

## Dear Fellow Clotter

We have a somewhat smaller newsletter for you this time.

With the workshop and ASM fast approaching, Grace Gilmore has included some final details for your information. Megan Sarson has written a short update on the recently formed Ethiopian Haemophilia Society.

As part of his President's report, Chris Ward has included a report on the ISTH SSC meeting held in Vienna and Scott Dunkley has provided a report on the Haemophilia World Congress held in Istanbul.

And last, but not least, Tim Brighton has updated us on the developments of the clinical trials group.

Many thanks to all who contributed to this edition.

Emma Perrin

### ASTH WORKSHOP/ HAA2008

The program for both the ASTH workshop and the HAA has been finalised.

The ASTH workshop covers a number of interesting current issues and can be viewed on the web site. It should provide some stimulating discussions and be a chance to catch up with colleagues and exchange ideas.

The day ends with a sundowner from 4.30 till 6pm, kindly sponsored by Siemens Medical Solutions Diagnostic. Registration forms can be found on the web site.

The program for the HAA can be found by clicking on: [www.fcconventions.con.au/HAA2008/](http://www.fcconventions.con.au/HAA2008/)

There are a number of excellent symposia planned with a blending of prominent speakers from around Australia and New Zealand and our international guests. Themes covered include basic and applied aspects of thrombosis and haemostasis. The Welcoming Reception and Conference dinner will give you a taste of local WA wines and produce.

Don't forget to apply for a travel grant.

Grace Gilmore

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## HAEMOPHILIA 2008 WORLD CONGRESS

The guest editors of the 'State of the Art'\* from the International Congress of the World Federation of Haemophilia held in Istanbul this June were tellingly Paul Giangrande and our own Alison Street. Paul, the quintessential English gentleman with whom many of us have spent time at Oxford, is handing over the reins of 'WFH vice-president medical' to Alison. This is a position of great honour and importance and reflects Alison's standing in the Haemophilia community globally and in Australia.

The Congress attracted more than 4200 participants from over 115 countries making it the largest WFH Congress ever. Istanbul itself was stunning and a more than capable host for such a meeting, though the tax on international wine caused some concern.

Delegates ranged from patients and family members to the super-specialised bleeding disorder professionals, entities that perhaps only the United States can support, and thus, there was a wide range of concurrent sessions targeting many levels.

Mark Skinner, the President of WFH and a haemophiliac himself, summarised the global situation. The gap between developed and developing is obviously large and typically reflects the country's gross domestic product (for example the FVIII IU per capita globally is around 1.25, versus Australia in the order of 6 IU/capita and those with a GDP <\$2000 of 0.02IU/capita) though cultural barriers also exist. The appropriately named GAP (Global Alliance for Progress project) was established to improve national care in 30 selected countries over a 10 year period. Currently is at its halfway mark, it has had considerable success. He also highlighted the importance of "being counted" and, through WFH support, the number of countries with registries has increased to 58% of affiliated countries. On the other end of the spectrum, the ABDR (Australian Bleeding Disorders Registry) nears completion of its re-development under the guidance of John Rowell (AHCDO), the HFA and NBA.

Updates on inhibitor biology and treatment were heard and controversy over the ideal tolerisation regime persist particularly surrounding the value of awaiting a fall in the pre-tolerisation inhibitor titre (the International ITI study had a death due to ICH whilst awaiting the titre to drop below the designated improved prognostic level of 10 BU), the role of immunomodulation with Rituximab, and the possible importance of plasma derived/VWF containing plasma products in the de-novo risk of inhibitor development (Sebastian Lacroix-Desmazes presented his elegant work, demonstrating reduced dendritic cell uptake of FVIII in the presence of VWF) as well as in tolerisation (the results of the OBSITI study were presented).

Perhaps for me the most interesting talks revolved around the increasing focus on laboratory measures of haemostasis in the diagnosis of haemophilia as well as the monitoring of by-passing therapy. John Lloyd presented the discrepant results he has found in the diagnosis of mild haemophilia A with one stage, two stage and chromogenic assays. Doctors Shima and Ingerslev discussed global assays of haemostasis.

David Lillicrap gave an excellent summary on the situation of molecular genetics and type 1 VWD, its relationship to disease severity (high likelihood if VWF levels <25% vs only 50% in general cohorts) and strong family history. He highlighted the incomplete penetrance of the disorder, and the influence of genetic modifiers such as the Y1584C mutation (found in around 20% of VWD cohorts and healthy donors with VWF levels <50%) and blood group O. Disappointingly he finished by saying "the extreme mutational heterogeneity and relative lack of knowledge concerning pathogenetic mechanisms precludes the use of genetic studies as a diagnostic aid".

WFH Buenos Aires in 2010 should stimulate many!

*Scott Dunkley*

\* State of the Art. Haemophilia 2008; Vol. 14 (Suppl. 3).

## FROM THE PRESIDENT

After years of anticipation and one well-publicised "false start", the next generation of oral anticoagulant agents is finally appearing. Earlier this year, both dabigatran, an oral antithrombin, and rivaroxaban, an oral anti-Xa agent were approved in the European Union for VTE prophylaxis following major orthopaedic surgery. Both agents have undergone an extended programme of clinical trials and appear to have excellent efficacy and safety profiles in the post-surgical setting, at least comparable to our current standard therapy of low-molecular weight heparin.

Having an oral agent which does not require monitoring, and lacks the diet and drug interactions of warfarin, could dramatically improve prophylaxis rates and make extended prophylaxis after hip replacement or fracture feasible. We expect that these drugs will be submitted for approval in Australasia in the near future, and hope that they will be accessible and affordable.

Many ASTH members have contributed to the development of new anticoagulants through their championing of clinical trials. They have had first-hand experience with

## FROM THE PRESIDENT *continued*

these new compounds and are keen to see alternatives to warfarin and the parenteral heparins. For many of us, though, our highest priority is to find agents which are as effective and safe for the treatment and secondary prophylaxis of VTE.

An increasing number of new (mostly oral) agents are undergoing initial and extended treatment trials of VTE right now, and the outcomes of these trials are eagerly awaited. All seem to have good initial activity and low bleeding risks, but there is still the risk of an unanticipated toxicity like ximelagatran's liver function abnormalities. We hope that Australia and New Zealand clinicians will continue to be major contributors to anticoagulation trials, despite the ever increasing burdens of paperwork and costs. Through the Clinical Trials Group, we should continue to advocate for simpler ethics and reporting systems, and for ASTH as a key local source of coagulation and trials expertise.

Many of our well-travelled experts were in evidence at last month's ISTH Scientific and Standardisation Committee meeting in Vienna. Held in alternate years to the major scientific congress, the SSC meetings have tended to attract the "cognoscenti" rather than a general audience, with workshops that often generated heated debate, but could take years to arrive at conclusions.

This year's meeting broke from tradition with an extra education day, record attendance numbers and stronger subcommittee programmes. ASTH was well represented at the meeting, with several of our senior clinicians and researchers active in the SSC and contributing reports.

For the platelet enthusiasts, there were entertaining sessions on the vexed issue of aspirin and clopidogrel "resistance" and solid progress was made on standardising optical platelet aggregometry – only 40 years after the technique was first developed! New platelet and coagulation assays were presented in satellite symposia and the vascular biology SSC analysed methods for measuring circulating endothelial cells and procoagulant microparticles. Even the antiphospholipid antibody workshop left me with a sense of optimism for once, as it worked towards a standardised set of assays and definitions.

The Austrian organisers and ISTH have worked hard to rejuvenate the SSC meeting, and it delivered a high-quality update in coagulation that set the scene for the detailed work of each committee. I'd urge all of you to make a date for the next SSC in Cairo 2010 and consider getting involved in the worldwide effort to fine-tune coagulation research and practice.

To finish, I have to remind you about another first-class coagulation meeting much closer to home (and with less camel dung underfoot). This year's HAA meeting in Perth is fast approaching and we've been delighted with the high number of quality abstracts submitted to the ASTH programme. The annual coagulation workshop on Saturday 18th October will again be a highlight for laboratory scientists and clinicians alike. Our local organisers, Ross Baker and Grace Gilmore, have attracted an outstanding lineup of international and local speakers – we hope you'll join us.

*Chris Ward*

## SECRETARIAT NEWS

Membership renewal notices went out to everyone at the beginning of July and there has been a good response. However, if you have forgotten to renew your membership, please complete the forms and send them back to me with your payment. If you've misplaced your renewal papers, drop me a line and I'll get a new set sent out to you.

And another thing to remember – keep checking the ASTH web site – activities, events and news items are posted regularly. If you know of something that would be worth putting on the site, do let me know – if you found it interesting, chances are other members would too.

The Scientific Workshop and HAA meeting are fast approaching. If you haven't already registered, it's another thing to add to your 'to do' list. The Workshop program and registration details are available from our web site, with registration closing on Friday 19th September. The Workshop is open to non members too so please tell colleagues who might be interested in attending the Workshop all about it.

### **Ethiopian Haemophilia Society Update**

Dr Kalid Asrat from the Black Lion Hospital in Addis Abeba, Ethiopia attended the World Federation of Haemophilia (WFH) Congress in Istanbul at the beginning of June sponsored by a grant from the Australia Haemophilia Center Directors' Organisation (AHCDO). I was invited to attend several meetings with Dr Asrat and, as a result of these meetings, there are some encouraging developments. The Black Lion Hospital received its first donation of Factor VIII treatment product at the end of June and a second donation is expected soon. Dr Asrat is also liaising with the WFH to initiate a twinning program with a **Haemophilia Treatment Centre in the US**, with an initial assessment visit planned for November and training being planned for nurses and laboratory scientists.

*Megan Sarson*

## CLINICAL TRIALS GROUP REPORT

The last ASTH CTG meeting occurred on the Gold Coast during the Annual HAA meeting. The group was keen to initiate some further investigator initiated studies in managing calf vein thrombosis and also HIT. Simon McRae has emailed a survey ([http://www.surveymonkey.com/s.aspx?sm=e2ak11kp4wPa1YAhWaZ4Zg\\_3d\\_3d](http://www.surveymonkey.com/s.aspx?sm=e2ak11kp4wPa1YAhWaZ4Zg_3d_3d)) to interested clinicians so please complete the survey.

This information will be important in the design of a management study. A small group is working on the HIT study design. The ASTH ITPI study was discussed and again a survey of sites looking at the response to high-dose dexamethasone and study feasibility will be soon distributed.

The ASPIRE Study ([http://www.ctc.usyd.edu.au/trials/other\\_trials/aspire.htm](http://www.ctc.usyd.edu.au/trials/other_trials/aspire.htm)) continues to gradually recruit patients. We have responded to the NH & MRC large project grant review. India is almost ready to recruit. A lot of progress has also been made in the UK with ethics and regulatory approvals and grant application to the British Heart Foundation all in progress. The total recruitment of ASPIRE and WARFASA is now 847 patients, with a target of 2000 required. We are almost half way.

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. This is also a very important clinical question, especially in light of several new antithrombotic drugs in the immediate pipeline.

A further ASTH CTG meeting is planned around the HAA in Perth. 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](mailto:t.brighton@unsw.edu.au)) or  
Douglas Coghlan ([douglas.coghlan@flinders.edu.au](mailto:douglas.coghlan@flinders.edu.au)).

Tim Brighton

## UPCOMING MEETINGS IN 2008

MEETING	WHERE/DATES	CONTACT
<b>12th Australasian College of Phlebology ASM and Workshops</b>	Gold Coast 6-11 September 2008	<a href="http://www.phlebology.com.au">www.phlebology.com.au</a>
<b>5th Congress of the Asia Pacific Society on Thrombosis and Haemostasis</b>	Singapore 18-20 September 2008	<a href="http://www.apsth2008.com">www.apsth2008.com</a>
<b>2008 BSHT/UKHCDO Annual Meeting</b>	Nottingham 1-3 October 2008	<a href="http://www.bsht.org.uk/">www.bsht.org.uk/</a>
<b>AIMS 2008 National Scientific Meeting</b>	Melbourne 13 -17 October 2008	<a href="http://www.aims.org.au">www.aims.org.au</a>
<b>Platelets 2008 International Symposium</b>	Massachusetts 15-18 October 2008	<a href="http://www.platelets2008.org">www.platelets2008.org</a>
<b>ASTH Scientific Workshop 2008</b>	Perth 18 October 2008	<a href="mailto:ASTH@bigpond.com">ASTH@bigpond.com</a>
<b>HAA2008 Joint Annual Scientific Meeting HSANZ/ANZBT/ASTH</b>	Perth 19-22 October 2008	<a href="http://www.fcconventions.com.au/HAA2008/">www.fcconventions.com.au/HAA2008/</a>
<b>32nd World Congress of the International Society of Hematology</b>	Bangkok 19-23 October 2008	<a href="http://www.ish2008.org">www.ish2008.org</a>
<b>31st Meeting of the Japanese Society of Thrombosis and Hemostasis</b>	Osaka 20-22 November 2008	<a href="mailto:yozaki@yamanashi.ac.jp">yozaki@yamanashi.ac.jp</a>
<b>The American Society of Haematology 50th Annual Meeting</b>	San Francisco 6-9 December 2008	<a href="http://www.hematology.org">www.hematology.org</a>