Dear Fellow Clotter

This is the first newsletter of the new council for 2010 and the continuation of a Queensland monopoly of the free press for the ASTH. Emma has passed on many useful tips, and Megan has been instrumental in guiding me towards a moving deadline before the end of 2010.

The appointment of a new president and council will hope to consolidate and strengthen the current success of the ASTH. The president's report is included in this newsletter.

Thank you to everyone who willingly contributed to the content of this newsletter and future contributors will be targeted from the remainder.

I hope that you find the content informative, and any suggestions and content for future editions are gratefully accepted.

Peter Wood

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## ASTH Council 2009-2011

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- CSL Bioplasma
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- Novo Nordisk
I sit writing this on a sunny, autumn day in Auckland with clear, blue skies and a just a hint of a winter chill.

2010 is off with a bang and the year is already accelerating ahead, promising to be a good one. 2009 seems such a long time ago but it was a busy year and the 2009 HAA Annual Scientific Meeting was a wonderful success. Congratulations to the organising committee (Doug Coghlan and Simon McCrae) for developing a thoroughly interesting programme and another great opportunity for us all to get together, share knowledge and have fun. Professor John Fletcher delivered an engaging Barry Firkin Oration and the invited overseas speakers, Paul Kyrle and Nigel Key, made excellent contributions, complemented by talks by our talented local speakers.

So what is new in 2010?

Changes and Thanks!

ASTH now has a new Council and President and, on behalf of Council and all the membership, I would like to extend a vote of thanks to the council members who have stepped down: Emma Jones-Perrin, Mark Smith and Chris Ward. I would like to make special mention of the contributions they made to ASTH during their time as Council members.

To Emma, huge praise and thanks for your hard work as editor of our newsletter – you always managed to gently encourage contributions from members so that we were kept up-to date with what was happening locally and internationally in the field of thrombosis and haemostasis. I imagine it is perhaps with some relief that you have handed the editor's job onto Peter Wood, a new Council member. Both Mark and Chris led the Council and the Society so admirably and with such skill and apparent ease that not only have they left the Society in its current robust situation, but they have left their successors with very hard acts to follow.

HAA 2010: Auckland 17-20 October

This year’s HAA Annual Scientific Meeting will be held in Auckland, New Zealand from 17-20 October 2010. We have three confirmed international speakers: Marc Roger from Ottawa, Canada, Mike Greaves from Aberdeen, Scotland and Andreas Greinacher from Germany.

We plan to focus on a number of topics with joint sessions with speakers from HSANZ and ANZSBT including haematological problems in pregnancy, management of acute coronary syndromes and bleeding during cardiac surgery and with new anticoagulants, risk profiling and decision analysis on longterm anticoagulation, pathophysiology and management of heparin-induced thrombocytopenia to name but a few. I think it is going to be a very interesting meeting and, as usual, we want to take the opportunity to showcase all of our local talent at the meeting so I may be in touch.

I have the onerous task of organising the social programme. Planning is well underway – the venue for dinner booked, tasting of the food arranged (I will be doing that – just to make sure it will be top quality, you understand) the band is booked and we will have a special guest performance by Don McGlashan, a fabulous NZ musician. So bring comfortable shoes because you are going to be dancing all night.

Grace is helping once more with organising the ASTH Scientific Workshop, which will be held in the Clinical Education Centre at Auckland City Hospital on 16 October. Mike Greaves has very kindly accepted our invitation to talk at the meeting and we hope to arrange a great session on the pitfalls of diagnosis of antiphospholipid antibodies as well as issues with anti-Xa assays, Factor XI deficiency, diagnosis of NAIT.

Speaker invitations and plans for the 2011 HAA in Melbourne and the 2012 meeting in Sydney are already underway but more news of those later. Such advance planning makes me giddy!


Tim Brighton, Huyen Tran, Simon McCrae, Sanjeev Chunilal, Laura Young and myself have been working hard for the past 18 months with colleagues from obstetrics, obstetric medicine, maternal-fetal medicine and obstetric anaesthesia developing NZ and Australian guidelines for the diagnosis, acute management and prevention of pregnancy-associated VTE. No mean feat can I tell you – the phrase “herding cats” springs to mind but nevertheless we have completed our final draft and hope to circulate the guidelines to Council for endorsement soon.

I hope to see many of you in Cairo for this year’s ISTH SSC meeting from 22-25 May. Also some of you may be interested in the International Society of Obstetric Medicine Meeting that will be held in Melbourne 1-3 October.

Well that wraps up all my news for the moment. Take care – I am off out into the sunshine (while it is still here!)

Claire McLintock
The HAA annual scientific meeting for 2009 was held in Adelaide in October. Blessed with unseasonably fine weather, the conference had over 1,000 attendees with ASTH members being well represented.

Despite the late withdrawal of Marco Cattaneo due to illness, those attending were still able to hear excellent talks from a strong panel of international speakers. Associate Prof Paul Kyrle, from Vienna, presented an in-depth overview of clinical and laboratory predictors of recurrent venous thrombosis, drawing largely on data from the large AUREC cohort study. He also presented a succinct overview of current strategies for the diagnosis of venous thromboembolism.

Dr Nigel Key, from UNC at Chapel Hill, gave a number of presentations around haemostasis and bleeding disorders. His discussion of the role of tissue factor in the normal haemostatic process, and also the possible contribution of microparticle associated tissue factor in pathogenic states such as cancer associated malignancy, was of particular interest. He also took part in an excellent masterclass focussing on management of patients with haemophilia and inhibitors.

Finally, and by no means least, those attended were treated to a number of dynamic talks by the pocket-rocket Benny Sorenson. Familiar to many Australian “clotters”, Benny talked with enthusiasm about the role of Fibrinogen in massive transfusion in a joint session with the ANZSBT. He also gave an overview of the emerging use of global coagulation assays such as thrombin generation and thromboelastography.

Whilst prospective trials using clinical endpoints demonstrating a clear improvement in outcome with the use of these assays are still not available, Benny gave a number of examples where these assays were used in the management of individual patients with clear benefit.

There was also a strong contingent of local speakers. A special commendation should go to Joanne Joseph who unflinchingly stepped into the breach to cover for the absence of Marco Cattaneo. Despite the difference in accent (and appearance), her talk clearly outlined the issues around failure of response, clinical or pharmacodynamic, to antiplatelet agents, and more than compensated for his absence.

Other highlights included an excellent overview by John Eikelboom of new anticogulant agents, and the Barry Firkin oration by John Fletcher highlighting his long involvement in improving outcomes for patients by advocating the use of appropriate thromboprophylaxis.

ASTH members are also to be congratulated for the high standard and quantity of abstract submissions. We hope that the upward trend in abstracts from our society continues this year at what looks to be an excellent meeting being planned in Auckland.

I look forward to seeing you all there.

Simon McRae

SECRETARIAT NEWS

Council Election
ASTH held online elections in October to elect the 2009-11 Council. Three of the existing Councillors retired – Chris Ward, Mark Smith and Emma Perrin – and I would like to thank them for their help over the last 6 years. Although the election was tightly contested, at the final count three new Councillors were elected: Sanjeev Chunlial (NZ), Jenny Curnow (NSW) and Pete Wood (Qld). The online voting seemed to be very easy to use and it was pleasing to see a large number of members taking the time to vote.

ASTH Workshop
Last year’s Workshop was another resounding success. There were even more delegates than in previous years, confirming that the Workshop’s reputation is growing. Feedback was also positive with the interactive sessions proving to be very popular. We will definitely try to include the interactive key pads in this year’s program! We also managed to secure more sponsors than last year, again proving that the formula of presentations, networking and posters seems to be working for our commercial supporters too.

Renewals
There are less than 20 members who have not renewed their memberships for 2009-10. Please, if you know you’re one of them, complete the forms and send payment to me asap – this will probably be the last newsletter you’ll receive as your name will drop off the mailing list soon. If you’ve misplaced your forms, drop me a quick email and I’ll make sure another set is emailed to you.

As always, a call for news items or interesting results to add to our website. Please feel free to send me anything you think other members will be interested in.

Megan Sarson
Four years after Hurricane Katrina hit New Orleans in August 2005 forcing a change in venue for the 47th Annual Meeting of the American Society of Hematology from New Orleans to Atlanta Georgia, the American Society of Hematology returned to New Orleans to hold its 51st Annual meeting.

After 24 hours of travelling, I was daunted at the prospect of a full day of education sessions with a 7.30am start. Nevertheless I was there at 7.30am to be educated about mucocutaneous bleeding disorders. Paula Bolton-Maggs from Manchester in the UK opened the session attempting to resolve the enigmas of Factor XI deficiency. I was pleased to hear some sense in relation to the bleeding reported in patients with mild deficiency or even normal factor XI deficiency. Perhaps it may actually be due to something else, ie these people may have VWD or a platelet function defect or some other modifier leading to a bleeding tendency. This is something I have thought for a long time, but it never seemed to be reported. I also think that often bleeding is over reported in many patients. I often recall what I was told by my mentor, Ahti Lammi, at The Children’s Hospital as a young and naïve haematology registrar, that when asking families if they have a bleeding problem, how many of them enthusiastically report “yes” and then report symptoms such as bleeding after cutting themselves shaving or nosebleeds as a child. There is a lot of poor quality data out there in the literature suggesting that carrier status of a factor deficiency is the cause of bleeding despite normal factor levels. It makes no sense to me. After an eloquent discussion on Factor XI by Paula Bolton-Maggs, Evan Sadler, from St Louis, spoke about low VWF as a risk factor for bleeding, a topic he has been talking on for quite a number of years now. He again confirmed the idea that mild bleeding symptoms are common in apparently healthy populations and have many causes, which can make it impossible to attribute bleeding to any single factor such as low VWF. He advises to treat low VWF (30-50%) as a risk factor and not as a disease and that it is not useful to label such patients with VWD. I think this is particularly important, all too often seeing patients inappropriately labeled with VWD. I think this is particularly important, all too often seeing patients inappropriately labeled with VWD. This session was concluded by Francesco Rodegherio giving an approach to the treatment of VWD using phenotypic and molecular data.

Bone marrow failure, congenital neutropenia, sickle cell disease and immunodeficiencies kept me entertained throughout the rest of the day, with sessions continuing until 5.30pm. I was exhausted but then it was time to check out some posters, another daunting task with literally thousands of posters on display throughout the course of the meeting.

Sunday morning had me back for more education. This time on thalassaemia and the role of newborn screening. It was interesting to hear how the newborn screening programs for sickle cell disease are run, and whilst many other haemoglobinopathies may be detected in this process, they are not all necessarily followed up because the law in many US states only mandates follow up for patients affected with sickle cell disease. At least they have screening for sickle cell disease. This is something not currently done in Australia, but with the recent migration patterns in Australia it is certainly something we need to think about. The team from California were pushing the concept of screening for alpha thalassaemia and whilst there certainly is a significant amount of alpha thalassaemia disease burden, I am not sure it truly fulfills the criteria of a disorder for which screening should be recommended. Unlike sickle cell disease where early diagnosis may make a significant difference by preventing death from sepsis or splenic sequestration, for Hb H disease there is no great advantage gained by early diagnosis.

Unfortunately Monday morning had me back at the convention centre for a 7am start to listen to the session on haemophilia inhibitors. Whilst the initial papers on genetic modifiers of the inhibitor risk were interesting, I wondered whether I should have stayed in bed a little longer. The data presented at times was contradictory and most of the risk factors identified to date are relatively weak, and there is not much one can do about these risk factors anyway. I did however wake up when Guenter Auerswald, from Bremer in Germany, presented his small study on early low dose prophylaxis regimen that appears to reduce inhibitor formation. This regimen consisted of once a week doses of 250 U of FVIII from the time of first treatment (av. age 10 mos and 1 exposure day) and was compared with a historical control group who had on demand therapy until starting standard dose prophylaxis after the first joint bleed (av. age 19 mos and 30 exposure days). There was a dramatic difference in inhibitor rate (3.8% in the early low dose group compared with 47% in the controls). This paper was interesting on several counts. If this does reduce inhibitor risk it would be an important advance. But I was also interested to see such a high inhibitor rate in the control group at 47%, way above what has been historically reported (15-30%) and the reason for this requires further investigation. The numbers in the trial were low and it will be interesting to see if the results hold in further studies.

Keith Hoots and Donna DiMichelle were overheard in the poster hall that evening postulating on reasons why the numbers were down. However, David Lillicrap reported to me the following day that the numbers were good with over 22,000 people attending. The local shopkeepers repeatedly
confirmed that there were over 20,000 doctors in town to whom they were offering a “special price”. The city of New Orleans was happy to host the biggest conference held there since Hurricane Katrina ravaged the city.

On Tuesday the conference wrapped up with just a half day of sessions. Many of the attendees rapidly departed the city, but I had another day. I took the opportunity on the advice of a Canadian Colleague to take the “Hurricane Katrina” bus tour of the city.

The graphic reality of the impact of Hurricane Katrina was truly appreciated from the windows of the Greyhound bus, with numerous vacant blocks of land where homes once stood, the abundance of motorhomes outside homes yet to be rebuilt as well as abandoned rotting homes still present 4½ yrs later. When Hurricane Katrina hit, it is estimated that about 80% of the city’s 500,000 citizens had already evacuated – predominantly those with the means to get out. Those that did not leave were trapped without water, without power and without food as 80% of the city flooded. The nightmare these people lived through has been well reported. The rebuilding is ongoing. The French Quarter escaped most of the flooding and is alive and well and open for business. The poorer suburbs are gradually being rebuilt and we saw a number of examples of the “Brad Pitt” houses in the hardest hit areas. I am sure New Orleans will continue to rebuild and whilst it will never be the same as before Hurricane Katrina I hope it can continue to retain its unique charm.

Julie Curtin, The Children’s Hospital, Westmead

ASTH Travel Grant Winners 2009
Steven Lazar Chee Wee Tan
Marie-Christine Morel-Kopp Nathalie Tjen
Tina Noutsas Huy Tran

ASTH Medal Winner 2009
Mohammad Al Tamimi (winning abstract on page 8)

ASTH Medal Runners Up 2009
Chee Wee Tan (Northern Blood Research Centre, NSW): Lepirudin Use and Laboratory Monitoring in Patients on Chronic Haemodialysis with a history of Heparin-induced Thrombocytopenia (HIT)

Huy Tran (Alfred Pathology Service, Vic): Thrombin Generation and Vitamin K Dependent Procoagulant Factors in Warfarinised Adult Patients

NEW MEMBERS
The ASTH would like to welcome the following members who have joined since the last newsletter

Ken Croll
Mohammad Al-Tamimi
Terry Fawcett
Shoma Baidya
Sharon Yong
Sunethra Athauda
Ofira Waldispuhl
Lubna Al-Zadjali
Valerie Rowland
Leo Gonzalez-Perez
Nicholas Viiala

Melissa Carmenzuli
Reanuga Gopal
David Yeung
Ritam Prasad
Thet Tin
Lacey Johnson
Leanne Sinclair
Lisa Marks
Lochlan Hayes
Raymond Banh

We would also like to welcome those new members who wish to keep their contact details private.

ASTH TRAVEL GRANTS 2010
The ASTH offers up to 6 travel grants to the value of $1000 to attend the Annual Scientific Meeting, this year in Auckland, NZ. The grant is conditional on the acceptance of a submitted abstract to the meeting.

There are also 3 additional study grants of $5000 which will allow the applicant to attend other meetings or spend a period of time in research. These grants will require the submission of a specific application form detailing the period of study, reason for study and a proposed abstract submission.

Full details and application forms are available through the secretariat (ASTH@bigpond.com).
The 5th ASTH Scientific Workshop was held on Saturday 17 October. It was an excellent day with 109 delegates.

Our first session started with Robyn Coleman bringing us up to date on Uncertainty of Measurement. Tom Exner followed with a presentation on the TEG. Roslyn Bonar from the RCPA gave us the results from two recent inhibitor QAP surveys and we finished with a controversial talk on INR and liver disease from Connie Solano.

Our session after morning tea was on HITTS. It was run by Simon McRae, who started with an overview, then Elizabeth Duncan, David Yeung and Tracy Dixon presented data on the variety of methods that are currently available. This session finished with a HITTS case study from Catherine Banks who had photos that probably didn't go well before lunch!

Unfortunately our International speaker, Prof Marco Cattaneo, was unable to make it to Australia due to illness. We still managed to fill in the session with Marie-Christine Morel-Kopp explaining Multiplate Impedance Aggregometry, Scott Willoughby covering Aspirin and Clodipogrel Resistance and Barry Woodhams giving us the latest on Microparticles.

Our final session was three case studies. Amanda Davis presented an APL case. Sue Rodgers gave us an entertaining VWD case that included audience participation. We finished with Dr Vaughan Williams showing us the world of paediatrics and how one must think outside the square sometimes.

The day ended with a sundowner kindly sponsored by Siemens Medical Diagnostic Solutions.

This year was the first time we had posters. We had eight posters and hope to have more at the next workshop. Our prizewinners for the day were Connie Solano and Marie-Christine Morel-Kopp.

I would like to thank the team in Adelaide for all their help, Sue Rodgers, Elizabeth Duncan, Brian Dale and Simon McRae.

I would also like to thank our sponsors for their continuing support and Helena Laboratories and Stago for production and supply of the workshop CDs

Please see below details for this year’s workshop.

Grace Gilmore
Some of you may have read the recent article in Blood and the commentary on ADAMTS-13 testing in TTP (Blood, 25 February 2010, Volume 115, Number 8, p1500 and same issue p 1475). These articles provide interesting background reading for the utility of testing.

ADAMTS-13 is not locally available for many sites and you may wish to consider referring samples. HAPS is now offering a testing service as detailed below.

ADAMTS-13 Activity and Antibody testing is now being offered in NSW by the Haematology Department at Hunter Valley

ADAMTS-13 and TTP?
ADAMTS-13 (A Disintegrin And Metalloprotease with Thrombospondin repeats member #13) is the major protease responsible for cleaving von Willebrand factor (vWF) and, as such, is responsible for control of vWF multimer length. In TTP, a severe deficiency of ADAMTS-13 activity, (<10% of normal plasma) causes accumulation of ultra-large vWF multimers which in turn leads to formation of platelet-rich thrombi in the microcirculation and to symptoms of end-organ ischaemia.

Deficiency of ADAMTS-13 is most commonly acquired (i.e. caused by inhibitory auto-antibodies directed against ADAMTS-13) and less commonly, congenital (i.e. caused by production of a dysfunctional ADAMTS-13 protein). Measurement of ADAMTS-13 and detection of ADAMTS-13 specific antibodies allows (in most cases) differentiation of congenital and acquired TTP from other thrombotic microangiopathies (e.g. HUS, atypical HUS, HELLP, PET etc).

Testing Principle
The assay employs fluorescence resonance energy transfer (FRET) technology to allow measurement of ADAMTS-13 activity in citrated plasma. A recombinant peptide containing the cleavage site for ADAMTS-13 as well as an auto-quenching fluorochrome is added to patient plasma at 37°C. Cleavage of the substrate by ADAMTS-13 uncouples the fluorochromes resulting in an increased fluorescence which is relative to ADAMTS-13 activity.

SAMPLE REQUIREMENTS

Sample Type:
Frozen citrated plasma (double centrifuged)

Pre-plasma Exchange Samples are Preferred

Volume required:
2 x 0.5mL aliquots (preferred)
1 x 100µL (minimum)

Assay Frequency:
Monthly or performed urgently as required.

Cost:
$160.00 Routine sample batched once a month.
$320.00 Urgent samples (830-1700 Mon-Fri).
$450.00 Urgent samples (after hours and weekends)

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Aim
The aim of this study is to evaluate the effect of coagulation on the surface expression of the platelet collagen receptor, glycoprotein VI (GPVI). We have previously shown that collagen, collagen-related peptide (CRP), snake toxins or anti-GPVI antibodies induce metalloproteinase-mediated ectodomain shedding of GPVI, generating an ~55-kDa soluble fragment (sGPVI), and an ~10-kDa remnant fragment that remains platelet-associated.

Methods
We used a newly-developed enzyme-linked immunosorbent assay (ELISA) to measure sGPVI levels in human plasma from healthy individuals, normal platelet-rich plasma where coagulation was experimentally induced, and plasma from patients with disseminated intravascular coagulation (DIC).

Results
Initial studies showed that plasma sGPVI levels in 192 healthy individuals were 19.5±15.4 (2×s.d.) ng/mL, and levels were independent of age, gender or common GPVI polymorphisms (associated with Gln317/Leu substitution). However, sGPVI levels were markedly elevated following coagulation:

First, while plasma sGPVI was independent of the anticoagulant used for blood collection (acetic acid-citrate-dextrose (ACD), citrate, or EDTA), collecting blood into a silica-coated coagulation tube and analysing serum from clotted blood showed markedly elevated sGPVI levels (124 ng/mL cf. 29 ng/mL in ACD-anticoagulated plasma). Second, inducing coagulation in normal citrated platelet-rich plasma by recalcification with or without added tissue factor resulted in increased sGPVI. This increase in sGPVI followed initial thrombin generation and peaked after 30 minutes at ~7-10-fold baseline levels. Shedding was strongly inhibited by hirudin (thrombin inhibitor) or GM6001 (broad spectrum metalloproteinase inhibitor), suggesting activated thrombin induced metalloproteinase-mediated GPVI shedding from platelets. Third, initial analysis of patients with DIC showed elevated plasma sGPVI consistent with increased GPVI shedding in vivo associated with coagulopathy.

Conclusions
These findings reveal that coagulation results in ectodomain shedding of platelet GPVI, and significant elevation of sGPVI levels in plasma. GPVI depletion limiting adhesion-dependent platelet activation may compensate for increased procoagulant activity in disease states.

No conflicts of interest to disclose.

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**UPCOMING MEETINGS**

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<td>ISTH SSC</td>
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<td>ASTH Scientific Workshop</td>
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<td><a href="mailto:grace.gilmore@health.wa.gov.au">grace.gilmore@health.wa.gov.au</a></td>
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<td>52nd ASH Annual Meeting</td>
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