PRCA. Differentiating benign causes from clonal haematological disorders is essential, and bone marrow examination may assist if no other apparent causes are identified.

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AN UPDATE ON THE IMMUNOPATHOLOGY OF IMMUNE THROMBOCYTOPENIA (ITP)

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Immune thrombocytopenia (ITP) is a bleeding disorder in which autoantibodies and/or cytotoxic T cells are directed against an individual's own platelets and/or megakaryocytes which leads to enhanced peripheral destruction and/or reduced bone marrow production, respectively. The cause of this disease is unknown and most research in ITP has concentrated on the characterisation of the anti-platelet autoantibodies. In the last 25 years, however, a relatively explosive body of research literature has arisen to shed new light on the complex immunopathogenesis of ITP. It is associated with three interrelated areas of autoimmunity pertaining to environmental, e.g., infectious influences, antigen presenting cell (APC) function and T cell abnormalities. It appears that the processes of apoptosis and deficiencies of CD4+ T regulatory cells are central events that lead to tolerance breakdown and induction of platelet autoimmunity. This lecture will update our understanding of the humoral and cell-mediated immunology of ITP and will highlight the recent literature which is beginning to suggest that platelets are not only the targets of autoimmune effector mechanisms but may actually control parts of the autoimmune pathogenesis suggesting the concept that the prey may become the predator.

WHAT HAEMATOLOGISTS NEED TO KNOW ABOUT VISCOELASTIC DEVICES IN BLEEDING PATIENTS

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The rationale for coagulation management in acute bleeding must be based on an understanding of the pathophysiological processes and functional assessment of the entire coagulation system leading to targeted replacement of platelets, fibrinogen and clotting factors or the use of anti-fibrinolytic agents. Standard coagulation assays such as prothrombin time and activated partial thromboplastin time are measures of clot initiation and do not test the entire cell based coagulation system only providing indirect correlation with the clinical picture in critical bleeding. Evidence is growing that viscoelastic assays, such as ROTEM or TEG are superior to standard coagulation tests in guiding critical bleeding coagulation management. ROTEM/TEG provides a quantitative global *in vitro* assessment of haemostasis with multiple end points reflecting the interaction between platelets, fibrinogen and clotting factors and fibrinolysis. The tests are

sensitive to qualitative and quantitative differences in the factors which influences clot generation and stability. Normal results in the presence of ongoing bleeding have a high negative predictive value of surgical bleeding rather than that associated with coagulopathy.

ROTEM/TEG provides useful tools for global assessment of haemostasis and hyperfibrinolysis and may be used to facilitate targeted, timely and appropriate use of blood components in trauma, surgical and obstetric patients.

UNFRACTIONATED HEPARIN MONITORING WITH ACTIVATED PARTIAL THROMBOPLASTIN TIME

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The activated partial thromboplastin time (APTT) is a global assay of coagulation initiated by the contact pathway and utilised for a variety of reasons, including screening for haemostasis or bleeding risk (e.g., 'haemophilia'). The APTT is also the current most utilised means of monitoring of unfractionated heparin (UH). In order to utilise the APTT for this purpose, the APTT reagent should be identified to be sensitive to UH, and show an upward 'linear' relationship according to UH concentration, particularly in the 'therapeutic range' (TR). The most common approach to establishing a TR for UH by APTT is to perform correlation studies against an anti-FXa assay and to identify the APTT range representing an UH level of 0.3–0.7 U/mL by anti-FXa,¹ with this anti-Xa range representing a common TR for UH.² There are many common pitfalls with this approach, including high variability in APTT according to anti-FXa according to individual variation, especially considering that anti-FXa testing represents a more discrete analyte compared to the global assay of APTT. Several additional confounders, including FXII deficiency and lupus anticoagulants, both not uncommon in patients on UH therapy, as well as many undefinable events, lead to poor correlation between APTT and anti-FXa.

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UNDERSTANDING THE PATHOPHYSIOLOGY OF TRANSFUSION-RELATED ACUTE LUNG INJURY (TRALI)

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Transfusion-related acute lung injury (TRALI) is characterised by the onset of respiratory distress and acute lung injury within 6