ASTH NEWSLETTER
The Australasian Society of Thrombosis and Haemostasis
Editor: Emma Jones-Perrin
Email: emma_perrin@health.qld.gov.au OR ae_perrin@optusnet.com.au Telephone: (07) 3350 8531 Fax (07) 3350 8879 **Vol 11, No 3 December 2005**

# Dear Fellow Clotter

Welcome to the final edition of the newsletter for 2005. Many thanks to all the contributors, your time and input are appreciated. In this issue you will find a report from the new ASTH President, Mark Smith and news from the ASTH secretariat, Megan Sarson-Lawrence. Also included are reports from the New and Emerging Technologies Group, the Clinical Trials Group, details of the ASTH Travel Grant winners for 2005 and upcoming meetings for 2006.

Congratulations to Vivien Chen (University of New South Wales) who won the AstraZeneca Medal and the $2000 prize at the recent HAA in Sydney. The runners up (Helena Liang and Vanessa Cole) both received $750 and all winners were presented with certificates. All three abstracts are included in this edition of the newsletter. Peter Castaldi delivered the Barry Firkin oration at the ASM in Sydney, his abstract "The Man and his Legacy" is included. A special thank you to Emmanuel Favaloro for his ISTH satellite meetings report.

*Vivien Chen receiving her prize from Glen Pater, Medical Director of AstraZeneca in Australia.*

Please find enclosed along with the newsletter a copy of the Presidents Report and the Treasurers Report presented at the recent AGM. Another three issues of the newsletter are planned for 2006. Contributions are most welcome.

Merry Christmas and hope you have a safe and happy New Year

*Emma Perrin*

## ASTH COUNCIL 2005-2007

| | | |
|---|---|---|
| Dr Mark Smith | President | *mark.smith@cdhb.govt.nz* |
| Dr Chris Ward | Vice-President & Treasurer | *cward@med.usyd.edu.au* |
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| Dr Murray Adams | Chair, New & Emerging Technologies Group | *m.adams@curtin.edu.au* |
| Mrs Emma Jones-Perrin | Newsletter Editor | *emma_perrin@health.qld.gov.au* |
| Dr Ali Bianchi | Vice-Chair, Scientific Programme Committee | *alessandra.bianchi@email.cs.nsw.gov.au* |
| Dr Paul Harper | Web Master, Discussion Group | *paulh@adhb.govt.nz* |
| Dr Douglas Coghlan | Clinical Trials Liaison | *douglas.coghlan@flinders.edu.au* |
| Dr Tim Brighton | Chair, Clinical Trials Group | *brightont@sesahs.nsw.gov.au* |
| Professor Hatem Salem | Executive Director | *hatem.salem@med.monash.edu.au* |

## FROM THE PRESIDENT

The Annual Scientific Meeting in Sydney this year marked the end of six year terms on council for several senior society members. Professor Hatem Salem completed a four year term as president. Hatem's enthusiastic and congenial approach to the society's activities has been inspiring. Under his tenure, the society has moved towards closer collaboration with its UK counterpart, the British Society for Haemostasis and Thrombosis. Professor Alex Gallus completed his term as vice-president. The council has appreciated the wise opinion and depth of experience offered by Alex, and will continue to look to his guidance, particularly in the field of clinical thrombosis research. Dr Tim Brighton completed his term as council treasurer, seemingly undaunted by the additional responsibility this year of helping to organise and run the successful ISTH meeting in Sydney. Tim will continue his role as clinical trials group chair. Thanks Hatem, Alex and Tim for your contributions to the society. The 2005 council elections proved interesting. The proportion of society membership that took time to cast a vote was 25%. A higher figure should be targeted in future, with a key council objective to deliver on issues of relevance to members. We welcome Alessandra Bianchi, Paul Coughlin, Doug Coghlan, and Claire McLintock to the council.

The ASTH secretariat office has moved from Perth to Melbourne. Thanks to Ross Baker and Leonie Klomp in Perth for their long and enthusiastic stewardship of the secretariat since the Society began. Our newly appointed project officer Megan Sarson-Lawrence will be based in the Melbourne office, a facility shared with the Australian Haemophilia Centre Directors Organisation. Megan has a wealth of experience in administration, including web site design, and will be an asset to the ASTH.

HAA 2005 was an excellent meeting. Two features of particular note were the Barry Firkin Oration and the AstraZeneca award winner. Peter Castaldi delivered the Firkin oration. He described the important scientific contributions of Firkin's many collaborators over the years, clearly illustrating his influence on high quality coagulation research. Vivien Chen was awarded the AstraZeneca medal for her Presidential Symposium presentation on the role of disulfide switching in activation of tissue factor. Her elegant work characterises mechanisms of protein chemistry fundamental to the initiation of the coagulation mechanism.

It seems the barrier provided by the Tasman Sea is diminishing. For the first time council has three members from New Zealand, a feature that will strengthen trans-Tasman collaborations. Additionally, looking forward to 2006, we expect New Zealand and Australia to establish a joint agency to regulate therapeutic products (including complimentary medicines), supported by regulatory framework and legislation. The focus will include pre-market evaluation, product licensing, controls on manufacture, and post-market surveillance. New Zealand will gain access to a broader range of technical expertise in the evaluation of complex products including medicines of biological origin. Both countries will benefit from a more simple evaluation process for clinical trial activity. The new agency will provide a "one-stop" shop for scientific and safety assessment of new molecules. A joint Australasian research application form for Ethics Committee assessment is a distinct possibility. This development should see New Zealand and Australia becoming a joint clinical research market, making the conduct of clinical trials across the region a more seamless process. This exciting development in trans-Tasman cooperation promises to enrich clinical coagulation research in both countries. The challenge is there for ASTH members to realise this opportunity.

Best regards and a safe and happy festive season to all.

*Mark Smith*

## SECRETARIAT NEWS

My name is Megan Sarson-Lawrence and I have recently been employed as the new ASTH secretariat. Originally from Manchester in the UK I have been in Melbourne for the past 15 years. I received a PhD in inorganic chemistry from the University of Birmingham and a Master of Women's Health from the University of Melbourne.

Prior to having children I worked at CSIRO but more recently I have worked as a project officer co-ordinating a scheme to facilitate multi centred clinical trials by streamlining ethics submissions – unfortunately it's still a work in progress but we must all live in hope!

I am currently also employed as a project officer by the Australian Haemophilia Centre Directors' Organisation, and so have already had some contact with the 'Haemostasis' part of ASTH.

As a consequence of my employment, the ASTH office has relocated from Perth to Melbourne. The new office contact details are

Postal: PO Box 217, Glen Iris, Vic 3146
Tel: 03 9388 8711
Fax: 03 9388 8722
Email: *asth@bigpond.com*

The ASTH office is only open 2 days per week, Wednesday and Thursday, but feel free to leave a message and I'll get back to you as soon as possible.

Since the secretariat position has been vacant for quite some time now my initial priority will be to re-establish routine business functions and catch up with membership processing. This years membership forms will be sent out in the near future, a bit later than in past years, but there are many 2004-05 memberships which have still not been processed – I appreciate your patience whilst things are being sorted out.

Once the back log has been cleared I look forward to developing relationships with members and ASTH sponsors and increasing the profile of the ASTH generally.

## NEW AND EMERGING TECHNOLOGIES GROUP REPORT

It has been a relatively quiet year for New and Emerging Technologies Group activities. This has been due mainly to a saturation of meetings in Sydney during 2005 that provided many opportunities for laboratory scientists. The ISTH, AIMS and HAA meetings were all held within the space of a few months and provided for a range of diagnostic laboratory interests.

Looking forward to next year, the NET Group is presently in the initial stages of planning for the 2006 scientific workshop. This is scheduled for Saturday 14th October 2006 to coincide with the Hobart HAA meeting, which commences the following day. Although the venue is yet to be confirmed it is probable that the workshop will be held at the Clinical School in Hobart and registration will be kept as low as reasonably possible. I would like to call for individuals interested in presenting at the workshop to contact me, and would especially encourage those with interesting case studies to contribute (M.A*dams@curtin.edu.au* or 08 9266 4316).

The 2004 workshop was very well attended with positive feedback and it is anticipated that the Hobart workshop will be similarly well received. A preliminary program should be available for distribution early in the new year to members along with details of registration.

Wishing everyone a safe and fun festive season.

*Murray Adams*

## THE MAN AND HIS LEGACY

*Peter Castaldi*
*Emeritus Professor, Westmead Hospital, Sydney, NSW, Australia*

There have been few medical academics in this country to match the influence and achievements that characterised the career of Barry Firkin. He was a prime mover in three key areas: clinical research with a basic bent: clinical medicine as practitioner, teacher and college examiner; and in communication through the Australian Society of Medical Research of which he was the principal founder and the Haematology Society of Australia in which he participated from the beginning. He had a cheerful engaging personality, a boyish ineptitude in the practical affairs of his household, a remarkable woman, Ruth for a wife who more than compensated and such a liking for golf that they moved next to a renowned Melbourne course when he retired from Monash in 1995.

He had a big impact on young physicians, a series of whom spent time doing research with him and all went on to productive careers in academic and specialist pathways . A feature of these experiences was the breadth of the studies in haematology including haemopoiesis, folate metabolism, PNH, Orotic aciduria, marrow grafting, as well as his preoccupation with platelets and von Willebrand Disease. Especially in the latter work he had the ongoing support of outstanding scientists. Margaret Howard was the pivotal person in the work with Ristocetin published in 1972 which opened up the field of study of primary haemostasis. Sharon Pfueller joined him in 1976 and was a great contributor in work on immune thrombocytopenia. His group at Monash thrived as the years went by and led by Hatem Salem, Shaun Jackson and Katrina Mitchell remain leaders in research.

He expanded his interest to the history of medicine and in his later years wrote about medical eponyms with Judith Whitworth, reflected on women in haematology over the years and wrote thoughtfully about the problems of recruitment and retention in academic medicine. He was a true leader with a passion for discovery and a rare commitment to the best in his discipline.

*From left James Wiley, Peter Castaldi and Hatem Salem*

The ISTH/SSC meeting was preceded for me by a Beckman Coulter Haemostasis day (Friday, 5th August, at the Maritime Museum). An 'hors d'oevre' to the main meal if you will. As usual at such industry-sponsored meetings, there was some obvious bias towards Coulter-IL products, and as the day developed it was made clear to us that the ACL Top was the only coagulation instrument worth owning. Nevertheless, the day provided a taste of haemostasis and there were two very well known international (keynote) speakers. After a brief 'welcome' from Beckman Coulter, Professor Sam Machin from the University College Hospital in London gave a talk on TTP diagnosis and treatment. TTP is a rare but serious and potentially fatal disorder. Machin sees around 5 or so new cases of acquired TTP/year, and he estimates a total of ~20 congenital TTP cases in the UK. TTP is thought to (usually) involve the loss of ADAMTS13 activity. ADAMTS13 acts to cleave ultra-large (UL) von Willebrand factor (VWF) in plasma, and in its absence this form of VWF can cause thrombotic complications in various organs. Diagnosis is usually on clinical grounds, although various assays attempting to assess plasma ADAMTS13 activity have been described (with some variable success). Treatment is typically by plasma exchange. Although recombinant ADAMTS13 has been developed, the rarity of the disorder may not provide the financial incentive required to provide this material as an ongoing therapeutic option. Potential future alternatives to diagnosis (eg flow based evaluations of reticulated platelets) and management (eg monoclonal antibodies to VWF or to CD20) were also noted.

The other key-note speaker was Professor Armando Tripodi, who spoke on Thrombophilia risk factors: Physiopathology and laboratory testing. He gave what was a fairly standard text-book talk[1] on the matter, noting the usual suspects (rare: Antithrombin (AT), Protein C (PC), Protein S (PS) deficiencies; common: activated Protein C Resistance (APCR), factor V Leiden (FVL) and prothrombin gene mutations (PGM)). Testing is recommended only in select cases (eg personal or family history of thrombosis), and some time after the thrombosis and cessation of oral anticoagulant therapy. He recommended the PC chromogenic assay, AT testing using an anti-Xa procedure, PS testing using the free PS assay, and APCR testing using the APTT based assay with and without factor V deficient plasma (FVDP) pre-dilution to detect APCR both due and not due to FVL. As is often the case in this contentious area of haemostasis, I have some personal 'biases' relating to thrombophilia testing[2-4] that I aired at the meeting. Firstly, I suggested that the RVVT based assay for APCR (even without FVDP predilution) gives better sensitivity to FVL than the APTT based assay (even with FVDP predilution). Professor Tripodi agreed with this view, but indicated that for some reason, RVVT-based assays were not as popular in Europe as APTT based assays. Then I suggested that for PC and PS assays at least, my calculations indicated that the potential false positive to true positive ratio was between 1:1 and 40:1[4], depending on various circumstances (which patients tested, what tests performed, etc), and should we instead be abandoning such tests? I'm not sure I was understood. You might be interested to know that I invited both Professors Machin and Tripodi to contribute to a Seminars in Haemostasis and Thrombosis issue on Thrombophilia that I recently guest edited. Professor Machin declined (prior commitments) but Professor Tripodi accepted.[1]

Other speakers for the day were various 'locals' or 'honorary-locals'. Emma Perrin from the Queensland Health Pathology Service (QHPS) gave a talk on establishing Quality Assurance across an area network, something she's had to grapple with recently up north. The network consists of four major Brisbane based laboratories and 33 other networked labs. The process is time consuming and otherwise unfunded (performed on top of other standard duties; a familiar story for laboratory scientists these days), but probably necessary for such a large network. I especially loved the term she used throughout the talk. What I would usually call a 'problem', Emma described 'lovingly' as an 'OQI' (an Opportunity for Quality Improvement). David Patterson from Canterbury Health Laboratories in Christchurch NZ (an 'honorary-local' for the day) presented a couple of interesting cases of falsely elevated D-Dimer possible due to 'heterophile' antibodies. I admit to previous ignorance of this, so it's always good to learn something new. Robyn Coleman from S&N in Queensland gave a talk on the VWF:Activity assay from IL. This is a new monoclonal antibody based VWF latex immunoassay that purports to provide a measure of VWF 'activity'. From what I can work out, IL's premise here is that since the antibody binds to VWF at the epitope that would otherwise bind to platelet glycoprotein-1b, this assay would therefore somehow reflect some measure of VWF activity. This doesn't make complete sense to me, as there is no inherent VWF activity attributable to the process of binding such an antibody. A few years ago, an ELISA assay was marketed as a VWF:Activity assay on a similar premise. Our laboratory published data at that time[5,6] suggesting that the assay was not so much a VWF:Activity assay, but rather a 'VWF:capture' assay that displayed some

preferential binding to high molecular weight (HMW) VWF. And in those studies, the VWF:CB was found to be a superior option for detection of HMW VWF. It is not clear if the new 'VWF:Activity' assay from IL uses the same antibody. Nevertheless, the IL assay principle (latex immuno assay) is different to the ELISA assay principle, and as highlighted by Robyn, the assay does appear to correlate with VWF:RCo in many sample test cases. Accordingly, we should not discount it's potential utility in VWD diagnosis until this is better evaluated. The RCPA QAP plans to include this assay under a new category in its VWF/VWD module from 2006. I will also mention that it's always a pleasure to see Robyn talk at these meetings, coming as she does from a non-public pathology institution. Other speakers for the day included Tom Exner (novel coagulation testing), Jenny Butler (ACL top) and various Beckman Coulter employees.

After the ISTH, Bayer sponsored a Stago-user's group meeting (13:00-20:00 Friday 12th). They apparently hadn't heard about the ACL-top, and throughout the day we got the impression that the Stago STA-R was the only coagulation instrument worth owning. Nevertheless, we were again treated to more brain food, and the meeting agenda was a real surprise, providing an eclectic mix of talks. There was a brief company talk regarding a software upgrade to the STA-R, but otherwise this was a peer-scientist driven meeting. An overseas guest (Dr Nicole Schlegal, Paris) spoke on antithrombotic drugs and monitoring. Steve Johnson (NZ 'honorary local') spoke on an APTT reagent evaluation, my good friends Margaret Aboud (PALMS) and Geoff Kershaw (RPA) spoke on APCR and LA respectively, Chris Holt (Victoria) spoke on a factor V inhibitor case, Vaughan Williams (SA) and Margaret Collecutt (Victoria) both spoke on the recent RCPA QAP inhibitor exercise (more on this later), and Leesa Ivey (WA) spoke on the new IL VWF:Activity assay (hey, sounds familiar) as performed on the STA-compact (oh!). Again, the VWF:Activity assay shows some correlation to standard 'functional' assays such as VWF:RCo and VWF:CB, so we will await the findings of future published studies to assess it true utility in the field. However, my award for best presentation at this meeting had to go to Vaughan Williams, who took us on an amusing personal journey through the recent RCPA QAP inhibitor exercise, warts and all. The talk related a step by step investigation of these samples, and it was such a pleasure to hear. Vaughan started his presentation by explaining the scenario (a 68 year old man scheduled for urgent neural surgery presenting with abnormal coagulation results). The primary site is unable to perform specialised tests of haemostasis, and so the sample has been sent for follow up in your referral centre. As Vaughan works in a Womens and Childrens centre, this he muses is their first mistake… He then went on a blow by blow study of each sample in turn. There were 8 samples in all, some more difficult than others. In addition to true inhibitors (a factor V inhibitor, a factor VIII inhibitor, and a lupus anticoagulant sample) the samples included EDTA, serum and heparin contaminated samples. In fact, the exercise (blind tested, lacking clinical details, unable to request repeat collections) was meant to be difficult and intellectually challenging, and we (ie myself and the RCPA QAP) were not expecting laboratories to get much more than about half the samples right. In fact, Vaughan didn't really score too badly in this exercise, as did many participants, so we (ie myself and the RCPA QAP) have been pleasantly surprised. Margaret Collecutt was so enthused by the exercise that she undertook additional studies on the effects of EDTA on coagulation tests. The report for this exercise was sent out in November.

**References:**


1. Tripodi A. A review of the clinical and diagnostic utility of laboratory tests for the detection of congenital thrombophilia. Semin Thromb Hemost 2005;31:25-32

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3. Favaloro EJ. Diagnostic issues in Thrombophilia: A laboratory scientist's view. Semin Thromb Hemost, 2005; 31: 11-16.

4. Favaloro EJ, Soltani S, McDonald J, Grezchnik E, Easton L. Laboratory identification of familial thrombophilia: do the pitfalls exceed the benefits? A reassessment of ABO-blood group, gender, age and other laboratory parameters on the potential influence on a diagnosis of protein C, protein S and antithrombin deficiency and the potential high risk of a false positive diagnosis. Laboratory Haematology, 2005; In Press (accepted for publication)).

5. Favaloro EJ, Henniker A, Facey D, Hertzberg M. Discrimination of von Willebrands Disease (VWD) subtypes: Direct comparison of von Willebrand Factor:Collagen binding activity/assay (VWF:CBA) with Monoclonal Antibody (MAB) based ELISA VWF-detection systems. Thromb Haemost, 2000; 84: 541-7.

6. Favaloro EJ. Detection of von Willebrand Disorder (VWD) and identification of qualitative von Willebrand Factor (VWF) defects: Direct comparison of commercial ELISA-based 'VWF:Activity' options. Am J Clin Path, 2000; 114: 608-18.


*Emmanuel J Favaloro*

# ASTRA ZENECA MEDAL ABSTRACTS

## WINNING ABSTRACT

## TISSUE FACTOR ACTIVATION INVOLVES DISULFIDE SWITCHING

*Vivien Chen*[1], *Michael Berndt*[2], *Wolfram Ruf*[3], *Philip Hogg*[1]

1 *University of New South Wales, Sydney* NSW, *Australia.*
2 *Monash University, Clayton, Victoria, Australia*
3 *The Scripps Research Institute, La Jolla, California,* USA

Tissue factor (TF), the essential cofactor for FVIIa, is required for activation of FX and FIX to generate thrombin. Transmembrane TF resides in a cryptic configuration on the cell surface with low procoagulant activity, however TF can be rapidly switched to an active configuration on exposure to certain stimuli. The nature of this switch is unknown. The extracellular part of TF consists of 2 fibronectin type III domains. The disulphide-bond in the membrane proximal domain (Cys186-Cys209) is atypical for fibronectin domains in that it links adjacent strands in the same ½-sheet, a cross-strand bond. The Cys186-Cys209 TF bond has the same unusual configuration as the disulphide-bond in the second domain of CD4, which controls CD4 function by switching between oxidized (disulphide) and reduced (dithiol) states (Matthias et al. Nature Immunol. 3,727, 2002). Ablation of the cross-strand bond severely impairs procoagulant activity (Rehemtulla et al. J. Biol. Chem. 266, 10294, 1991). Labeling with a biotinylated maleimide, we demonstrate that cryptic tissue factor is reduced at the domain 2 disulfide and oxidised on activation. In HL60 cells, membrane based tissue factor procoagulant activity is blocked by the mono-thiol alkylator N-ethylmaleimide but increased by formation of the disulfide via the thiol oxidiser, HgCl2 or thiol cross-linkers, bismaleimidohexane and bismalemidoethane. Using the VIC7 anti-TF antibody which recognises an epitope between aa181-214 in TF (Magdolen et al Biol Chem 1998) we demonstrate that activation of cryptic TF on HL60 cells correlates with a change in the conformation of the TF region that is constrained by the cys186-cys209 disulfide. These results indicate that the activation of TF involves a change of conformation of the domain 2 of extracellular TF caused by formation of the cross strand cys186-cys209 disulfide bond. This is likely to be the physiological change that facilitates productive binding of FIX and FX in coagulation.

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## RUNNER UP ABSTRACT

## GENETIC CONFIRMATION OF PROTEIN S DEFICIENCY

*Vanessa Cole*[1], *Quintin Hughes*[1,2], *Janelle Staton*[1], *Melissa Sayer*[1], *and Ross Baker*[1,3]

1 *Department of Haematology, Royal Perth Hospital, Perth,* WA
2 *School of Surgery and Pathology, University of Western Australia, Nedlands,* WA
3 *School of Medicine and Pharmacology, University of Western Australia, Nedlands,* WA

**Aim:** Congenital Protein S (PS) deficiency is associated with a 10-fold increased risk of venous thromboembolism (VTE). The diagnosis of PS deficiency is complicated by circumstantial factors including warfarin treatment, pregnancy, oral contraceptive use and hormone replacement therapy which lower PS levels. Our aim was to develop a simple technique for the detection of PS mutations.

**Methods:** We used PCR and combined single stranded conformational polymorphism and heteroduplex analysis (CSHA) to detect mutations within the PS gene (PROS1) and PS mRNA. Ninety-two patients presenting with a history of VTE and suspected PS deficiency were screened.

**Results:** Twenty-four patients were heterozygous for at least one PROS1 mutation. Seven novel (g-29a, K9T, P35P, T101A, G231R, intron k insert t exon 8 -16 and G340C) and five previously reported (E26A, T37M, R192K, S460P and intron a del att exon 2-67) mutations were detected. The K9T, E26A, T37M, T101A and G340C mutations affected residues conserved in PS among different species. The first three were present in the GLA-domain of PS and may decrease its affinity for negatively charged phospholipids. Three mutations (T101A, R192K and G231R) were located in the PS epidermal growth factor-like domains and are predicted to affect protein folding, the binding of calcium ions or interaction with activated protein C. The G340C mutation was present in the sex hormone binding globulin domain may disrupt protein folding or secretion. The relatively common heerlen mutation (S460P) accounted for half of the mutations detected. This mutation destroys a glycoslylation site. One patient was heterozygous for a splice mutation in which exon 2 was spliced out. This exon is necessary for carboxylase recognition and contains a cleavage site required for protein secretion.

**Conclusions:** CSHA is a valuable tool for the detection of PS mutations and aids in the genetic confirmation of PS deficiency.

## RUNNER UP ABSTRACT

# A COMMON ANCESTRAL GLYCOPROTEIN (GP) IX GENE MUTATION (ASN45SER) CAUSES BERNARD-SOULIER SYNDROME (BSS) IN EUROPEAN FAMILIES FROM NORTHERN EUROPE AND AUSTRALIA

HPH Liang[1,2], MC Morel-Kopp[1], JM Clemetson[3], KJ Clemetson[3], R Kekomaki[4], H Kroll[5], K Michaelides[6], EGD Tuddenham[6], K Vanhoorelbeke[7], CM Ward[1]

1 Northern Blood Research Centre, Department of Haematology and Transfusion Medicine, Royal North Shore Hospital, St Leonards, Australia
2 Discipline of Medicine, University of Sydney, Camperdown, Australia
3 Theodor-Kocher Institute, University of Berne, Berne, Switzerland
4 Finnish Red Cross Blood Transfusion Service, Helsinki, Finland
5 Institute for Clinical Immunology and Transfusion Medicine, Giessen, Germany
6 Haemostasis and Thrombosis Research, MRC Clinical Sciences Center, Hammersmith Hospital, London, United Kingdom
7 Laboratory for Thrombosis Research, IRC, K.U.Leuven Campus Kortrijk, Kortrijk, Belgium

Bernard-Soulier syndrome (BSS) is an extremely rare hereditary bleeding disorder, caused by mutations occurring in the *Glycoprotein* (GP) Ibα, GPIbβ and GP9 genes that encode for the corresponding subunits of platelet GPIb-V-IX adhesion receptor complex. BSS has been reported in many populations, mostly behaving in an autosomal-recessive manner. While the great majority of BSS mutations are unique to a single individual or family, the GP9 1828A>G Asn45Ser single nucleotide substitution, which we have identified in an undocumented Australian Caucasian, has already been reported in multiple unrelated Caucasian families from various Northern and Central European countries. Consequently, we performed a haplotype study to determine whether the GP9 1828A>G Asn45Ser mutation is an ancient 'mutation' in the European population, or indicates a 'hot-spot' for mutagenesis in the GP9 gene. The haplotypes of GP9 1828A>G Asn45Ser mutation carriers and 100 Caucasian controls were established by single nucleotide polymorphism screening using allele-specific PCR and DHPLC techniques. Haplotype analysis of 19 BSS patients from 15 unrelated Northern European families (including 2 compound heterozygote siblings from a British family previously published, and 17 Asn45Ser homozygotes), showed that 14 of these BSS patients from 11 of the Asn45Ser homozygote families share a common haplotype at the chromosomal region 3' to the GP9 gene. Hence, the results suggest that the GP9 1828A>G Asn45Ser mutation in these families is ancient, and its frequent emergence in the European population is the result of a founder effect rather than recurrent mutational events. Association of the GP9 1828A>G Asn45Ser mutation with variant haplotypes in 4 other Northern European BSS families raised the possibility of a second founder event, or rare recombinations in these families. Additional members from these 'atypical' lineages would be needed for haplotype screening to resolve this question.

# ASTH TRAVEL GRANT WINNERS 2005

## (EACH WINNER RECEIVED $750)

**International Normalised Ratios Measured at Home with a Point of Care Device Diverge from Hospital Laboratory Results when Starting Warfarin**

Dolly Daniel, Babara Farrelly, Alexander Gallus, Douglas Coghlan, Jenny Osmond, Brodie Hearne
Haematology Department, Flinders Medical Centre, Adelaide, SA, Australia

**A Comparison of Enoxaparin and Unfractionated Heparin in Combination with Tirofiban during Percutaneous Coronary Intervention: Effects on Inhibition of Coagulation and Activation of Platelets**

Emma Perrin[1], Michael Ray[1], Peter Wood[1], Darren Walters[2]

1 Department of Haematology, Queensland Health Pathology Service, Prince Charles Hospital, Brisbane, Queensland, Australia
2 Cardiac Program, Prince Charles Hospital, Brisbane, Queensland, Australia

**Afibrinogenaemia Due to a Compound Heterozygosity for Two Termination Events in the Aα Chain**

Linda Saravanan[1], Mark Kirkland[1], Robin Lowen[2], Peter George[2], Stephen Brennan[2], Philip Campbell[1]

1 Department of Clinical Haematology and Medical Oncology, Andrew Love Cancer Centre, Geelong Hospital-Barwon Health, Geelong, Victoria, Australia
2 Molecular Pathology Laboratory, Canterbury Health Laboratories, Christchurch, New Zealand

# ASTH TRIALS GROUP

The ASTH Clinical Trials Group (CTG) met at the ASPIRE Investigators meeting in May 2005 and also during the ISTH in Sydney during August 2005. Meetings are planned but not yet formalised for 2006. Welcome to Dr Douglas Coghlan from Flinders Medical Centre who now co-chairs the CTG.

The ASPIRE study is the major undertaking of the CTG. This study examines the benefits of low-dose aspirin as prophylaxis against recurrent venous thrombosis after initial warfarin therapy in patients with unprovoked DVT or pulmonary embolism. There are now 224 patients enrolled from 23 actively recruiting sites. A further 4 sites are yet to enrol patients and a further 20 sites awaiting ethics approval. The Trial Management Committee is committed to find 50-60 sites across Australia and New Zealand so more sites are welcome to join the project. The recruitment period will be about 2 years ending in December 2007. The companion study in Italy, the WARFASA Study, has now recruited 124 patients. Further international collaborations are being explored in the UK, other European sites, Nth America and Asia.

A major discussion topic in the management of patients with vein thrombosis is the prediction of recurrence. A sub-study of the ASPIRE study, the PREDICT study, will be examining the ability of residual thrombus, plasma D-dimer, and other clinical and laboratory parameters to predict late recurrence of vein thrombosis. Unfortunately our application to the National Heart Foundation was unsuccessful. Given the importance of this substudy the ASTH CTG have agreed to support the PREDICT study in 2006 so sites should expect approaches for this sub-study early in 2006 once logistics of the study are solved.

Primary Immune Thrombocytopenia remains an interest for the ASTH CTG. There are now at least 2 novel small molecular weight peptides with thrombopoietin agonist activity in clinical studies amongst the group. The protocol for the randomised study of oral dexamethasone versus oral prednisone for acute initial therapy of adult ITP, the ASTH ITP1 study, is almost complete and will be circulated to the group in 2006.

The ASTH CTG is always keen to receive new members and new ideas. Interested people or any enquiries may be directed to Tim Brighton (*t.brighton@unsw.edu.au*).

*Tim Brighton*

# UPCOMING MEETINGS IN 2006

| MEETING | WHERE/DATES | CONTACT |
|---|---|---|
| **46th British Society of Haematology ASM** | Edinburgh<br>3-5 April 2006 | *www.b-s-h.org.uk* |
| **XIXth International Symposium on Technological Innovations in Laboratory Haematology** | Amsterdam, The Netherlands<br>25-28 April 2006 | *www.islh.org* |
| **Platelets 2006 Symposium** | Ma'ale Hachamisha, Israel<br>11-14 May 2006 | *www.med.unc.edu/**isth***<br>(Haematology link) |
| **19th International Congress on Thrombosis** | Tel Aviv<br>14-19 May 2006 | *thrombosis2006@kenes.com* |
| **2006 World Federation Haemophilia World Congress** | Vancouver<br>21-25 May 2006 | *www.wfh.org* |
| **52th Annual Scientific and Standardization Committee Meeting** | Oslo, Norway<br>28 June -1 July 2006 | *www.med.unc.edu/isth/*SSC2006/ |
| **18th International Society of Fibrinolysis and Proteolysis Congress** | San Diego<br>27-31 August 2006 | *www.med.unc.edu/**isth***<br>(Haematology link) |
| **4th Asian-Pacific Congress on Thrombosis and Hemostasis** | Suzhou, China<br>21-23 September 2006 | *www.apcth.org.cn*<br>**Deadline for abstracts May 31, 2006** |
| **British Society for Haemostasis and Thrombosis Annual Meeting** | St Helier, Jersey<br>4-6 October 2006 | *www.bsht.bham.ac.uk* |
| **ASTH Workshop** | Hobart<br>14 October 2006 | *m.adams@curtin.edu.au*<br>*emma_perrin@health.qld.gov.au* |
| **8th HSANZ/ANZBT/ASTH Annual Scientific Meeting** | Hobart<br>15-18 October 2006 | *www.cdesign.com.au/*HAA2006 |
| **AIMS National ASM** | Hobart<br>23-27 October 2006 | *www.aims.org.au* |
| **The American Society of Haematology 48th Annual Meeting** | Orlando, Florida<br>9-12 December 2006 | *www.hematology.org* |