

**P030**

## Six Patients with Acquired Haemophilia A Successfully Treated with Rituximab

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### Introduction

To describe six patients with acquired haemophilia A treated successfully with Rituximab in South Australia.

### Method

Clinical information was provided by the treating physicians, and both treatment modalities and responses were correlated with laboratory results.

### Results

Six patients (5 females, 1 male) with median age 62.5 years (range 24-84) presented with prolonged median APTT 83.5s (range 62 to 99). Four patients had inhibitor titre between 10-12 BU/ml; another two patients 16.5 and 460 BU/ml; the median baseline FVIII was 0.04 iu/ml (range <0.01 to 0.18). All patients presented with bleeding, predominantly mucocutaneous bleed, one patient had muscle bleed which was initially diagnosed as deep venous thrombosis. One patient had recurrent retroperitoneal bleed. All bleeds were treated with recombinant VIIa, maximum cost was \$752,652 incurred for retroperitoneal bleeding.

	Type of Bleed	Etiology	Rx for AH
46F	retroperitonealX2	Myasthenia	pred+ivlg+ Rituximab +azathioprine
24F	muscle,	post-partum	Pred, Rituximab
78M	mucocutaneous	lymphoma	Rituximab combination chemo
45F	DVT, muscle	idiopathic	pred, ivlg, Rituximab
84F	haematuria,haemathrosis	idiopathic	pred,cyclo,Rituximab
83F	mucocutaneous, muscle	idiopathic	Pred, Azathio, ivlg, cyclo,Rituximab

Rituximab was used as second/third line agent after immunosuppressive and cytotoxic agents in four patients with recurrent bleeding/relapse, and intolerant of steroid; three also had immunoglobulin as an adjuvant treatment. One patient had Rituximab up-front because of underlying lymphoproliferative disease. All six patients achieved complete remission following Rituximab therapy.

### Conclusion

Monoclonal anti-CD20 antibody (Rituximab) treatment is used in lymphoma and autoimmune disorder such as Rheumatoid Arthritis. Acquired haemophilia A is a rare acquired bleeding disorder with auto-antibodies to FVIII, and Rituximab is currently being used for refractory/relapsed cases, rather than up-front because of its cost, however it would be cost-effective for antibody eradication in patients with high titre inhibitor or major bleed on presentation given the significantly higher cost of bypassing agent such as recombinant FVIIa to treat life-threatening bleeding.

*No conflict of interest declared*

P031

## **Analysis of Blood Product Management and Outcome in Patients Having Massive Blood Transfusion in a Tertiary Hospital - A Retrospective Study**

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### **Aim**

Massive blood transfusion (MBT) is arbitrarily defined as the replacement of more than one blood volume within a 24 hour period. A retrospective study was performed at Liverpool Hospital, NSW, to determine the clinical aspects, transfusion practices and mortality in patients who had MBT from October 2007 to March 2009.

### **Methods**

Patients who were transfused  $\geq 10$  packed red cells in a 24-hour period were included in the study. Demographics, clinical details, lab parameters and number and type of blood products given during the 24 hours of MBT were collected on all the patients. Standard methods were used for statistical analyses.

### **Results**

There were 72 MBT episodes, one third of which were associated with cardiac surgery. Based on the underlying conditions for MBT, three groups were identified: - surgery: 52%, spontaneous bleeds: 28% and major trauma: 20%. The number of blood components transfused and recombinant FVIIa used in the three groups were not significantly different, but a higher platelet/PRBC transfusion ratio was observed in surgical patients. The overall mortality was 30.5% and was lowest in surgical (24%) and highest in trauma patients (50%). A significantly higher number of PRBCs (P value: 0.0004). and FFPs transfusions (P value: 0.026) with lower platelet/PRBC ratio was seen in patients who died (P value: 0.018). The FFP/PRBC ratio was not significantly different between the patients who survived and died (P value: 0.33). Mortality was highest in the group of patients who received more than 30 units of packed cells in 24 hours. The total number of packed red cells used in these 72 patients in 24 hr period was 7.5% of the total PRBCs used in the hospital in the 18 month period. Total FFP units, platelets, cryoprecipitates used were 16%, 8% and 37% of the total and overall the total blood products used in these patients were approximately 11 % of the blood products used in the 18 month period in Liverpool hospital.

### **Conclusion**

Patients with MBT used approximately 11% of the total hospital blood products in the same period thereby imposing a considerable strain on the blood resources. Prospective studies with a larger number of patients are required to determine the optimal blood product ratios and efficacy of rVIIa in patients with massive blood loss.

*No conflict of interest to disclose*

A263

**P032**

## **Thromboprophylaxis, Just Do It. The Peter Mac Experience**

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### **Introduction**

Venous thromboembolism (VTE) is the commonest cause of preventable deaths in hospitalized patients. It is also a major complication of cancer, occurring in 4%-20% of patients and is one of the leading causes of death in cancer patients. Despite an insurmountable body of scientific literature over 50 years supporting thromboprophylaxis, it remains grossly underutilised. Studies have shown that multiple strategies are required to increase the rates of thromboprophylaxis assessment and prescribing.

### **Aim**

To assess and improve thromboprophylaxis rates in medical and surgical inpatients at the Peter MacCallum Cancer Centre.

### **Method**

We employed a multi-interventional approach comprising:

- Audit and feedback thromboprophylaxis rates in hospitalized patients pre implementation of mandatory VTE risk assessment on all inpatients.
- Introduce a simple hospital thromboprophylaxis guideline
- Introduce a mandatory thromboprophylaxis tool requiring assessment and/or prescription on all inpatient hospital drug charts, including rewritten charts.
- Develop & distribute a thromboprophylaxis education booklet
- Raise awareness through a hospital education campaign including a grand round
- Follow up audit to assess efficacy of interventions

### **Results**

Our preintervention cohort comprised 212 patients, 17 receiving therapeutic anticoagulation were excluded. 117 patients were male. 81 (38%) were surgical patients. All tumour streams were represented with the exclusion of haematological malignancies. 91/195 evaluable (47%) had thromboprophylaxis prescribed, 52% in surgical patients and 37 % in medical patients. LMWH was the treatment prescribed in 91% of cases, unfractionated heparin in 9%. 19/104 receiving no pharmacological thromboprophylaxis were prescribed TED stockings. The post intervention audit is currently in progress with preliminary results showing significant improvement in thromboprophylaxis prescription rate in the surgical, and a modest increase in medical patients.

### **Conclusion**

Thromboprophylaxis rates were congruent with recent literature and were suboptimal for both medical and surgical inpatients. Multiple and mandatory tools or systems are required for tackling this pivotal issue.

*No conflicts of interest to declare*

P033

## Use of Factor VIII Inhibitor Bypassing Agents in Bleeds Due to High Titre FVIII Inhibitors. Which Agent to Use? Three Cases Illustrating Treatment Decisions

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### Aims

In high titre FVIII inhibitors the decision to use either FVIII bypassing agents rFVIIa (NovoSeven: Novo Nordisk) and aPCC (FEIBA: Baxter) depends on the severity of bleed and response to initial therapy. We conducted a retrospective analysis of patients presenting with bleeding and Factor VIII inhibitors to assess the efficacy of recombinant Factor VIII and FEIBA.

### Methods/Results

Patient 1: 54 year old male bled after gum biopsy and developed a deltoid haematoma due to a FVIII inhibitor. There was a minor response to 4 doses of rFVIIa. Immediate improvement in the gum bleed and shoulder haematoma occurred after aPCC. Six months later he developed a haematoma in the left ankle (concurrent with a rise in FVIII inhibitor) which resolved after a single dose of rFVIIa 270mcg/kg. Two days later the haematoma progressed and responded to aPCC.

Patient 2: 59 year old male with mild haemophilia A presented with a tense haematoma in the right upper arm causing ulnar neuropathy. Factor VIII 26% and inhibitor screen was negative. He was treated with rFVIII responding over 7 days when inhibitors were detected (66 BU/ml): rFVIII was ceased and aPCC was administered. This was associated with further improvement in the haematoma and neuropathy.

Patient 3: 41 yr male with mild haemophilia A required surgical decompression for a spontaneous intracranial bleed under cover of recombinant Factor VIII. Further surgery was required after 6 months. Four weeks later he presented with haematuria: FVIII inhibitor 0.9 BU/ml rising to 14 BU/ml. Two doses of rFVIIa did not reduce the haematuria which settled after a single dose of aPCC.

### Conclusion

Each bleed is unique and requires individual management. Treatment decisions are required every 6-12 hours in the first 24 hours then daily depending on response which may require changing agents. Routine laboratory monitoring is not available for inhibitor bypass therapy although thrombin generation and thromboelastography may assess efficacy. Therefore regular clinical evaluation is critical for effective and economical use of expensive therapies.

*MFL received travel sponsorship from Novo Nordisk*

A265

**P034**

## **Retrieval Rate of Radiologically Inserted Filters**

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### **Aims**

To look at the retrieval rate of intravenous filters inserted following various indications.

### **Methods**

Retrospective review of filter insertions done at a single centre between 2005-2009.

### **Results**

Out of the 73 patients who had filter inserted, a major reason for filter insertion (in 46 cases) was because of contraindications to therapeutic anticoagulation. Out of these 46 patients: filters were successfully removed in 14 cases, filter removal was not attempted in 28 cases, in only one case filter removal was attempted unsuccessfully and outcome of three cases were unknown. Retrieval rate in this patient population was 32.55% (excluding the unknown). Filter insertion was carried out due to contraindications to prophylactic anticoagulation in seven patients; out of these five had it removed successfully. In three patients, filter was indicated because of failure of anticoagulation and none of them had it removed. The reason for filter insertion in six patients was chronic thromboembolic pulmonary hypertension and insertion was carried out to prevent further clots and none of these were removed. Five out of seven patients who had prophylactic placement of filter had it removed. Reasons for not attempting filter removal were: persisting indication (13), lack of follow up (9), patients who died within one month of insertion (7) and who died more than one month of insertion (8). The overall retrieval rate was 37.87%. There was no immediate complication related to filter insertion apart from failure to engage caval side wall in one case. Long term complications included IVC thrombus in two cases. Even after filter insertion, two patients were found to have new pulmonary embolism filter insertion.

### **Conclusions**

The overall retrieval rate in our cohort of patients was 37.87%. Reasons for not attempting retrieval include persisting indication and lack of follow up. Overall filter insertion appears to be a safe procedure.

*No conflict of interest to disclose*

P035

**Cyclical Thrombocytopenia and Neutropenia Associated with Rebound Thrombocytosis – A Case Report****David Connor**<sup>1</sup>, Joanne Joseph<sup>1,2</sup><sup>1</sup>*Department of Haematology, St Vincents Hospital, Sydney, NSW, Australia*<sup>2</sup>*University of New South Wales, Sydney, NSW, Australia*

Cyclical thrombocytopenia is an extremely rare condition characterised by periodic fluctuations in the platelet count. In some cases, rebound thrombocytosis may also occur. Here, we present a case of cyclical thrombocytopenia and neutropenia associated with rebound thrombocytosis in a 33 year old female originally considered to have immune thrombocytopenic purpura (ITP), but who failed to respond to typical ITP treatments including splenectomy.

Full blood count, serum luteinising and follicle stimulating hormones (LH, FSH), oestradiol, progesterone and C-reactive protein (CRP) levels were assayed 2-3 times per week for a total of 2 cycles. Reticulated platelets were also measured using flow cytometric analysis of thiazole orange staining of platelets. Serum samples were collected for performing thrombopoietin assays at a future date. The patient was not on any therapy designed to increase the platelet count during this period. Platelet count varied spontaneously from 8 to 1,249  $\times 10^9/L$  throughout a single cycle and cycle length was approximately 28 days duration. The patients platelet count was  $< 20 \times 10^9/L$  for a total of around 10 days. Each increase in platelet count was accompanied by an increase in the reticulated platelet count. The patient's neutrophil count also appeared to cycle, however the peak neutrophil count preceded the peak in the platelet count. The fluctuation in the neutrophil count was closely matched to serum CRP levels. Oestradiol levels also appeared to increase prior to the peak in platelet count.

The cyclical thrombocytopenia and neutropenia in this patient appear to be related to phases of the menstrual cycle. This may have potential therapeutic implications for this condition.

*No conflict of interest to disclose*

**P036**

## **Venous Thromboembolism During Autologous Stem Cell Transplantation for Haematological Malignancies**

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### **Aim**

To establish the risk of VTE during autologous stem cell transplant.

### **Method**

A retrospective review of all patients undergoing autologous stem cell transplant for haematological malignancies at our institution was undertaken to determine the incidence of radiologically confirmed symptomatic VTE and the presence of concurrent risk factors.

### **Results**

One hundred eighty four patients had follow up for at least one month following discharge and were included in the analysis. There were two deaths within the follow-up period (1 graft failure, 1 progressive disease). Non-Hodgkin lymphoma (NHL) and myeloma were the most common indications for transplant, with BEAM and melphalan, respectively the most common conditioning regimens. Twelve patients had a history of prior VTE, of whom three had pharmacological prophylaxis, which was withheld during severe thrombocytopenia in two cases.

A total of four (2.2%) patients had confirmed VTE. None had had a prior event. Three events were related to central venous catheters. Only one patient (0.5%) had a VTE not associated with a venous catheter, developing an above knee deep vein thrombosis after discharge. Two of 9 patients with peripherally inserted central catheters (PICC) developed catheter associated thrombosis, which was the only significant risk factor. No patients in this cohort had veno-occlusive disease of the liver.

### **Conclusion**

Autologous stem cell transplant with BEAM or melphalan has a low risk of venous thromboembolism. The use of PICC lines may carry a higher risk of thrombosis.

*No conflicts of interest to disclose*

P037

**Patients' Risk of Recurrent Venous Thromboembolism (VTE) is Associated with Hypercoagulable Overall Haemostatic Potential (OHP) Assay Results****Jennifer Curnow**<sup>1,3</sup>, Marie-Christine Morel-Kopp<sup>1,2</sup>, Ninfa Rojas<sup>1</sup>, Margaret Aboud<sup>1</sup> and Christopher Ward<sup>1,2</sup>*1 Northern Blood Research Centre, University of Sydney**2 Department of Haematology, Royal North Shore Hospital, Sydney NSW**3 Department of Haematology, Concord Repatriation General Hospital, Sydney, NSW, Australia*

The ability to stratify patients according to risk of recurrent VTE would improve the risk-benefit ratio for use of long term anticoagulation in individual patients. The use of global coagulation assays, such as the OHP, for this purpose, may also provide insights into the mechanisms of hypercoagulability. We aimed to determine whether OHP assay results either during, or on completion of, warfarin therapy, were predictive of recurrent VTE. We conducted a prospective cohort follow up study of 134 consecutive VTE patients, recruited at Royal North Shore hospital from July 2005 to May 2008. OHP assays, D-dimer and coagulation factors were performed in all patients whilst on warfarin. In a subgroup of 40 patients, assays were also performed one month after warfarin cessation. Median duration of follow up was 18 months. 53% (71/134) patients were male with mean age 48.6 years (range 19-85). 80% had proximal DVT or PE, with 80% events spontaneous. 61% patients had a thrombophilia. 56% (75/134) patients ceased warfarin during the study period. 11% (8/75) had a recurrent VTE. Risk of VTE recurrence was associated with a positive D-dimer (OR 1.43, CI 0.19-10.6), hypercoagulable OHP (OR 1.64 CI 0.3-9.0), elevated fibrin generation (OR 4.8, CI 0.26-90) and reduced fibrinolysis (OR 2.30 CI 0.17-30).

Even whilst patients remain anticoagulated, hypercoagulable OHP assay results may predict risk of recurrent VTE, if warfarin is subsequently ceased. Incorporation of OHP results into a clinical prediction rule for stratification of VTE recurrence risk, may assist in decisions regarding duration of anticoagulation in individual patients, and should be further investigated.

*No conflict of interest to disclose*

**P038**

## **The Pharmacogenetic Basis of Clopidogrel Resistance: CYP2C19 Genotype in a Suspected Myocardial Event Population**

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### **Aim**

Clopidogrel, a widely used anti-platelet agent for primary and secondary prevention of arterial thrombosis, is administered as a pro-drug. Clopidogrel is metabolised to its active metabolite by the hepatic cytochrome P450 2C19 (CYP2C19) enzyme. Recent studies demonstrate that single nucleotide polymorphisms (SNP's) in the CYP2C19 gene result in significantly reduced production of the active metabolite of clopidogrel (Hulot et al, *Blood*. 2006). Additional studies demonstrate that patients with CYP2C19 gene SNP's, including CYP2C19\*2, \*3, \*4 and \*5, have reduced production of the active metabolite of clopidogrel and increased coronary, cerebrovascular, and coronary stent thrombosis (Simon et al and Mega et al, *N Eng J Med*. 2009, Collet et al, *Lancet* 2009). We were interested in determining the CYP2C19\*2 allelic frequency in a population of patients presenting for assessment of a suspected myocardial event as these patients may be receiving or considered for anti-platelet therapy.

### **Method**

Non-identifiable patient samples referred to a pathology practice for troponin levels (n=99) were analysed. DNA was extracted from whole blood using the Roche Diagnostics Magnapure and CYP2C19 was genotyped using the Sequenom Massarray technology. CYP2C19 gene alleles studied were: CYP2C19: \*2, \*3 & \*17.

### **Result**

34% of patient samples were heterozygous for CYP2C19\*2 whilst 3% were homozygotes for CYP2C19\*2. In a sub-group of samples with an elevated troponin level (>0.05µg/L) (n=18) 55% were heterozygous for CYP2C19\*2 with no homozygotes detected.

### **Conclusion**

Our results highlight the significant prevalence of the CYP2C19\*2 deficient allele in patients assessed for a suspected myocardial event. Interestingly, consistent with a recent report regarding stent thrombosis (Giusti et al *Am J Cardiol* 2009), a high CYP2C19\*2 prevalence was noted in patients with confirmed cardiac damage. As cardiac patients may be receiving or considered for clopidogrel treatment determination of CYP2C19\*2 genotype may be of benefit in assessing the potential efficacy of therapy.

### **Conflict of Interest Statement**

*This research was supported by Gribbles Pathology, Melbourne, Victoria, Australia. The company provided genotyping results for this study.*

**P039****Genetic Screening for FVIII mutations in Haemophilia A Patients at Fremantle Hospital****Tracy Dixon**<sup>1</sup>, Tony Calogero<sup>1</sup>, Michael Leahy<sup>1</sup>, Ratna Dubey<sup>2</sup>, Barney Rudski<sup>3</sup>1. *Haematology, PathWest Laboratory Medicine WA Fremantle Hospital*2. *Molecular Genetics, PathWest Laboratory Medicine WA Princess Margaret Hospital*3. *Molecular Genetics, Institute of Medical and Veterinary Science, Adelaide.***Aim**

To screen all Haemophilia A patients attending the clinic at Fremantle Hospital in order to characterise the FVIII mutation responsible for the Haemophilia, and correlate this with the patient's phenotype

**Method**

To date 16 patients have had samples referred for genetic analysis. Initial screening for the Intron 22 inversion was undertaken at Pathwest, Princess Margaret Hospital via DNA extraction from peripheral blood leucocytes followed by PCR and southern blotting methodology.

Those found to be negative for the rearrangement were subsequently referred to the Institute of Medical and Veterinary Science for further investigations. PCR and direct sequencing of the DNA was then used to screen the entire coding region and splice junctions of the FVIII gene.

Further data analysis was undertaken, by screening of patient records and laboratory results.

**Results**

Out of 13 results received, 5 (38%) of patients were positive for the intron 22 rearrangement that is associated with severe Haemophilia A. 4 patients (31%) were found to have missense mutations in exons 1 (2), 7, 8 and correlate to mild disease. There was one instance of inhibitor formation in a patient having a mutation in exon 7. Of the remaining 4 patients, one possessed a nonsense mutation in exon 14 presenting as mild disease and the other 3 related patients were shown to have a frameshift mutation in exon 26. Clinically, a moderate to severe bleeding syndrome has resulted in these patients. 3 mutations that are described have not been previously reported on the HAMSTeRs database for FVIII mutations.

**Conclusion**

Isolation and characterisation of the FVIII gene defect in haemophilia A patients, although expensive, may be important for genetic counselling of affected patients and their family members. Further evaluation may be indicated to determine whether specific genotypes may be associated with certain phenotypes, including propensity to inhibitor formation.

*No conflict of interest to declare*

**A271**

**P040**

## **Aspirin for Primary Prevention of Cardiovascular Disease: A Meta-Analysis of Randomized Controlled Trials**

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### **Background**

Aspirin reduces the risk of myocardial infarction (MI), stroke and death in patients with clinically manifest vascular disease but the benefits are less certain when aspirin is used for primary prevention of cardiovascular events

### **Aim**

To determine the benefits and harm of aspirin compared with no aspirin in primary prevention of cardiovascular disease.

### **Method**

Meta-analysis of randomized controlled trials of aspirin for primary prevention was conducted. Eligible studies were identified using MEDLINE, EMBASE, Cochrane library and CINAHL databases; review of bibliographies of relevant publications and a related article search. Outcomes of interest were: all cause mortality, cardiovascular mortality, the composite of MI, stroke or cardiovascular death, and bleeding complications. 2 reviewers independently extracted study information and data. Data were pooled from individual trials using the DerSimonian-Laird random-effects model and relative risks (RR) with 95% confidence intervals (CI) were computed.

### **Results**

8 studies enrolling a total of 96,726 subjects were included. Aspirin reduced all-cause mortality (RR 0.94; 95%CI 0.88-1.00), the composite of MI, stroke or cardiovascular death (RR 0.87; 95%CI 0.82-0.93), and MI (RR 0.8; 95%CI 0.66-0.98) but did not significantly reduce cardiovascular mortality (RR 0.94; 95%CI 0.82-1.08) or stroke (RR 0.93; 95%CI 0.81-1.07). Aspirin increased the risk of major bleeding (RR; 1.69 95%CI 1.38-2.08), gastrointestinal bleeding (RR 1.38; 95%CI 1.16-1.65) and hemorrhagic stroke (RR 1.36; 95%CI 1.01-1.84).

### **Conclusion**

Aspirin therapy in subjects with no prior history of cardiovascular disease reduces the risk of cardiovascular events, MI and overall mortality but at the expense of increased bleeding.

*No conflict of interest to disclose*

P041

**Laboratory Monitoring of Oral Anticoagulation in Lupus Anticoagulant Patients**

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**Aim**

International normalised ratios (INR) may be affected by the presence of a lupus anticoagulant (LA), making it difficult to monitor these patients when on oral anticoagulant (OAC) therapy. It has been reported that Factor X activity may be a preferred method for monitoring, as different thromboplastins have variable LA sensitivity. We evaluated our test systems to assess LA interference with INR reagents.

**Method**

Samples from OAC patients with LA (n=9) and without LA (n=8) were collected from our INR clinic. INRs were performed with two different thromboplastins viz. ThromborelS and HemosIL Recombiplastin as well as Factor X (chromogenic), LA screening, B2 Glycoprotein antibody (B2GP) and Cardiolipin Antibodies (ACA). A subgroup of LA positive patients were tested with the CoaguChek XS instrument.

**Results**

Result variation was evident in both the LA positive and LA negative groups when comparing the two thromboplastins. The difference in the LA positive group ranged from 0.0 – 1.1 INR units whereas the LA negative group ranged from -0.3 – 0.6 INR units. If therapeutic FX levels of 20-40% were applied, all LA positive patients were in range. In this group, Thromborel S INR results of 2/9 patients were out of range compared to 4/9 with Recombiplastin. In the LA negative group, 3/8 Thromborel S results and 3/8 Recombiplastin results were out of range. Two patients demonstrating significant differences between thromboplastins had markedly elevated B2GP and ACA with inaccurate results using the CoaguChek XS.

**Conclusion**

Significant discrepancies existed within the three INR test systems. We suggest laboratories be aware of their thromboplastin sensitivity to LA, especially in the Point of Care setting, or investigate an alternative approach.

*No conflict of interest to disclose*

A273

**P042**

**Audit of the HemosIL D-Dimer HS Assay with Radiological Diagnosis of Venous Thrombo-Embolicism in Patients Presenting to an Emergency Department in a Tertiary Teaching Hospital**

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**Aim**

To evaluate the utility of an automated D Dimer assay for exclusion of VTE in patients presenting to our Emergency Department with a low- or intermediate pre-test probability of VTE.

**Methods**

In October 2008, the automated latex immunoassay HemosIL D-Dimer HS replaced the qualitative Simplify D-Dimer assay in our laboratory. A threshold of 0.23mg/mL is reported to provide 100% negative predictive value for VTE in low or intermediate pre-test risk patients. Our laboratory information system identified all D-Dimer tests ordered from our Emergency Department between October 2008 and June 2009. Requests for patients with non-VTE provisional diagnoses were excluded. For patients with possible VTE, a search of the Radiology Database identified venous duplex ultrasound, CT pulmonary angiogram or ventilation perfusion lung scans, and the results were noted. The Emergency Department database identified all patients with the discharge diagnosis of DVT or PE during this period, including those without a D-Dimer test, enabling calculation of the incidence of VTE in this population. Results for patients with both a D-Dimer test and radiological imaging performed were analysed to determine the sensitivity, specificity and negative predictive value for the HemosIL D Dimer HS assay.

**Results**

435 patients were considered to have VTE included in their differential diagnosis. Of these, 314 D-Dimer tests were ordered. An emergency discharge diagnosis of VTE was made for 129 patients, 121 of these did not have a D-Dimer test performed. Of the 314 patients with a D-Dimer test, 113 had confirmatory imaging performed. 7 patients demonstrated venous thrombosis (2 positive USS, 4 positive CTPA and 1 positive on both). The sensitivity, specificity and negative predictive value of the HemosIL D-Dimer HS assay for the diagnosis of VTE was 100%, 28.3% and 100% respectively. Statistical analysis demonstrated a significant p value ( $p=0.05$ ) for comparison of D-Dimer values according to the presence or absence of thrombosis.

**Conclusion**

A threshold HemosIL D-Dimer HS assay level of 0.23mg/L provided a 100% negative-predictive value for exclusion of VTE in patients with a low or intermediate pre-test probability in our institution. Correlation with pre-test clinical risk assessment and D-Dimer level is essential to aid the diagnostic process in patients with probable venous thrombo-embolism. The diagnostic algorithm is being correctly applied with patients with a high pre-test probability proceeding directly to radiological imaging without a D-Dimer test being performed.

*No conflict of interest to disclose*

P043

**A Method to Determine If an Association Exists Between Stroke and Autoantibodies Directed Against Folate Receptor****Quintin Hughes**<sup>1,2</sup>, Graeme Hankey<sup>3</sup>, Jim Thom<sup>2</sup>, Ross Baker<sup>1,2</sup>*1 Centre for Thrombosis and Haemophilia Research, Murdoch University. Perth, Western Australia. Australia.**2 Department of Haematology, Royal Perth Hospital. Perth, Western Australia. Australia.**3 Stroke Unit, Royal Perth Hospital. Perth, Western Australia. Australia.***Aim**

A correlation between antiphospholipid autoantibodies and venous thromboembolism has been well documented, although debate continues as to whether a link exists with vascular thrombotic risk. Autoantibodies directed against folate receptor alpha (FR $\alpha$ ) are reported to be a risk factor for pregnancy complications including sub-fertility and neural-tube defect. We aimed to investigate if FR $\alpha$  autoantibodies are a risk factor for stroke.

**Method**

Chinese Hamster Ovary (CHO) cells stably transfected with FR $\alpha$  and non-transfected, FR $\alpha$  negative, CHO cells were plated out on 96-well plates and fixed with gluteraldehyde. After blocking with fetal calf serum and bovine serum albumin, patient sera was added to FR $\alpha$  and FR $\alpha$ - wells in duplicate. A horse radish peroxidase labelled, antihuman IgG/IgM/IgA secondary antibody was added, followed by the addition of a colourmetric substrate that was quantitated using standard spectrophotometric techniques. 100 first ever stroke patients and 100 age/sex/postcode matched controls were investigated using the method and quartile analysis performed.

**Result**

There was no significant statistical difference between the two groups, although the 75<sup>th</sup> quartile of the stroke cohort was greater than that of the control group.

**Conclusion**

The results suggest that autoantibodies directed against the alpha form of folate receptor are not a direct risk factor for stroke. However, the greater representation of strongly sero-positive samples detected in the stroke cohort may warrant further investigation. The cell-based ELISA method we have developed may have applications in the assessment of other pathologies where FR $\alpha$  autoantibodies may be involved in the development or progression of the disease.

*No conflict of interest to disclose*

A275

**P044**

## **Evaluation of a Clinical Pathway to Enable Patient Self-Monitoring of Anticoagulation**

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### **Aim**

Previous studies suggest that self-monitoring (PSM) of the international normalised ratio (INR) may improve the outcomes of oral anticoagulation therapy through increasing the time spent within the target range (TTR), and improving both consumer satisfaction and participation in healthcare. The purpose of this study was to develop, implement and evaluate a pathway to enable people taking warfarin to monitor their own therapy in the community setting.

### **Method**

A structured training program was developed to facilitate the transition of consumers from usual care to PSM using the existing Home Medicines Review (HMR) model. Consumers were recruited through their community pharmacies and, in collaboration with their general practitioners, received intensive one-on-one warfarin education and training in using the CoaguChek XS point of care INR monitor by a trained HMR accredited pharmacist. PSM was undertaken for six months. Outcome measures included TTR, quality of life, warfarin knowledge, and consumer satisfaction.

### **Result**

Twenty-eight patients with a minimum six-month history of anticoagulation treatment were recruited from Tasmania and New South Wales. Sixteen (57.1%) were male and 64.3% required anticoagulation for atrial fibrillation. At baseline, the mean TTR was 64.8%. The mean baseline warfarin knowledge score was 72.4% using a validated warfarin knowledge questionnaire. Qualitative feedback from consumers and general practitioners has indicated a high level of satisfaction with both the training program and PSM. Qualitative and quantitative results after six months of PSM will be reported.

### **Conclusion**

Using the proposed model, trained pharmacists successfully identified and trained suitable consumers to undertake PSM. Initial qualitative feedback has been positive. Future investigation of both qualitative and quantitative data will aim to provide objective data to support these positive findings. This shared model could be used to identify suitable candidates for PSM and provide Australians with access to appropriate training and support.

*No conflict of interest to disclose*

**P045****An Unusual Case of Rapid Development of an Acquired Factor V Inhibitor****Sarah Kamel<sup>1</sup>**, Ellen Maxwell<sup>1</sup>, Kate Burbury<sup>2</sup>, Max Wolf<sup>2</sup>, Robyn Coleman<sup>3</sup><sup>1</sup> *Melbourne Pathology, Collingwood, Victoria, Australia*<sup>2</sup> *Cabrini Hospital, Malvern, Victoria, Australia*<sup>3</sup> *Sullivan Nicolaides Pathology, Taringa, Queensland, Australia***Introduction**

We present a case of a spontaneous Factor V (FV) inhibitor complicating cholangitis, in the absence of bovine thrombin exposure.

An 85 year old male admitted with fever, abdominal pain and deranged liver function secondary to cholangitis demonstrated isolated mild prolongation of prothrombin time (PT 17secs: RR 10-14 secs). Abnormal coagulation results progressed, peaking 3 weeks from admission (PT 59 secs, APTT 110 secs: RR 23-35 secs). Daily therapy with vitamin K was unsuccessful. Normal plasma failed to correct the abnormalities, suggesting the presence of an inhibitor. Factor assays demonstrated a FV level of 0.04 U/ml (RR 0.50-2.00) with inhibitor strength of 5.9 Bethesda units. Endoscopic Retrograde Cholangiopancreatography performed under fresh frozen plasma and prior to completion of investigations, was not complicated by bleeding. The inhibitor remains detectable but clinically silent 8 weeks after initial detection.

**Conclusion**

Most acquired FV inhibitors result from exposure to bovine thrombin in fibrin glue. This patient had no recognised invasive vascular procedures and the aetiology of his FV inhibitor remains unclear. A contribution from sepsis and antibiotic exposure is presumed. Aetiology, natural history and therapy of FV inhibitors are discussed.

*No conflicts of interest to disclose*

**P046**

## **Utility of the HemosIL™ D-Dimer Assay as a Screening Tool in Outpatients Presenting with a Suspected Deep Venous Thrombosis**

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### **Background**

An elevated plasma D-Dimer level is a sensitive but non-specific marker of thrombosis. D-Dimer has been advocated as a screening test for excluding deep venous thrombosis (DVT) among patients presenting with suspected DVT, thereby reducing unnecessary radiological investigations and anticoagulation.

### **Aim**

To perform a single centre retrospective analysis of the sensitivity and specificity of an elevated D-Dimer among outpatients presenting with suspected proximal DVT.

### **Methods**

Using a data extraction algorithm, consecutive outpatients with proximal DVT confirmed on ultrasonography (US) were identified. An age- and sex-matched control group was identified using outpatients who presented with suspected DVT but had the diagnosis excluded by US. US and D-Dimer testing were performed within 72 hours of presentation. Clinical pre-test probability was not performed. D-Dimer measurements were performed using HemosIL™ D-Dimer HS kits on the ACL TOP™ automated coagulation analyser. A positive result was defined as  $\geq 0.2$ mg/L. The impact of alterations to the reference range was also evaluated. Statistical analysis was performed using MedCalc software.

### **Results**

Eighty-seven patients with proximal DVT and controls were identified in both groups. The D-Dimer was positive in all but one patient with a proximal DVT. Using statistical analysis the calculated sensitivity and specificity for a positive D-Dimer defined as a level of  $\geq 0.2$ mg/L were 98.85% (95%CI: 93.8%-100%) and 27.59% (95%CI: 18.5%-38.2%), respectively with a negative predictive value (NPV) of 95.8% (95%CI: 78.9%-99.9%). ROC curve analysis demonstrated that augmenting the cut-off to  $\geq 0.22$ mg/L resulted in a modest increase in specificity 31.3% (95%CI: 21.5%-42%) with only a small reduction in sensitivity 97.7% (95%CI 91.9%-99.7%) and NPV 92.9% (95%CI 76.5%-99.1%).

### **Conclusion**

This study demonstrates the HemosIL™ D-Dimer assay has a high NPV at a cut-off of  $\geq 0.2$ mg/L amongst patients presenting with suspected DVT. Changing the cut-off to  $\geq 0.22$ mg/L may improve specificity and reduce unnecessary US, with only a slight reduction in sensitivity. The cost: benefit ratio of increasing the cut-off level to 0.22mg/L requires validation in a prospective study.

*No conflict of interest to disclose*

P047

## Effect of a Single Indian Meal on Platelet Function and Coagulation

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### Aim

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in Australia and New Zealand. Increased platelet aggregation and hypercoagulation play significant roles in the aetiology of cardiovascular disease. Garlic, ginger, onion, and tomatoes have independently been shown to modify platelet aggregation. The aim of this study was to demonstrate a combination of these dietary components in a meal in modifying platelet aggregation and coagulation.

### Methods

Twenty healthy volunteers were recruited with informed consent and tested pre- and post-Indian meal. Investigations included platelet aggregometry, flow cytometry, platelet function analyzer (PFA-100), overall haemostasis potential (OHP), thrombin generation (CAT), and thrombelastography (TEG). Statistical analyses were performed using the Wilcoxon method.

### Results

Changes in platelet aggregation were varied from subject to subject; reduced platelet aggregation was observed in response to low dose adrenaline, arachidonic acid, and U46619 (TXA<sub>2</sub> mimetic) while aggregation increased in response to high dose platelet agonists ADP, adrenaline, arachidonic acid, and collagen. Flow cytometry showed reductions in platelet-monocyte (P=0.022) and platelet-granulocyte aggregates (P=0.025). No significant difference in platelet function was observed using the PFA-100 assay. We observed reduced thrombus formation as determined by OHP, TEG and CAT. This was evident as reduced fibrin generation (increased lagtime and decreased maximum slope, OHP), significantly decreased clot strength (P=0.048) (reduced maximum amplitude, TEG), which is dependent on number and function of platelets and its interaction with fibrin, and delayed start of thrombin generation (CAT).

### Conclusion

The results of this pilot study suggest that the consumption of an Indian meal, containing garlic, ginger, onion, tomato and other spices, has a mild hypocoagulant effect. This effect is likely due to changes in platelet function and interactions with fibrin. Future studies are underway to investigate the benefits to cardiovascular health of these dietary components.

*No conflict of interest to disclose*

A279

**P048**

## **Garlic and its Potential in Cardiovascular Disease: A Review**

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<sup>3</sup> Department of Cardiology, Royal North Shore Hospital, St Leonards NSW, Australia

### **Aim**

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in Australia, the United Kingdom and the United States. Increased platelet aggregation plays a significant role in the aetiology of CVD, and is complex involving multiple mechanisms with platelet hyperactivity being one of the most important factors responsible for CVD incidence. It is proposed that garlic modifies CVD risk by inhibiting platelet aggregation, increasing HDL-cholesterol and reducing triglycerides. This presentation aims to review the current literature of garlic and CVD and the potential mechanisms involved.

### **Methods**

A PubMed and EBSCO literature search was conducted using the search terms “garlic”, “cardiovascular disease”, “platelet aggregation” and “aggrogometry” in human studies for publications dated from 1966 to October 2008.

### **Results**

The studies using in-vitro methods of garlic on platelet aggregation found significant inhibition of platelet aggregation while using the platelet agonists ADP, arachidonic acid, collagen and epinephrine. Intra-platelet calcium was also inhibited. In ex-vivo studies, garlic consumed by subjects found platelet aggregation induced by ADP, collagen and epinephrine was also inhibited. Triglycerides were found to be reduced, HDL-cholesterol increased and fibrinolytic activity also increased. Preliminary results in our research centre have also shown inhibition of platelet aggregation.

### **Conclusion**

Garlic has the potential to reduce cardiovascular risk via inhibiting platelet aggregation, reducing triglyceride levels, and by increasing fibrinolysis and HDL-cholesterol levels. Modifying these risk factors can have favourable effects on cardiovascular health and the regular consumption of garlic can be suggested in treatment protocols of patients with increased cardiovascular risk, such as those with diabetes.

*No conflict of interest to disclose*

**P049****An Interesting Case of HIT**

**Nick Michalopoulos;** Jeanene Lam  
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74 year old female underwent MV replacement (day 1). Pre-op platelet count was 283.

Following CPB platelets dropped to 36. She returned to theatre due to bleeding. 280mg of heparin was administered on each occasion in theatre. During that time she was transfused platelets, FFP, cryoglobulin and novo-7. Transfusion of another bag of single donor platelets on day 2 resulted in a platelet rise to 93. On day 6 the platelet count dropped to 23 with no evidence of bleeding or sepsis. During day 7 - 11 she was transfused with 5 single donor units (total platelets transfused was 15) at which time the platelet count stabilized. She was discharged from hospital 25/03/2009 with a platelet count of 203.

HIT testing was performed using ELISA (GTi diagnostics IgG and IgGAM) and platelet aggregation methods.

On day 1 (post-op) the initial screening test performed using IgG ELISA was negative.

On day 6 a repeat HIT test was requested and was found to be positive by ELISA IgG and by platelet aggregation. Results will be tabled.

Supplementary (using IgGAM ELISA) and retrospective testing was performed on samples between day 1 and day 6 which showed a graduation in the OD which was clearly negative on day 1 and becoming a clearly positive OD by day 6.

PTP score (based on the 4T's) for day 1 and day 6 was 2 (low risk) and 5 (intermediate risk) respectively.

**Conclusion**

HIT was confirmed on day 6.

This case raises several points:

1. Was the initial negative result due to: HITS not being present or simply serologically not detectable?
2. Despite the low risk clinically (as assessed by the 4T's), consideration of HITS testing should not be excluded.
3. HITS should still be considered as a differential diagnosis of thrombocytopenia <5 days of heparin exposure, despite the negative laboratory HITS (ELISA) test.

*No conflict of interest to disclose*

**A281**

**P050**

## **Comparison of Platelet Function and Reticulated Platelet Fraction in Three Groups of Thrombocytopenic Patients**

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### **Aim**

Bleeding risk can be dependent on platelet numbers, function and maturation. This study aims to investigate the platelet function in three different low platelet groups: ITP, bone marrow recovery post-chemotherapy and in Myelodysplasia.

### **Method**

From 34 participants, 12 were selected as suitable for this study based on study criteria: 3 ITP, 2 Myelodysplasia and 7 post-chemotherapy. EDTA and 0.109M citrate blood samples were collected from each patient and tested within 3 hours.

1. Platelet count was determined on the CELL-DYN Sapphire and verified using Anti-human CD61 monoclonal antibody on the same analyzer.
2. Platelet function was performed on the DiaMed Impact-R measuring Surface Coverage (SC) indicating platelet adhesion, and average size of platelet aggregates (AS) indicating platelet aggregation. Reference range for SC and AS were established from 12 healthy subjects (5M, 7F).
3. Reticulated platelet fraction (representing the immature platelet population) was determined by anti-RNA and CD41 using a BD FACSCalibur flow cytometer. Gate settings were determined based on 3 normal samples for each assay. Results were expressed as reticulated platelet percentage (RP%) and absolute reticulated platelet numbers.

### **Result**

ITP – all patients had platelet counts above  $100 \times 10^9/L$  showing normal SC and AS.

Myelodysplasia – both patients had low platelet counts and low SC and AS.

Chemotherapy – 2 patients with normal platelet counts had normal SC and AS, 1 patient with normal platelet count had borderline SC but low AS, 4 patients with platelet counts below  $100 \times 10^9/L$  had low SC and low/normal AS. A relationship could not be demonstrated between platelet function and reticulated platelet fraction.

### **Conclusion**

This study suggested normal platelet function in ITP, reduced in Myelodysplasia and variable in post-Chemotherapy. No relationship could be shown between platelet maturation and function.

*No conflict of interest to disclose*

P051

**A Single Institution Experience with Retrievable Inferior Vena Caval Filters****Tina Noutsos**, Lay Tay, Simon McRae*Institute of Medical and Veterinary Science, Adelaide, South Australia, Australia***Introduction**

Retrievable inferior vena cava (IVC) filters are recommended in the presence of a short term absolute contraindication to anticoagulation (AC) in patients with a recent history of venous thromboembolism (VTE). However there is marked variation in clinical practice regarding filter insertion, with the procedure being associated with a potentially significant complication rate. We report recent experience with IVC filter insertion at the Royal Adelaide Hospital.

**Methods**

A retrospective audit was conducted on all retrievable IVC filters inserted between January 2006 and September 2008.

**Results**

123 retrievable IVC filters were inserted. 89/123 (72%) filters were inserted for prevention of PE in patients with recent venous thrombosis unable to receive therapeutic anticoagulation due to active bleeding in 61 pts (50%), and planned surgery in 31 pts (25%). 6 were inserted for recurrent VTE despite therapeutic anticoagulation. 25 (20%) were inserted for non evidence based indications including 24 for primary PE prophylaxis in trauma patients, and 1 for atrial fibrillation and bleeding on AC. Only 37/123 (30%) of filters were removed at a median time of 22 days (range 7-502 days). Of the 86 filters left insitu, after a median follow up of 116 days (range 0-846 days) 12 failed attempted removal, 6 remained permanently for medical reasons and 28 patients died with the filter in situ. There were 8 definite complications including 3 complete IVC occlusions; 1 IVC perforation; 2 IVC wall penetrations without perforation; 2 misplaced filters and 1 filter fracture. Possible IVC filter complications included VTE distal to the filter in 5 patients, 2 fatal PEs with filter in situ, 11 filters with in situ thrombus and 2 episodes of bacteraemia post insertion.

**Conclusion**

Filters were often used in settings which did not strictly meet standard clinical indications. Retrieval rate of temporary IVC filters was low (30%). There was a small but significant complication rate.

*No conflicts of interest to disclose*

A283

**P052**

## **Is IVC filter insertion always safe? : Report of two cases**

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### **Introduction**

In patients with contraindications to anticoagulation or those with recurrent DVTs, despite anticoagulation, placement of an IVC filter may be indicated. Occasionally, penetration of the IVC wall by filter components occurs in 3-38% of the total cases depending on the type of IVC filter used. Among those symptomatic penetration is very rare occurring in approximately in 0.3%. Here we present two cases of IVC filter penetration in our centre.

### **Case-1**

A 32 years old female, developed extensive lower limb DVT following the hormonal therapy for hirsutism. She developed bilateral pulmonary embolism (PE) with extension of thrombus to distal IVC. Left iliac thrombectomy was performed and temporary IVC filter inserted through internal jugular vein (IJV). A CT venogram performed after 6 days showed an appropriately placed IVC filter. Six weeks after the insertion of the IVC filter she developed postprandial abdominal pain. CT venogram demonstrated extension of one limb of filter perforating the posterior wall of second part of duodenum. Filter was successfully removed with resolution of symptoms.

### **Case-2**

A 61 years old woman with a history of recurrent PE presented with chest pain while on therapeutic enoxaparin. She was treated with heparin and had an IVC filter placed under CT scan guidance. Fifteen minutes after insertion of the filter, she developed severe pain in central abdominal and back. A CT scan performed demonstrated struts beyond the IVC wall abutting the aorta. Filter was removed successfully with resolution of abdominal and back pain.

### **Discussion**

In these two patients the IVC filter used were 'recovery vena cava' filter and 'Celect' IVC filter. Kalva et al (2006) shown in a large retrospective study that a incidence of penetration of the 'recovery' IVC filter seen in 27.5% on a follow up abdominal CT scan at a mean of 80days. Though there are case reports of similar complication with 'Celect' IVC filter, the exact incidence has not been reported. The majority of the patients with IVC filter penetration remain asymptomatic while less than one percent of patients become symptomatic.

### **Conclusion**

These cases demonstrate that penetrations can cause symptoms that require IVC filter removal. Safety of IVC filters remain an important issue in the management of these patients.

*No conflicts of interest to disclose*

P053

## Big Bleeds in Little People: Paediatric Use of rFVIIa Reported to the Haemostasis Registry

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### Background

Recombinant activated factor VII (rFVIIa, NovoSeven) is approved for the treatment of spontaneous and surgical bleeding in patients with haemophilia A or B and with inhibitors. Over the past years rFVIIa has increasingly been used for indications outside the approved areas, particularly in trauma, cardiac surgery and other critical bleeding episodes. Use in these areas remains controversial.

### Methods

Monash University established the Haemostasis Registry in 2005 to monitor the use of rFVIIa throughout Australia and New Zealand. More than 80 hospitals contribute data to the Registry including all major users of rFVIIa in Australia and New Zealand. This study examines the cohort of paediatric cases reported to the registry.

### Results

Between Jan 2002 and May 2009, 224 cases of rFVIIa use in children aged 16 years and under have been reported to the Registry. The major indication was in bleeding following cardiac surgery (49%) with haematology/oncology (12%) and trauma (12%) formed the next largest groups. Just under one half of the cases (46%) were infants less than one year of age (28% <4 weeks of age) and primarily related to cardiac surgery. Most patients (68%) received a single dose of rFVIIa with a median (IQR) dose of 121 (96-182) mcg/kg. Neonates were more likely to receive higher doses [160 (98-207) mcg/kg] but this was not associated with a higher rate of thromboembolic adverse events.

### Conclusions

Within the paediatric population, rFVIIa is most often used in the setting of cardiac surgery with a wide range of doses in neonates. This study does not allow conclusions regarding efficacy, nor comparison of adverse events rates with non-treated patients. The desire to minimise exposure to blood transfusion may be contributing to the increase in paediatric off-label use of rFVIIa. It is therefore important that in the absence of clinical trial data, independent monitoring of all aspects of rFVIIa use is continued.

*The Haemostasis Registry is funded through an unrestricted educational grant from NovoNordisk Pharmaceuticals Pty Ltd. The company is not involved in the collection, analysis or interpretation of the data, nor do they have the right to veto publication of results.*

A285

**P054**

**A Case of Life Threatening Thrombosis in a Neonate Who is a Compound Heterozygote for 3 Thrombophilia Gene Mutations**

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**Clinical Data**

A male neonate was admitted on Day 4 to NICU with failure to thrive, hyperbiliribinaemia and thrombocytopenia. ABO incompatibility and sepsis were ruled out. A diagnosis of right sided renal vein thrombosis was confirmed by ultrasound. Thrombus extended to inferior vena cava and also involved left portal vein leading to deranged liver function tests and cardiac dysfunction due to hypertension.

Investigations revealed heterozygosity for factor V leiden, prothrombin 20210 and antithrombin gene mutations.

The child was treated with enoxaparin and platelet transfusion. The dose of enoxaparin, which started at 0.8mg/kg BD, was increased gradually to 3.3 mg/kg due to the suboptimal anti Xa levels, consequent to low antithrombin(31%). Antithrombin concentrate was infused during his inpatient period. The patient was also supported for a short period with protein C concentrate infusion until clinically stable, despite his protein C level of 21% being at the lower end of the normal range for a neonate(21-65%). Repeat ultrasound at 6 months of age showed significant clot regression, and enoxaparin has been discontinued.

**Discussion**

Neonatal life threatening thrombosis due to thrombophilia is rare and the diagnosis can be challenging. The reference ranges for various coagulation parameters in neonates are different to the adult population and this must be considered when interpreting paediatric coagulation results. The maintenance dose of enoxaparin is higher in neonates, when compared to adults. Therapeutic strategies for neonatal thrombosis are variable and range from supportive care alone to specific anticoagulation or even thrombolysis.

*No conflict of interest to disclose*

## P055

### **Prevention of Deep Venous Thrombosis (DVTs) in Patients Undergoing Hip or Knee Replacement Surgery with Low Molecular Weight Heparin Therapy (LMWH) or Outpatient Calf Compression Device (CCD) After a Short Course of LMWH: A Randomised Prospective Equivalent Study**

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#### **Aim**

To test whether a combination of 5 days of post-operative LMWH therapy and outpatient CCD is as effective in preventing DVTs as 2 weeks of LMWH therapy.

#### **Method**

Patients undergoing hip or knee replacement surgery at St. George Private Hospital were randomly assigned to either 2 weeks of LMWH therapy (group A) or 5-7 days of inpatient LMWH and CCD for 2 weeks at home (group B).

Exclusion criteria:

- Age <18 or >85
- morbid obesity
- gross lower limb oedema, or skin ulcerations
- active malignancy
- recurrent venous thrombosis
- current anti-coagulation therapy
- severe mental disorders
- severe language difficulties

All patients were subjected to lower limb Doppler study before discharge (day 5 or 7) and 4 weeks post-operatively. All patients with DVTs or cardiorespiratory symptoms were subjected to lung scan examination. Patients were also assessed for increased pain, leg swelling, bruising, haematoma, and wound infections.

#### **Results**

84 patients were enrolled for the study, with 3 patients withdrawn for non-compliance and 2 lost to follow-up. There were 42 female and 37 male patients with a mean age of 72 (range 52-84). 40 patients were enrolled to group A and 39 in group B. There were 3 cases of DVT in each group and one case of asymptomatic pulmonary emboli in group B. There were no significant differences between group A and B in minor haematoma (2 and 1 patient respectively), and minor infections (5 and 7 patients respectively). Leg swelling was more marked in group A (11 patients) compared with group B (1 patient).

#### **Conclusion**

There was no increased incidence of DVT in patients receiving a shorter duration of LMWH and CCD compared with 2 weeks of LMWH therapy. Group B had significant leg swelling reduction, perhaps related to longer CCD use. There were no significant differences in terms of bleeding and minor infections.

This small study may have a significant impact on reducing the use of LMWH in patients undergoing orthopaedic surgery and hence overall costs of pharmaceutical expenditure without compromising patient care or increasing the risk of DVT.

*No conflict of interest to disclose*

## **A287**

**P056**

**Outcomes of Paediatric Immune Thrombocytopenia in Queensland: A 5 Year Single Centre Experience**

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**Aim**

To review the clinical and haematological outcomes of children treated for ITP at Royal Children's Hospital, Brisbane, and to apply the recently published standardised terminology to this cohort.

**Summary**

The last 5 years has seen renewed interest in the management of ITP both in children and adults, as a number of new treatment options have become available for use in this condition. Recently an attempt to standardise the terminology used in ITP was published on behalf of an International Working Group (IWG). We will present data obtained from a retrospective chart review for 90 children treated for ITP from November 2003 to November 2005, including symptoms and platelet count at presentation, responses to first-line therapy, range of second-line therapies utilised, and long-term haematological outcomes. The impact of the revised terminology on outcome definitions will be examined.

*No conflict of interest to declare*

P057

## Heparin Induced Thrombotic Thrombocytopenia Testing – A Comparative Study of 4 Commercial Kits

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### Background

Heparin Induced Thrombotic Thrombocytopenia (HITT) is a clinicopathologic syndrome caused by an antibody-mediated reaction to heparin-platelet factor 4 complexes. Our institution previously used the particle agglutination gel card method to screen for HITT, with confirmatory testing done by Carbon-14 serotonin release assay where clinically indicated. Supply problems with gel cards prompted us to evaluate other available test systems.

### Aim

To compare diagnostic accuracy of four commercially available HITT screening tests: STAGO ELISA, DiaMed Gel Card, GTi and Zymutest.

### Method

We performed a prospective observational study of 35 consecutive patients requiring HITT testing. All samples were initially tested using the STAGO ELISA method and then stored at minus 30 degrees for subsequent testing with all four kits. All testing was performed according to the manufacturer's specifications.

### Results

Of the 35 samples tested, 10 were positive by STAGO ELISA, 9 by DiaMed, 8 by GTi and 6 by Zymutest. Only the GTi test includes a confirmatory step which demonstrates heparin dependence, a feature of true HIT antibodies. Of the 8 samples positive by the GTi test, only 1 did not show heparin dependence - this sample was positive with the STAGO test. Using the STAGO ELISA method as the reference, the sensitivity and specificity of the other tests were determined, and are as follows: DiaMed sensitivity 60%, specificity 84%; GTi sensitivity 70%, specificity 96%; Zymutest sensitivity 70%, specificity 100%. The Zymutest showed the greatest correlation with STAGO ELISA results (100%), while the DiaMed method had the greatest rate of false positive (33%) and false negative(33%) results. All samples have been sent for C14 serotonin release assay- when available, these results will be used as the gold standard test for comparison of other methods and included in the final poster.

### Conclusion

This study highlights the difficulty in laboratory diagnosis of HITT, with high false-positive and -negative results with the currently used DiaMed test, and variable correlation between the test methods. Careful test selection and assessment of pretest probability of HITT will greatly increase diagnostic accuracy.

*No conflict of interest to disclose*

A289

**P058**

## **Therapeutic Response to FVIII: VWF Concentrate in Acquired von Willebrand Syndrome: A Case Report**

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*The Queen Elizabeth Hospital, Adelaide, Australia*

### **Background**

Acquired von Willebrand Syndrome (AVWS) is a heterogeneous bleeding disorder occurs in association with a variety of underlying conditions. The clinical and laboratory findings are similar to congenital vWD and characterised by mucocutaneous bleeding and a decrease in Ristocetin cofactor activity (vWF:RCo) and Collagen binding activity (vWF:CBA). Accelerated removal of vWF rather than decreased synthesis is the underlying mechanism.

Though the focus of management is the treatment of underlying condition, additional measures to correct the haemostasis defect is essential during acute bleed or invasive procedures.

Management options include desmopressin, factor VIII:vWF concentrate and immunoglobulin. Although immunoglobulin's effect is longer lasting the onset is slower and may not sufficient as a single agent when urgent haemostasis support is needed. This necessitates the use of desmopressin or FVIII:vWF during such settings but their duration of action is greatly shortened due to accelerated clearance in this condition.

### **Case**

We report a case of acquired von Willebrand disease associated with Ig G monoclonal gammopathy of uncertain significance. VWF studies showed decreased vWF:RCo, vWF CBA, vWF antigen and RCo/Ag ratio confirming Type 2A von Willebrand syndrome. FVIII:vWF concentrate (biostate) was administered and assays were repeated at 0,1,2,4,6,24 hours. We observed that vWF antigen level and activity persisted only for 6 hours and 2 hours respectively confirming the accelerated clearance of infused products. The non parallel nature of the decay is consistent with preferential removal of high molecular weight multimers which are haemostatically more active. High dose immunoglobulin infusion resulted in more lasting effect.

### **Conclusion**

The duration of action of biostate was greatly reduced in acquired vWD and this is important to recognise during perioperative or acute bleed scenarios. The extent of this reduction may vary depending upon the underlying conditions. Further studies are needed to evaluate this.

*No conflict of interest to disclose*

P059

**Congenital Factor X Deficiency presenting with Severe Bleeding in the Newborn Period****Chee Wee Tan**<sup>1,2</sup>, Juliana Teo<sup>3</sup>, Sabine Zimmerman<sup>2</sup>, Margaret About<sup>1,4</sup>, Christopher Ward<sup>1,2</sup><sup>1</sup>*Northern Blood Research Centre, University of Sydney, NSW, Australia.*<sup>2</sup>*Department of Haematology & Transfusion Medicine, Royal North Shore Hospital, St. Leonards, NSW, Australia.* <sup>3</sup>*Department of Haematology, The Children's Hospital at Westmead, Westmead, NSW, Australia.* <sup>4</sup>*Pacific Laboratory Medical Services (PaLMS), Royal North Shore Hospital, St. Leonards, NSW, Australia***Aim**

Bleeding in the neonatal period is potentially life-threatening and can be a diagnostic challenge. We present a 3 day old female who presents with severe cutaneous bleeding.

**Case**

The infant was the first child of unrelated Caucasian parents, with normal vaginal delivery at 37<sup>+5</sup> weeks. The mother had epilepsy treated with lamotrigine, a drug not considered to cause fetal coagulopathy. There was no family history of abnormal bleeding. IM vitamin K was administered at birth. Severe periumbilical bleeding and cutaneous bruising was noted on Day 3. There was also persistent bleeding from previous venepuncture sites and heel-pricks. Haemoglobin on Day 3 was low, 130 g/L, falling to 75 g/L within 12 hours. Initial coagulation profile showed a marked coagulopathy with PT >200 secs, APTT >150 secs, with full correction on mixing tests. Fibrinogen levels were normal. Bleeding stopped and coagulopathy was corrected with FFP but not with repeated vitamin K administration. Factor studies showed an isolated severe FX deficiency (<1 U/mL, <1%). Periumbilical bleeding recurred on Day 11, and oro-pharyngeal bleeding at 5 weeks resulted in Hb of 51 g/L; bleeding was successfully treated with Prothrombinex. Prophylaxis with twice weekly Prothrombinex via a Hickman catheter was commenced at 6 weeks of age. Prophylaxis will be changed to FX concentrate when available. FX levels were at the lower limit of normal in both parents. Mutation analysis is in progress.

**Conclusion**

Congenital Factor X deficiency is a rare autosomal recessive bleeding disorder which can manifest with severe bleeding. It should be considered in infants with mucocutaneous bleeding which do not respond to vitamin K. Mixing tests and factor studies should yield the diagnosis. Treatment is with FX-containing products such as FFP, Prothrombinex, or FX concentrate. Future prenatal testing in this family may be considered with identification of a mutation.

*No conflict of interest to disclose*

A291

**P060**

## **The Sensitivity of Thrombin Generation and an Assay for Procoagulant Phospholipids to Platelet-Derived Microparticles**

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STA-Procoag-PPL (Stago, France) is an automated clotting test able to detect procoagulant phospholipids (PPL). This assay monitors the decrease in clotting time caused by the sample PPL in the presence of a fixed amount of FXa and calcium. We studied the influence of platelet derived microparticles (PMP) on both the PPL assay and thrombin generation (TG).

PMP were obtained by activation of a platelet concentrate with calcium ionophore. A PMP range from 500 to 20000MP/μl was prepared in normal platelet poor plasma (NPPP). This range covers the expected normal count of circa 655MP/μl for males and 1775MP/μl for females [1].

The MP count and size were assessed in all preparations before and after freezing using flow cytometry with Megamix beads (Biocytex, France). PPL was assessed on the STA-R and TG was determined using the Calibrated Automated Thrombogram (CAT) with the PRP-reagent (1pM tissue factor, no phospholipid) as trigger (reagents and instrument Stago, France).

PPL clotting times measured for normal MP counts are consistent with the normal range established for STA-Procoag-PPL (61-83 sec for normal plasma double centrifuged for 15' at 2500g and stored frozen at <-20°C). The clotting times correlate with log MP count ( $r=0.998$ ).

As expected, as the PMP count increases, the STA-Procoag-PPL clotting time decreases. The TG peak correlates positively ( $r=0.954$ ) while lagtime correlates negatively ( $r=0.943$ ) with the logarithm of the PMP load. Endogenous Thrombin Potential is not altered since the procoagulant surfaces accelerate TG but do not affect the global thrombin potential of a plasma sample.

The correlation of STA-Procoag-PPL with C.A.T. suggests a strong relationship between both assays for estimating procoagulant potential level. These results deserve further investigation on microparticles derived from other cellular origins.

### **Reference**

1: Robert S et al, J Thromb Haemost 2008; 7: 190-7.

**Disclosure of interest:** All authors are Stago employees

P061

**Changes in Coagulation Observed in Early and Late Foetal Loss**

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Many recurrent miscarriages in patients without any know causes are characterized by defective placentation and/or microthrombi in the placental vasculature. However, in 50% of cases the cause of foetal loss remains unknown. Because of the key role thrombomodulin (TM) and tissue factor (TF) in coagulation and embryonic development we performed a study using new specific activity assays for these 2 factors (both prototype assays) in samples collected from patients with early (n=30), late (n=32) pregnancy loss (all with no known causes for the loss) and normal pregnancy (n=35) We also measured procoagulant phospholipids (PPL, STA Procoag PPL, Stago, France) and free Tissue Factor Pathway Inhibitor (f-TFPI, Asserachrom free TFPI, Stago, France).

The plasma levels of TF, TM, PPL (PPL reflected by a shortening clotting time) were significantly higher in cases than in controls subjects. In addition the ratio TF/ f-TFPI were higher in patients than in controls. Patients with late pregnancy loss had a higher TF/f-TFPI ratio than patients with early pregnancy loss (p>0.001). The combinations of these different parameters reveal an increase in procoagulant activity and suggest that endothelial damage or activation may be involved in the pathogenesis of these pregnancy losses. The use of these 2 new activity assays and PPL may help in assessing the prognosis of pregnancy loss.

**Table**

	<b>Normal Pregnancy</b>	<b>Early Pregnancy Loss</b>	<b>Late Pregnancy Loss</b>
<b>TM (%)</b>	96	148	133
<b>TF (pM)</b>	1.18	3.65	3.92
<b>TF/f-TFPI ratio</b>	0.20	0.31	0.41
<b>PPL (sec)</b>	42.6	35.46	38

**Disclosure of interest:** P VanDreden, B Woodhams and A Rousseau are full time employees of Diagnostica Stago.