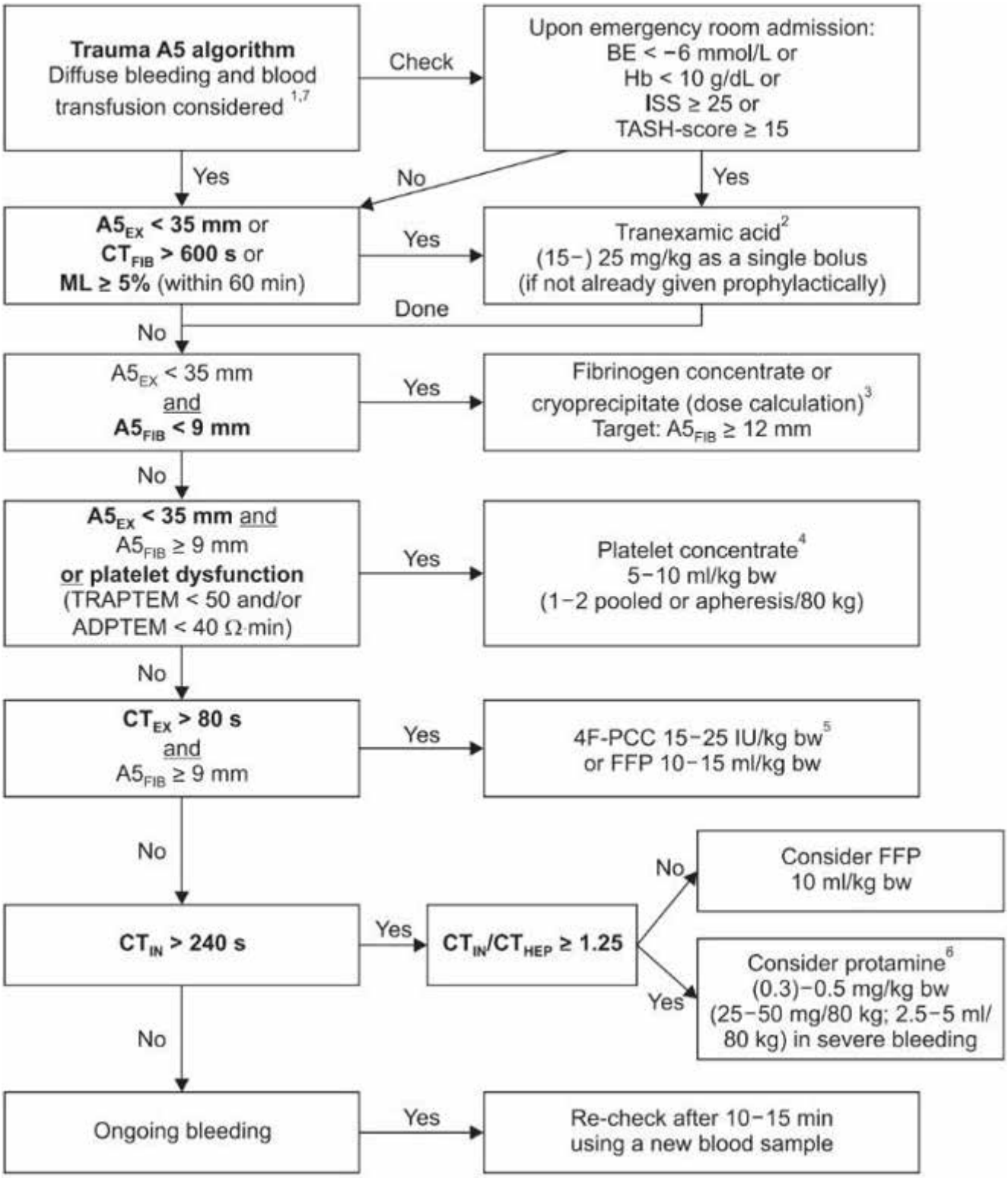
Cardiovascular Algorithm



Liver Transplantation Algorithm



Trauma Algorithm



Obstetric Algorithm

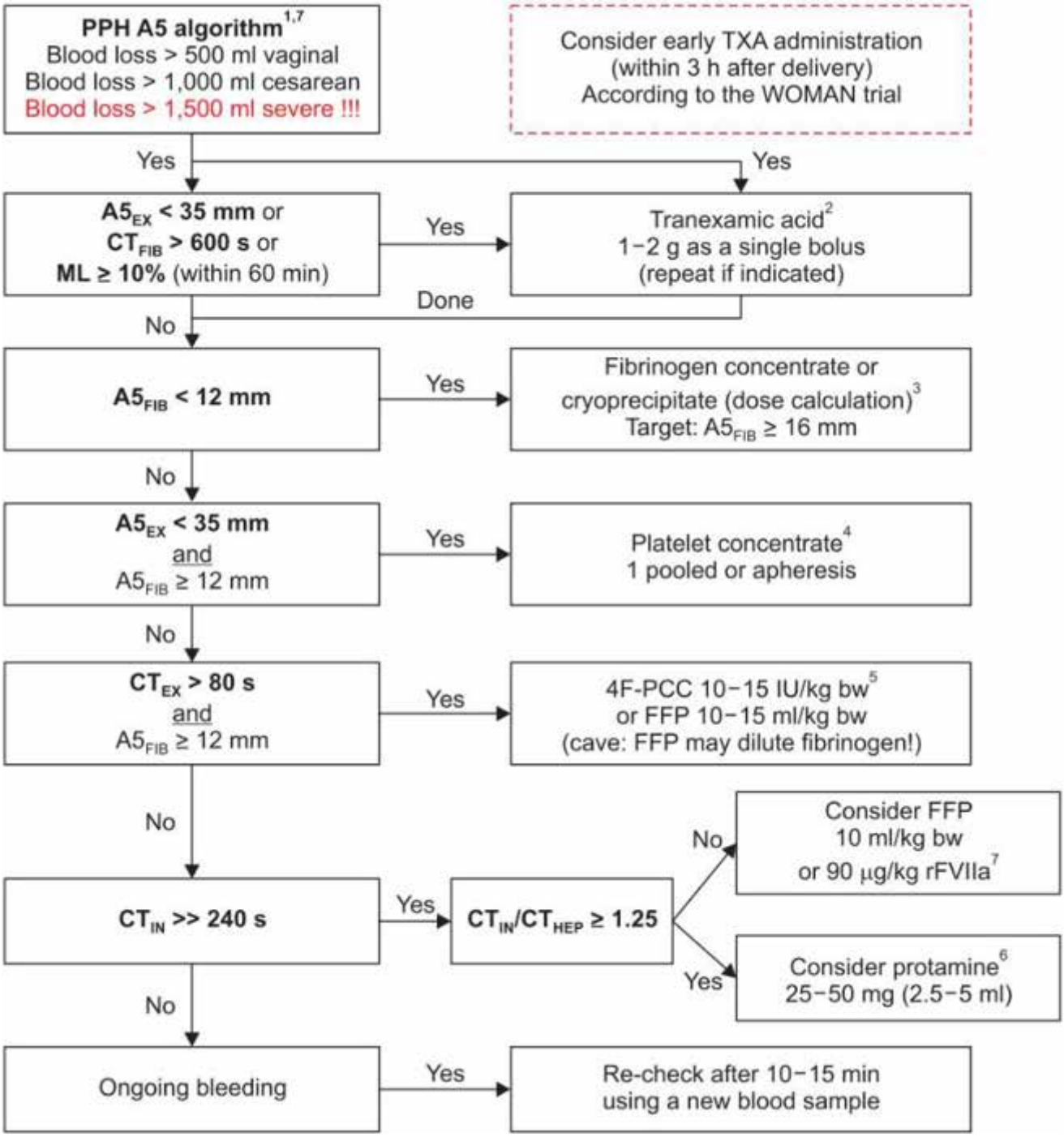


***Figure 15**. ROTEM® based algorithms for cardiovascular, trauma, obstetric and liver transplantation in which the target values for therapeutic interventions have been validated by setting specific interventional trials (Görlinger* et al *2019).*

blood component therapy, reducing coagulopathic blood loss and subsequent RBC transfusion (Redfern *et al* 2019).

Cardiac

Management of cardiovascular patients during cardiac surgery presents a range of unique challenges. Many of these patients are on anticoagulation and antiplatelet regimes prior to surgery or require initiation and management to prevent thrombosis and thrombolytic events following the use of cardiopulmonary bypass (Rali *et al* 2020). Post operative bleeding is a well- known and a serious complication of cardiac surgery and this bleeding has been attributed to increased rates of re-exploration, blood transfusion requirements as well as the length and cost of hospital stay (Elassal *et al* 2021).

Heparin is widely used to achieve anticoagulation during cardiac surgery, particularly during cardiopulmonary bypass. Protamine sulphate is required for reversal of heparin, but it is known to inhibit platelet function and serine proteases that are involved in coagulation with evidence suggesting that protamine overdose can lead to anticoagulant effects, further contributing to bleeding complications (Koster *et al* 2014; Hanke *et al* 2021). The use of ROTEM® has been shown as a valuable tool for heparin-protamine management. HEPTEM is used to confirm the presence of heparin in a sample which impacts the CT INTEM (Figure 16a), and by reviewing the ratio of CT- INTEM:CT-HEPTEM, effects of heparin excess can be distinguished from those of protamine excess (Figure 16b) (Mittermayr *et al* 2005).

Blood loss in cardiac surgery and the immediate post op period has been shown to be lower when VHA are used to guide transfusion management, with a reduction in the transfusion of RBCs, FFP and prothrombin complex concentrate and an increase in administration of tranexamic acid (Redfern *et al* 2019; Kuiper *et al* 2019) In addition to this there is evidence that the number of patients who experienced post operative bleeding requiring urgent re-exploration surgery was also decreased (Redfern *et al* 2019).

Cirrhosis and liver transplant

VHA have now been used extensively in liver transplants as an effective testing option for haemostatic monitoring to detect coagulopathy and to guide haemostatic therapy. The value of SCT in this setting is questionable due to the long turnaround time and the inability to reflect complex haemostatic changes in real time (Park 2020).

Liver transplantation is frequently complicated by coagulopathy associated with end-stage liver disease that is often multifactorial, contributing to complex haemostatic challenges faced during the operation. Decreased coagulation factors, antifibrinolytic factors and endogenous anticoagulant factors can add to both bleeding episodes and thrombotic events. There are various stages during liver transplantation which impact the state of coagulation and by having a POC device available for use in the theatre suite to provide real-time results is of great benefit. In one study of liver transplantation (Poon *et al* 2015), 80% of the cases revealed transient coagulopathy and fibrinolysis after reperfusion of the graft which is often reflected in the EXTEM and APTEM traces. With careful VHA monitoring to ensure normalization of haemostasis, this transient condition reversed without the need for additional treatment.

A recent study comparing the predictive value of SCT (PT, aPTT, fibrinogen concentration and platelet count) with ROTEM® assays in liver transplantation found that although the PT and aPTT were predictive of post operative bleeding, neither fibrinogen concentration nor

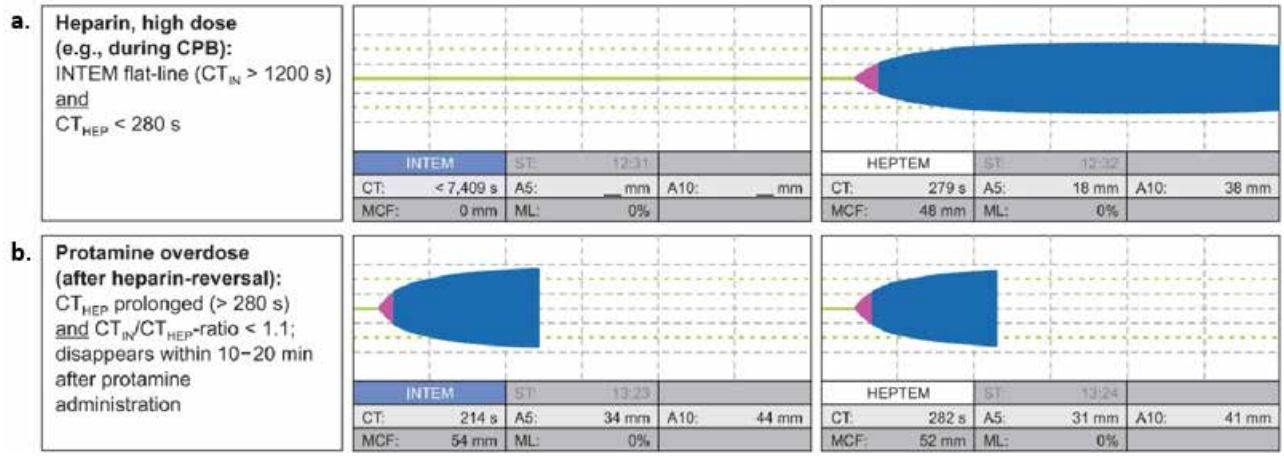


***Figure 16**. ROTEM® traces with a) heparin effect b) protamine overdose (Görlinger* et al *2019). Reproduced with permission (CC BY 4.0).*

platelet count were shown to have positive predictive value (Dötsch *et al* 2017). The CT-EXTEM and CFT- INTEM as well as the A10 and MCF-FIBTEM were predictive of bleeding, although other assay parameters were not as valuable. This study also showed that ROTEM® has a greater predictive value for impaired fibrin polymerization related coagulopathy (Dötsch *et al* 2017). International guidelines have been published that support the use of thromboelastography over SCT in the management of patients in intensive care units with acute liver failure (Hartmann *et al* 2023a). As with all in vitro testing, there are limitations. VHA testing may underestimate the haemostatic capacity because they are not sensitive to the effect of von Willebrand factor (vWF), which is often found to be significantly elevated in cirrhotic patients (Al Moosawi *et al* 2021).

SCT such as INR or platelet count should not be used to guide pre-procedural blood product transfusion in cirrhotic patients, but ROTEM® parameters associated with hypo coagulation (in particular a MA of < 30mm) have appeared to predict procedure related bleeding (Zanetto *et al* 2021). Hartmann *et al* in 2023 concluded that VHA guided therapy in patients with cirrhosis enhances patient blood management by decreasing the use of blood products without increasing complications (Hartmann *et al* 2023a).

Trauma

Trauma-induced coagulopathy is an imbalance of the dynamic equilibrium between procoagulant and anticoagulant factors, platelets, endothelium and fibrinolysis. Development of this condition is life-threatening and associated with high morbidity and mortality. Both TEG® and ROTEM® (particularly the FIBTEM assay which correlates well with standard fibrinogen concentration tests), can predict massive transfusion and can detect a developing a coagulopathy much earlier than SCT (Brill *et al* 2021; Winearls *et al* 2017. The most recent European guideline on management of major bleeding and coagulopathy following trauma recommends VHA and/or SCT can be used for early and frequent monitoring of haemostasis (Rossaint *et al* 2023).

There are various parameters in VHA that can be used to guide resuscitation therapy after trauma. VHA testing can occur within minutes of presentation and a growing body of evidence suggests that this approach may improve survival while reducing the volumes of blood products transfused (Brill *et al* 2021; Maegele 2023). Figure 17a shows a prolonged CT and CFT and reduced MCF in the EXTEM and no clot formation in the FIBTEM and Figure 17b is a trace from the same patient post treatment based on a local algorithm.

There have been conflicting results in some trials comparing patient outcomes in groups using VHA guided treatment versus SCT in haemostatic resuscitation in trauma. Gonzalez *et al* in 2016, reported that survival at 28 days was higher in the VHA guided cohort, with a decrease in plasma and platelet use in these patients compared to those utilising SCT. This trial concluded the use of VHA to guide haemostatic therapy in trauma improves survival and promotes appropriate use of blood products. On the other hand, the iTACTIC trial concluded there were no difference in overall outcome between VHA augmented protocols compared to SCT augmented protocols, although a significant limitation of this trial was that nearly three quarters of the patients were not coagulopathic at baseline measurements (Baksaas-Aasen *et al* 2021). This highlights the need for further large-scale randomized control trials to support the growing evidence for use of VHA for bleeding management.

Obstetrics

Fibrinogen depletion early in post-partum haemorrhage (PPH) is independently associated with severe PPH. FIBTEM test parameters correlate well with fibrinogen levels, and the FIBTEM A5 was demonstrated to be superior to Clauss fibrinogen in predicting progression to severe haemorrhage (Amgalan *et al* 2020). ROTEM® based algorithms have been developed taking into account this hypercoagulable state and when the A5 FIB is less than 12 mm fibrinogen concentrate in a PPH is recommended in comparison to the trauma algorithm where fibrinogen concentrate is recommended when the A5 FIB is less than 9 mm (Görlinger *et al* 2019) (Figure 15). An example of a severe post-partum haemorrhage, with the ROTEM sample collected after receiving tranexamic acid and an initial dose of cryoprecipitate, indicates that further product would be required to correct coagulopathy if bleeding was still present is shown in Figure 18.

Women become more hypercoagulable as pregnancy progresses and this state persists throughout labour with the addition of the activation of the fibrinolytic system to compensate for the hypercoagulable state. VHA testing is a valuable tool which can detect these changes and the differences between labouring and non-labouring women have now been shown. Lee *et al* in 2020, demonstrated a significant decrease in the onset of clot formation (CT EXTEM/INTEM & CFT INTEM), with an increase in parameters related to clot firmness (A5/A10/MCF FIBTEM/EXTEM/INTEM), supporting that women in labour are in a hypercoagulable state (Lee *et al* 2020). Figure 19 is an example of a ROTEM® trace displaying hypercoagulable features as reflected by the increase in the amplitudes of EXTEM, INTEM and FIBTEM. This specimen was collected from a patient experiencing post-partum haemorrhage (PPH).

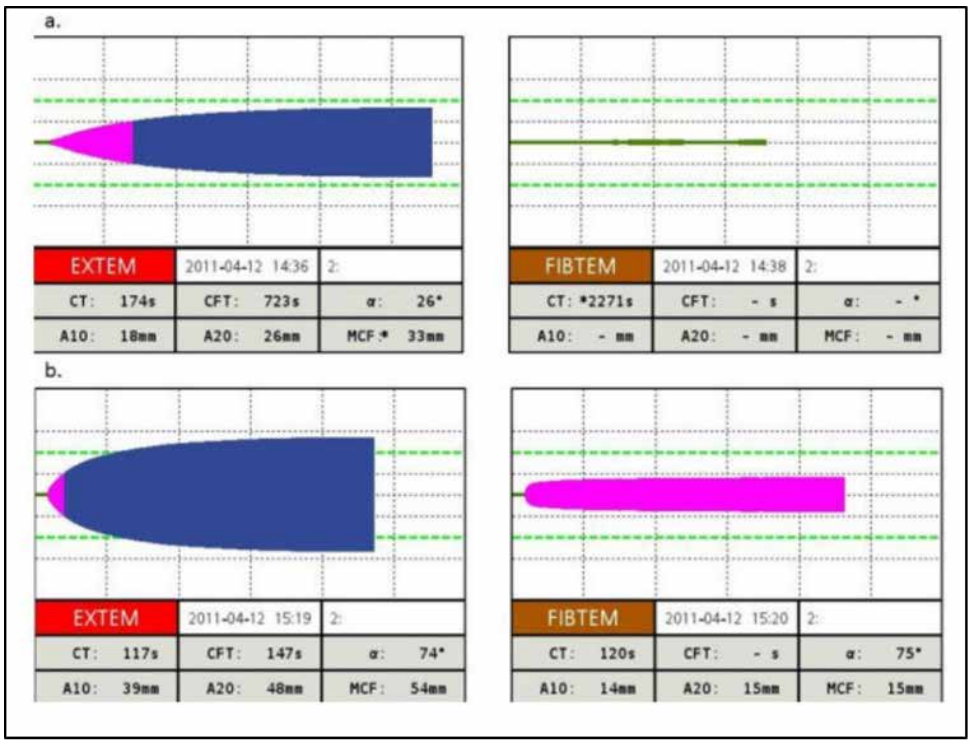


Figure 17. *ROTEM® examples from trauma patient. a. is upon admission where EXTEM clotting time (CT) and clot formation time (CFT) are prolonged, maximum clot firmness (MCF) is reduced and no clot formation in the FIBTEM. b. correction of these values can be seen in both EXTEM and FIBTEM after the patient received treatment including tranexamic acid, fibrinogen concentrate and prothrombin complex concentrate (Schöchl* et al *2012). Reproduced with permission (CC BY 4.0).*

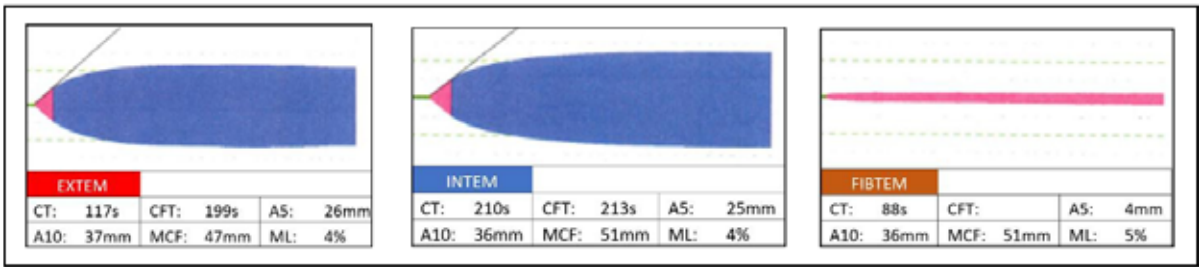


Figure 18. *ROTEM® example from patient experiencing severe PPH where the clotting time (CT) is prolonged, the maximum clot firmness (MCF) and amplitude (A) in both the EXTEM and INTEM are decreased and the amplitude in the FIBTEM is low suggesting further product is required if still bleeding.*

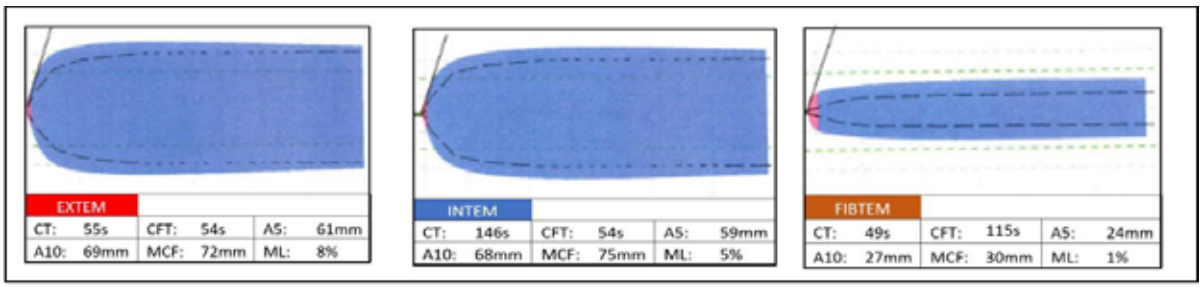


Figure 19. *ROTEM® example from a patient experiencing post-partum haemorrhage although trace shows hypercoagulable features such as increased clot firmness and amplitude (A) in EXTEM, INTEM and FIBTEM.*

Clinical outcomes of patients with severe PPH managed with and without VHA guided transfusion management have been compared. VHA patients received significantly fewer transfusions (RBCs, FFP and platelets) than those following standard massive transfusion protocol. This cohort was also found to have a lower incidence of hysterectomy and shorter post-partum hospitalisation, resulting in benefits to both patient outcome and the cost of care (Snegovskikh *et al* 2018).

Emerging Uses

Pre-op screening

There are a variety of clinical areas with active research into viscoelastic testing. These include the use of pre-surgical platelet function tests (using platelet mapping assays) in cardiothoracic and vascular surgery, the assessment of patients prior to cardiac surgery and pre-operative screening in patients with cirrhosis undergoing invasive procedures (Hartmann *et al* 2023b).

Bleeding complications associated with invasive procedures in patients with cirrhosis continue to be a concern for clinicians. Many guidelines recommend the correction of INR and platelet counts using FFP and platelets prior to procedures to prevent bleeding complications. Studies have now shown that the use of VHA before invasive procedures resulted in a reduction in the use of blood products with significantly altered INR and platelet count, without increasing the risk of procedure related bleeding (De Pietri *et al* 2016). Pre-operative VHA analysis has also proved useful in predicting transfusion requirements in liver transplant recipients, allowing for better preparation and lower blood product requirements prior to surgery (Fayed *et al* 2015). In patients with decompensated liver cirrhosis, TEG® parameters that are associated with hypocoagulability appear to predict procedure-related bleeding, although further research is required to establish whether correction of the abnormal parameters reduces the bleeding risk in this patient group (Zanetto *et al* 2021).

Chronic kidney disease (CKD) is associated with both bleeding and thrombotic tendencies, involving cellular (platelet function), plasma (coagulation cascade and fibrinolysis) and endothelial abnormalities (Abdelmaguid *et al* 2022). The use of ROTEM® in assessing coagulopathy in CKD demonstrated a prothrombotic state, with reduced CFT, increased MCF and hypofibrinolysis, but did not indicate risk of bleeding due to a hypo-coagulable state (Abdelmaguid *et al* 2022). This is likely to be due to standard ROTEM® assays not being sensitive to platelet dysfunction and platelet assays could be utilized in this condition.

DOAC monitoring

The use of direct oral anticoagulants (DOACs) has become increasingly common although there remain limited reversal options available. DOACs are a group of coagulation factor inhibitors including direct thrombin inhibitors (dabigatran) and direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) (Moser and Smock 2021). As bleeding risk continues to be a concern for prescribing physicians, there is a need for early assessment of residual DOAC activity if a patient presents with bleeding or there is an acute need for surgical intervention (Ten Cate *et al* 2017).

There are first line SCT currently such as PT and aPTT which can be used to screen for rivaroxaban and dabigatran respectively, but results can be highly variable based on the concentration of the DOAC and the reagent (thromboplastin) used in the assay (Ten Cate *et al* 2017). Secondary quantification assays (drug specific anti-FXa inhibitor levels and diluted thrombin time test with dabigatran calibrators) may be useful but have limited application where fast turnaround times are required in an emergency where time is critical (Ten Cate *et al* 2017).

The application of VHA to assess a patient's coagulation status is well established and there have now been numerous studies assessing VHA utilisation in the assessment of residual DOAC activity (Korpallová *et al* 2021). Standard ROTEM® tests (EXTEM/INTEM CT) can detect dabigatran, edoxaban and rivaroxaban but is insensitive to apixaban (Curry *et al* 2018). Experience in this area is still limited and there has been some variability reported where treatment with FXa inhibitors often present with a clotting time within normal range, but then others have found that by using modified

ROTEM® reagents (addition of saturating phospholipid vesicles and small amounts of TF), they could distinguish between treated and untreated patients with a good sensitivity (90%) and high specificity (85%) (Pailleret *et al* 2019).

Sahli *et al* in 2022 found the effects of DOAC plasma levels in various VHA can provide fast and essential information regarding DOAC activity although quantification with DOAC 'unspecific' VHA are still not sensitive enough in comparison of anti-Xa measurements performed in the laboratory (Sahli *et al* 2022).

Interestingly an observational study by Groene *et al* (2021) showed that the ClotPro device enables detection of anticoagulants DOACs. They found 100% specificity and sensitivity to detection of dabigatran and improved detection of the FXa inhibitors but were unable to differentiate between them (Groene *et al* 2021).

At this stage, the assessment of haemostasis competence in patients treated with DOACs requires specialized reagents and testing, with specific assays still in various stages of approval for commercial use (Volod *et al* 2022).

Summary

VHA provide a wholistic view of coagulation and with the use of a variety of assays run concurrently allow the process of clot initiation, amplification, strength, and stability to be assessed in real-time. Utilising whole blood, VHA allow for the assessment of not only the plasma protein contributions to clotting, such as fibrinogen and clotting factors, but also how the quantity and interaction of cellular components, in particular platelets, can contribute to haemostasis.

SCT were developed primarily for screening for factor deficiencies and to monitor anticoagulation therapy, but are limited in their application for the management of acute haemorrhage, to diagnose coagulopathy and are poor predictors of bleeding.

Advancement of VHA technology over the last 75 years has resulted in the development of POC devices that have proven utility in clinical situations where rapid, reliable and useful results can have profound impact on patient outcome.

Evolvement from the first generation of these devices has seen an increase in stability allowing further use as a true POC test at the patient's bedside, with specialist training in manual pipetting techniques also being removed with the introduction of cartridge technology. Further development of specific assays and platelet mapping is underway, addressing some of the limitations in current assays in detecting platelet factor receptor defects and von Willebrand's disease.

Being able to access meaningful parameters within minutes of test initiation and subsequently applying established algorithms to assist in transfusion management is of great benefit in clinical scenarios where early intervention, such as in critical bleeding, is known to improve patient outcomes. Use of VHA guided transfusion management algorithms in other areas such as cardiac surgery, liver transplantation and obstetrics has been established and recommended in several national and international guidelines as a part of patient blood management as there is now a large volume of evidence to support a decrease of allogenic blood product transfusion when utilising this technology.

It has been noted in many research and review papers that although there is growing evidence to support the use of VHA, particularly in critical bleeding, there continues to be a lack of level 1 evidence from high quality randomised controlled trials. This may contribute to a degree of questionability among clinicians around the application in clinical scenarios. With new and emerging technologies being developed, as well as further research and evidence being published in patient cohorts outside of those where the use is already established, it can be expected that the utility of VHA will only continue to grow.

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Implementation of photobiological warning markings for equipment and instruments in the Australian Standard AS ISO 15189:2023 accredited medical laboratory

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Introduction

Equipment and instruments that incorporate photobiological lamp products to support diagnostic capacity are commonly used in the medical laboratory (Sveinbjornsson and Gizurarson 2022). The medical laboratory must implement relevant risk control measures to protect laboratory personnel from optical radiation hazards as outlined in Clause 5.6 of AS ISO 15189:2023. The main objective of this paper is to enhance the medical laboratory's awareness of requirements relating to the provision of relevant risk control measures through warning markings for Exempt Group (RG 0), Risk Group 1 (RG 1) (low-risk), Risk Group 2 (moderate-risk) and Risk Group 3 (high-risk) lamp products (Section 6 of AS/NZS IEC 62471:2011). Selected organisations were identified to provide relevant information to support communication of hazard information to laboratory personnel and these were the Institute of Electrical and Electronics Engineers (IEEE), the International Electrotechnical Commission (IEC), the International Labour Organization (ILO) and the International Organization for Standardization, Standards Australia, and Standards New Zealand.

Contemporary challenges

The risk control measures relating to hazard information communication in the medical laboratory should include the display of relevant warning markings to inform laboratory personnel about optical radiation hazards to ensure the exposure remains acceptable and within the exposure limit (Gutteling 2018). Implementation of relevant measures to address the areas of vulnerability in the medical laboratory operations should be in alignment with the medical laboratory good professional practice commitment as stated in Clause 5.5 a of AS ISO 15189:2023. This paper does not cover the emission aperture label requirements in Clause 201.7.101.3 of AS IEC 60601.2.57:2014.

Optical radiation warning markings

The medical laboratory is to ensure that appropriate warning markings are displayed as listed in Subclause 9.5.1 of ISO 15190:2020 and in accordance with the risk group classification in Section 6 of AS/NZS IEC 62471:2011. The markings must be durable, permanently affixed, and legible according to Clause 201.7.101.2 of AS IEC 60601.2.57:2014, so that laboratory personnel can recognise the optical risk without the necessity for exposure to optical radiation. The optical radiation warning markings must display the following information outlined in Clause 201.7.101.2 and Clause 201.7.101.4 of AS IEC 60601.2.57:2014. There must be a warning sign as shown in ISO 7010-W027 (2011-05), Table 7 of ISO 7010:2019 with specified layout requirements (Subclause 6.4 of ISO 3864-1:2011) (Figure 1). There must also be a separate explanatory marking

***Figure 1**. **Optical radiation hazard warning sign [ISO 7010-W027 (2011-05)]**. The warning sign should be placed on the lamp product with the explanatory marking.*

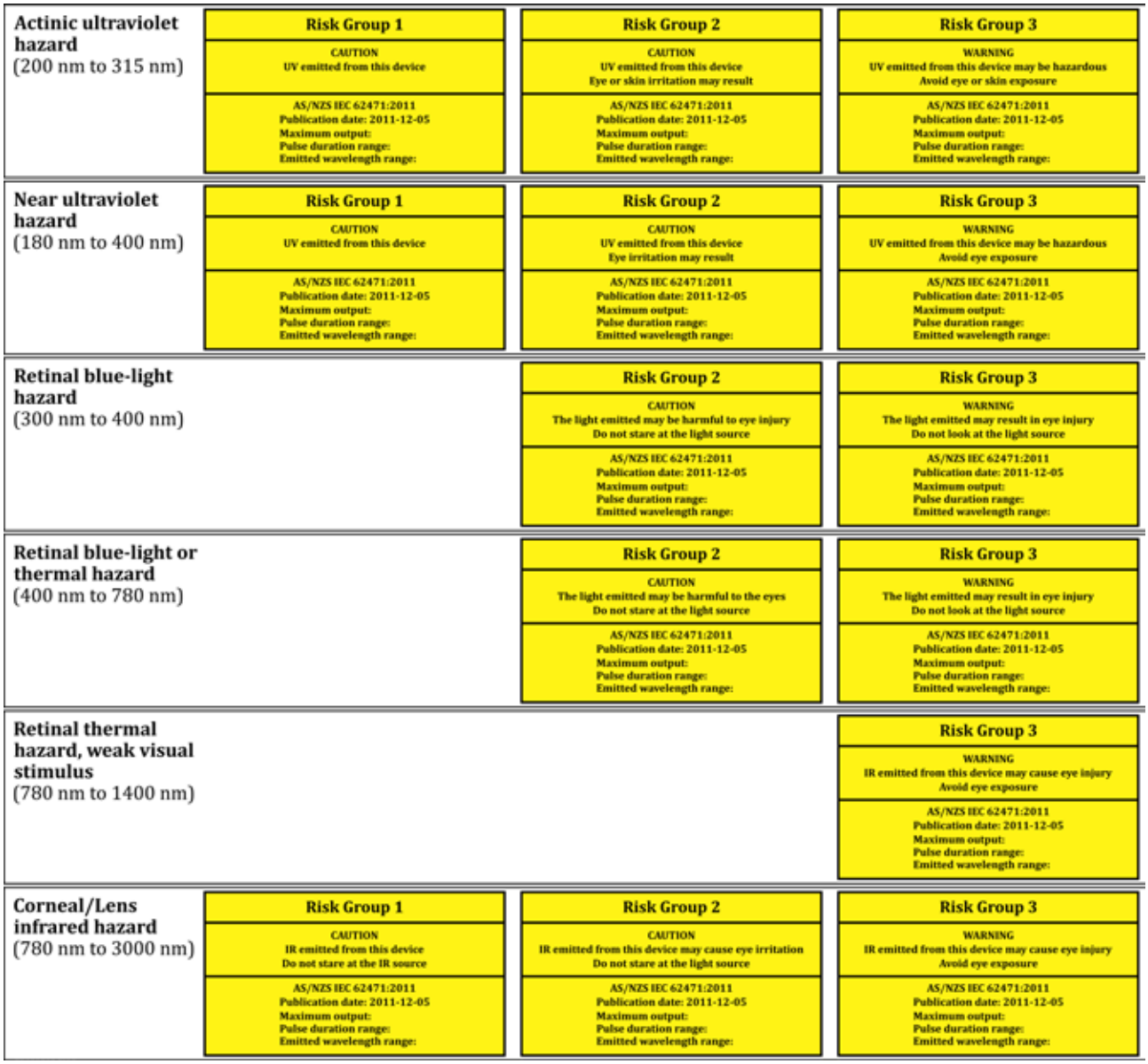

***Figure 2**. **Photobiological lamp product warning markings**. The explanatory markings that include the product risk group numbers and relevant information according to AS IEC 60601.2.57:2014 should be used in AS ISO 15189:2023 accredited medical laboratories to support good professional practice in Australia.*

containing safety information. The text panel must state the hazard-related risk group number excepting RG 0 and RG 1 emitting only in the wavelength range of 300 nm to 780 nm. In addition, the signal word for harm to laboratory personnel (Caution or Warning) must be visible and supplemented with safety information (Subclause 6.3 of ISO 3864-2:2016) as well as guidance on control measures; although wording that conveys an equivalent meaning is acceptable (Figure 2). The name and publication date of the Joint Australian/New Zealand Standard to which the product was classified must then appear along with the maximum output of optical radiation, the pulse duration range (if appropriate), and the emitted wavelength range (Figure 2).

Placement considerations of warning markings

The medical laboratory is to ensure appropriate warning markings are clearly visible and unambiguously legible during maintenance or operation as specified in Clause 201.7.101.2 of AS IEC 60601.2.57:2014. There is a potential practical shortfall however because the warning effectiveness is likely to be reduced if the warning information is visible only during the maintenance. The medical laboratory should investigate the availability and suitability of ways to display the markings continuously during normal use to communicate hazard information to laboratory personnel. Implementation of warning markings that are visible during both maintenance and normal use should eliminate or minimise the

optical radiation risks to laboratory personnel in the medical laboratory.

Further considerations

The medical laboratory should also take further notes from the IEC, the IEEE, the ILO, and Standards Australia. The ILO provides prevention and control measure recommendations for optical radiation, including the placement of warning labels (ILO 2001). Standards Australia provides information relating to the warning sign dimensions [ISO 7010-W027 (2011-05)] and it should be ≥ 2.75 mm high [Clause 5.2 a) of AS 61010.1—2003]. The IEC and the IEEE provide information relating to the text font size and it should be ≥ 14 point in bold according to Subclause 9.10.1 of IEC/IEEE 82079-1:2019 to maintain reasonable visibility.

The present study suggests that the optical radiation warning markings should be clearly visible during normal use by trained, authorised, and competent operators to promote continual situational awareness. The medical laboratory must, to the extent that is reasonably achievable, implement effective risk control measures to minimise optical radiation hazards in a consistent manner by displaying the hazards explicitly to laboratory personnel.

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Acute mast cell leukaemia case study

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Abstract

Mast cell leukaemia (MCL) is a rare subtype of systemic mastocytosis (SM), characterised by clonal proliferation of the mast cells in the bone marrow and other organs. According to the World Health Organization (WHO), MCL must meet SM diagnostic criteria and possess additional features such as the presence of atypical mast cells in bone marrow, peripheral blood and extracutaneous organs. Acute mast cell leukaemia has a significantly worse prognosis than other subtypes of SM. Some treatment options are available for acute MCL cases including tyrosine kinase inhibitors (TKIs), chemotherapy, and allogenic stem cell transplants.

The following case study describes the diagnostic and therapeutic approaches for a patient with acute MCL who completed consolidation therapy for FMS-like tyrosine kinase 3 (FLT3)-positive acute myeloid leukaemia (AML). Neoplastic mast cells were observed on the peripheral blood film and in the bone marrow (BM) nine months after the initial FLT3-positive AML diagnosis. Several tests were conducted including a BM examination, immunohistochemistry, molecular test and serum tryptase level analysis, in accordance with WHO criteria for acute mast cell leukaemia diagnosis. Due to the absence of a KIT D816V mutation and the patient's age, the treatment options were limited. As targeted MCL treatment was not feasible, the patient was provided supportive care.

Keywords: ***Systemic mastocytosis, mast cell leukaemia, KIT D816V mutation, tyrosine kinase inhibitors***

Introduction

A mastocytosis is a clonal proliferation of mast cells in one or more organs (Georgin-Lavialle *et al* 2013; Zheng *et al* 2018; Jafari *et al* 2019). Based on the clinical and pathological presentation, mastocytosis is classified into systemic mastocytosis (SM), cutaneous mastocytosis (CM), and mast cell sarcoma (Joris *et al* 2012; Jafari *et al* 2019). A rare disease, SM has an estimated incidence rate of 13 cases per 100,000 people and generally occurs in adults (Galura *et al* 2020). The release of mediators and infiltration of mast cells causes symptoms of the condition. These symptoms include hypertension, rash, pruritus, musculoskeletal pain, and fever (Jafari *et al* 2019; Galura *et al* 2020).

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A diagnosis of SM is confirmed by the presence of mast cell infiltration in at least one extracutaneous organ, most commonly the bone marrow (Bae *et al* 2013; Galura *et al* 2020; Zanelli *et al* 2023). SM is further classified according to its disease-specific features, including indolent SM (ISM), smouldering SM (SSM), aggressive SM (ASM), SM with an associated hematopoietic neoplasm (SM-AHN), and MCL (Georgin-Lavialle *et al* 2013; Valent *et al* 2014; Jafari *et al* 2019; Zanelli *et al* 2023). MCL is a rare form of SM that accounts for less than 0.5% of all SM cases (Georgin-Lavialle *et al* 2013; Zheng *et al* 2018; Galura *et al* 2020). The disease is characterized by the leukaemic spread of mast cells across multiple organs, including the liver, peritoneum, spleen, bones, and bone marrow (Valent *et al* 2014; Zanelli *et al* 2023). A diagnosis of MCL requires the presence of SM diagnostic criteria and at least 20% atypical/immature mast cells in a bone marrow as defined by the World Health Organization in 2022 (Khoury *et al* 2022; Zanelli *et al* 2023) (Table 1).

Depending on the presence of organ damage (C-findings), MCL is divided into acute and chronic variants (Galura *et al* 2020; Zanelli *et al* 2023).

***Table 1**. Diagnostic criteria for systemic mastocytosis (Adapted from Zanelle* et al *2023).*

2022 WHO: The diagnosis of SM can be made when the major criterion plus one minor criterion or at least three minor criteria are fulfilled.
Major criterion
• Multifocal dense infiltrates of MCs (≥ 15 MCs in aggregates) in BM biopsy and / or other extracutaneous organs.
Minor criteria
• > 25% immature or atypical or immature MCs in BM biopsy or BM smear or other extracutaneous organs. • Any kind of *KIT* mutation in BM, blood or other extracutaneous organs. • MCs expressing CD25 with or without CD2 (in addition to normal MC markers). • MCs expressing CD30. • Persistently elevated serum tryptase level (> 20 ng/mL), unless there is an associated myeloid neoplasm, in which case, this parameter is not valid.

WHO: World Health Organization; **SM:** Systemic mastocytosis; **BM:** Bone marrow; **MCs:** Mast cells; **CD:** Cluster of differentiation

Most patients (60-90%) experience the acute form of MCL which develops rapidly and aggressively, resulting in massive organ damage. The chronic form of MCL has a prolonged course without rapid organ damage, but progression to acute MCL appears to occur over a variable period (Valent *et al* 2014; Zanelli *et al* 2023).

Acute MCL has a poor prognosis, with a median survival of less than six months (Bauer *et al* 2017; Zheng *et al* 2018). There are limited treatment options for acute MCL and little data on treatment (Joris *et al* 2012; Bauer *et al* 2017; Zanelli *et al* 2023). A molecular analysis of the *KIT* Proto-Oncogene (*KIT*) gene is essential for selecting the appropriate treatment (Joris *et al* 2012; Georgin-Lavialle *et al* 2013; Galura *et al* 2020). This case report describes the laboratory findings and prognosis of a patient with acute MCL without *KIT* D816V mutation.

Case report

A 64-year-old male was admitted to the hospital with a history of completing consolidation therapy for FLT3-positive AML in December 2021. The patient commenced maintenance treatment with ongoing transfusions and in February 2022, a BM aspiration was performed due to abnormal laboratory results. The laboratory findings were notable for a decreased white blood cell count (1.40 x 10^9/L; RR 3.5-11.00 x 10^9/L), neutropenia (0.60 x10^9/L; RR 1.7-7.0 x10^9/L), anaemia (haemoglobin 94 g/L; RR 130-180 g/L), and thrombocytopenia (11 x 10^9/L; RR 150-450 x 10^9/L). A microscopic examination of the peripheral blood film revealed some abnormal mononuclear cells with heavily granulated cytoplasm, with granules overlying the eccentric nucleus and with cytoplasmic budding (Figures 1A and 1B). This patient had a marked increase in serum tryptase 515.0 µg/L (RR 0.0-11.4 µg/L).

Bone marrow examination demonstrated a hypocellular marrow with reduced three lineage haematopoiesis. Approximately 44% of cells were intermediate to large atypical round granular cells, favoured to be abnormal mast cells. These cells had a single round or bilobed eccentric nucleus with variable granules in the cytoplasm (Figures 2A and 2B). Approximately 5% of cells were typical blasts with some having monoblastic appearance. About 50% of the abnormal granular cells showed metachromatic staining of cytoplasmic granules with toluidine blue stain (Figure 3). Flow cytometry analysis showed approximately 36% of the total nucleated cells were intermediate to large immature myeloid cells, and their immunophenotype was CD45 +/HLA-Dr+(high)/ CD 117 +(bright)/CD 34-/CD10+/CD2+ (dim)/CD 25+/CD4+.

A cytogenetic analysis of bone marrow cells revealed a normal male karyotype (46, XY) with no abnormalities. No mutations were detected in molecular analysis, including the most frequently detected mutation, *KIT* D816V.

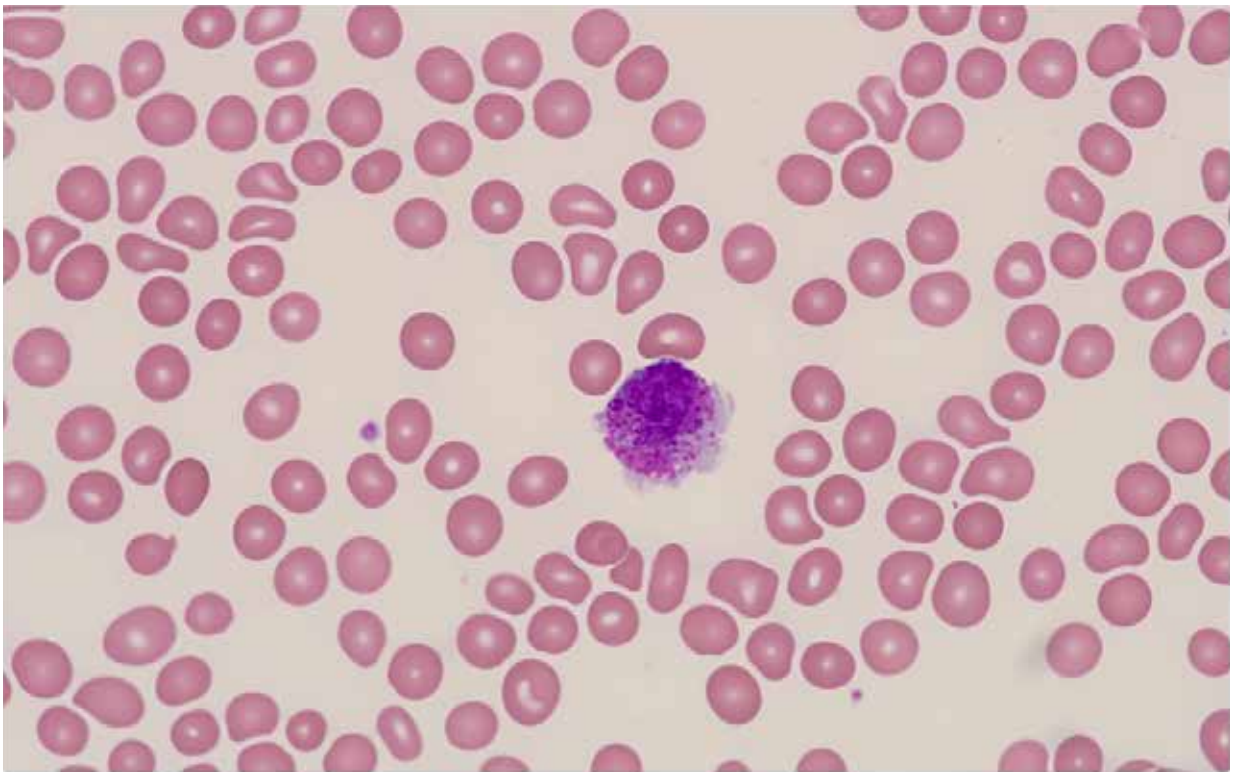

***Figure 1A**. Peripheral blood film showing a circulating atypical mast cell with cytoplasmic budding.*

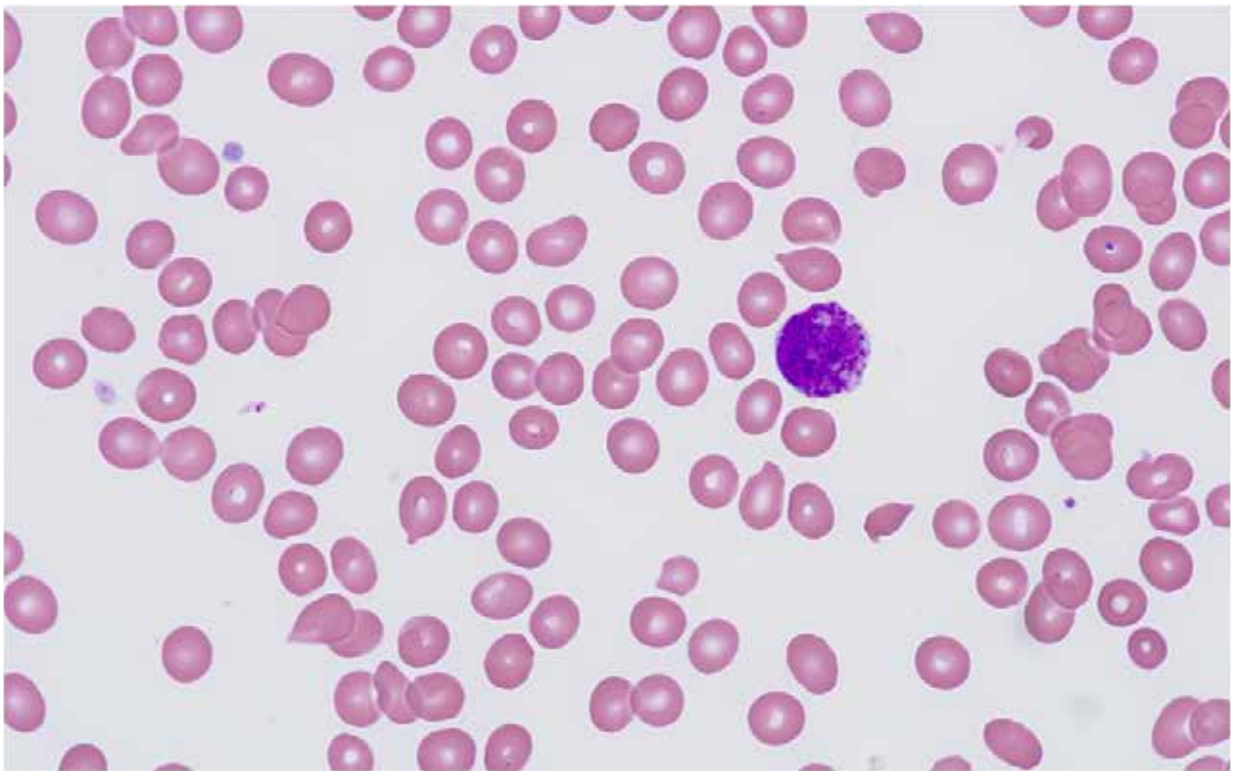

***Figure 1B**. Peripheral blood film showing an atypical mast cell with metachromatic granules.*

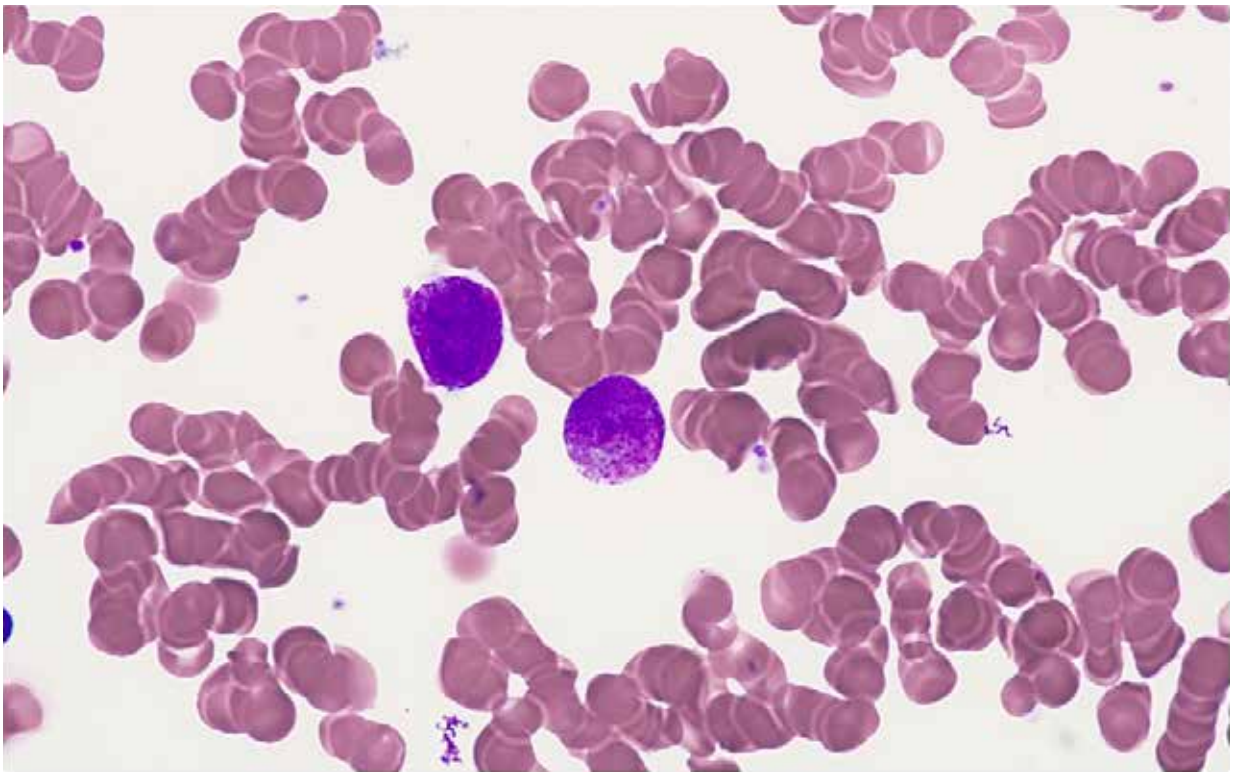

***Figure 2A**. Bone marrow aspirate showing atypical mast cells with a bilobed eccentric nucleus and variable granules in their cytoplasm.*

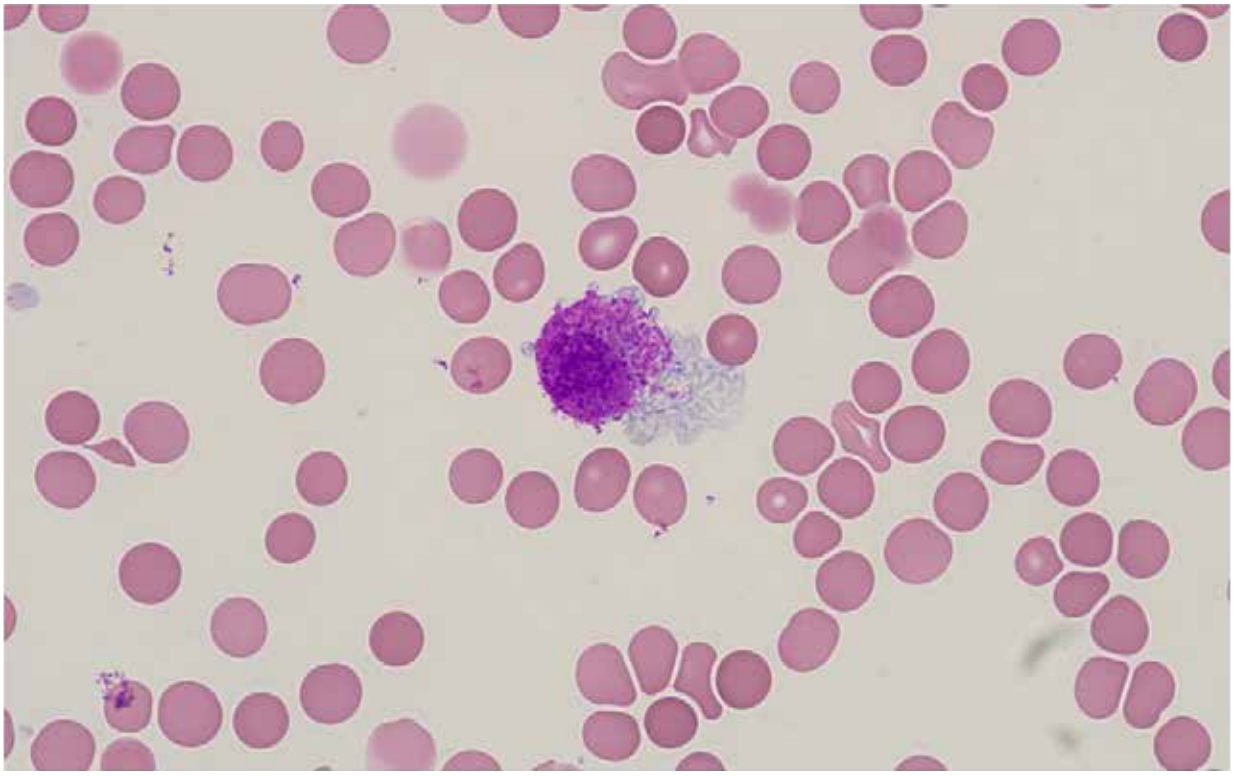

***Figure 2B**. Bone marrow aspirate smear showing a neoplastic mast cell with a single round eccentric nucleus moderately large purple-pink granules in the cytoplasm with long cytoplasmic tendrils.*

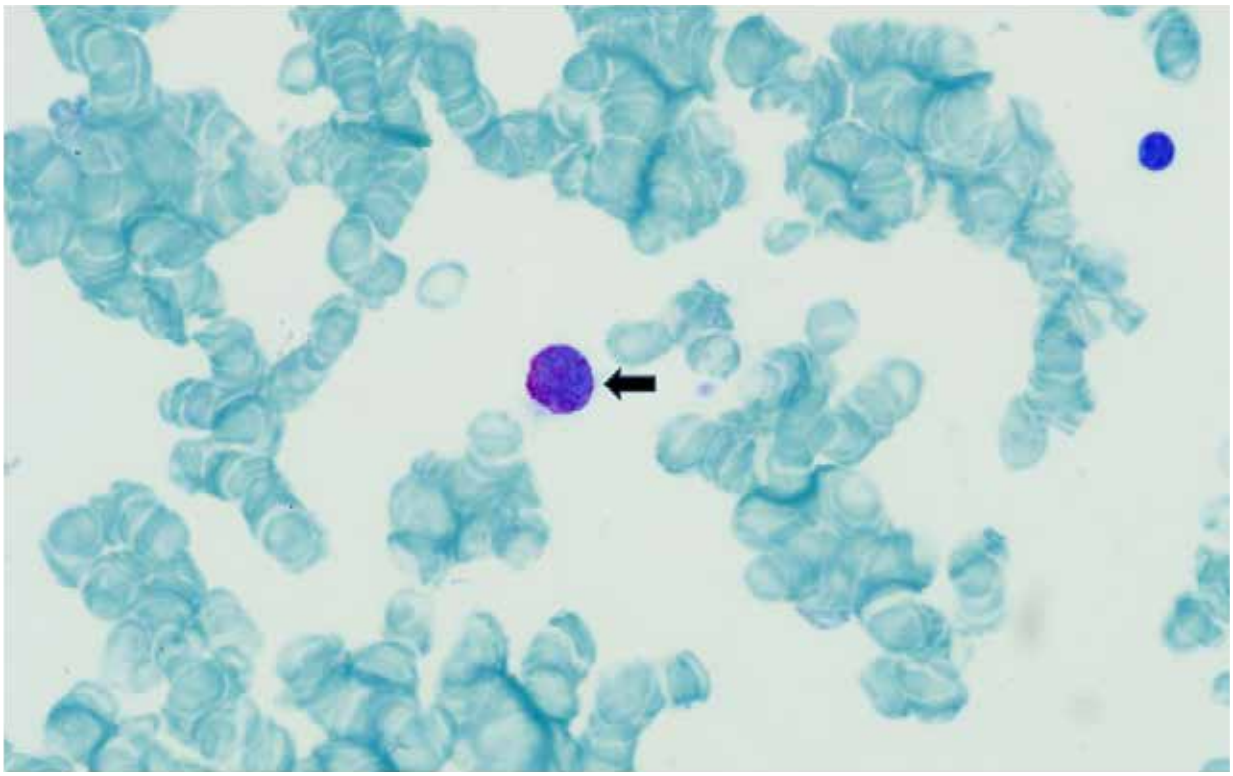

***Figure 3**. Toluidine blue stain showing medium-sized round or oval mast cell with densely packed purple metachromatic granules in the cytoplasm (black arrow).*

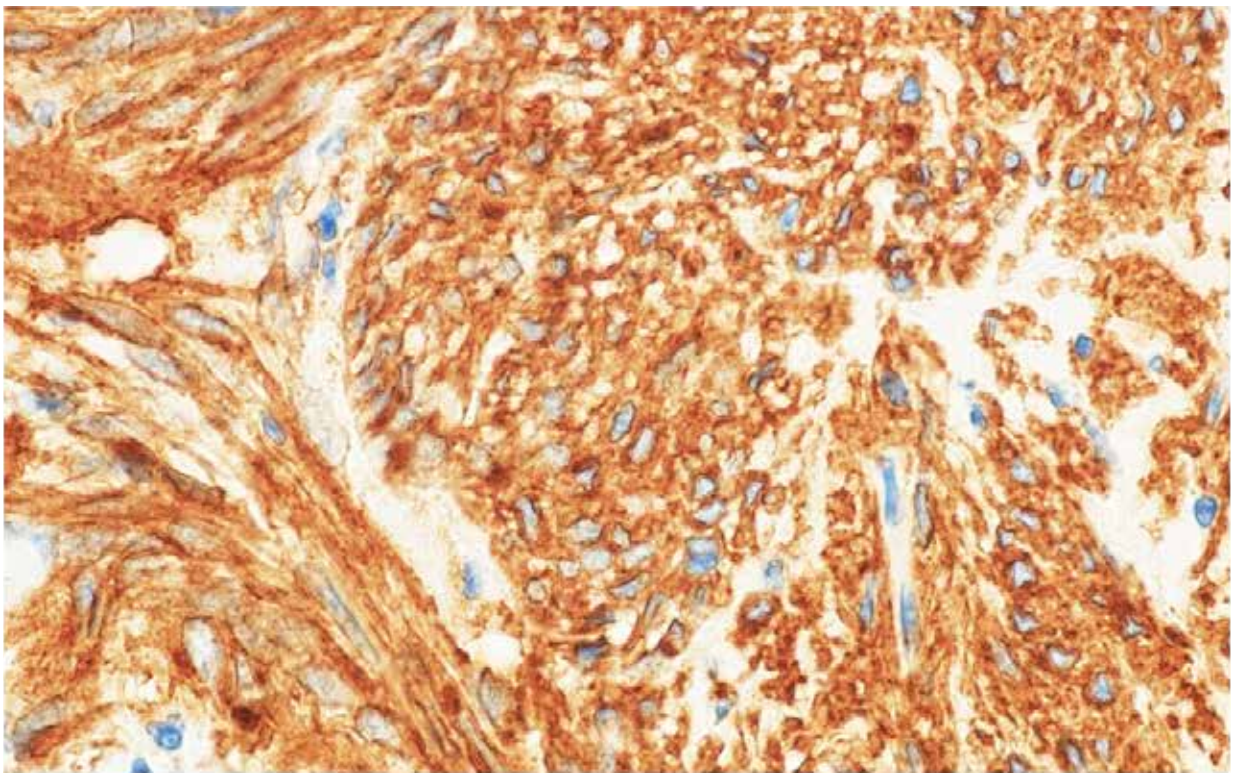

***Figure 4A**. Immunohistochemical staining of bone marrow biopsy in which mast cells are positive for CD117.*

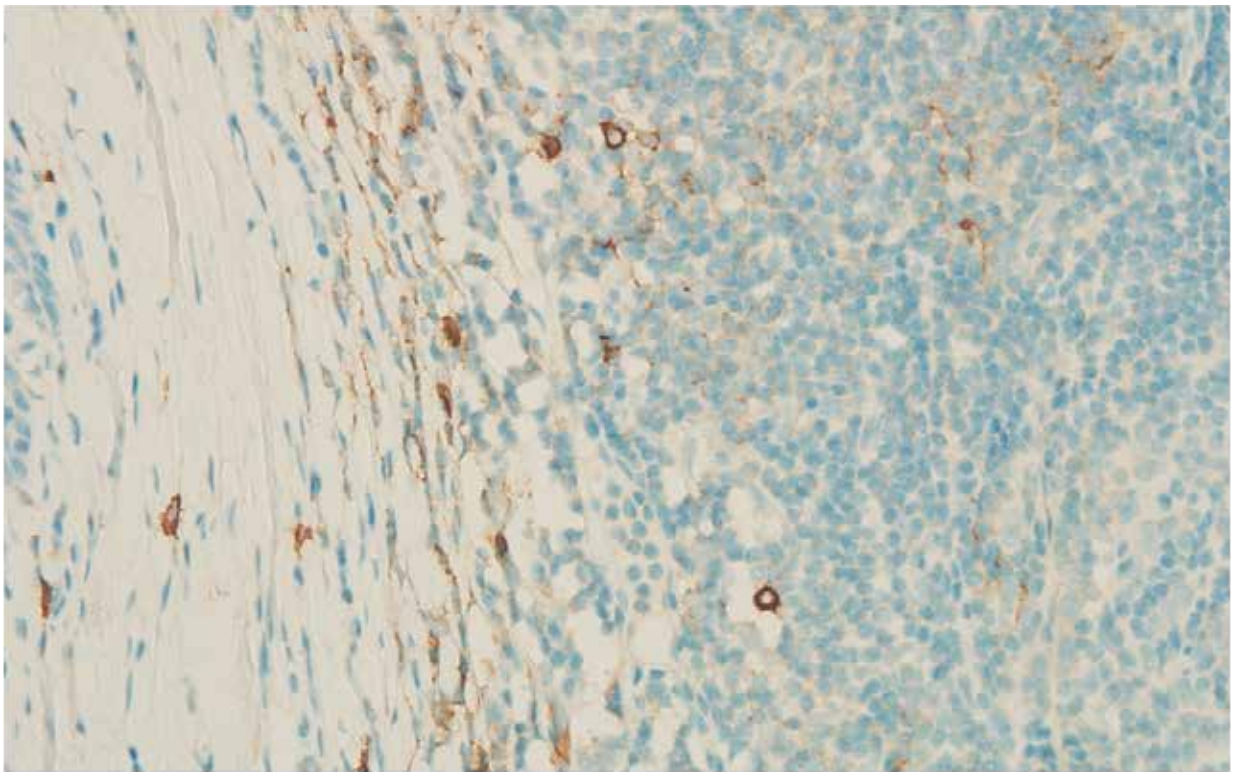

***Figure 4B**. Immunohistochemical staining of bone marrow biopsy showing a weakly positive reaction for mast cell tryptase.*

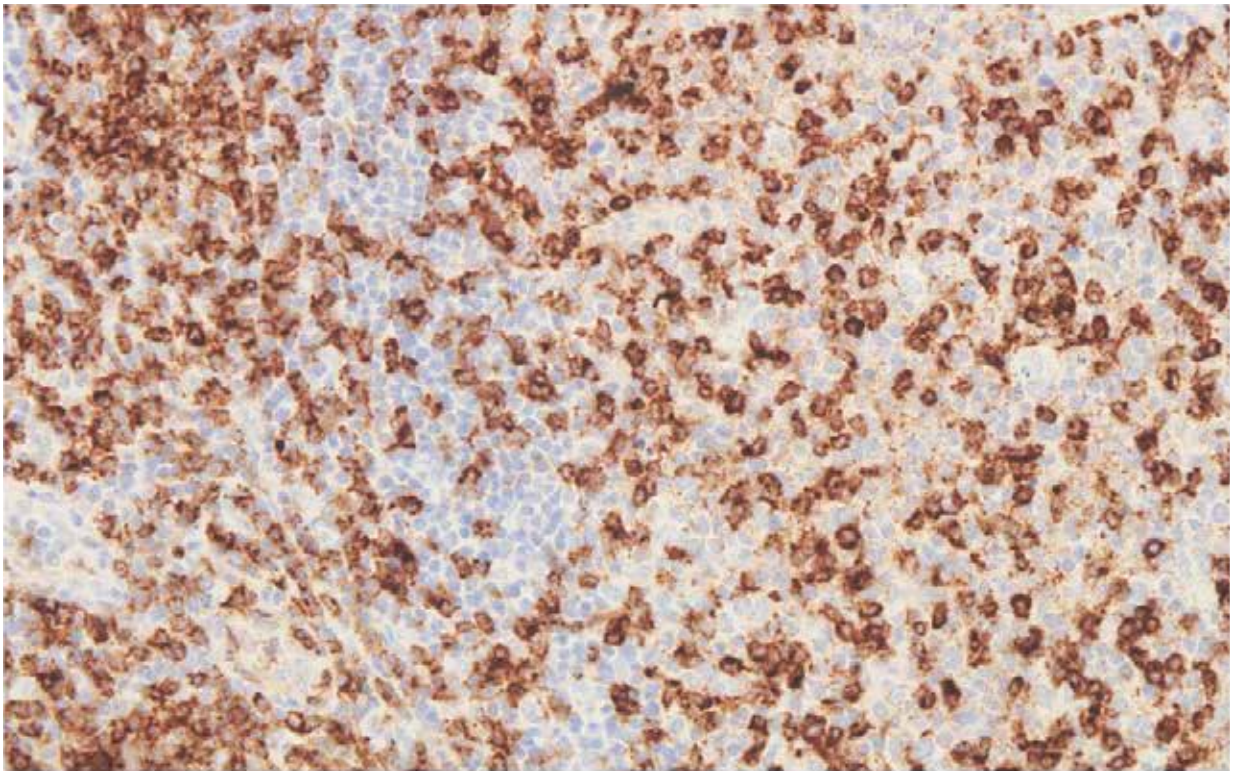

***Figure 4C**. Immunohistochemical staining of bone marrow biopsy showing an increased number of neoplastic mast cells positive for CD2.*

Immunohistochemistry revealed a strong positive of CD117, CD 2 and weekly positive in mast cell tryptase (Figures 4A-C).

The laboratory results of this patient fulfilled the diagnostic criteria of SM, with approximately 44% of atypical immature mast cells in bone marrow and elevated serum tryptase level (> 20 ng/mL). Cytopenia caused by infiltration of neoplastic mast cell was identified as a C-finding of acute MCL.

Discussion

As an aggressive form of mastocytosis, acute MCL is a very rare disease. It is characterized by the proliferation of atypical mast cells and frequently affects multiple organs. Most acute MCL cases present with cytopenia, hepatic dysfunction, hypersplenism, malabsorption, osteolytic lesions, and weight loss, known as C-findings (Galura *et al* 2020; Zanelli *et al* 2023). For its diagnosis, acute MCL must meet the criteria for SM and organ function impairment, as well as leukemic involvement of the bone marrow. (Galura *et al* 2020; Pardanani 2021; Zanelli *et al* 2023). The heterogeneity of acute MCLs clinical and morphological features often makes diagnoses difficult and the clinical course of the disease unpredictable (Valent *et al* 2014).

Atypical mast cells are classified into three subtypes based on their morphological characteristics: metachromatic blasts and atypical mast cells I and II. A metachromatic blast exhibits a blast-like nuclear morphology with numerous metachromatic granules (Bae *et al* 2013; Valent *et al* 2014). The atypical mast cell type I has elongated cytoplasmic projections, oval eccentric nuclei, and hypogranulation. Unlike type I mast cells, type II mast cells normally exhibit bilobed or polylobed nuclei (Bae *et al* 2013; Valent *et al* 2014). As shown in this case study, MCL and aggressive forms of SM commonly display more pronounced cellular atypia, such as metachromatic blasts or atypical mast cell type II (Bae *et al* 2013; Zanelli *et al* 2023).

It is essential to perform immunophenotyping in order to identify abnormal mast cells (Galura *et al* 2020). The key markers for identifying abnormal mast cells in SM are tryptase, CD117+, CD25+ and CD2+. Despite this, tryptase and CD117 expression alone do not indicate the neoplastic nature of mast cells (Georgin-Lavialle *et al* 2013; Galura *et al* 2020; Zanelli *et al* 2023). The immunohistochemical expression of CD25 and/or CD2 is currently recognised as a minor diagnostic criterion for SM, as the expression of these markers is indicative of clonal infiltrates of mast cells (Joris *et al* 2012; Zanelli *et al* 2023). Neither of these antigens is expressed in normal mast cells, myeloid precursor cells or immature mast cells from other myeloid neoplasms (Galura *et al* 2020; Zanelli *et al* 2023). Mutations in the *KIT* gene are also hallmarks of the disease (Joris *et al* 2012; Pardanani 2021). The deregulation of the *KIT* gene, including overexpression and gain of function mutations, has been discovered in several types of cancer in humans (Cruse *et al* 2014). Mutations in codon 816 of *KIT* cause constitutive activation of KIT kinase in adult-type mastocytosis (Joris *et al* 2012; Georgin-Lavialle *et al* 2013). There are several types of activating *KIT* mutations, which respond differently to KIT inhibitions based on the site and type of mutation (Joris *et al* 2012; Georgin-Lavialle *et al* 2013). The *KIT* D816V mutation occurs in more than 80% of adult patients with SM, particularly in the aggressive forms, with a frequency greater than 95% in patients with MCL (Joris *et al* 2012; Zanelli *et al* 2023). However, several studies have found that *KIT* D816V mutations are not always positive, as illustrated in this case study (Joris *et al* 2012; Galura *et al* 2020; Zanelli *et al* 2023). This information is useful in predicting drug resistance and in supporting individualisation of therapy based on the response of specific mutant proteins to specific drugs (Joris *et al* 2012; Georgin-Lavialle *et al* 2013; Pardanani 2021).

The treatment options for acute MCL include TKIs, chemotherapy and allogeneic stem cell transplantation (allo-SCT) (Georgin-Lavialle *et al* 2013; Galura *et al* 2020; Pardanani 2021). Allogenic stem cell translation may also be an effective treatment option for MCL (Georgin-Lavialle *et al* 2013; Galura *et al* 2020; Pardanani 2021). According to some reports, the graft reduces the mast cell burden after transplantation. Due to the limited ability of this treatment to completely eradicate the disease, allo-SCT is yet to be proven in MCL patients and, as of now, requires further evaluation (Georgin-Lavialle *et al* 2013; Bauer *et al* 2017). One of the most promising therapeutic options is the use of TKIs, such as avapritinib or midostaurin, which have been shown to possesses a potent inhibitor of the *KIT* D816V mutation (Galura *et al* 2020). Unfortunately, the patient in this case study did not have the *KIT* D816V mutation and therefore could not be treated with TKIs. Another possible treatment option was cladribine, but it has only been utilized in a very small number of acute MCL cases and has demonstrated relatively low efficacy (Joris *et al* 2012). After careful discussion with the patient and his family, supportive care was provided, including platelet and red cell transfusions every one to two weeks.

In conclusion, it can be challenging to diagnose acute MCL due to its rarity. An early diagnosis may increase the chances of successfully administering treatment and extending patient survival time.

A thorough understanding of the morphology and classification of acute MCL based on the novel criteria is essential for appropriately guiding diagnosis. In

addition, molecular analyses of the *KIT* gene are critical in determining the appropriate treatment. An appropriate drug selection can facilitate effective treatment of subsequent relapses and prevent the occurrence of resistance.

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Viaduct Events Centre 16-18 August 2023

Oral and poster presentation abstracts

O1: Data and Digital ethics

M Adriaansen[1]

[1]*Te Whatu Ora Waitematā*

There is no disputing that medical laboratory tests are critical for patient diagnosis and treatment. However, numerous publications and organisations claim laboratory tests are used by clinical staff in the diagnosis of at least 70% of patients disorders (or variations of this claim), without any evidence. The origin of this claim arose from a publication in 1996 that stated that "*Laboratory services may make up 5% of a hospital's budget but leverage 60-70% of all critical decision-making such as admittance, discharge, and medication*" (1).

This publication has been cited 78 times in the PubMed database to date with virtually all just stating the original statement or various versions thereof, without critical comment. It has also frequently been stated on the web sites of various originations, including the NZIMLS where it states that "*Medical laboratory scientists analyse patient speciments/samples sent to the laboratory producing results in the diagnosis of 70-80% of all patients disorders.*"

The 70% claim, or variations thereof, were challenged in 2011 by Hallworth who argued that these claims were not evidence-based and stated that "*Various 70% claims should be resisted in favour of more specific and evidence-based indices of added value*" (2). Despite arguments for objective evidence, many publications and organisations continue to state the 70% claim without critical discussion. As medical laboratory professionals, we should resist making this 70% claim (or one of the various versions) in favour of more specific statements that must be evidence-based.

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O2: Quality in the Pacific Laboratory - Past, Present and Future

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[1]*Pacific Pathology Training Centre*

As medical laboratory technicians, scientists, and managers, we understand the importance of Quality in our services and the impact of poor-quality laboratory results on a patient's management and outcome. All laboratories are required to be accredited in developed countries such as New Zealand and Australia. However, in the Pacific, quality and quality improvement is challenging. Laboratories in the Pacific struggle to be aligned to ISO15189, and accreditation, currently unreachable.

The Pacific Pathology Training Centre (PPTC) has worked closely with Pacific countries and donor partners to improve the quality of laboratory services for over 40 years. The PPTC provides short term centre-based courses in Wellington, in-country on-site courses for LQMS and section specific training, short term training attachments with New Zealand accredited medical laboratories, distance learning Diploma programme, an External Quality Assessment programme, facilitate the design and delivery of Laboratory container systems, and the provision of reagents and equipment for Pacific Island laboratories. In addition, the PPTC conducts annual external SLIPTA audits for selected countries to assess the level of performance in terms of alignment with the ISO15189 standard.

Over the years, there have been many improvements in the laboratories, however, limitations in resources, in-country politics and attitudes have been hindering progress. From personnel, equipment, procurement, and infrastructure problems to name a few, sustainability of quality improvement within these low resources Pacific Island laboratories is somewhat challenging.

The future of Pacific laboratory quality improvement must be a multi-faceted, fully understood and supported teamwork approach. It must involve government and donor investment and support, laboratory leadership and empowerment to conduct work, an appropriate and effective laboratory organisation structure and uplifting culture, proper clinical guidance and advice, open and clear stakeholder collaboration, and monitoring and evaluation to ensure effective outcomes of activities by the laboratories, donor partners and governments Ministries Of Health.

Future improvements in the Pacific laboratories must be driven and owned by the PIC laboratories themselves. At the same time, they must be supported by organisations such as the PPTC and other donor partners. The limited resources in Pacific Island laboratories are the main challenge, however, improvement in quality can be done in a stepwise, systematic approach. PIC governments must invest in Laboratory Quality Management Systems to ensure sustainable laboratory quality improvement in their countries. High quality of services in laboratories ensures better treatment and management, and the best outcomes for the Pacific Island people.

O3: A smooth sea never made a skilled sailor

L Aspin[1]

[1]*Labtests*

The thing I enjoy most about my job (apart from my team of course) is process improvement; making things easier for the team, better for the patient and faster for the requestor. From 2009 to 2020 we consistently met our KPIs and continued to improve our processes and quality of service with the help and support from the team and our suppliers.

In 2019, we started a project for the upgrade of our automated solution to Total Lab Automation (TLA). We knew this was a necessary step; our analysers were ready for retirement, we had nearly maxed out our ability for process improvement and we needed to plan for future increases in testing within our region. The bonus of course was getting to use the latest technology and start moving in to the future of laboratory testing. After a long process, a decision was made as to which supplier which we would be working with and from there the fun began.

Sunday 13th December 2020, we went live and as you all probably know, the fun stopped that day.

So what went wrong? That discussion is for another time. This talk is about "If I could start over, what would I do differently", and while you may think that will be a long list, it really isn't. In fact, I doubt very much that what I say surprises you; after all, we are scientists.

The path we travelled was difficult; the turbulent waters and heavy swells we endured were the roughest seas we have ever seen, however, we know what is needed in order to break through the storm clouds, and when we finally get there it will be magnificent!

O4: Manipulations and Their Need in Cellular Therapies

G Atkinson[1]

[1]*New Zealand Blood Service*

The New Zealand Blood Service (NZBS) is responsible for processing and manipulating all stem cell collections (regardless of source), throughout New Zealand. Working with Te Whatu Ora physicians to fit patients need and disease state through their treatment. The Manipulations come in several forms from the most common plasma reduction and cryopreservation to cell selection for enrichment or depletion.

This presentation will explain these methods, the equipment and resources required for them to be undertaken and their role in patient care. We will also discuss what the future holds for the Cellular Therapy space in regards methods, facilities and the new HealthNZ space.

O5: An update on consultation

B Besley[1]

[1]*Medical Sciences Council New Zealand*

The Medical Sciences Council of New Zealand (the Council) is one of eighteen New Zealand health responsible authorities appointed by the Minister of Health under the Health Practitioners Competence Assurance Act 2003 (the Act). The Council is responsible for the administration of the Act regarding two separate health professions - the profession of medical laboratory science and the profession of anaesthetic technology.

The primary responsibility of the Council is to protect the health and safety of the public. The Council ensures this by implementing mechanisms that ensures medical laboratory science practitioners and anaesthetic technicians are competent and fit to practise (e.g., registration, annual practising certificates, setting the scopes of practice for the professions).

This presentation will cover an overview of the regulation of medical laboratory science practise in New Zealand, the purpose of the Health Practitioners Competence Assurance Act 2003 (the Act) and the Council's legislated functions under the Act. The presentation will also cover registration and professional standards requirements for practitioners as well as the Council's business priorities and workplan.

O6: Using big data to improve antibiotic prescribing in relation to microbiology lab results

M Bloomfield[1]

[1]*Wellington Southern Community Laboratories*

Wellington Southern Community Laboratories performs infection diagnostics for the entire Capital, Coast and Hutt Valley health districts, including all public and private, community and hospital testing. By combining laboratory data with routinely collected community prescribing data, we have created a dataset that provides real-time information that can be used to assess antibiotic prescribing responses to microbiology tests on a large scale. We have used this to identify a number of areas where prescribing may be suboptimal and microbiology tests may be unwittingly driving unnecessary antibiotic usage. This talk will discuss

some of our findings and interventions using this dataset, in relation to throat swab culture, wound swab culture and sputum culture, where we have been able to improve prescribing in relation to these tests by utilising changes in reporting or laboratory comments.

O7: Fresh blood: tales from the neonatal unit

P Bradbeer[1]

[1]*Starship Children's Hospital*

A series of interesting cases in neonates.

O8: The Future of Spectral Flow Cytometry in the clinical setting - Translation to the Clinic for the Monitoring of Infectious Diseases

A Brooks[1]

[1]*University of Auckland*

The COVID-19 pandemic has had a profound impact on the world, both in terms of public health and in terms of our understanding of the immune system. One of the most important lessons that we have learned from the pandemic is that the immune response can be highly complex and unpredictable. In some cases, the immune system responds in a way that is either inadequate or even harmful. This can lead to a variety of long-term health problems, including long COVID and myocarditis.

Translational research in this area is needed to develop new treatments that can target the underlying causes of immune dysfunction and to develop diagnostic tools for effective immune monitoring. Specifically, there is a critical need to improve our understanding of the underlying mechanisms and immune dysfunction associated with long COVID and other post-viral conditions. However, no currently available diagnostic tests are sufficient to detect the underlying pathology.

Spectral cytometry is a critical tool that can be used to dissect immune function. This technology allows researchers to measure the expression of multiple immune markers on individual cells, providing a more comprehensive view of the immune response. Spectral cytometry has been used to study the immune response to COVID-19 infection, and it has the potential to be used to develop new diagnostic tools for long COVID and other post-viral conditions associated with immune dysfunction. The rapid implementation of diagnostic tools to assist in infection management has been critical throughout the pandemic. However, a focus on post-acute illness management has been lacking. Spectral cytometry has the potential to fill this gap and help us to better understand and treat long COVID and other post-viral conditions.

O9: I really do care - Our national High sensitivity Troponin I study

V Buchan[1]

[1]*Te Whatu Ora Canterbury*

For many years, the Point of Care Testing community has been anticipating the release of a high sensitivity troponin assay for use at the point of care. Dr Martin Than (Te Whatu Ora Waitaha ED SMO), through his renowned work in the cardiac chest pain pathway space has made this a reality, securing a grant to investigate the opportunities the release of the first such assay may bring. When initially approached regarding the project, Vanessa did not have the time available to dedicate, however the interest was too strong and this presentation will attempt to showcase the journey of the iCare faster project, where the clinical and pathology worlds have collided and what we've learnt along the way.

O10: NGS - Advances in Diagnostic Haematology

I Caldwell[1]

[1]*Auckland City Hospital*

Genomic characterisation of haematological neoplasms has become increasingly important for accurate diagnosis, prognostication and therapeutic decision making. While morphological assessment still plays a crucial role, many diseases are now genetically defined. Current disease classifications in both the WHO 5th edition and ICC are dependent on the use of high throughput sequencing (HTS) to detect somatic mutations. Additionally, a number of germline mutations that are associated with a predisposition to haematological malignancy are now recognised and can be detected through the use of HTS.

This talk will demonstrate the clinical utility of using next generation sequencing targeted gene panels in the diagnosis of haematological malignancy by presenting a range of cases to show how integration of molecular data is required for contemporary disease classifications.

O11: Iatrogenic Anaemia - A Case study

R Cameron[1]

[1]*Pathlab Rotorua*

Introduction

Iatrogenic anaemia (IA) is generally thought of as anaemia caused by excessive collection of blood samples from a patient undergoing care in a hospital facility. There are also other causes that are not so frequently discussed in a laboratory sense. A recent case of Haemolytic Disease of the Foetus and Newborn (HDFN) in our small laboratory and the follow up care showed IA as an unexpected result of treatment.

Case Details

Rh D HDFN is a rarity in our hospital with most being dealt with in larger specialised facilities. The textbooks give a very good description of the aetiology of Rhesus HDFN and most cases follow a fairly similar and expected progression. Occasionally, we see one that doesn't fit our expected model.

A pregnant mother with a history of immune anti-D presented for an Antenatal screen for her 5th child. Pre-natal care began. After multiple intra-uterine transfusions (IUT), her baby was born prematurely at approximately 32 weeks. Mum and baby were transferred to our hospital after 4 weeks for ongoing care. Neonatal transfusions require specialised products that are sourced from regional hubs. This presentation will discuss this case including some of the issues we faced as a smaller blood bank providing transfusion support and a case that didn't seem to follow the plan.

- Previous history
- Intra-uterine Transfusions (Briefly)
- New-born care and transfusions
- Haematology perspective
- Results and Outcomes
- Effects of IUTs on erythropoiesis

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O12: What happens to donated blood?

R Charlewood[1]

[1]*New Zealand Blood Service Auckland*

New Zealand Blood Service collects nearly a quarter of a million donations a year. But to what end? We know that blood donations save lives – but how? Historically, blood was collected and transfused simply as whole blood. Indeed, in some parts of the world, this is still the case. But an anaemic patient doesn't need plasma, and a patient with immunodeficiency doesn't need red cells. So modern blood services separate and process blood donations into a variety of products that can be used to treat a wide range of conditions.

Within New Zealand Blood Services, blood is separated into red cells, plasma, cryoprecipitate and platelets. Some specialised products are also produced such as IgA-deficient plasma, rare blood groups red cells, cryopreserved platelets.

Almost half our donations are purely plasma, collected on specialised machines that return the red cells and platelets to the donor. Most of this plasma is sent to the Melbourne plant of one of the world's big plasma fractionators, CSL Behring. There, plasma is separated into some of its key proteins, purified and bottled, making yet another range of products for patients.

O13: Cryopreserved platelets - a novel approach for major haemorrhage as well as highly refractory patients in New Zealand

R Charlewood[1]

[1]*New Zealand Blood Service Auckland*

Platelets can be cryopreserved using 5% dimethylsulphoxide (DMSO), the same cryoprotectant used in stem cell cryopreservation. To minimise DMSO toxicity, the initial platelet component with added DMSO is centrifuged and the supernatant removed, leaving a platelet plug and 15-20 mL plasma with 5% DMSO. The platelets are frozen in one compartment with fresh frozen plasma in another, allowing for rapid thawing and issuing. Although studies of the platelets have shown signs of activitation of some of the platelets, functionally the platelets behave as they should though are cleared faster than liquid platelets.

Building on the experience of the military's use of frozen platelets in conflict zones, NZBS and Auckland Hospital took part in a trans-Tasman pilot trial, CLIP, evaluating cryopreserved platelets in elective cardiac surgery patients. This trial showed that there were no differences in median blood loss up to 48-h between study groups, or in quantities of study platelets or other blood components transfused. There were no differences in multivariable adjustment for imbalances in baseline patient characteristics did not find study group to be a predictor of 24-h blood loss, red cell transfusion or a composite bleeding outcome. The median platelet concentration on the day after surgery was lower in the cryopreserved platelet group but this was expected as cryopreserved platelets are partially activated. The follow-on full trial, CLIP-II, is also underway with results expected at the end of the year.

NZBS has also cryopreserved platelets for highly refractory patients with multiple HLA antibodies and these have been transfused to symptomatic patients with good outcomes.

With this data, cryopreserved platelets are now being piloted in a small blood bank for use in major haemorrhage. If this proves successful, we anticipate wider rollout of cryopreserved platelets across the smaller blood banks across the country.

O14: Triaging Muscle Biopsies

A Charlton[1], S Prasad[1], D Tottle[1]

[1]*Te Toka Tumai LabPlus, Auckland City Hospital, Auckland, New Zealand*

Introduction

Fresh muscle biopsy in the anatomical pathology laboratory is an uncommon specimen requiring specialised triage in the cut-up room. Fresh muscle needs to be triage within 2 hours for optimal enzyme histochemistry. Most artefacts are due to delays in transportation before triage, suboptimal freezing and poor orientation.

In NZ, for laboratories more than 2hrs transport away from the muscle reference laboratory, it is necessary to triage and freeze the muscle on site. Then you can send the frozen muscle overnight on dry ice to the reference laboratory.

Method

At LabPLUS Auckland Hospital, we traditionally froze loose muscle biopsies in hexane cooled with dry ice (-78°C). Recently, to reduce freezing artefact and improve orientation, we moved to mount orientated muscle on a cork disc and freeze using hexane cooled with liquid nitrogen (-176°C).

Demonstration and discussion

Histopathology staff encountering fresh muscle biopsy require training in muscle biopsy triage. In this session, we will perform a live demonstration of muscle biopsy triage, including equipment, materials, dissection, and freezing. We will discuss tips and pitfalls.

Resources

Liquid nitrogen method video: https://youtu.be/7rgFJB_EiLw

Dry ice method video: https://youtu.be/Ysl4Mo6Pv3s

Dry ice method poster: https://tinyurl.com/ycy8yjp3

O15: Bleeding Disorders of Unknown Cause

L Chen[1]

[1]*Middlemore Hospital*

Bleeding discorders of unknown cause – this presentation goes over the approach to patients who have a history of bleeding with no reproducible abnormalities on standard blood tests; the investigations that are required and treatment recommendations.

O16: Acronyms relevant to medical emergencies - a brief review

W Chiu[1]

[1]*Middlemore Hospital*

This talk gives an overview of some of the commonly used acronyms for medical emergencies and related conditions. The objective is to aid laboratories involved with specimen registration to gain a better understanding of the terms used by medical staff, fostering a timely response at the laboratory level. Intraosseous samples obtained under desperate situations for biochemistry testing will be discussed in more detail.

O17: Embracing R in the clinical laboratory: building a 'Shiny App' for Metabolic Screening Results Interpretation

J Chu[1]

[1]*Canterbury Health Laboratories*

Data Science has been growing exponentially across the medical industry in Aotearoa New Zealand. As a result, there has been considerable discussion on clinical laboratories relying less on propietary spreadsheet software such as Excel in favour of statistically powerful and open-source software, such as Posit using the programming language R. By all accounts, this will give rise to more reliable and reproducible analysis, leading to better patient outcomes.

At Canterbury Health Laboratories, screening for Inborn Errors of Metabolism (IEMs) is performed predominantly through tandem mass spectrometry. The spectrometry software outputs the data in the form of hundreds of cells for analysis in an Excel template. The large amount of data is hard to interpret and relies on software that can sometimes be unreliable or present barriers to use for laboratory staff. Furthermore, the number of steps involved and opportunity for error in analysis and interpretation is considerable.

In the present proof of concept, we aimed to develop a 'Shiny' application as an eventual replacement for the current tool used currently in Excel. The application demonstrates how R can be utilised in the laboratory for tasks requiring complex statistical analyses and visualisations. We will discuss how this adds extra levels of safety for patients, and reproducibility for scientists. Lastly, we will present opportunities and challenges in establishing a pipeline to facilitate the development of such applications in Aotearoa.

O18: EUCAST Rapid antimicrobial sensitivity testing use, validation, and evaluation

S Clements[1]

[1]*Pathlab*

In December of 2019, The European union Committee on antimicrobial susceptibility testing (EUCAST) released a method for Rapid antimicrobial sensitivity testing (RAST) directly from blood culture bottles within 4-8 hours. The method includes 7 species of bacteria commonly isolated from blood cultuires, and a wide range of commonly used first and second line antibiotics. A method for detection of Methicillin resistance in *Staphylococcus aureus*, and presumptive detection of Extended spectrum beta-lactamase (ESBL) in *Escerichia coli* and *Klebsiella pneumoniae*, and Carbapenemase in *E. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumanii* is also included. RAST was validated in our laboratory for the purpose of resistance mechanism detection. High sensitivity and specificity across all tested species was observed for this purpose. RAST was then implemented in the laboratory and found to have a positive impact on patient management and antibiotic use, with faster isolation and antibiotic switching in MRSA and ESBL positive patients. The advantages, limitations, and improvements that could be made to RAST will be discussed.

O19: Scientific and Technical Professional Leader Role

P Coles[1]

[1]*Te Toka Tumai LabPlus*

Within the Medical and Allied Health workforces, the Professional Leader role has been well established. This has not been the case for the Scientific and Technical workforce. The introduction of this new role at Te Toka Tumai, Auckland has sought to rectify this missing representation and aims to enhance professional advocacy, promote professional excellence and equity. The presentation will explore the establishment of the role, scope, and future opportunities of the Scientific and Technical Professional Leader role. It will cover various aspects of this role, including details on the primary purpose and responsibilities, contribution to strengthening professional accountability for quality assurance, compliance, competence, professional governance and local oversight of professional standards. In addition, the challenges faced by the scientific and technical professional leader as well as the benefits and opportunities associated with this role, will be discussed. Attendees will gain a deeper understanding of the importance of the role and its influence in shaping

the future workforce and the profession as a whole.

O20: The rise and fall of ICSI. What's next?

DD avydova[1]

[1]*Fertility Associates Ltd*

Intracytoplasmic sperm injection (ICSI) has been used in assisted reproduction for several decades. Originally developed to treat severe male infertility, its use became extended. As for many other techniques, it had its ups and downs, from ''use ICSI for all cases'' to ''ICSI causes autism in kids''. So where are we with it now and is this technology still developing and how?

A Retrospective analysis of ICSI indications and results from 5 New Zealand IVF clinics (Fertility Associates) over the last 30 years will be presented. This will include not only main laboratory KPIs but also live birth data. Review of modern ICSI techniques currently used and being tested worldwide will also be presented, as well as preliminary data from Fertility Associates' recent trial of piezo-ICSI technique.

ICSI illustrates how new technologies in assisted reproduction are adopted and how experience over time is required to assess and refine these technologies.

O21: The Clinical Scientist Role

M de Hora[1]

[1]*Te Toka Tumai LabPlus*

A clinical scientist is a medical and healthcare professional who supports other clinical staff in their work with patients. Their work is very broad and can include laboratory and testing work, research, and management. There are many different areas of clinical science, including biochemistry, immunology, microbiology, genomic, informatics, inherited metabolic disease, haematology, and toxicology. Clinical scientists are expected to support laboratory service development, specialist service delivery and troubleshooting. This will include the provision of analytical, interpretive, and advisory services within laboratory departments which enables the delivery of strategic objectives with directorates within the hospital environment.

On a day-to-day basis, Clinical Scientist use specialised scientific knowledge to advise clinicians on the requirements for diagnostic testing on patients. They should ensure a safe and effective service, undertake appropriate relevant research work to solve diagnostic or therapeutic problems within their field. They have an ongoing responsibility to provide strategic direction, as well as the teaching and training of scientists, technicians, and registrars.

The clinical scientist roles, including the consultant scientist role was introduced in LabPlus in 2021. In this presentation the experience of working as a clinical scientist is discussed as well as the experiences of transitioning from a medical scientist role, including training requirements and the support needed to ensure the role is successfully implemented in departments.

O22: The power of lab data

G Devenie[1]

[1]*Te Toka Tumai LabPlus*

Laboratories collect a vast amount of data. Historically the way we displayed this data was via complex searches into Excel spreadsheets to produce static graphs and tables. Business Intelligence platforms, e.g. Power BI, Clik, Tableau, can interrogate data dynamically and display charts and tables on the fly.

This presentation will be about two dashboards that were created for LabPlus. Diagnostic Genetics needed, an open requests/overdue dashboard. Lab Management, wanted a workload monitor for registration, test and billables.

O23: "The itch you can't scratch" - Allergy Testing of LabPlus

N Devi[1]

[1]*Te Toka Tumai LabPlus*

Allergy is considered to be an important public health problem in developed countries. Allergic reactions (hypersensitivity reactions) are inappropriate responses of the immune system to a normally harmless substance. This response is triggered by an antigen which has penetrated body surfaces e.g. skin, respiratory or gastrointestinal tract. Some of the symptoms include watery eyes, runny nose, skin rash, and hives. In extreme cases it can lead to acute anaphylaxis, which is potentially fatal. There different types of allergic reactions are immediate anaphylactic, cytotoxic, immune complex and cell mediated reactions. A detailed clinical history and physical examination is carried out by allergy specialist to establish and confirm diagnosis. The various types of allergens may include:

- Aeroallergens–grasspollen,treepollen,fungi,animals, storage mites, dust mites, cockroaches, latex
- Food- fruits, vegetables, fish, shellfish, meat, diary,

grains, treenuts, legumes, egg, sesame, mustard, coconut, yeast and other fresh items

- Drug – penicillin, local anaesthetic, general anaesthetic and steroid drugs
- Insect stings – honeybee, Vespula, Polistes

Skin prick, intradermal and blood test (specific IgE) are the commonly used testing method for the diagnosis for allergy. It is a safe and easy way to investigate. The skin prick test involves the introduction of a small amount of a standardised allergen extract into the upper layer of the skin, usually on the lower forearm. A lancet is used to penerate through it, without causing any bleeding. The resulting release of mediators causes characteristic indurations of the skin (called "wheal") and erythematic/ redness of the skin (called "flare"). The size of the wheal is compared to the reaction obtained with a positive and negative control. This test cannot be used in the presence of any widespread skin disease or if the patient is on antihistamine medication. Although the risk of an adverse reaction is minimal, adrenaline should always be available during these tests. Patients with a history of drug allergy anaphylaxis should be tested by an intradermal skin test using defined concentrations of the putative drug solution prior to surgery. Positive skin prick test to an allergen showing large reactive wheals indicate allergy and these allergens should be avoided. It is best for patients to avoid the allergens they have had reactions to until they see the Clinical Specialist so these allergies are correctly diagnosed.

O24: Patient Blood Management - More than just Gatekeeping

R Donegan[1], G Manpreet[1]

[1]*CNS Middlemore Hospital*

The concept behind Patient Blood Management (PBM) involves the implementation of effective medical and surgical methods and techniques to prevent peri-interventional anaemia, the rationalisation of blood products and the setting of good blood management measures to optimise patient safety and outcome.

Counties Manukau Health have found it is far more complicated than that. The system implemented at CMH actively targets pre surgical anaemias through direct referral whilst running an inpatient service that offers support and guidance to medical staff.

We will present case studies, patient experiences, outcomes, successes and future opportunities. Like many found, Covid presented challenges for healthcare delivery in Aotearoa. With theatre lists being delayed we had to look at how to best support our patients through this period. The delays presented us with an opportunity in which we could support patients that were confronted with inoperable diagnosis. The aim was to work with patients and their whanau to ensure a goal of quality of life and prevent unnecessary hospital admissions which comes at a cost to health care and a disruption in the daily lives of our people.

PBM requires a multidisciplinary and multi technique approach to limit potentially inappropriate use blood products. It's about alternatives, optimization intervention and education. What we give our patients, when we give it to them and what can be done differently. We will present our experiences achievements and importantly the outcomes for the patients of South Auckland.

Many of the achievements would not happen without the many teams we work with. The laboratory service is one part of the process so thank you, and we hope you will enjoy this presentation.

O25: Patient Blood Management in New Zealand: from the rear mirror to the road ahead

G Duarte[1]

[1]*New Zealand Blood Service*

Patient Blood Management implementation has been recognized as an urgent matter by the World Health Organization. PBM has been demonstrated to improve patient outcomes, whilst making evidenced-based use of resources. The current lecture is going to provide an overview of what was achieved so far, and as the New Zealand PBM working group commences its work, what lies in the road ahead.

O26: Emicizumab for Haemophilia A treatment

N Eaddy[1]

[1]*Auckland City Hospital*

Haemophilia A is a rare inherited bleeding disorder in which the blood does not clot properly due to a lack of the clotting factor VIII. This can lead to spontaneous bleeding as well as bleeding following injuries or surgery. The mainstay of treatment has been replacement of the missing factor requiring lifelong regular infusions. Emicizumab (tradename Hemlibra), a humanised bispecific monoclonal antibody has been a breakthrough in the treatment of this disorder. This talk will discuss the

antibody – its mechanism, use and laboratory features.

O27: Sailing into the future with antimicrobial resistance in Aotearoa: where have we come from and where are we headed?

J Elvy[1]

[1]*Awanui Labs*

Antimicrobial resistance (AMR) is a growing concern within Aotearoa New Zealand and globally. This talk will address past, present and future AMR threats with a particular emphasis on emerging AMR mechanisms of interest yet to hit our shores.

O28: HART register

S Faamoe[1], AC Wyseur[1]

[1]*Department of Internal Affairs*

The Department of Internal Affairs (DIA) is responsible for establishing and maintaining the Human Assisted Reproductive Technology (HART) Register under the Human Assisted Reproductive Technology Act 2004. The HART register holds information about donors, donor-conceived persons and parents/guardians who have been involved in fertility treatment that involves the use of donated material through fertility service providers.

The HART register is a restricted register so has strict rules around who can access information. However, it does allow access for donor-conceived persons to find out information about their genetic origins and donor information which could lead to also locating their siblings. It also allows donor access to certain information. Only donor-conceived persons, or donors, using approved fertility service providers can be recorded on the HART register.

O29: Type 1C vWD

G Faulhaber[1,2]

[1]*Waikato Hospital*

[2]*Pathlab*

Von Willebrand Disease (vWD) is the most common inherited bleeding disorder. It has an autosomal inheritance pattern, with an estimated prevalence between 0.6 to 1.3% of the population. Current classification divides the disease into three main groups:

- Type 1 – a quantitative deficiency; Type 2 – a qualitative defect; Type 3 – Absence of factor.
- Type 1 vWD is the most common variant, with about 70-80% of cases.In the last 20 years, many advances in the understanding of physiopathology were made.
- Type 1 vWD is composed of a highly heterogenous group of mechanisms leading to the reduction factor levels and bleeding phenotype.

About 30% of patients do not have any detectable mutation in the vWF gene, making it clear that very complex network interactions are required to lead to a reduction of vWF levels. Some described mechanisms include reduced synthesis of normal vWF, intracellular retention of vWF and enhanced clearance of VWF.

Recently, the variant with enhanced clearance has been nominated type 1C, given some peculiar findings.The presentation will review the last data about this subgroup.

O30: Microbiology and antimicrobial resistance control: an overview of work facilitated by the Pacific Region of Infectious Disease Association

J Ferguson[1]

[1]*Pacific Regional Infectious Disease Association*

The Pacific Region Infectious Diseases Society (http://pridanetwork.org) utilises a multi-faceted approach to achieve best management and control of infectious diseases including:

- Development of long-term relationships with infectious disease professionals in the Pacific and South East Asian region
- Practical development of diagnostic microbiology and laboratory quality management
- Post-graduate professional development courses in diagnostic microbiology for scientists and doctors
- On-the-ground training – one on one mentoring, teaching ward and laboratory rounds, workshops, seminars and practical sessions
- Guideline, operating procedures and policy development related to microbiology, including antimicrobial susceptibility testing, infection prevention and control and infectious diseases
- Resource optimisation – knowledge of correct diagnosis and appropriate management allows scarce resources to be used optimally
- Development of online pan-Pacific forums

This presentation will provide an overview of recent developments, focusing particularly on PRIDA programs that relate to diagnostic microbiology and laboratory quality management.

O31: Return to Family - Tissue

J Ferguson[1]

[1]*Te Toka Tumai LabPlus*

Coronial specimen management is an obscure area, in that not many medical laboratory technicians (with a scope of mortuary practice) and scientists in New Zealand have the opportunity to develop their expertise in this particular workspace.

Our contract is with the Ministry of Justice, rather than the Ministry of Health, and we rely on both the laboratory team for our test results, and radiologists to provide final radiology reports from CT scans, skeletal surveys and so forth. We interact as well with consultant pathologists (e.g. neuropathologists) who provide the expertise to assist in reporting for complex brain injury cases. Homicide and suspicious cases are performed with the utmost of attention to detail, in both procedure and record keeping, so they will hold up in court when a forensic pathologists case goes to trial. We have 2 main workspaces termed 'clean' and 'dirty' – an administration area, along with operating theatres plus a deceased holding room and CT scanning room (rather than a laboratory testing workspace).

As coronial cases are part of the judicial system (coroners in New Zealand are lawyers rather than pathologists), the management of specimens is in some ways similar and other ways dissimilar to those employed in the main laboratory. Specimens taken at post-mortem are retained in storage until a coronial case is closed by the coroner and the final findings issued. Only at this point (for a proportion of cases - several years down the track) is authorisation given to either return samples to family or dispose of them to collective cremation. This makes accurate and consistent record keeping of paramount importance, as another staff member, often years later, is reviewing records held to determine the types and quantities of specimens that have been retained in storage that must be located (freezers, cut-up room, post-mortem blood cards in case files, material held in Anatomical Pathology, Diagnostic Genetics or off-site).

This presentation will give a broad overview of the coronial process from start to finish, including pointers for effective specimen management and information on how our service performs annual residual specimen auditing.

O32: What's Fuelling You?

D Gallagher[1]

[1]*Te Whatu Ora Waitematā*

Focusing on the Quality systems used within the Petrochemical industry, this presentation discusses:

- the New Zealand Fuel industry
- the standards and Quality systems used in the petrochemical laboratory
- what the medical field can learn from these systems
- 91 octane fuel quality in the Auckland market

Denese is a fuel quality expert, having worked 13 years in New Zealand's leading petrochemical laboratory. Within the petrochemical laboratory, Denese spent time as a bench technician, a Key Technical Person, a trainer, a report authoriser, a method developer, a method expert, and a quality expert.

Drawing upon her expertise in the petrochemical field, Denese has created this presentation as a learning tool for what a good quality system looks like, and what medical laboratories should aim for in terms of quality systems.

O33: How Forensic Anthropology can assist Forensic Pathology

K Galvin[1]

[1]*Te Toka Tumai LabPlus*

This presentation will briefly explain what forensic anthropology is and how it can contribute to the forensic mortuary environment. It will also demonstrate how and why forensic significance is important to this discipline and what forensic anthropology can do to identify and interpret forensic significance. Examples and a case study will highlight how this field can be utilized and why we should use forensic anthropology to provide insight into relevant mortuary casework. Finally, we will ask the question of how this niche field can be further employed to provide answers in the forensic context.

O34: Organ Donation

S Garland[1]

[1]*Organ Donation New Zealand*

Organ Donation New Zealand (ODNZ) is the national service for deceased organ and tissue donation. Its primary responsibility is to coordinate organ and tissue donation from deceased donors in New Zealand.

ODNZ work with health professionals throughout New Zealand to ensure there are nationally consistent processes for donation and all families of potential donors are offered the option of organ and tissue donation. The service also provides education and training for health professionals as well as supplying information to the media and the public.

Today Sue will share information and stories about organ and tissue donation and the integral part that all the different health care professional teams play to ensure a donation proceeds for the purpose of life saving and life changing transplantation.

O35: Two Minutes to Midnight

A Gee[1]

[1]*Pathlab Waikato*

Clinical presentation

Mr S is a 59 year old male presenting with diarrhoea and fatigue, while Mr D is a 35 year old male who presents with fevers, chills and body aches. Both patients have a history of recent overseas travel.

Discussion

Diseases endemic to the countries visited by both patients ought to have been considered, however in both cases the initial clinicians only requested a complete blood count (CBC) and general chemistry. The cause of both patients' symptoms were discovered on their blood films in what could have been described as an incidental finding. This demonstrates the important role that the medical laboratory plays in diagnosing patients.

O36: Abnormal phagocyte function in X-linked Chronic Granulomatous Disease

J Gojer[1]

[1]Te Toka Tumai LabPlus

X-linked Chronic Granulomatous Disease (XL-CGD) is a rare inherited immunodeficiency characterised by the inability of phagocytes to kill certain pathogens. Patients with XL-CGD suffer from chronic inflammation and are vulnerable to frequent bacterial and fungal infections. XL-CGD mainly affects males due to genetic defect of cytochrome b-245 beta chain (CYBB) gene located on the X-chromosome. Females are carriers if they have a defective CYBB gene on one of the X chromosomes and could pass the defective X chromosome to male descendants. Affected XL-CGD males and carrier females can be diagnosed with two main laboratory methods namely dihydrorhodamine (DHR) test and genetic testing. DHR tests the ability of the neutrophils (a type of phagocyte) to produce activated oxygen compounds essential for killing pathogens. Genetic testing is performed to ascertain the exact genetic defect. Two XL-CGD cases will be presented in this talk.

O37: CSF Oligoclonal Bands Test: Is it MS or Not?

K Govender[1]

[1]*Te Toka Tumai LabPlus*

Multiple Sclerosis (MS) is one of the most common diseases of the Central Nervous System. It is an immune mediated disease. There are approximately 4000 people in New Zealand with MS. MS usually affects people between the ages of 20 to 40 years of age. Cerebrospinal Fluid (CSF) Oligoclonal Bands Test is one of the biomarkers used to assist in the diagnosis of MS. A description of the CSF Oligoclonal Bands Test at LabPlus along with some interesting case studies will be presented.

O38: Diagnostic Transmission Electron Microscopy: The Evolution of Resolution

C Gray[1]

[1]*Te Toka Tumai LabPlus*

Introduction

Transmission Electron Microscopy (TEM) is a specialised, but essential diagnostic modality that aids diagnosis through ultrastructural examination of laboratory prepared tissue. It is predominantly used in native renal biopsy diagnostics but can be used for the ultrastructural examination of a diverse range of tissue specimens.

Outline

I will present an illustrated overview of how specimens are prepared to be viewed in the TEM. I will emphasise the importance of glutaraldehyde fixation and contrast this with artefact created when the wrong fixative is used. I'll follow this with a gallery of images, including some artefacts we encounter in the EM lab.

O39: McLeod Syndrome & Paroxysmal Cold Haemoglobinuria

R Haack[1]

[1]*NSW Health Pathology*

Case 1 – McLeod Syndrome (MLS)

Clinical Presentation

Patient was referred for Coomb's negative haemolysis and splenomegaly. Laboratory studies showed CK 2250 U/L, Hb 176 g/L, haptoglobin < 0.08 g/L, reticulocytes 157x10^9/L and LDH 521 U/L. Blood film showed marked acanthocytosis. Neurological symptoms included facial tic, learning difficulties, depression and anxiety. Red cell phenotyping showed reduced expression of Kell antigens (K-,k,Kp(a-b-),Kx-). Serology for Kx expression confirmed absence of Kx antigen. Genetic testing confirmed deletion in XK gene including the 5' UTR and part of exon one, supporting the observed Kell system serology and is consistent with probable KX:-1 (McLeod) Phenotype. His asymptomatic siblings with normal blood films and elevated CK, had the same phenotype consistent with the McLeod Phenothype.

Discussion

MLS is an X-linked disorder, characterised by acanthocytosis and neuro-cardiac manifestations. MLS is caused by deletions in the XK gene that is responsible for producing the XK protein that attaches the Kell protein. The absence of Kx antigen is known as the "McLeod phenotype". Creatinine kinase is elevated in all patients with MLS and an effective screening test in subjects with Coomb's negative haemolysis and acanthocytosis.

Case 2 – Paroxysmal Cold Haemoglobinuria (PCH)

Case Presentation

A three-year-old presented with "port stained" urine post respiratory tract infection. Blood film analysis identified florid peripheral granulocytic erythrophagocytosis. DAT was strongly positive for C3d and cold agglutinin screen was negative. Donath-Landsteiner testing was done by a referral lab and was negative.

Discussion

PCH is a rare haemolytic anaemia where biphasic haemolysis is triggered by the Donath-Landsteiner antibody affecting mostly young children who present with symptoms of brisk intravascular haemolysis including haematuria. Positive confirmation is by the detection of bi-phasic haemolysis however low sensitivity occurs due to consumption of the antibody and complement during haemolysis. Florid erythrophagocytosis can be used to positively confirm PCH.

O40: Clozapine - the drug and its monitoring

J Harrington-Knapton[1]

[1]*Te Whatu Ora Counties Manukau*

Treatment resistant schizophrenia is often associated with severe burden of disease, poor quality of life, and functional impairment. It is defined by the persistence of symptoms despite two or more trials of antipsychotic medications and occurs in approximately 30% of people diagnosed with schizophrenia. Clozapine is a second generation antipsychotic indicated for use in people with treatment resistant schizophrenia. Its unique, and sometimes life threatening, side effect profile gives rise to numerous considerations in prescribing, monitoring, and side effect management. This presentation will discuss the indications, pharmacology, side effects, and monitoring of clozapine, along with patient experience, and treatment outcomes.

O41: Low Risk Chest Pain Pathway. Initial data from a primary care POC troponin initiative

S Hartnell[1]

[1]*Te Whatu Ora Waitematā*

Primary Care Urgent Clinic POCT Troponin I: Evaluation of results from across the 4 Auckland districts. Does it really save our health dollars and improve patient care and support our hospitals?

O42: The importance of Newborn Screening - a collection of case studies

N Heather[1]

[1]*Te Toka Tumai LabPlus*

Newborn bloodspot screening is available and publicly funded throughout New Zealand and Australia. Bloodspot cards are used to test for over 20 serious inherited conditions. Each year, around 50 babies in New Zealand and 300 babies in Australia with serious inherited conditions are picked up and diagnosed early through their newborn screen. This talk will illustrate the impact of early identification through newborn screening on babies and their families.

O43: Ethics and Medical Laboratory Science in New Zealand

R Hewett[1]

[1]*Te Toka Tumai LabPlus*

The NZIMLS has a code of ethics as does the Medical Sciences Council of NZ, both related to our roles as Medical Laboratory Technicians and Scientists and the practice of our profession. So which once has precedence or relevance and do we really understand what is meant by ethics and which ethical theories, if any, are applicable to our practice? Do they actually alter our behaviour or reinforce our already existing moral conduct?

This presentation will discuss the ethics of healthcare and those theories most relevant to Medical Laboratory Science as well as highlighting the most appropriate legislation designed to ensure patient safety, privacy and autonomy in New Zealand.

O44: Moving from glass to pixels: Digital Pathology and the impacts on the Lab

C Hills[1]

[1]*Te Whatu Ora Waitematā*

Digital pathology is transformative technology, changing the way anatomical pathology can be delivered across the world. From scanning the humble glass slide, the digital format opens up the specialty to computational analysis and AI based tools, leading to efficiency gains and new ways of reporting. There has been gradual adoption of digital pathology across the last few years and it is set to become routine practice by the end of the decade. So how will this new technology effect the day-to-day running of the AP lab, including grossing, processing, quality control and workflow? This talk will go through the basics of digital pathology implementation and what to expect when the scanners arrive in your department.

O45: Application of College of American Pathologists Checklists to Laboratory Procedure Manuals

M Hitchcock[1], M Narsa[1]

[1]Anatomic Pathology Services Auckland

Objective: To demonstrate and discuss the practicalities of using College of American Pathologists (CAP) laboratory checklists in preparation of New Zealand (NZ) laboratory procedure manuals.

Methods: The authors will discuss the availability of the thoroughly researched checklists prepared by CAP for their thousands of member labs, and their practical attributes. Based off the same ISO regulations we work to, they could enable consistency in organization of lab procedures across the multiple sites Te Whatu Ora / Health NZ operates throughout the country. The consistency may be at an overall structure level, or incorporate very granular approaches to documenting laboratory procedures.

Conclusion: NZ labs each prepare their own policies and procedures. In this era of mass merger of all former district health boards under one ownership structure, it may be productive to develop consistency in our laboratory manuals. This overseas developed model produced by pathologists and medical laboratory scientists is available as a potential reference.

O46: Quality Update ISO15189:2022

B Holiss[1]

[1]*International Accreditation New Zealand*

Most medical laboratory staff will by now be aware that an updated version of ISO15189 has recently been released and many will possibly know that the new standard places a greater emphasis on minimising risks to patients. However, laboratory staff are probably not yet sure how the revision of ISO15189 will affect the daily operation of the laboratory at the bench level. While the majority of the changes may not be noticed immediately by many, the significant change in the philosophy of the new standard will eventually impact on all laboratory staff members.

Since there will not be time to cover all the changes in the new standard I will focus more on some of the issues that have emerged in laboratories that have already applied to transition to ISO15189:2022. The areas I will discuss are: impartiality and confidentiality, lines of communication, responsibility and authorization, risk management, facility controls, equipment calibration, competency and service agreements (including for PoCT).

O47: PoC testing and its pivotal role in the HCV Test and Treatment Programme

T Hollings[1]

[1]Southern Community Laboratories

In New Zealand there are an estimated 50,000 people living with Hepatitis C, many of whom are undiagnosed and unaware of the risks of the virus. The World Health Organisation (WHO) aims to eliminate hepatitis as

a major public health threat by 2030. Awanui labs in collaboration with the MoH and the Southern Hepatitis C steering group, are developing an HCV 'test and treat' programme which utilises Point of Care testing to improve equity of access to testing and treatment of HCV. This presentation covers the journey to date; the challenges, successes and the next steps.

O48: Phinterless Collection - prelabelled specimen tubes for eCollection

L Hopley[1]

[1]*Te Whatu Ora and Digital Services*

Introduction and context

Evolution of eCollection. Paper orders, and patient labels onto specimen vials are status quo in a lot of our laboratory specimens, but we know that's time intensive for everyone and very error prone. We took the plunge into eOrdering with "bedside" printing of the specimen label, affectionately called the "phinter" as it's phone and printer held together on a simple chassis – this has saved a lot of time for the ordering person and pre-analytical staff, as we pre-allocate specimen IDs that print on the label at the bedside but it's still KLUNKY for the ordering person who is also collection – as its two different devices, the collecting person as the "phinter" is still bulky and needs paper and power, still leaves room for error, specifically of the specimen tube type, and the specimen ID makes the specimen unique to that laboratory and thus doing nothing for the movement and decanting of specimens

COVID gave us the next step - because it was a single specimen - we could create the paperless collecting system or "phinterless" solution by pre labelling the vial with a unique number - and using scanning associated that with the right person at the bedside. Eliminating the need for paper or stickers out in the field (literally).

We are now working on the next step of the evolution – the collection tubes who already have a pre-printed colour coded label, with unique IDs, so we can do "phinterless" collecting of all specimens.

Key message

Visibility of the possible eCollection methods, with a view to the future paperless "phinterless".

Collection of laboratory specimens:

- pre-printed order and patient labels with speciment IDs
- print at the "bedside" patient label with specimen ID
- use a unique ID on the speciment tube as the speciment ID AFTER using scanning to associate it with the person at the bedside

Open up the world of paperless/phinterless collection and improve the ability to move large amounts of specimens in a high demand environment.

O49: Climate change: implications for population health in Aotearoa New Zealand

J Hosking[1]

[1]*University of Auckland*

Climate change has been called a leading threat to population health. Conversely, responding well to climate change could be one of our biggest opportunities to improve health. This presentation discusses the underlying common causes of climate change and several major health issues. It also identifies how some of our most important responses to climate change can also have major 'co-benefits' for health. Examples include healthier and more sustainable cities, improvements to diets and food systems, and warmer, healthier homes. We have already made some progress in several important areas. However, there are significant opportunities to further improve our responses in future, with large potential benefits for population health and health equity, as well as for broader social well-being and the health of our environment in Aotearoa New Zealand.

O50: What happens to the Flow Cytometry Samples

K Hughes[1]

[1]*Te Whatu Ora Auckland*

The LabPlus Flow cytometry laboratory at Te Toka Tumai Auckland City Hospital undertakes a wide variety of immunophenotyping, transplantation and immune deficiency laboratory testing.

The quality of the samples received by the flow lab plays an important role in determining the subsequent quality of both the test results and the analysis performed. Thus the important role of pre-analytics will be discussed. The role that sample collection plays is an important one that can affect the accuracy of the results.

An overview and novice's guide to the flow lab's processes and testing methods for immunophenotyping will be covered to provide an understanding of the journey a sample takes after it leaves the pre-analytical section, with a focus on the importance of correct specimen collection,

adherence to transportation requirements and timely reception and processing in the flow laboratory.

O51: Therapeutic Venesections

S Hutton[1]

[1]*New Zealand Blood Service*

Haemochromatosis. (Haemo = blood, Chromat = colour, Osis = disease) - hereditary genetic condition - This condition affects 1 in 200 New Zealanders and is believed to be the most common genetic disorder in the world. People diagnosed with Haemochromatosis, absorb too much iron and become "iron overloaded". This accumulation of iron can be stored in organs such as the liver, pancreas and the heart and over time can cause severe organ damage.

In the early stages of the condition, there are often no symptoms, but as iron accumulates sufferers may experience:

- Tiredness / Lethargy / Fatigue.
- Abdominal discomfort.
- Joint pain.
- Low libido.
- Discolouration (Bronzing) of the skin.

Polycythemia vera. Is a rare blood disorder in which the bone marrow makes too many red blood cells. People diagnosed with Polycythemia produce extra blood cells which increases the likelihood of bleeding, bruising and clotting. Symptoms only develop overtime and can start with:

- Headaches / Dizziness.
- Fatigue.
- High blood pressure.
- Blurred or double vision.
- Tinnitus.

A recognised treatment for both these conditions is THERAPEUTIC VENESECTION.

Venesection - means taking a unit of blood, the red cells and the iron in those cells from a patient. NZBS Therapeutic Venesection Clinics across the country, care for 3 types of patients with these conditions:

1. Patients who do not meet the criteria to be a Whole Blood donor but require venesections, e.g. Patients with vCJD risk.
2. Patients who are able to be a Whole Blood donor but may require venesections more often than every 84 days.
3. Patients who are able to be discharged from our care and become a regular Whole blood donor once their condition is stable.

Since 2020 we have cared for approximately: **2,500 patients**. Please talk to your friends and family about this condition, as early diagnosis can prevent long term complications. If this presentation raises any health concerns regarding Haemochromatosis or Polycythemia vera, please seek medical advice.

O52: Lyme disease serology at LabPLUS: The transition from indirect immunofluorescence screening assay to use of the Euroimmun IgG and IgM line immunoassays

Y Hwang[1]

[1]*Te Toka Tumai LabPlus*

Historically, LabPLUS has been testing Lyme disease serology using an indirect immunofluorescence screening assay (IFA), which interpretation of reactive result was often difficult due to interference by presence of ANA or Treponemal-specific antibody. Recommended best practice is for screen reactive sera to be referred to overseas laboratories for confirmatory testing by Western Blot (WB) however due to added costs, requestor's demand to have sera referred for WB testing has been very low. The Euroimmun Lyme disease IgG and IgM line immunoassay (LIA) is widely accepted to have equivalent, if not, superior test performance characteristics to the first-generation WB. To validate the performance of the Euroimmun LIA method and to determine if the Euroimmun LIA was negatively impacted by ANA or Treponemal-specific antibody, four serum panels were assembled as follows: EQA reference panel (n=5), ANA/ Treponemal antibody reactive sera panel (n=19) to test for interference, retained historical sera with two screen assay results (IFA and ELISA)(n=15) and unselected freshly retained sera where Lyme serology was requested (n=52). Euroimmun LIA was performed on these four serum panels using a fully automated Euroimmun EuroblotONE LIA processor. From the results obtained in this method validation, the Euroimmun LIA had significantly higher levels of assay specificity than the IFA screening system, yet retained sufficient assay sensitivity to identify true positive cases. Also, Euroimmun LIA does not appear to be impacted by presence of ANA or Treponemal antibody as only single serum with high ANA titre (> 1280) gave independent IgM reactivity by LIA.

In conclusion, change in methodology to LIA will make a cleaner testing system with easier interpretation of results and negates the requirement to refer specimens for confirmatory testing which will add value to the delivery of serological results for cases of suspected Lyme disease.

O53: Arts in Health and Well-being, a review on the inclusion and benefits of arts in holistic healing

D Jayaraj[1]

[1]*LabPlus*

Artistic Director and Choreographer, Tapasya School of Dance, New Zealand

Cultural Ambassador, Sree Sankara School of Dance, India

The recent pandemic, Covid-19 has changed the lifestyle of the general population. We see a steady increase in anxiety, depression and unhappiness which is an indicator of a steep decline in the mental and physical well-being.

History speaks that one of the ancient manuscripts of Arts, "Natyashastra" was created to contribute towards the well-being of a then distraught society.

Arts practice has been proven to release the "feel-good" hormone Dopamine which helps to battle against loneliness, anxiety, and depression. Arts is a universal language and often doesn't need to be explained in words, it can be reflected in your emotions. It goes beyond different cultures, religions, ethnicities, and languages. Arts allows self-expression and is a therapeutic tool.

Any form of art (visual or performing) can be a medicine for the psychosomatic well-being of an individual. Participation in creative arts encourages everyone in the society to connect, be active and keep learning. Having social contacts and taking part in activities outside the home are known to be factors that help to protect the physical and mental well-being. Arts projects improve empowerment for people with mental health difficulties and are a promising approach for improving mental health symptoms and social inclusion.

Though participatory arts have been found to be beneficial, it has always been difficult to quantitatively measure its positive outcome because of the tension that exits between the philosophical differences of creative arts and health care systems. We should aim at educating the society on the benefits of arts in daily life so that more research and resources are invested into this field of study.

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2. The Arts in Heath, Evidence from the International Literature. Susan Bidwell, Population Health and Community Engagement March 2014.

O54: Polio and vaccination in 2023

R Jenkins[1]

[1]*Labtests*

The World Health Organisation set out to eradicate poliovirus in 1998, and there are pockets of wild poliovirus 25 years later.

What is being done about this, how big is the threat to the rest of the world and why is vaccination so important in New Zealand? Buckle up for a glimpse of the past, and the way forward.

O55: What's Happening in the Land of Oz?

S Just[1]

[1]*Australian Institute of Medical and Clinical Scientists*

The Australian Institute of Medical and Clinical Scientists (AIMS) is the peak professional body representing medical scientists working throughout Australia in all disciplines of laboratory medicine. AIMS provides overseas member, stakeholder and partner services including a university accreditation program. This is to ensure the minimum requirements standards are met for bachelor and master degree courses offered by Australian and overseas universities. AIMS assesses the qualifications of medical scientists, medical laboratory technical officers and pathology collectors wishing to migrate to Australia under the Government's skilled migration program. AIMS continuing professional development program (APACE) is designed to ensure members maintain their knowledge and skills in their chosen field of laboratory medicine. The Certification of Medical Laboratory Scientific workforce (CMLS) scheme in Australia is a voluntary scheme that provides a framework for the recognition of the qualifications and experience of medical laboratory scientists.

O56: Beware of Naked Ladies

A Karpik[1]

[1]*Middlemore Hospital*

This presentation is a case history of a patient with an acute onset of illness with abnormal morphological findings in her blood film. The case discusses the patient's initial presentation to our ED department, laboratory findings, the diagnosis and eventual outcome.

As our patient's history is revealed, the evils and virtues of "Naked Ladies" are exposed and we consider the "chaos" they can bestow upon us.

O57: When heartache isn't love or myocarditis: causes of cardiac troponin increase after COVID-19 vaccination and infection

S Kawamoto[1]

[1]*Te Toka Tumai LabPlus*

Clinical presentation: Three young adult patients with chest pain presented at the Emergency Department. Elevated high sensitivity Troponin I (hs-cTnI) levels were observed, while the electrocardiogram remained normal. Patient 1 had received the mRNA-1273 (Moderna) vaccine for COVID-19 five days prior, patient 2 had received a second dose of Moderna vaccine three weeks before admission, and patient 3 had confirmed COVID-19 infection based on reverse transcription PCR test.

Discussion: In these otherwise healthy young adults, the presence of a normal electrocardiogram and unchanged serial measurements of cTn suggested immunoassay interference with hs-cTnI rather than myocarditis. Although false positive cTn increases due to immunoassay have been reported in various conditions, their occurrence following COVID-19 infection or vaccination has not been previously described. Notably, macrotroponin complexes were identified in all three patients, indicating a potential immune response from the mRNA-1273 vaccination or COVID-19 infection.

Conclusion: Distinguishing between immunoassay interference and myocarditis can be challenging when diagnosing elevated cTn levels based on traditional criteria, especially in cases related to COVID-19 infection or vaccination. Clinicians and laboratory staff evaluating patients with suspected acute or long-term cardiac complications following COVID-19 infection or vaccination should be aware of the potential for false positive cTn increases due to assay interference.

O58: Cervical specimens: the why and how of macroscopy

D Kenwright[1]

[1]*Wellington SCL*

Accurate orientation and dissection of cervical specimens depends on understanding the anatomy of the cervix, the pathology being looked for and thee type pf procedure performed. In this talk we will describe the types of cervical specimens and what they consist of, the commonly encountered pathology and macroscopic reporting requirements, and how to dissect and orientate small biopsies, LLETZ and cone biopsies.

O59: POC Evaluation of the HemoScreen full blood count analyser

C Kot[1]

[1]*NSW Health Pathology*

The HemoScreen is a PoC device used to perform a Full Blood Count (FBC). The analyser measures whole blood samples, which are prepared inside disposable units, termed cartridges. It requires 40uL of venous whole blood added to a sampler, which is inserted into the cartridge. The cartridge is then loaded into the analyser for preparation and measurement. The cartridge is preloaded with all required reagents. After analysis, the results are displayed and can be saved, printed, or exported to another digital system.

The HemoScreen Analyser provides 20 standard FBC parameters in approximately 6 minutes. The HemoScreen technology utilises a physical phenomenon known as viscoelastic focusing, which causes cells to align in a single cell-plane. Once the cells are stained and focused, images are visually processed using machine vision algorithms. Leukocytes are classified based on their staining properties and morphology, whereas absolute counts are obtained by counting the cells contained in a chamber of predetermined volume.

Based on the outcome of the validation, it was concluded that the device was "fit for purpose" as a screening device in PoC settings and can be implemented across NSW with caveats.

O60: Overview of Newborn Screening Programme in New Zealand

S Krishna[1]

[1]*Te Toka Tumai LabPlus*

Newborn Screening Programme is one of the most successful screening programmes in New Zealand. It has been in place in New Zealand since 1969. Each year almost all babies born in New Zealand are screened and about 50 babies are identified with an inherited disorder.

The screening samples are collected from babies 24 hours to 48 hours after birth. Specimens are collected by heel prick onto filter paper and sent to the laboratory for testing. The newborn screening lab measures a variety of metabolites and hormones to screen for metabolic and endocrine disorders, phenylketonurina, cystic fibrosis, congenital hypothyroidism and severe combined immunodeficiency. Now over 20 inherited disorder are included in the New Zealand Newborn Screening Programme.

O61: Cardiovascular tissue banking in NZ; Our Experiences, Our Perspective

S Kumar[1]

[1]*New Zealand Blood Service*

The implantation of the homograft came into clinical practice in the 1960's where by Donald Ross in year 1962 at Guys Hospital in London and Sir Brian Barret Boyes in 1964 at Greenlane Hospital in Auckland preformed this procedure successfully. Thus, cardiovascular tissue banking came into practice. This presentation will look at the history and current process of heart valve banking. Including the antibiotics used, types of homograft and it's usage and the impact homograft usage is making to the people of New Zealand. Finally elaborating on tissue donation and the importance of tissue in medical practices from sourcing donations to processing tissue to implantation.

O62: Enhancing Employability of Medical Laboratory Science Graduates

A Kundur[1], B King[1], I Singh[1], A Hicks[1], I Cassady[1]

[1]*Griffith University, Parklands Drive, Gold Coast, Queensland, Australia*

Objective

Medical Laboratory Science (MLS) is a dynamic field that is constantly evolving. Hence, as educators we have the responsibility to prepare future graduates with comprehensive knowledge and skills necessary for the workplace. In Griffith University MLS program, we use horizontal scaffolding of case studies across Hematology, Histopathology, Biochemistry, Transfusion Science and Microbiology. This approach teaches students to apply cross-disciplinary knowledge and adopt a holistic approach to reach a final diagnosis. The Bachelor of MLS teaching team in collaboration with public and private pathology service providers, have developed an innovative and employment-focused curriculum. This focus is to bridge the any knowledge and experience gap between our graduates and the pathology service providers, potential employers, as well as accreditation bodies such as the Australian Institute of Medical and Clinical Scientists (AIMS).

Methods

Our aim is to significantly enhance the employability skills of MLS graduates through the development and deployment of a one-week intensive training workshop that students must attend prior to commencing clinical placement. This micro-credentialled workshop provides students with specialised training that utilises virtual and face-to-face delivery formats with a focus on industry specialist material such as pre-analytical error training, 3D virtual pathology simulations, telepathology, NATA and understanding of NATA requirements and ISO15189 standards. Student surveys on the effectiveness of pre-placement workshops before and after completing clinical placement were conducted.

Results

The students either strongly agree or agree that pre-placement workshops enable them to better prepare for their placement, help them in their job interview, identify their skills and attributes that employers need and helped them to develop employability skills.

Conclusion

These results strongly indicate the effectiveness of pre-placement workshops in enhancing student confidence and preparedness at

placement and subsequent employment.

O63: Introducing Non-Invasive Fetal RHD Genotyping in New Zealand

P Kwan[1], R So[1], S Kirwan[1]

[1]*Clinical Development Team, New Zealand Blood Service*

Objective

NZBS will introduce non-invasive fetal *RHD* genotyping as a screening tool to avoid unnecessary administration of anti-D immunoglobulin in pregnancy, which aligns with international best practice and NZBS strategic goals of clinical excellence, by expanding our services to suit the healthcare needs of the people of New Zealand.

Methods

We reviewed the key considerations for implementing a real-time quantitative PCR assay for fetal *RHD* genotyping, including testing methodology with respect to the choice of *RHD* exons, sampling time points during gestation to achieve optimal assay performance and strategies for repeat testing and reporting algorithm, in accordance with the latest international best practice guidelines.

Results

Due to the existence of *RHD* variants, two or three of the *RHD* exons 4, 5, 7 and 10 are commonly targeted for fetal *RHD* genotyping internationally. Results would be considered highly accurate when testing is performed with samples from 11^{+2} weeks' gestation, with sufficient cell-free fetal DNA available for reliable detection in maternal plasma. Based on the performance characteristics established for a commercially available CE IVD marked assay kit, the Free DNA Fetal Kit RhD® (Sensitivity: 100%; Specificity: 98.1%) was chosen to be validated for fetal *RHD* genotyping at NZBS.

Conclusion

Validation of the assay will be performed in accordance with international recommendations to ensure appropriate assay performance and applicability for safe clinical use, covering analytical detection limit, range and linearity, precision, robustness, assay sensitivity and specificity

O64: What more can we learn from the aviation industry?

O Lau[1]

[1]*Te Toka Tumai LabPlus*

Air travel once was very dangerous, with many flights ending in disaster, especially in the early '90s. However, through learning and an extreme focus on safety and risk management, air travel is now considered the safest form of transportation. Conversely, preventable medical errors are the third leading cause of death in developed countries, behind cancer and cardiovascular disease. The aviation industry serves as an excellent blueprint for addressing safety concerns and offers invaluable lessons that all healthcare organisations can draw from.

Over the years, the healthcare sector has adopted numerous safety principles and risk management approaches from aviation, such as the checklist approach, incident and risk management systems, and the black box thinking approach. So, what more can we learn from aviation?

This presentation centres around a crucial facet of safety often referred to as the 'soft side.' I will delve into the realm of human factors, exploring the influences on our behaviour and performance, particularly those that have the potential to lead to errors. By drawing parallels with aviation and examining its best practices, we can unlock valuable insights for the improvement of safety in healthcare organisations.

O65: Improved Strategy for Detection of Dermatophyte Infection

E Lau[1]

[1]*Canterbury Health Laboratories*

Dermatophytes are the major cause of superficial mycoses. Accurate confirmation of the aetiology and mycological identification is necessary to initiate appropriate therapy. Inappropriate use of antifungals risk development of antifungal resistance, or adverse side effects due to drug interactions; some of which can be life-threatening.

There are significant challenges in diagnostic mycology where traditional and time-consuming culture methods are compounded by a limited number of experienced scientists with expert knowledge in this area. Molecular diagnostic methods such as the Dermatophyte Polymerase Chain Reaction (PCR) is a powerful tool with its increased sensitivity and significantly reduced turnaround time for results. Rapid results give clinicians the confidence to make informed decisions and advice on treatment or further diagnostic options.

The flow-on benefit will be improved diagnostic reliability of results for appropriate clinical decision and patient care.

The poster will present on our recent findings, specimen processing algorithm and the implementation of Dermatophyte PCR testing at Canterbury Health Laboratories, Christchurch Hospital.

O66: Development and validation of drug screening in urine by liquid chromatography time-of-flight mass spectrometry (LC-QTOFMS)

H Madhavaran[1]

[1]*Te Toka Tumai LabPlus*

Introduction

In an analytical toxicology laboratory, numerous therapeutic and illicit drugs in biological samples need to be identified and reported in a timely manner. Due to comprehensive data acquisition capability, LC–QTOFMS analysis provides a reliable technique for identifying many known and unknown analytes in several matrixes and has proven to be one of the most efficient methods in systematic toxicological analysis.

Methods

We developed and validated a LC-QTOFMS screening method for the detection of therapeutic and illicit drugs in urine samples. This method was developed on a Shimadzu LCMS-9030-QTOF. The LC analysis was performed with an auto sampler, column oven and a binary pump (nexera series). For the separation a shimpac biphenyl analytical column was used.

Results

The approach we have taken for method validation which is a complex and labour intensive process for broad screening assays is to choose a sub-set of "model" compounds (69 drugs). Qualitative validation for 69 compounds included linearity, matrix effects, recovery, carryover and extract stability. The extraction procedure is a simple dilution of human urine with mobile phase and internal standard solution and filtration after enzymatic hydrolysis. The identification of the compounds was based on exact mass, retention time, isotopic score fit and library similarity index. To assess the performance of the QTOF in patient samples, 450 historical qualitative samples were analysed on the QTOF system and the concordance was over 70%.

Conclusion

Compared to the established gas chromatography-mass spectrometry procedure, the developed LC-QTOF-MS screening method showed in the majority of cases the same or even more findings. The capability of TOF instruments to collect all generated ions permits retrospective data analysis. Thus, a sample can easily be reprocessed and searched for a given substance without re-injection.

O67: Infective Endocarditis: In search of the cause…

S Mahar[1]

[1]*Pathlab*

Infective endocarditis (IE) is potentially fatal infection of the endocardium, the tissue of the heart chambers and heart valves. The diagnosis of the cause is ideal to optimise treatment and to improve outcomes. The diagnosis can be tenuous and culture negative endocarditis remains a treatment challenge.

This is a presentation of patient with infective endocarditis where the diagnosis was elusive and treatment challenging.

O68: *Candida auris* the new emerging multi-drug resistant organism

W McKinney[1]

[1]*Te Toka Tumai LabPlus*

Candida auris is a new emerging multi-drug resistant fungal pathogen that was first described in Japan in 2009, it has now been reported in over 40 countries. New Zealand can now be added to the list with the first reported case in January 2023. *C. auris* is a skin commensal that exhibits antifungal resistance and primarily causes healthcare associated infections. Transmission occurs by contact with contaminated surfaces or medical equipment. Screening of patients that have been hospitalised overseas is essential to detect colonisation and prevent hospital outbreaks. Auckland City Hospital has now updated the multi-drug resistant organism (MRO) screening protocol to include *C. auris* using salt Sabouraud dulcitol (SSDB) broth and CHROMagar Candida Plus. We recently validated a modification of SSDB, with the addition of vancomycin to inhibit gentamicin and/or chloramphenicol resistant Gram-positive bacteria during screening. Two case studies will be presented with emphasis on laboratory isolation and identification.

Disclosure: No conflicts of interest.

O69: Cervical Cancer Screening in the Pacific Islands

S Meharry[1]

[1]*Auckland University of Technology*

Cervical cancer is a common form of cancer in women worldwide including the Pacific Island Countries and Territories (PICT's). Mortality rates with cervical cancer are high in the PICTs and can be related to a number of factors including lack of available resources and cultural acceptance of screening, which contribute to this high rate. Cervical cancer screening methods have evolved from cell morphology observations to the more specialized techniques of molecular testing. High-risk Human Papilloma Virus (HPV) genotyping and liquid-based cytology are the most common methods and have been "gold standard" tools used in cervical screening for some time now. However, in the Pacific Island Countries and Territories (PICTs), there is great disparity in the use of such methods. These disparities in testing have seen an increase in cervical cancer morbidity and mortality rates.

Here, we consider the factors necessary to develop a low-cost effective and acceptable cervical cancer screening programme made accessible to all women in the Pacific Islands and thereby decrease the mortality rates and improving outcomes for women in the PICTS.

Keywords: ***Cervical cancer, Pacific Islands, Human papilloma virus (HPV)***

O70: Massive Haemorrhage Pathway

S Mercer[1]

[1]*New Zealand Blood Service*

Haemorrhage causes 60% of trauma deaths that occur within the first six hours after injury[1]. Up to fifty percent of these deaths are often preventable[1]. In March 2019 the Accident Compensation Corporation contracted the Health Quality & Safety Commission to support the National Trauma Network to improve knowledge and skills across the New Zealand trauma system[1]. The Critical Haemorrhage Project ("the Project") engaged an expert reference group including the NZ Blood Service to develop a national critical bleeding bundle of care[2] ("the Bundle"). The bundle, adjustable for local context and scale, has been designed to support ambulance services, emergency departments, intensive care units and surgical teams in rapid decision making and optimising patient access to definitive control of bleeding[1].

Achieving appropriate blood product delivery is an important part of the bundle's co-ordinated clinical approach to improving care for critically bleeding patients[2]. Code Crimson and Code Red has become the activation terms to accelerate clinical care for trauma patients[3]. Patients with obstetric haemorrhage, large blood loss surgery, transplants, and gastro-intestinal haemorrhage, who were out of scope of the project, are expected to benefit from the improved guidance[2]. The Adult Massive Haemorrhage Pathway ("MHP") released in 2022 is a modified version of the previous Massive Transfusion Protocol. The new Code Crimson, Standard and Obstetric pathways are a "complex set of concurrent processes utilising an algorithm that standardises the management and transfusion of adult patients with massive bleeding and shock or coagulopathy"[4]. Stat packs are delivered to the patient as soon as the MHP is initiated, providing early access to red cells and fresh frozen plasma to maintain blood volume while clinical teams assess their patient for ongoing transfusion needs. This quality improvement initiative has been implemented in 54% of NZ hospitals with a further 13% in final stages and the remainder in planning phases[5].

O71: Haematology in Pregnancy

E Merriman[1]

[1]*North Shore Hospital*

Management of haematological problems occurring during pregnancy will be reviewed, including thrombocytopenia, microangiopathic haemolytic anaemia, antiphospholipid syndrome, lymphoma, acute leukaemia and myeloproliferative disorders. Illustrative real-life cases will be used throughout.

O72: Neonatal haematology: a clinician's overview

M Meyer[1,2]

[1]*Middlemore Hospital*

[2]*University of Auckland*

Blood disorders are common in the NICU setting, owing partly to severity of illness but also to the immunocompromised state of preterm and to a lesser extent term infants. Anaemia is almost universal in the very preterm infant with reduced red cell production and the frequent requirement for blood sampling (some of our smallest infants have a total blood volume of around 40ml!). White cell anomalies are also common with transient low or raised neutrophil counts possible in response to maternal conditions and sepsis. Low platelet counts may also occur in response to acute illness . In our experience severe NAIT is uncommon in Maaori and Pacific peoples, with confirmation of this from a large survey of

cord blood samples. Coagulopathies are usually easily managed but interpretation of results can be difficult because of uncertainty of normal ranges. Haemolytic jaundice is often due to ABO incompatibility, Rh disease being much less common following antenatal prevention.

O73: Beyond the stain: Is PCR the Future of Vaginosis Diagnosis?

B Mills[1]

[1]*Canterbury Health Laboratories*

Vaginal swab analysis, commonly including culture and Gram stain, represents one of the high-volume sample processes in a clinical microbiology laboratory. However, Gram stain interpretation can be subjective, even with an experienced operator. As an alternative to Gram stain or wet-mount, molecular analysis of the vaginal microbiome is non-subjective and rapid, potentially enabling an improved service for the clinicians. The BD Max vaginal panel (MAX VP) is an automated qualitative multiplex molecular test for the direct detection of BV, Candida species (*C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. dubliniensis*), *C. glabrata*, *Pichia kudriavzevii* (*C. krusei*) and *T. vaginalis*, from vaginal swabs, performed using the BD Max System. We present to you our study, performed at Canterbury Health Laboratories to compare the performance of the BD Max vaginal panel against routine laboratory procedures for the detection of BV, Candida spp, and *T. vaginalis*.

O74: Safety, risk management and excellence: from extreme environments to the hospital

S Mitchell[1,2]

[1]*Auckland City Hospital*

[2]*North Shore Hospital*

Hospital care of complicated patients is rife with opportunities for error and omissions that may impact negatively on outcomes. This has much in common with adventure in extreme environments. Three extreme environment adventures (taking arterial blood gas samples from an elite freediver at 60m depth, underwater exploration of an extremely deep cold-water cave, and the Thailand cave rescue) achieved positive outcomes despite numerous challenges and hazards. They combined elements of meticulous planning, teamwork, communication and simulation that have direct relevance to improving outcomes in the healthcare setting. These adventures will be described, along with some of the tools available to healthcare professionals that apply the same operational principles for optimizing outcomes.

O75: McLeod phenotype

D Murphy-Devlin[1]

[1]New Zealand Blood Service

McLeod syndrome is a rare X-linked neurohaematological disorder which is defined by absent Kx red blood cell antigen and weak expression of Kell antigens (McLeod phenotype). This may lead to it being accidentally detected in routine screening of apparently healthy donors. The NZBS Reference Laboratory occasionally receives referrals for these red cell phenotyping tests as a screening test for suspected McLeod syndrome. Two case studies that were tested by NZBS Reference Laboratory will be discussed.

O76: A personal perspective: Insights, challenges and learning's from the Northern region

S Musaad[1]

[1]*Te Whatu Ora Northern Region*

The Northern Region POCT Network is one of several clinical networks under the auspices of the Regional Labs Harmonization programme. The Network is working towards developing a cohesive and sustainable POCT service for the Northern Region. A service that meets the needs of our population, particularly in the community, and that functions within a quality framework. The talk describes the principles and insights of the Network, and importantly lessons learnt so far!

O77: A suspected anaphylactic reaction to DMSO

A Nalder[1]

[1]*New Zealand Blood Service*

I will give a brief introduction to Allogeneic Haematopoietic Progenitor Cells (HPC) and T-cell including the processing performed by the New Zealand Blood Service (NZBS) and their use in cancer treatment. I'll then introduce our case study, an anaphylactic reaction that occurred at the start of the infusion of cryopreserved allogeneic HPC cells. I will provide details of the steps that were taken to ensure the transfusion was allowed to continue and the methods used to control the reaction in the following weeks while the patient underwent T-cell infusions.

O78: Strengthening diagnostic microbiology in LMIC: the Timor-Leste example

T Oakley[1]

[1]*Menzies School of Health Research*

Low-resource settings have a high burden of infectious disease and antimicrobial resistance, however, often lack the capacity for effective diagnostic microbiology. Issues faced in low- and middle-income countries such as Timor-Leste include infrastructure, technical, and equipment challenges which can be difficult to overcome. This talk will outline the barriers and enablers for capacity-building activities for microbiology in LMIC using the example of Timor-Leste, which has undergone significant change since 2019.

O79: Unexpected and disconcerting - when natural conception coincides with fertility treatment

M Olds[1]

[1]*Fertility Associates Ltd*

Identical twins occur in 1-2% of pregnancies after a single embryo transfer (SET). This is well known 'side effect' and well-explained as part of patient information giving. It is also possible to have twins of different sexes after SET, where natural conception occurs in the same menstrual cycle as the transfer of a frozen-thawed embryo. This is much rarer and totally unexpected by people who have experienced infertility for many years. When this occurs, people are naturally concerned about whether the clinic accidently transferred two embryos instead of one, and whether they received the correct embryo(s). A recent very unusual case prompted us to review our experience over 35 years, and to calculate how likely this event might be for different groups of patients and for different types of embryo transfer cycles. This talk will also cover how we navigated an investigation of our processes while balancing patient care as the information of this case slowly came to light.

O80: Development of the Northern Region Benchmarking/Baseline Tool

F Osborne[1]

[1]*Te Whatu Ora Northern Region*

As the health system works towards national clinical networks that will have regional operating models to deliver efficient, equitable and quality service to its diverse population it is important that we are able to understand and demonstrate the business of pathology and connect it with quality and workforce management. Northern Region Labs Harmonisation Programme engaged Beeston Consulting Ltd, a UK company that provides benchmarking services to the NHS, to work in partnership with laboratory teams to construct a consistent 'baseline model' for both private and public Northern Region laboratories. The Labs Benchmarking / Baseline Tool provides a regional summary and overview of the pathology service for the first time. The region can now compare three datasets (financial, tests, workforce) over a five-year period on a common platform and advance regional service analysis. The exercise itself has been valuable in assessing and identifying where data sets are comparable, and where they are captured inconsistently between pathology services. A longitudinal view of the lab service speciality allows trend analysis which can be applied to strategic planning of the delivery of services going forward. Beeston also provided peer group comparison with the services they had in their benchmarking archives. These insights provide opportunities on how to improve the data to effectively support regional pathology service management. This presentation will share the northern region's experience in the development of the tool and the lessons learnt.

O81: Following the White Rabbit: A journey into a competency matrix

C Osborne[1]

[1]*Te Toka Tumai LabPlus*

Have you ever wondered what you need to do to take that next step into a new role? Have you ever asked someone and been given vague answers. Come and have a listen as a new skills matrix, for laboratory IT, is presented. We will have a look at some of the benefits and the journey taken to get to a working prototype.

O82: Rapid genetic testing and what it means for the future of healthcare in Aotearoa New Zealand

J O'Sullivan[1]

[1]*Liggins Institute*

Precision health is a fast-growing field that uses emerging technology to understand all available genetic, health and environmental information to predict, prevent, diagnose, and treat disease with great accuracy for individuals and their whānau. Genomic methods can significantly contribute to all facets of precision medicine, from diagnosis to prevention, therapeutic intervention,

and management of acute and chronic illnesses. DNA based methods are already having a considerable impact across healthcare in fields that include acute and chronic disease. Internationally over 20 studies have demonstrated the clinical utility of rapid genome sequencing for neonates. As a result, researchers have argued that rapid genome sequencing should become the standard of care in critically ill infants and be used as a first-tier test. In the Liggins Institute Newborn genomics programme, we are focusing on rapid whole-genome sequencing of parents and children (i.e. a trio) for the identification of diseases that have genetic components. In this talk I will discuss how we have gone about setting up this project, our quality assurance, where we are starting and our future challenges.

O83: Malaria PCR

E Otte[1]

[1]*Canterbury Health Laboratories*

Malaria diagnostics represent a continuous challenge in non-endemic settings. The current gold standard is microscopy of stained blood films, but the method is time-consuming and laborious.

Submicroscopic infections and keeping microscopy skills up to date is equally challenging.

For these reasons we decided to develop a Plasmodium species PCR for the BD MAX platform.

The ease of use of the platform allows for 24/7 speciation of malaria parasites in our laboratory.

O84: ISTH 2023 Congress Update

J Phillips

Three interesting presentations highlighting new developments relevant to the haemostasis laboratory, selected from the recent ISTH Congress in Montreal will be reviewed. Firstly, a late-breaking abstract from Andreas Greinacher describing insights into identification of HITT, VITT and a newly described phenomenon, spontaneous VITT. Secondly, a novel modification of the Bethesda assay for the emicizumab era described by Bert Verbruggen. Finally, insights into the multiple roles of 'coagulation' factor V gleaned from the Grant medal plenary lecture by Bjorn Dahlback.

O85: Mutual Learning with Medical laboratory Scientists in Precision Medicine and Genomics

C Print[1]

[1]*University of Auckland*

Precision medicine is having substantial impact internationally on both clinical care to benefit current patients, and molecular research to benefit future patients. As precision medicine, including genomic analysis, expands in NZ, we need to rapidly grow the numbers of clinical and research laboratory experts with experience in this area. In this talk Cris will highlight some opportunities for NZ laboratory scientists to expand their skills in precision medicine and genomic analysis.

O86: Updating Aotearoa New Zealand's human reproductive research guidelines: public perceptions on the use of human embryos in research

K Reader[1]

[1]*Advisory Committee on Assisted Reproductive Technology*

Assisted reproductive technology (ART) in Aotearoa New Zealand is regulated under the Human Assisted Reproductive Technology Act 2004 (HART Act). Under the HART Act, the Advisory Committee on Assisted Reproductive Technology (ACART) is required to issue guidelines and advice to the Ethics Committee on Assisted Reproductive Technology (ECART) on assisted reproductive procedures, including human reproductive research. The HART Act defines human reproductive research as any studies that use or involve gametes or embryos. The current guidelines for human reproductive research, titled Guidelines for Research on Gametes and Non-viable Embryos, were published in 2005. It is timely to review these now with a view to providing updated guidelines that enable society to benefit from developments in ART while reflecting the views and attitudes of today.

ACART consulted the public from November 2022 to March 2023 seeking specific feedback on possible types of research, including the purposes of the research and the risks and benefits. ACART asked submitters to comment on the ethical/moral matters they believed were important. This feedback will now be used to develop new guidelines which will be the subject of a second consultation prior to advising the Minister of Health on finalised guidelines for ECART. A summary of the submissions outlining submitters' thoughts on research using human gametes and embryos will be presented.

O87: What's new at Otago?

C Ronayne[1]

[1]*University of Otago*

Despite the doom and gloom about Otago University in the media, the team in the medical laboratory science programme are forging ahead. We have seen increased student numbers over the last few years in both our undergraduate and post-graduate courses. Several new initiatives are underway to improve student engagement and learning, including developing a simulation laboratory to reduce telephone anxiety. We are also exploring alternative revenue streams, such as workshops and laboratory testing to assist researchers. These could also be tailored short courses for diagnostic laboratory educational requirements.

In 2024, our honors programme (BMLSc(Hons)) begins, which will shorten the time required for graduates to attain post-graduate qualifications. This means students will have just one clinical placement, and a research placement, for which we are happy to provide ideas and assistance.

We have a current proposal with Medical Sciences Council New Zealand to have a Postgraduate Diploma of Medical Laboratory Science approved as a bridging course, for graduates of other science programmes (BSc etc) who are currently working as medical laboratory technicians to upgrade to medical laboratory scientists. We plan to offer this by distance.

As always, we greatly appreciate the support, time and input of the profession, particularly our clinical placement hosts.

O88: Looking through the lipid glass: Is everything as it seems?

CL Ronayne[1], IM Morison[1], RJ Hancox[2]

[1]*Pathology Department*

[2]*Department of Preventative and Social Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand*

Objective

Plasma lipid testing is a key component of cardiovascular disease (CVD) screening. The last national survey of lipid levels was in 2009 and no studies have investigated lipids in the southern region of NZ. The aim of this study was to investigate changes in plasma lipid levels over time in Otago adults.

Methods

We performed retrospective analysis of 883,793 community-requested lipid profiles from adults aged 18 to 100 years of age living in the Otago region from 1995-2021.

Results

Over the 27-year period, mean total cholesterol (TC) levels fell from 6.38 mmol/L (95% CI 6.33-6.42) to 5.25 mmol/L (5.23-5.26) in women and from 6.17 mmol/L (6.14-6.21) to 4.83 mmol/L (4.81-4.84) in men. Low-density lipoprotein cholesterol shows a similar decline. High-density lipoprotein cholesterol (HDLc) peaked in 2006 at 1.66 mmol/L (1.65-1.66) for women and 1.36 mmol/L for men (1.36-1.37), declining to 1.57 mmol/L (1.56-1.58) and 1.26 mmol/L (1.26-1.26) respectively in 2021. Plasma triglycerides (TG) show a U-shaped distribution, falling to 1.39 mmol/L (1.38-1.40) for women and 1.55 mmol/L (1.53-1.56) for men in 2010, then increasing to 1.68 mmol/L (1.67-1.69) and 1.98 mmol/L (1.96-1.99) in 2021. Recent studies suggest TG to HDLc ratio (TG:HDLc) and remnant cholesterol (consisting of very low and intermediate density lipoprotein cholesterol) are strong risk factors for myocardial infarction, stroke and all-cause mortality. Both show U-shaped distributions in the Otago population, with 2021 mean values exceeding the recommended targets.

Conclusion

While traditional markers of CVD risk appear to be improving in Otago, increasing levels of alternative markers, TG:HDLc and remnant cholesterol, are concerning. There is a need for further monitoring and investigation of their association with CVD morbidity and mortality.

O89: New Zealand Blood and Organ Service Response to Auckland Flooding and Cyclone Disasters: From Business Continuity Plan to Cleanroom Suite Recommissioning

G Roufail[1]

[1]*New Zealand Blood Service*

The Cleanroom Suite at the Cellular and Tissue Laboratory (CTL) at the New Zealand Blood and Organ Service Donor Centre in Auckland, was severely flooded and compromised. This affected the laboratory's ability to cryopreserve life-saving Cellular Therapy Products collected within the Auckland and Waikato regions.

Discussion

Business Continuity Plan (BCP) was activated to facilitate distribution of CT products around the organisation's other CT laboratories throughout the country for timely processing, while the clean room underwent recommissioning. The BCP was coordinated by the Cellular Therapy Operations Support Officer to align and fit with logistical obstacles resulting from the flooding and cyclone, and fitting in our ongoing 'business as usual' workload.

O90: Update on the Classification of Myeloid Neoplasms (Who And Icc)

A Ruskova[1]

[1]*Auckland City Hospital*

Since the early 1980-ies the global haematology community has benefited from and enjoyed the use of a single world-wide accepted classification of the myeloid neoplasms. The classification was pioneered by the FAB (French-American-British) group and followed successfully by 3 editions of the WHO classification of the tumours of haematopoietic and lymphoid tissues - the 3rd (2001), 4th (2007) and revised 4th (2017).

In 2022 this unison was disturbed by the emergence of two independent classification – the 5th edition of the WHO classification and the International Consensus Classification (ICC); both produced by teams of well-known and highly regarded experts and each having their own merits. This division necessitates the simultaneous use of two different classifications and nomenclatures leading to upset and confusion for professionals and patients alike. Although the vast majority of authors from both sides acknowledge and agree that a unified classification is of utmost importance and the only sensible way forward, for now, we have no choice but get familiar with and use both classifications in our everyday practice.

The talk outlines the most significant changes introduced by the two classifications in respect to the myeloid malignancies with emphasis on Myelodysplastic Neoplasms/Syndromes (MDS) and Acute Myeloid Leukaemia. The common concepts, trends, similarities and differences will be discussed.

O91: Guidelines for the Laboratory Diagnosis of Malaria

R Saddoy[1]

[1]*Pathlab Waikato*

Laboratory tests used in the diagnosis of malaria continue to grow. However, careful film examination of thick and thin blood films remains the gold standard for diagnosis. This presentation revises and reviews the basic procedures in malaria testing and outlines the recent updated guidelines for the laboratory diagnosis of malaria published by the British Society for Haematology.

O92: HPV primary screening for cervical cancer prevention: making it happen

M Sage[1]

[1]*National Cervical Pathology Training Service*

On 12th September 2023, the National Cervical Screening Programme in Aotearoa New Zealand will change the primary cervical screening test from cytology to a test to detect high-risk types of Human Papillomavirus (HPV). Using an HPV screening test will allow sampling using a vaginal swab sample, rather than requiring a speculum examination to sample cells from the cervix for cytology. Screening for HPV is a more sensitive test than cytology for identifying those with high-grade lesions on follow-up. Changing the test per se will reduce cervical cancer rates, with further benefit gained from the increased coverage that offering a test that can be performed using a vaginal swab sample will bring.

Because of the complexities of changing the screening test, a new NCSP cervical screening register has been built and will go live on 12th September 2023.

Changing the screening test has major consequences for the laboratory sector. This talk will outline what these changes have been and will entail as New Zealand moves through this period of transition into the era of HPV primary screening.

O93: Pacifica culture in Phlebotomy

V Salanoa-Taituave[1]

[1]*Labtests*

Aotearoa New Zealand is home to almost 400,000 people who identify as Pacific Islanders. This accounts for just over 12.5% of the population. Health statistics indicate that Pasifika people are less likely to interact with the health system and experience barriers to access healthcare which

contributes to the inequity in health outcomes. I will be touching on points of importance for Pasifika population and how this can be translated in the world of Phlebotomy.

O94: Triving in an ever-changing world

D Sanders[1]

[1]*Raise Mental Health*

Today's world is always changing, presenting us with continual challenges and serious life issues. At times, these can affect us in such a way, that we are often left feeling overwhelmed and exhausted.

For many professionals and families, the impact has often challenged our ability to, not only cope, but thrive.

In my work as a trauma counsellor and C.I. responder, I am always amazed at the human spirit's desire to thrive and overcome adversity.

I have witnessed and learnt that having hope for the future is very much about how we view our struggles and respond to them.

It is my hope that our session will explore some of these wonderful principles and tools that always seem to benefit us in the midst of difficult times.

Our session will look at:

1. Acknowledging the changes and stressors of life
2. Principles internally and externally, that allow us to become resilient and thrive
3. Tools and tips on ways to Love life, feel refreshed and see hope in the midst of an ever-changing, and sometimes chaotic life.

My hope is that our time together will leave you feeling enriched and hopeful about the future.

O95: Biotin Interference in Immunoassays at LabPLUS

R Sargon[1]

[1]*Te Toka Tumai LabPlus*

Roche, along with many other manufacturers of immunoassay kits, utilise biotin-streptavidin binding in their immunoassay methods. It has been known for several years that over the counter biotin supplements and biotin therapies can raise blood levels to a point where biotin can interfere with these immunoassays potentially leading to mis-diagnoses[1,2]. Amongst the strategies to minimise the effect of high endogenous biotin levels on immunoassays, is the release of re-engineered immunoassays that are more resistant to biotin interference. LabPLUS is currently updating existing immunoassays on the cobas e801 platforms for biotin resistant assays as they become available. Recently the biotin resistant versions of AFP and Free T4 were evaluated against their original versions. A number of immunoassays have already been converted to biotin resistant versions while others have yet to be converted.

The objective of this small study was to determine if the manufacturer's claims of biotin resistance could be supported. A small number of sample pairs for each assay were run; one was spiked with 1000 mg/L biotin while the other was "non-spiked". By comparing the recoveries of each pair for each assay, the degree to which the existing and the biotin resistant immunoassay versions are affected by biotin was demonstrated. The biotin resistant version of all assays showed marked resistance while the original, non-biotin resistant immunoassay versions all demonstrated varying degrees of biotin interference.

The manufacturer's claim of biotin resistance for the new assays is supported. With such assays becoming available and with better education, is there still the need for the same degree of concern for potentially high endogenous biotin containing samples? Is a strategy of targeting questionable samples with off-line, manual biotin evaluation sufficient or is there a place for a more automated method that could be run on every sample received in the laboratory?

Disclosure Statement

There are no conflicts of interest. No financial support provided by any individual or organisation.

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O96: Mobilising Blood Collection during a National Disaster

L Scott[1]

[1]*New Zealand Blood Service*

In our little slice of paradise at the bottom of the world, New Zealand is unfortunately not immune to disasters. Whether they are natural or man-made they can have a profound effect on our service and our teams. Severe flooding, arson, pandemics, terrorist

attacks, and earthquakes, as an essential service, the New Zealand Blood Service is required to navigate them all, providing a constant supply of blood and blood products to our fellow kiwis in need.

The ability to manage and respond in such situations starts long before the event. National response plans, business continuity preparedness and recovery plans are essential to any organisation. For any plans to work, the ability to respond and recover begins with us. Our teams on the ground.

When these disasters threaten not only "BAU" but our own well-being, we discuss how the Donor Services teams of the New Zealand Blood Service build resilience and be change ready through culture, leadership and relationships enabling them to prepare, mobilise, recover and grow in the event of a disaster.

O97: The 70% claim. Is it evidence-based?

R Siebers[1]

[1]*Wellington School of Medicine and Health Science*

There is no disputing that medical laboratory tests are critical for patient diagnosis and treatment. However, numerous publications and organisations claim laboratory tests are used by clinical staff in the diagnosis of at least 70% of patients disorders (or variations of this claim), without any evidence.The origin of this claim arose from a publication in 1996 that stated that "*Laboratory services may make up 5% of a hospital's budget but leverage 60-70% of all critical decision-making such as admittance, discharge, and medication*" (1).

This publication has been cited 78 times in the PubMed database to date with virtually all just stating the original statement or various versions thereof, without critical comment. It has also frequently been stated on the web sites of various originations, including the NZIMLS where it states that "*Medical laboratory scientists analyse patient specimens/samples sent to the laboratory producing results in the diagnosis of 70-80% of all patients disorders*".

The 70% claim, or variations thereof, were challenged in 2011 by Hallsworth who argued that these claims were not evidence-based and stated that "*Various 70% claims should be resisted in favour of more specific and evidence-based indices of added value*" (2). Despite arguments for objective evidence, many publications and organisations continue to state the 70% claim without critical discussion. As medical laboratory professionals we should resist making this 70% claim (or one of the various versions) in favour of more specific statements that must be evidence-based.

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O98: Brain banking and neuropathology of X-Linked Dystonia Parkinsonism – A scientific humanitarian effort

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[2]*Department of Anatomical Pathology, LabPlus, Auckland City Hospital, Auckland, New Zealand*

Objective

X-linked dystonia-parkinsonism (XDP) is a hereditary recessive neurodegenerative disease that is endemic to Panay in the Philippines. While the disease presents with widespread atrophy, the striatum appears significantly affected. However, detailed neuropathological studies characterising the human XDP striatum and basal ganglia are largely limited. We have set up the first brain bank in the Philippines to understand XDP neuropathology.

Methods

To advance our understanding of disease impact in the human XDP striatum, immunohistochemical studies were conducted on post-mortem striatal tissue from a cohort of 12 XDP and 5 age-matched neurologically normal cases. A suite of well-characterised antibodies coupled with automated analysis was conducted to detail disease-related neurochemical and pathological changes in the striatal sub-compartments, and investigate cell populations of medium spiny neurons (MSNs) and interneurons.

Results: Neuroanatomical delineation of the XDP striatal compartments, through enkephalin, DARPP-32, and $GABA_A$ receptor β2/3 subunit immunolabelling, revealed "patches" of enhanced immunoreactivity which are likely to be preserved striosomes, rather than preserved matrix. Furthermore, calbindin expression, typically localised to the matrix, appeared to be upregulated within striosomal "patches" of the XDP striatum, suggesting pathological restructuring of the striosomal and matrix sub-compartments in XDP. At the cellular level, the XDP striatum presented with selective neuronal vulnerability, as indicated by > 50% loss of both calbindin+ MSNs and choline acetyltransferase+ (ChAT) interneurons in both the XDP caudate nucleus and putamen. Furthermore, morphological analysis of $ChAT^+$ interneurons indicates a disruption in cellular

morphology within the XDP cohort, evidenced by a reduction in somal size and number of processes.

Conclusion: This study is part of an ongoing investigation to elucidate the neurochemical and phenotypical dysfunction of the human XDP striatum. This study will extend to key outputs of the striatum and other basal ganglia nuclei to understand the XDP neuropathology, to identify potential targets for future therapeutic strategies.

O99: Haemovigilance in New Zealand

M Smith[1]

[1]*New Zealand Blood Service*

This presentation will delve into some of the history of haemovigilance and examine why it is important. We will clarify the scope of haemovigilance, which is wider than many realise.

We will also take a look at some of the areas where NZ has made safety improvements and highlight areas for focus going forward.

O100: Operation Deans - DVI Response to Christchurch Mass Shooting

S Stables[1]

[1]*Te Toka Tumai LabPlus*

On Friday 15th March 2019, a lone gunman entered two mosques in Christchurch committing New Zealand's worst mass murder which resulted in the deaths of 51 people. The offender was quickly apprehended, and he eventually pled guilty to 51 counts of murder, 40 counts of attempted murder and one charge of committing a terrorist act. This presentation will detail how the mass fatality response to this tragedy was conducted, and how this operation was adapted to ensure the victims were returned to their families as soon as possible so that the religious requirements of the deceased and their families could be honoured.

O101: Primary spinal epidermal lymphoma – a case report with flow cytometry confirmation

T Taylor[1]

[1]*Southern Community Laboratories*

Primary spinal epidural lymphomas (PSEL) are a rare finding and seldom reported in the literature. A rare case of PSEL is described that presented with a T12/L1/L2 mass causing neurological weakness due to spinal cord compression. A soft tissue biopsy from the epidural space submitted for flow cytometry revealed the presence of a clonal B-cell population. Although spinal epidural lymphomas can occur in up to 2.8% of B-cell lymphoma cases, the occurrence of a genuine PSEL case is significantly rarer. The histological and flow cytometry findings confirmed B-cell Non-Hodgkin's Lymphoma (NHL) involvement within the epidural cavity without tumour involvement within the Lumber vertebrae or external soft tissue. The immediate patient care involved tumour shrinkage to restore neurological function and targeted radiotherapy and chemotherapy to suppress further tumour expansion.

Key words: ***non-Hodgkin's lymphoma, spinal epidural lymphoma, flow, cytometry, neurological function***

O102: Pathology workforce for the future - the role of the NZIMLS

T Taylor[1]

[1]*New Zealand Institute of Medical Laboratory Science*

This presentation will look at the Te Whatu Ora workforce plan from a professional perspective.

O103: NSWHP Clinical Scientist Training Programme

V Thomson[1]

[1]*NSW Health Pathology*

In 2018 NPAAC introduced the term Clinical Scientist in the updated publication '*Requirements for the Supervision in the Clinical Governance of Medical Pathology Laboratories*'. The RCPA followed with a position statement in 2019 on the definition and role of a Clinical Scientist.

Pathologist workforce shortages particularly in Chemical Pathology, Genetic Pathology and Immunopathology introduced a conversation in NSW Health Pathology to establish a Clinical Scientist trainee programme, with the aim to support clinical governance of the over 60 public laboratories across the state of NSW and succession planning in sub-specialty areas.

The RCPA Faculty of Science was founded in 2009 to train and develop a career path for senior Scientists working within the field of pathology and developed a Fellowship of the Faculty of Science by examination. This qualification is one of several qualifications defining a Clinical Scientist.

This presentation will outline the Clinical Scientist

trainee programme established at NSW Health Pathology in 2019, with a preference for studying the RCPA Fellowship of the Faculty of Science by examination.

O104: Virtual Microscopy Pilot Project

V Thomson[1]

[1]*NSW Health Pathology*

NSW Health Pathology has 62 medical pathology laboratories in 15 Local Health Districts, spanning a state of almost 810,000 km^2 and a population of over 8 million. Tweed Heads is 8.5 hours north of Sydney, Broken Hill 13 hours west and Deniliquin 8 hours southwest of Sydney. Couriers do not always operate everyday and only about 80% of laboratories perform blood cell morphology onsite.

In 2019 NSW Health Pathology commenced a program to replace aging haematology FBC analysers across the state with one standard brand, implementation of standard middleware and then implementation of Cellavision digital morphology at three pilot sites. The DM9600 was implemented at John Hunter hospital laboratory, DM1200 at Coffs Harbour laboratory and the small DC-1 at Kempsey laboratory. The analysers use artificial intelligence to classify images, and the scanners contain high-precision mechanics and advanced imaging solutions. All three scanners use the same software ensuring ease of use, can be connected in a networked environment, enabling images to be shifted between sites for remote review and an advanced RBC module is also available. An online academy is available, an education platform offering a range of training resources for beginners to advanced practitioners, as well an online proficiency software for internal competency assessment and training of staff.

This presentation will outline the process of setting up the systems, benefits, and limitations of performing morphology in a digital environment.

O105: Intra-individual variability of volunteer response to anti-D sensitised red blood cells in the Monocyte monolayer assay (MMA)

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[3]*Faculty of Health, Queensland University of Technology, Brisbane, Queensland, Australia*

Objective

A complication of pregnancy and/or transfusion is development of antibodies to red blood cell (RBC) antigens. When these RBC-antibodies are of clinical significance the result is often life-threatening transfusion reactions. Due to the difficulty in finding compatible (antigen-negative) RBC units, the monocyte monolayer assay (MMA) is a useful tool to investigate and predict whether antigen-positive RBCs will be safe to transfuse. This study evaluated variation in responses to anti-D sensitised RBCs that serve as a positive control in the MMA.

Methods

Whole blood was collected from healthy volunteers and peripheral blood mononuclear cells (PBMC) were isolated using Sepmate ficoll density gradient tubes (Stemcell Technologies). Monocytes from isolated PBMCs were incubated with RBCs sensitised with anti-D plasma (1 hour, 37°C, 5% CO_2). The monocytic index (MI%) (the proportion of monocytes with phagocytosed or adherent RBC) was calculated after microscopic analysis. Monocytes from eight different individuals were collected multiple times (n=2-4) and used in separate MMAs.

Results

Based on a 20% MI as a cut off for the anti-D sensitised RBC, four individuals in separate MMAs had %MI less than 20. Three volunteers had responses less than the cut off with results being less than 10% MI. Volunteer 1 showed the biggest variation with a range of 1.64-33.5 MI%.

Conclusions

Individual-to-individual and changes in responsiveness at different times affect the outcome of the testing in the MMA. Pooling of 2 or more individuals' monocytes may mitigate a low response; however, for reliable MMA testing development of a panel of individuals who provide consistent responses is desirable. Investigation of techniques for evaluation of the response other than a direct read of phagocytosis/ adherence may provide more consistent results with lower individual-to-individual variation.

O106: A better nights' sleep – by Integration of an Electronic Witnessing System into our Embryology Laboratory

L van Maanen[1]

[1]*Repromed Auckland*

Preventing the mismatching of samples during assisted reproductive treatments, is critical to the safe management of client's gametes and embryos. History has shown, such errors are catastrophic to all individuals involved which is thus a huge responsibility and constant source of stress for embryologists and their lab managers.

The requirement to double witness each individual movement of eggs, sperm and embryos between tubes, dishes, and devices, became mandatory in Australasian clinics in 1998. These manual witnessing steps, necessitate an additional staff member to essentially shadow an embryologist's every technical movement throughout the day. Theoretically the addition of this cumbersome and labour-intensive system was to eliminate mismatches, but the presence of human error remains (Rasouli *et al* 2021). The concept of automating witnessing steps was therefore an attractive option for many years, and there are now a range of sophisticated products on the market that utilise radio frequency or barcode scanning systems to do so.

This presentation explores the journey of our clinic with the implementation of an Electronic Witnessing System. We report, not only the challenges and benefits, but also the unexpected wealth of analytical capabilities that allows us to effortlessly measure KPIs that relate to workflow efficiency, technical compliance, trend analysis and comparative data for benchmarking against other service providers. Ensuring we are aware of potential pitfalls and gaps is also essential when utilizing any automated system. But at the end of the day, our Electronic Witnessing System has indeed provided us with a better nights' sleep.

O107: Time=Life

L Wang[1]

[1]*Te Whatu Ora Waitematā*

My topic is "Time = Life": master your time to master your life. My interest in this topic started with my teenage daughter. I wanted to help her manage her time well with her study. Then I found it also helped me with my own time management. I would like to share my study with everyone to make the most of your time to achieve the goals you set for yourself, and to live a meaningful life.

O108: Real World Point of Care Testing – The good, the bad and the downright messy

S Williams[1]

[1]*Te Whatu Ora Waitematā*

An interactive series of short talks based around real life results and patient outcomes from our primary and secondary care clinics/units that use POCT devices across Waitemata and the region. Different analysers will be highlighted along with some good and may be not so good things about them while reviewing actual patient results, trying to ascertain the clinical problem(s) and the actual outcomes that were observed.

Analysers included (but not limited to):

- Radiometer ABL Blood Gas Analyser
- Druker QBC Star Haematology/Diff Analyser
- Abbott iSTAT and iSTAT Alinity

O109: Clinical STEC in Aotearoa New Zealand, a significant endemic communicable disease: Current knowledge and future focus

J Wright[1]

[1]*Environmental Science and Research*

The Institute of Environmental Science and Research Limited (ESR) performs national reference and surveillance testing and administers the national communicable disease notification database on behalf of New Zealand's Ministry of Health. The New Zealand (NZ) surveillance case definition for disease caused by Shiga toxin-producing Escherichia coli (STEC) requires the detection of stx genes or isolation of an STEC in the presence of clinically compatible illness i.e., acute diarrhoea, haemolytic uraemic syndrome (HUS) or thrombotic thrombocytopaenia purpura (TTP). From 2015, culture independent diagnostic testing of faecal samples referred for microbiological analysis has been progressively introduced across NZ and currently > 85% of all faecal samples are routinely screened for stx genes. Whole genome sequencing (WGS) analysis for all STEC isolates confirmed at ESR became routine in 2019 and together, these technological advances have clarified both the full extent of STEC, and the specific types associated with this disease in NZ. In 2022 STEC was the third most common cause of bacterial diarrhoea in NZ with a case rate of 19.9 cases per 100,000 population.

O110: Glycosylated Ferritin

O Yi[1]

[1]*Te Whatu Ora Manukau*

Glycosylated ferritin (GF) is an in-house method developed on the Roche platform at Middlemore Hospital laboratory that is fully validated and accredited by IANZ. The method principle utilises the property of concanavalin A (a lectin) to bind glycosylated proteins.It is an useful tool in the investigation of hyperferritinaemia particularly in the diagnosis of adult onset Still's disease. It can also be useful in other disease such as haemophagocytic lymphohistiocytosis, hereditary hyperferritinaemia cataract syndrome and benign hyperferritinaemia. As we know from RCPA eQAP, there is a wide difference in ferritin results among different assay platforms. GF was measured on some of the eQAP samples as well as ferritin assay calibrators to see if the differences can be explained by the percentage of GF in these samples.

O111: Time travelling into the future of immunology: a glimpse of the new era of automation in immunofluorescence imaging

Z Yiu[1]

[1]*Labtests*

Imaging utilising the technologies of a computer-aided immunofluorescence microscope is the future of diagnostic laboratories in immunology. Immunoassay analysers specifically the EUROPattern Microscope Live and the EUROpattern Microscope facilitate the analysis and classification of immunoassay slides. The software programme has the ability to produce high-resolution immunofluorescent images which can be automatically classified by pattern recognition and calculation of antibody titre by deep-learning. Across the diagnostics panels, antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), autoimmune liver diseases, and antigen-expressing cells can be identified and titred by EUROpattern Classifier. In laboratories with high volumes of patient samples, automation plays a large role in facilitating work output and producing more accurate results with fewer human errors. Despite the advantages of automation, implementing new technologies should be considered in all aspects before integrating an automation system, while maintaining a proper balance between manual labour and operations.

P1: Awareness and health literacy of cervical cancer screening modalities amongst participants, in Auckland, New Zealand

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Objective

The World Health Organization (WHO) estimates high-risk Human Papillomavirus (hrHPV)-associated cervical cancer (CxCa) is the 2nd most common cancer in women aged 15-44 consequently, launched a campaign for CxCa elimination by 2030 [1]. In New Zealand (NZ), CxCa prevention practices are based on a 3-yearly cytology screening model using the Papanicolaou (Pap) test through cytology-based platforms since 1990, this model has resulted in 50% reductions in the incidence of CxCa in women aged 20-69 relative to increasing incidence of cervical precancers in women aged 20-24 from 1985 to 2013 [2]. Commencing in July 2023, exclusively 5-yearly molecular primary hrHPV screening will become available for women aged 25-69 with a self-sampling option [3].

Hypothesis

There is comparable awareness and literacy of CxCa *between Nationalities and Genders*.

Aim

Conduct awareness-assessment-surveys (AAS) for gaps in CxCa and hrHPV association.

Methods

The study methodology was based on cross-sectional awareness-assessment- surveys (AAS) for CxCa and hr-HPV association knowledge and literacy of anonymised data to prepare this research from two Medical Centres in Auckland City; Tamaki Health Clinic (March-October 2020) and Browns Bay Family Doctors (October 2020-January 2021).

Results

Independent-Samples-Mann-Whitney-U (ISMWU) tests revealed no statistical significance (p=0.347) between literacy and Nationality of 302 participants: 219 (72.8%)

NZ, 82 (27.2%) Other; however, revealed significance (p=0.000) between literacy and Gender: 242/301 (80.4%) Women, 59/301 (16.6%) Men. Chi-Square testing revealed significant literacy of CxCa and hrHPV association in younger age-groups (p=0.000): 15-20[13/301(4.3%)] but lower literacy for 20-29 [69/301(22.8%)].

Conclusions

Study participants aged 20-29 revealed significantly lower literacy of CxCa exclusive of Nationality. Therefore, with imminent introduction of primary hrHPV CxCa screening in women aged 25-69 in NZ, health literacy initiatives should ideally target younger ages (i.e., 15-25) to optimize CxCa prevention in NZ, and WHO campaigns.

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P2: Where The Sun Doesn't Shine – A Case Report

T Arroyo[1], R Beazley[1]

[1]*Pathlab Waikato*

A 55-year old male presented with a 4 week history of a black lump on the perimeatal area. Based on clinical presentation a differential diagnosis of melanoma or hemangioma was given. The initial sample from an incisional biopsy concluded a mucosal malignant melanoma diagnosis. Subsequent margin clearance biopsies were then retrieved. Routine histology staining using haematoxylin & eosin was used in conjunction with three immunohistochemistry antibodies (SOX10, Melan-A, & Ki-67) to aid in accurate diagnosis. Melanoma is the most common skin cancer in New Zealand, and is caused by a pigment known as melanin.[1] One of the rarest forms of melanoma found in the distal urethra is discussed further in this case report. Mucosal malignant melanoma involves organs not commonly exposed to UV rays, thus making diagnosis very rare. Furthermore, diagnosis is primarily achieved in the advanced stages resulting in poor clinical outcomes and prognosis.[2]

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P3: Usefulness of the Sysmex XN-2000 Body-Fluid HF-BF Panel to Detect Early Malignancy in Pleural Fluid and Ascites Fluid

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[1]*University of Otago, Dunedin, New Zealand*

[2]*Southern Community Laboratories, Dunedin, New Zealand*

Objectives

The microscopic examination and cellular analysis of body fluids (BFs) is critical for accurately diagnosing many diseases. BF cell counts have previously been performed manually, but automation allows for faster and more accurate analysis. The BF mode on the haematology analyser, Sysmex XN-2000, differentiates cells into polymorphonuclear and mononuclear white blood cells (WBC) and high-fluorescent cells (HFC). The aim of this study is to evaluate the performance of HFC in the detection of malignant cells in pleural and ascites fluid, and to establish a cut-off value to aid in the early diagnosis of malignancy.

Methods

A total of 200 BF samples, including 42 malignant, from preceding years were reviewed to establish a cut-off value to investigate. Samples received during the permitted time frame were analysed on the Sysmex XN-2000, and if greater than the established cut-off of 4.2/100WBC, were sent to cytology for manual microscopy.

Results

In pleural and ascites fluids, malignant cells were not detected by cytological microscopic examination in all samples that were received over the data collection period.

Conclusion

In conclusion, the BF mode on the Sysmex XN could be an alternative method for BF cell counts, with the HF-

BF parameter acting as a screening tool to determine whether samples require further investigation by microscopy, but has its limitations. Therefore, in cases where the concentration of HF-BF is greater than the cut-off, or there is clinical suspicion of malignancy, additional microscopic review will be required.

P4: Verification of serum free light chain quantitation and a new reference interval for freelite assay on the Optilite turbidimeter. (The Binding Site)

B Chan[1], B Li[1,2], C Rollo[1]

[1]*Protein Chemistry, Canterbury Health Laboratories*

[2]*Department of Pathology, University of Otago*

Overview

Canterbury Health Laboratories currently quantitate serum free light chains (sFLC) on the BNII nephelometer (Siemens), however in certain patients with high SFLC levels, the analyser is unable to detect antigen excess and the serum reference interval used for SFLC is based on a single assay method (Freelite assay) and instrument (BNII nephelometer), established by Katzmann *et al*. Method comparison and verification of a recently established diagnostic range by Morales-Garcia *et al* measured on the Optilite turbidimeter was performed to determine if it could be a more suitable alternative and verify if the new diagnostic range should be adopted.

Method

93 patient serum samples and 7 RCPAQAP samples were selected to be analysed on the Optilite turbidimeter. The SFLC concentration were compared to the Siemens BNII nephelometer. 21 patient serum samples, with no demonstratable renal impairment, inflammation and no paraprotein on serum protein electrophoresis (SPE) were selected to verify the reference interval established by Morales-Garcia *et al*. A Box and Whisker distribution and Passing-Bablok regression plots were produced using MedCalc software.

Results

The Passing-Bablok regression for kappa and lambda (mg/L) showed a systematic and analytical difference between analysers. (kappa y= -0.497+0.941x and lambda y= -0.108+0.980x). The Kappa/Lambda FLC ratio for the 21 patient serum samples was within the established diagnostic range by Morales-Garcia *et al* (0.65-2.56 mg/L) and 6/21 were outside the diagnostic range established by Katzmann et al. (0.26-1.65 mg/L).

Conclusion

The Optilite turbidimeter and the BNII nephelometer SFLC quantitation were comparable and any variation were not clinically significant and did not change the reporting outcome. Optilite turbidimeter was also able to detect antigen excess in patients not detected by BNII nephelometer. Verification study confirms the established diagnostic range by Morales-Garcia *et al*. Based on these findings, its recommend that all laboratories verify their own diagnostic range on the Optilite turbidimeter.

P5: Evaluation of BIOPHEN™ FVIII variant kit on STAR MAX 2®

S Jamati[1]

[1]*Waikato Hospital*

Introduction

Haemophilia A is a genetic disease occurring as a consequence of a genomic defect in the long arm of the X chromosome, causing in a deficiency of factor VIII (FVIII). The majority of cases are sex linked but, approximately 30% of haemophilia arise from de novo variants. (1) Treatment for haemophilia A traditionally involved replacing FVIII with recombinant products. (2) Emicizumab (Hemlibra) is a humanized bispecific antibody designed to imitate the role of factor VIII and bind activated factor IX and factor X together to continue the coagulation cascade. (3) The benefit of Emicizumab is the prevention or reduction of the frequency of bleeding episodes. However it interferes with the Activated partial thromboplastin time (APTT), 1-stage factor assays and Bethesda assays (clotting-based) for FVIII inhibitor titres. The interference causes an overestimation of clotting results (4).

Objective

Evaluate the BIOPHEN™ Factor VIII variant kit (bovine) against the BIOPHEN™ FVIII: C kit (human) for the purpose of introducing the BIOPHEN™ Factor VIII variant kit for patients on emicizumab.

Method

Patient samples were drawn in 3.2% sodium citrate tubes. 50 patient samples from those with no known bleeding disorder, haemophilic A (severe, moderate or mild), von Willebrand disease (acquired or congenital) were analysed. A further 8 external quality control vials from RCPA were analysed. Samples had a FVIII Chromogenic assay using the BIOPHEN™ Factor VIII variant kit and the BIOPHEN™ FVIII: C kit performed in parallel. Precision studies were run on BIOPHEN™ Factor VIII variant kit.

The Reference Interval (RI) was established using 50 healthy donors collected from New Zealand Blood Service. Each donor sample had a chromogenic FVIII run using the BIOPHEN™ Factor VIII variant kit.

Results

Pearson Correlation was 0.99 between the BIOPHEN™ Factor VIII variant kit and the BIOPHEN™ FVIII: C kit in patients who were not on emicizumab. The hypothesized mean difference of the kits was 0.

Conclusion

The Pearson correlation showed excellent association between BIOPHEN™ FVIII: C kit and BIOPHEN™ Factor VIII variant kit. Furthermore, the BIOPHEN™ FVIII: C kit measured both the FVIII and emicizumab while the BIOPHEN™ Factor VIII variant kit measured FVIII exclusively. A combination of both kits are required to quantitate emicizumab.

References

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Disclosure of interest statement

Roche Products (New Zealand) Limited provided support in the form of a grant for this assay validation. The assay validation was independently organized and Roche had no involvement in the design or validation process. The content and the clinical opinions expressed are those of the authors and may not reflect those of Roche.

P6: Haemoglobinopathy testing – A Lab's perspective. Is it a Needle in the Haystack?

V Mala[1]

[1]*Te Whatu Ora Waikato*

Objective

This poster is intended to raise awareness and provoke discussion around haemoglobinopathy testing in NZ hospital Labs. Identify processes and consider a national programme going forward.

Discussion

Haemoglobinopathy is not a National programme as NZ is not considered high risk. Currently DHB labs have their own separate processes in place for Haemoglobinopathy/thalassaemia as incidental findings. Some requests are clinician driven.

Discuss

Some of the important Haemoglobinopathies, thalassaemias and Sickle cell. Briefly discuss the local demographics, immigrant population and the risk of thalassaemia traits.

What are the implications of incidental findings for patients? National programme – is NZ ready? Is there a need? What will it look like from a Laboratory's point of view? Unnecessary testing and Iron deficiency – resources and responsibilities.

Is there a need for national standardisation going forward across Te Whatu Ora labs? "Red cell indices are suggestive of iron deficiency and or thalassaemia. Further studies are recommended, exclude iron deficiency before testing for thalassaemia" Is anyone taking note?

Does it need to be GP/PHO driven requests? What if there's no GP? Patients coming through ED – what about these?

These are some of the questions and discussions to be had on the poster. I will present some statistics, information and references but mostly intending to would be interested to see what laboratory processes are, and the future of Haemoglobinopathy testing from the attendees of the conference.

P7: A case of *Aggregatibacter aphrophilus* in the bloodstream

M Patel[1]

[1]*Auckland University of Technology*

A 46-year-old male had a case of *Aggregatibacter aphrophilus* (*A. aphrophilus*) in the bloodstream. The patient had a history of asymptomatic small membranous ventricular septal defect and mild aortic regurgitation, which increased the risk of infective endocarditis due to *A. aphrophilus*. The organism is difficult to visualize in the direct examination of blood cultures; as a result, multiple attempts were required to directly examine the organism in gram stains. Matrix-Assisted-Laser-Desorption-Ionisation-Time-of-Flight (MALDI-TOF) identified the organism as *Aggregatibacter* (*Haemophilus*) *aphrophilus comb.nov* with 99% accuracy. Guidelines from the European Committee for Antimicrobial Susceptibility Testing (EUCAST) are used for determining the antimicrobial susceptibility of organisms; however, as there were no guidelines for *A. aphrophilus*, the minimum inhibitory concentrations for penicillin and ciprofloxacin were determined. This led to directed therapy of oral augmentin and ciprofloxacin for three weeks to be given. The patient was also given a transthoracic echocardiogram to check for infective endocarditis, which was negative for any heart valve damage.

P8: Coeliac Disease – A Case Study

V Wales[1]

[1]*Auckland University of Technology*

Coeliac disease is an intestinal reaction to dietary gluten. The disease affects the cells lining the small bowel. It can be managed by gluten-free diet intake. However, some individuals do not respond well to the diet.

P9: Determining the Optimal Input DNA Concentration Range for AmpFLSTR® Identifier™ Assay

H Ward-Hayes[1], A Dixon-McIver[2]

[1]*University of Otago, Dunedin, New Zealand*

[2]*Igenz, Auckland, New Zealand*

Objective

Forty randomly selected buccal swabs were retrospectively analysed to determine an optimal DNA concentration range for the AmpFLSTR Identifiler assay to generate complete DNA profiles.

Method

DNA profiles obtained from the samples previously run using the AmpFLSTR Identifiler assay, were categorised as Passed (obtained a complete profile), Rerun (required a rerun with adjusted test parameters to obtaining a complete profile) or Fail (where no or an incomplete profile was obtained). DNA concentration was quantified on the QUBIT and quality was assessed on the Nanodrop to determine an optimal range which would reduce the number of re-runs and fails. Other factors such as sex, age and collection location were also examined to determine if they affect the DNA profile outcome.

Results

The existing protocol using a standard 1 in 15 dilution had a 62.5% pass rate, along with 20% Rerun rate and 17.5% Fail rate. DNA concentration ranged from 0.263 ng/uL to 6.54 ng/uL with no clear correlation between DNA concentration and the ability to yield a complete DNA profile. Quality was assessed using absorbance ratios 260/280 and 260/230, and values between 1.08 and 1.88 and 0.25 to 1.07 were obtained, respectively. Again, with no correlation to pass rates. There was also no correlation to pass rate between age, sex or collection location found.

Conclusion

This investigation found there was no optimal DNA concentration range which could be implemented to reduce the number of failed samples and in turn to reduce cost and time to generate a complete profile and obtain a result for the client. Collection location, age and sex did not appear to have an impact on pass/failure rate.


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Journal-based CPD No. 94
Page 1 of 2

Questions relating to the article *'Evolution of viscoelastic haemostatic assays'* at page 153 of this issue.

1.	Viscoelastic haemostatic assays (VHA) results are based on whole blood coagulation.	True/False
2.	Haemostasis is the body's physiological mechanism that leads to the prevention and cessation of bleeding from a blood vessel.	True/False
3.	If plasma fibrinogen levels are high, a clot with sufficient firmness and quality cannot be formed.	True/False
4.	Fibrinogen assays can be used to investigate a prolonged PT or aPTT.	True/False
5.	A measurement in VHA is the observation of the transition from a viscous to elastic state and the measurement of the shear elastic modulus.	True/False
6.	The strength of the clot is determined by the interaction of platelets, fibrinogen and FXIII.	True/False
7.	The most recent European Guideline on management of major bleeding and coagulopathy following trauma recommends VHA methods can be used for early and frequent monitoring of haemostasis.	True/False
8.	Next generation VHA devices have exchanged pipetting of blood samples to cartridge technology.	True/False
9.	TEG® 5000 and ROTEM® Sigma are examples of first generation VHA devices.	True/False
10.	A lack of standardisation across institutions and devices is a limitation of VHA devices.	True/False

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Journal-based CPD No. 95
Page 2 of 2

Questions relating to the article '*Acute mast cell leukaemia case study*' at page 178 of this issue.

1.	Mast cell leukaemia is a common subtype of systemic mastocytosis.	True/False
2.	Systemic mastocytosis has an estimated incidence rate of 13 cases per 10,000 people.	True/False
3.	A mastocytosis is a clonal proliferation of mast cells in one or more organs.	True/False
4.	The acute form of mast cell leukaemia develops rapidly and aggressively, resulting in massive organ damage.	True/False
5.	A diagnosis of systemic mastocytosis is confirmed by the presence of mast cell infiltration, most commonly in the bone marrow.	True/False
6.	The presence of systemic mastocytosis diagnostic criteria and at least 20% atypical/immature mast cells in a bone marrow is required for diagnosis of MCL as defined by the World Health Organization in 2022.	True/False
7.	*KIT* D816V mutation was not detected in this study.	True/False
8.	Acute MCL must meet the criteria for SM and organ function impairment, plus leukemic involvement of the bone marrow.	True/False
9.	Atypical mast cells are classified into three subtypes; atypical mast cells I, II and III.	True/False
10.	Acute mast cell leukaemia has a significantly worse prognosis than other subtypes of SM.	True/False

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Articles should be submitted in electronic format to programs@aims.org.au. If an article is too large to be submitted by email, it should be submitted on an or USB stick.

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The abstract should be approximately 150 words and should make sense when read alone or in conjunction with the article. The abstract should be a concise overview that describes the important details of the article including the purpose of the study/investigation, basic procedures (study subjects/experimental animals/observational and analytic methods) and the results and principal conclusions. New and important aspects of the work and its implications may also be included. References should not be included.

Three to ten keywords may be listed. Authors are advised to comply with the terms from the Medical Subject Headings (MeSH) list from Index Medicus (see http://www.nlm.nih.gov/mesh/). Keywords should be given below the Abstract.

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The style of writing should conform to acceptable English usage. Do not use slang, medical jargon or unnecessary abbreviations. Accepted spelling is the first choice given in the latest edition of the Macquarie Dictionary.

Wherever possible, observational or experimental articles should be divided into sections headed:

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- Materials and methods
- Results
- Discussion
- References

For other types of articles such as commentaries, reports and reviews, use an appropriate format or consult the Editors for guidance. Do not include a separate section for conclusions, these should be given in the discussion.

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Clearly state the purpose of the article leading the reader from the known to the unknown. Summarise the rationale for the study and state the question to be answered as appropriate. Give only strictly pertinent references, and do not review the subject extensively.

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Present the materials and methods in a logical sequence. Describe the selection of the observational or experimental subjects (patients or experimental animals, including controls) clearly. Notification of ethics approval must be given where relevant. Identify the methods, apparatus and procedures in sufficient detail to allow other workers to reproduce the results. Give references to established methods, including statistical methods. Adequately describe new or substantially modified methods. Identify precisely all drugs and chemicals used, including generic name(s), dosage(s), and route(s) of administration. Do not identify patients or hospitals without consent.

Results

Present the results in the same sequence as given in the Materials and methods; use tables and illustrations where these will help the reader understand the work being presented. Do not repeat in the text all the data in the tables or illustrations.

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Indicate the new and important aspects of the study and emphasise the conclusions that follow. Do not repeat in detail data given in the Results section and do not add new data. Include in the Discussion the implications of the findings and their limitations and compare the observations to other relevant studies. Recommendations may be included if appropriate. Link the conclusions with the goals of the study and answer the experimental question stated in the Introduction. However, avoid unqualified statements and conclusions not completely supported by your data. Avoid claiming priority and alluding to work that has not been completed. State new hypotheses when warranted, but clearly label them as such.

Acknowledgements

Acknowledge individuals who have made substantial contributions to the study including technical work and financial support. Authors are responsible for obtaining consent from all the individuals acknowledged by name as inclusion may be interpreted as an endorsement of the article's contents.

References

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Throughout the body of the manuscript cite the author/s name and the publication year in parentheses as in the following examples:

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Online documents:

National Center for Biotechnology Information. OMIM: online Mendelian inheritance in man. http://www.ncbi.nlm.nih.gov/omim. Accessed February 25, 2007.

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Number tables consecutively with Arabic numerals and supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes, not in headings. Explain in footnotes all non-standard abbreviations used in each table.

For footnotes, use the following symbols in this sequence:

* † ‡ § ¶ ** ††

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Colour illustrations may be submitted on a USB stick. Images should be scanned at a minimum of 300 dpi.

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Photomicrographs must have internal scale markers and the magnification must be stated. Symbols, arrows, or letters used in the photomicrographs should contrast with the background.

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Use only standard abbreviations (see list of commonly used abbreviations).

Avoid abbreviations in the title. The full term for which an abbreviation stands must precede its first use in the text unless it is a standard abbreviation for a unit of measurement.

Report measurements in the units in which the measurements were made. In most countries the International System of Units (SI) is standard.

Commonly used abbreviations

Abbreviation or Symbol	Standard Units of Measurement
g	gram
g	gravity
Hz	hertz
h	hour
IU	international unit
K	kelvin
kg	kilogram
L	liter, litre
m	meter, metre
min	min
M	molar
mL	millilitre
mol	mole
N	newton
nm	nanometre
p	probability
rpm	revolutions per min
s	second
wk	week
yr	year

Additional information

The following are useful sources of information. The first two publications are used by the AJMS as standard references.

Style Manual Committee. Council of Biology Editors. *Scientific style and format: the CBE manual for authors, editors, and publishers.* 6th ed. Cambridge University Press, 1994.

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Changes to Certification arrangements for the Medical Laboratory Science Profession

From April 2023, the Australian Council for the Certification of the Medical Laboratory Scientific Workforce (CMLS) Board are no longer accepting applications for certifications directly. Instead, professional bodies operating CMLS approved CPD schemes will be able to issue certification on behalf of the Council for their members who meet the requirements for certification as detailed on the CMLS website.

What this means for AIMS members utilising APACE

AIMS Members using the APACE scheme to track their professional development activities can now apply to be certified through the AIMS National Office.

AIMS National Office will now issue Certification to APACE users who have:

- Completed their required CPD activities;
- Been issued their APACE certificate;
- Provided a competency assessment signed by your employer **as part of your AIMS Membership**.

AIMS Members will have access to their APACE record and submission system in the AIMS Members' Area. To get started, follow the step-by-step guide detailed at: https://www.aims.org.au/apace/certification-cmls.

Why become Certified?

Your status as a certified medical laboratory professional is a public guarantee that you are qualified, competent, and continuing your professional development.

If you would like more information on Certification, contact the AIMS National Office via email at: programs@aims.org.au.

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The **Australian Journal of Medical Science** (AJMS) will consider for publication any paper relevant to the field of Medical Science.

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- Immunology
- Microbiology
- Molecular biology

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