

Dear Fellow Clotter

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SECRETARIAT NEWS

Preparations for the ASTH Scientific Workshop are well under way so mark Saturday 17 October in your diary now. The poster session will be something new at this year's workshop, with posters being shown both at the Workshop and afterwards at the HAA meeting.

Following on from delegate feed back last year, it was decided that there was enough support to hold the poster

session in light of the number of delegates who do not go on to attend the HAA meeting. Please get behind this new session and think about what you could submit.

The web site continues to be updated regularly but it would be great if you could let me know if there's something you'd like to share with other members which I can add to the site. Perhaps you've read an interesting article or have some interesting results yourself. Do you know of another site which would we could link to? Just drop me a line with any suggestions.

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

Michael Robinson
Sue Russell
Joanne Perel
Chris Barnes
Paul Zerafa
Ferenc Szabo
Ram Suppiah

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

Megan Sarson

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HAA CONFERENCE 2009 – ADELAIDE

On behalf of the organising committee, I would like to invite you all to this year's HAA conference, to be held in Adelaide from 18-21 October 2009. Along with the normal opportunity the conference offers to network and socialise with your colleagues, this year's scientific program offers something for all ASTH members, regardless of whether your area of interest is thrombosis, bleeding disorders, or platelets and arterial disease.

In the area of venous thrombosis, the main visiting speaker is Professor Paul Kyrle from Vienna. Amongst other things, he will be presenting some of his groups' extensive work on using laboratory and clinical markers to help stratify the risk of recurrent venous thrombosis. Other talks will cover recent results of new anticoagulant trials (with John Eikelboom making the pilgrimage back down under to talk to this topic), diagnosis of venous thrombosis, post-thrombotic syndrome, and thrombophilia testing for pregnancy complications, and various other topics of interest.

Nigel Key from Chapel Hill leads the list of speakers in the area of bleeding disorders. He will be speaking on a range of topics from tissue factor and micro-particles, to management of inhibitors in patients with haemophilia.

Again, his presentations will be complemented by talks from a strong local contingent of speakers.

In the area of platelets and arterial disease we are very fortunate to have Professor Marco Cattaneo coming to speak. He will be addressing the hot topic of testing for anti-platelet drug resistance, as well as mechanisms and diagnosis of platelet function disorders. Talks by other speakers will cover testing for ADAMTS13, and the vexed issue of peri-operative management of anti-platelet therapy.

The main scientific program will again be complemented by the ASTH workshop, to be held the day prior to the main conference. Professor Cattaneo will also be speaking on platelet function testing at the workshop. There will also be the usual social events, presenting the chance to indulge in some of South Australia's finest produce (and I don't mean the Adelaide Crows).

So again, on behalf of the organising committee, I would like you all to make the trip down south (north for the Tasmanians). We are looking forward to seeing you all in October.

Simon McRae

ASTH SCIENTIFIC WORKSHOP 2009

The 2009 ASTH workshop will be held on Saturday 17 October at the University of South Australia, City West Campus. We will be in the Allan Scott Auditorium in the Hawke Centre.

We are pleased to announce that international invited speaker, Prof. Marco Cattaneo, will give a presentation on platelet function testing. The program is currently being finalised and we will inform you when the registration forms are on the website. If you have an interesting case, weird results you would like to talk about and discuss or a hot topic, please don't hesitate to contact me by end of May to be included in the program. Please send me a brief outline of your 10-15 minute presentation.

Morning tea, lunch and afternoon tea is included as well as a sundowner from 4.30pm-6pm.

Registration for the workshop is separate from the HAA.

This year we would like to try something different. We are keen to get the young scientists involved. We would like to call for posters from young scientists. These will be displayed next to the trade and prizes will be awarded at the end of the day. Please send me a brief outline of your poster.

Look forward to seeing you at this year's meeting.

Please let me know if you require further information or assistance.

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IT'S RAINING ANTICOAGULANTS

Hatem H. Salem

Australian Centre for Blood Diseases

They are coming from everywhere, Apixaban, Rivaroxaban, Dabigatran, Lepirudin, Idraparinux, Ultra Low Molecular Weight Heparin and the list goes on. They are all new anticoagulants, some are parenteral other oral. They are all effective in preventing the development of venous thrombosis and from the studies published to date appear to be very promising for the treatment of established thrombosis. What a transformation!

Only a few years ago, we just had the Heparins (unfractionated and low molecular weight) and Warfarin. Now we are spoilt for choices. While parenteral anticoagulants will always have a role, most clinicians are more excited at the prospect of the new oral drugs. These fall into two groups, direct anti-thrombin of which Dabigatran is the only one, and direct anti-Xa such as Apixaban and Rivaroxaban.

The debate is still unsettled and probably will never be as to which the better anticoagulant approach is; inhibiting thrombin or Factor Xa. The likelihood of head-to-head comparison will probably never happen, and even if it did, one will only conclude that one approach is better at the particular dose used. What is more relevant, is that from the studies published to date, both the anti-thrombin and anti-Xa drugs appear to be highly effective with a reasonably wide therapeutic window, a predictable gastro-intestinal absorption and a safety profile comparable to current anticoagulants. Regular monitoring of the clotting time may therefore be a thing of the past when using these new drugs.

The two front runners are Rivaroxaban and Dabigatran. The clinical program for Apixaban lags a little behind but is nevertheless at a reasonably advanced stage. Dabigatran is a potent non-peptidic direct thrombin inhibitor. It was designed by a structure-based approach using of bovine thrombin complexed to a direct inhibitor. The drug was found not to be orally active, and was therefore modified to a prodrug (Dabigatran Etxilate) to modify its physicochemical property and enable it to be absorbed. The drug has potent anticoagulant effects after oral administration. Rivaroxaban on the other hand is a small molecule which binds tightly and specifically to factor Xa thereby inhibiting its activity and limiting thrombin generation. The drug inhibits free factor Xa, Xa that is part of the prothrombinase complex as well as clot-associated factor Xa.

Both Dabigatran and Rivaroxaban have been fully evaluated as thromboprophylactic agents in patients

undergoing major lower limb arthroplasty (the Renovate/Remodel program and the Record program respectively).

These extensive and well performed studies were very similar in their design and utilised venography as the objective end point for efficacy. In these studies, both drugs were shown to be highly effective thromboprophylactic agents. The studies have recently been published (1-4) and have also been presented at several international meetings. As a result both drugs have received TGA approval for use as thromboprophylactic agents in patients undergoing knee or hip replacement.

The results of the treatment studies (deep vein thrombosis and pulmonary embolism) are pending. The application of these new drugs to patients in atrial fibrillation is particularly important. Several studies involving Idraparinux (once a week injection), Rivaroxaban, Apixaban and Dabigatran are currently underway. In all these studies the comparator is Warfarin. One study (Dabigatran) has completed recruitment whereas the others are in advanced recruitment stage. Approximately 15,000 subjects have or are planned to be recruited in each study with a substantial number of warfarin naïve patients. The answers are eagerly anticipated.

In addition to venous thrombosis and atrial fibrillation, the new anticoagulants are also been evaluated in patients with arterial thrombosis, specifically acute coronary syndromes. While we expect their introduction to be slow, my expectation is that in 10 years from now, Coumarins will be relegated to the museum but will maintain their role as the number one rodenticides.

- 1) Eriksson, B. I. *et al.* Oral dabigatran etexilate vs. subcutaneous enoxaparin for the prevention of venous thromboembolism after total knee replacement: the RE-MODEL randomized trial. *Thromb. Haemost.* **5**, 2178–2185 (2007)
- 2) Eriksson, B. I. *et al.* Dabigatran etexilate versus enoxaparin for prevention of venous thromboembolism after total hip replacement: a randomised, double-blind, non-inferiority trial. *Lancet* **370**, 949–956 (2007)
- 3) Eriksson BI, Borris LC, Friedman RJ, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after hip arthroplasty. *N Engl J Med* 2008;358:2765-2775.
- 4) Lassen MR, Ageno W, Borris LC, et al. Rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty. *N Engl J Med* 2008;358:2776-2786.

5TH CONGRESS OF THE ASIA-PACIFIC SOCIETY ON THROMBOSIS AND HAEMOSTASIS



In September last year, the 5th APSTH Congress was held in Singapore. Organised by the haematologists of the Singapore College of Physicians, and chaired by Dr Tien Sim Leng, the Congress attracted over 500 delegates and featured 52 invited speakers, including 6 Australians.

Attendees came from many Asian and Pacific rim countries, and provided many different perspectives on the diagnosis and treatment of coagulation disorders. The Congress was held in a large hotel overlooking the Singapore river – only a few steps away from the airconditioned interior, and you were definitely in the tropical zone.

A series of excellent plenary lectures and concurrent sessions covered the full range of venous and arterial thrombosis, inherited and acquired coagulopathies and specialised areas such as paediatric and obstetric disorders. Our “own” experts featured in the plenaries, with comprehensive reviews by Beng Chong (new therapies in ITP), Alex Gallus (VTE guidelines) and John Eikelboom (antithrombotic therapy in the acute coronary syndrome). Symposia with an Asian focus included snake toxins and herbal therapies affecting haemostasis, animal thrombosis models developed in Taiwan, Japan and Korea, and a VTE session comparing prophylaxis guidelines and examining

the emerging evidence for VTE rates in Asian patients that are not markedly different from European studies. Laboratory testing was also well covered, with sessions on new D-dimer and platelet function assays.

The congress highlighted the established strengths of Asian researchers in basic science and the developing interest in clinical trials. Many of the trials of new antithrombotics are now being conducted in Asian countries as well as Western ones – this offers not only great opportunities for recruitment, but will also test whether the safety profile is really different between ethnic groups, an often-expressed concern from clinical

haematologists based in Asian countries. We can also learn from the vast stores of traditional and herbal medicines, which are now being rigorously tested for activity, and from technological advances in automation and diagnosis.

Platelet biology was a particular focus of this meeting, thanks to the UK-Japan Platelet Conference which began one day prior to the Congress and for a joint morning session. This is the third such conference held since 2002, bringing together platelet scientists from both regions, for vigorous discussion and networking over a cool ale. The standard of the presentations was excellent, highlighting new developments in platelet signalling, disease-predicting polymorphisms and animal and *in vitro* models of thrombus formation.

In the latter category, Dr M Emerson reported a non-invasive model of platelet-triggered thrombosis in mice (using pulmonary scintigraphy) which would greatly simplify the study of gene knockouts. Two intriguing papers from Japan (Drs N Takayama and Y Matsubara) reported the generation of megakaryocytes and platelets from inducible pluripotent stem cells, and from cultured adipocytes – these raise the possibility of “growing” platelets to order, from non-haemopoetic tissues. The ongoing large-scale “Bloodomics” collaboration in the UK and Europe also featured, in a plenary by Dr W Ouwehand on platelet polymorphisms and thrombosis. Finally, there were new prospects for the clinicians, such as using platelet-derived microparticles to monitor antiplatelet therapy.

As always, the opportunity to “compare notes” with colleagues from other countries, and to discuss new collaborations was invaluable – this continued on the city tour, an APSTH tradition on the final day, which took in the orchid gardens, Chinatown and Hindu temple and the ultramodern downtown, just days before the inaugural Singapore Grand Prix. Prof Hatem Salem and I represented Australia at the APSTH council, and can confirm that both the APSTH and a satellite platelet conference (UK-Japan-Australia) will be held in Melbourne in 2012, concurrent with the HAA meeting. We see this as a great opportunity to promote our field in the region, and establish stronger links with Asian clinicians and researchers. For those who can't wait that long, the next APSTH congress will be held in Bali from 14-16 October 2010. Hope to see many of you there!



Paul Harrison (UK platelet group) with Chris Ward in the National Gardens.

Chris Ward

WOMEN'S HEALTH ISSUES IN THROMBOSIS AND HAEMOSTASIS

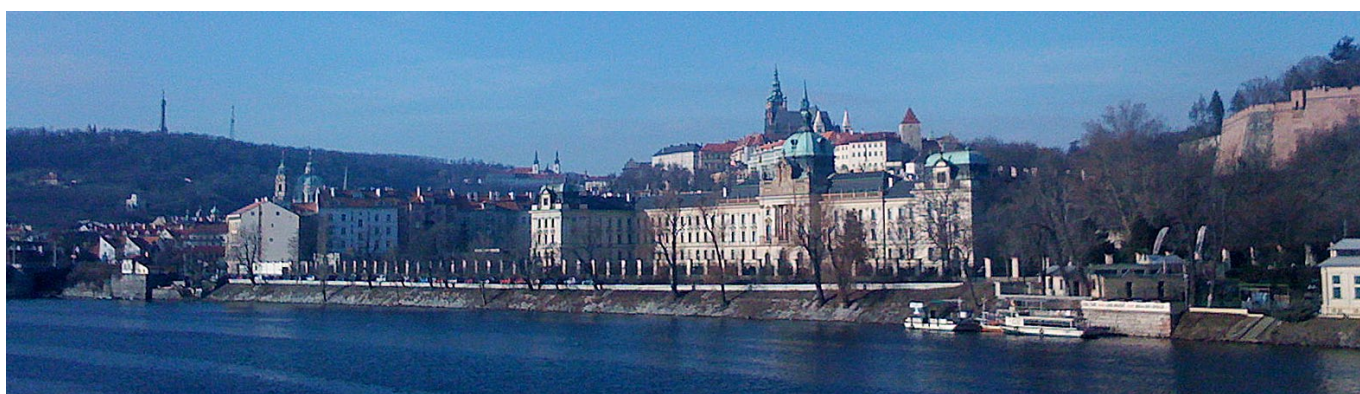
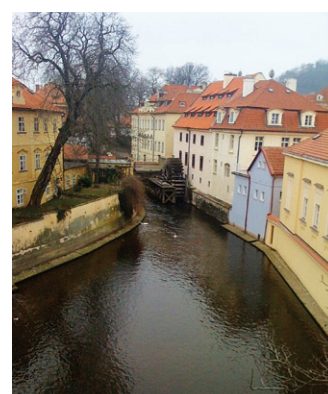


Prague, February 2009 – the setting for the 3rd International Symposium on Women's Health Issues in Thrombosis and Haemostasis. With all the usual suspects and all the usual subjects. This biannual conference is an excellent way to review the most up-to-date opinions on what is happening in this field. It is small enough to catch up with friends and colleagues from around the world and an excellent way to remind oneself why Christmas is much better in summertime. Most of the eminent speakers in this area are invited to give talks but as we know, the data in this field is not rapidly evolving so it is probably only worthwhile going to the meeting every other year if your focus for attendance is on updating your clinical knowledge rather than building relationships. It is an excellent forum for identifying where gaps in our knowledge in this field lie and discussing with like-minded clinicians to fill the gaps. In particular this year there were excellent presentations on microparticles and placental haemostasis and Anath Karumanchi, from Harvard gave an excellent talk on Angiogenesis and Preeclampsia – summarizing current knowledge of the role of sFlt and endoglin in pathogenesis of this important pregnancy complication. Scott Nelson from Glasgow gave an excellent talk about thrombosis in assisted reproductive techniques. Marc Rodger from Ottawa, Canada provided an excellent summary of

Thrombophilia and Gestational Vascular Complications – suggesting as many of us know there are insufficient data to recommend routine testing for thrombophilias in women with pregnancy complications at this stage as it is not clear that their increased prevalence in women with these conditions plays a causal role. Most importantly, being at the meeting gave me an opportunity to invite Marc to be one of the Society's invited speakers at the 2010 HAA meeting in Auckland. I am happy to report that he enthusiastically said yes! I also caught up with Mike Greaves from Aberdeen at the conference – Mike is one of the editors of the Journal of Thrombosis and Haemostasis and also is coming to Auckland in 2010. I thought we could have a pregnancy focus for that meeting – but I digress... The Symposium is also attracting more proffered papers giving young investigators a chance to present.

All of the abstracts for the conference, providing excellent reviews of the topics covered, are available in a special supplement of *Thrombosis Research* 2009 volume 123, Supplements 2 (S1-165) and 3 (S1-29). I certainly would recommend looking out for the 4th WHITH in 2011 – I am not sure where – another central European destination, I am sure. I have suggested Cracow – would love it to be St Petersburg but I think that would be too cold.

Claire McLintock





Australian governments have funded the redevelopment of the Australian Bleeding Disorders Registry (**ABDR**) to provide a clinical tool for specialist staff in designated treatment centres and clinics and to improve treatment outcomes for patients with bleeding disorders across Australia. It was implemented in December 2008.

This redevelopment has been undertaken by the National Blood Authority (**NBA**), in collaboration with the Australian Haemophilia Centre Directors' Organisation (**AHCDO**), Haemophilia Foundation Australia and all Australian governments.

The ABDR will be used to register all patients who require clotting factor replacement therapy, in order to gain a better understanding of the incidence and prevalence of bleeding disorders. This information will also be used to understand demand for, and to facilitate ordering of, clotting factor product.

Statistics currently available on people with bleeding disorders underestimate the total number requiring access to clotting factor product. By registering your patients, you will increase the accuracy of these statistics to ensure there is sufficient product available to meet the clinical needs of your patients.

How will this change the way I treat my patients?

It won't! Patients will continue to access treatment and clotting factor product the same way they do now.

What do I need to do?

Register your patients by completing the ABDR Patient Registration form and faxing it to your nearest Haemophilia Treatment Centre or Bleeding Disorders Clinic. Copies of the ABDR Patient Registration Form and a contact list for treatment centres and clinics can be downloaded from www.ahcdo.org.au.

What about patient privacy?

Only the health care team and support staff involved in providing medical services have access to the personal information of their patients. Other authorised users only have access to limited, depersonalised and/or summary information where all identifying information is removed to protect patient privacy.

Where can I get more information?

For more information about the ABDR and the registration of patients visit www.ahcdo.org.au or call **AHCDO** on (03) 9885 1777 or info@ahcdo.org.au.

UPCOMING MEETINGS IN 2009

MEETING	WHERE/DATES	CONTACT
XXII International Symposium on Technological Innovations in Laboratory Hematology	Las Vegas 11-14 May 2009	http://www.islh.org
XXII Congress ISTH with 55th Annual SSC Meeting	Boston 11-16 July 2009	http://www.isth2009.com/
2009 BSHT/UKHCDO Annual Meeting	Newcastle Upon Tyne 7-9 October 2009	www.bsht.org.uk/
AIMS 2009 National Scientific Meeting	Adelaide 12-16 October 2009	www.aims.org.au
ASTH Scientific Workshop 2009	Adelaide 17 October 2009	ASTH@bigpond.com grace.gilmore@health.wa.gov.au
HAA2009 – Joint Annual Scientific Meeting HSAZ/ANZBT/ASTH	Adelaide 18-21 October 2009	www.fcconventions.com.au/HAA2009/ Abstract submission closes 13 July 2009
APSTH-JSTH joint Symposium	Osaka, Japan 20-22 November 2009	http://www.jsth.org/apsth/information/0008.html
The American Society of Haematology 51st Annual Meeting	New Orleans 5-8 December 2009	www.hematology.org
20th Congress of the International Society for Fibrinolysis and Proteolysis	Amsterdam 24-28 August 2010	www.isfp2010.org