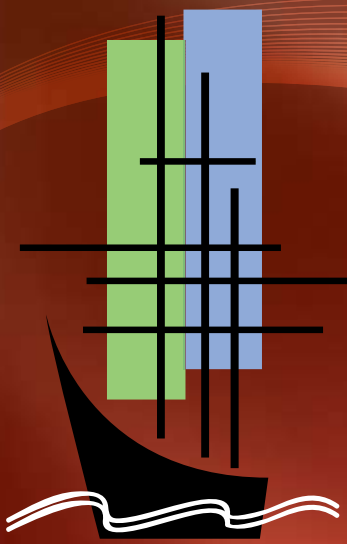




ISTH 2009 DAILY

XXII CONGRESS INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS



INSIDE

LATE-BREAKING RESULTS

Latest data released on five trials

page 2

HISTORY FROM THE BEGINNING

ISTH was founded 40 years ago

page 4

SNAKE BITE TREATMENT

Research ongoing about when, if to administer fresh frozen plasma

page 6

YOUNG INVESTIGATORS

Four Pier M. Mannucci Awards announced

page 8

TUESDAY AT A GLANCE

Ongoing
Oral Communications, State-of-the-Art Lectures, Abstract Symposia, Nurses' Sessions

9:45 a.m. – 10:30 a.m.

Plenary Lecture: Contribution of Allosteric Disulfide Bonds to Regulation of Hemostasis (Philip Hogg)

3:00 p.m. – 3:15 p.m.

ISTH General Membership Assembly

3:15 p.m. – 4:00 p.m.

Presidential Plenary Abstracts

4:00 p.m. – 4:15 p.m.

ISTH 2009 Congress Awards Presentation

4:15 p.m. – 5:00 p.m.

Presidential Plenary Abstracts

6:30 p.m. – 7:30 p.m.

Technical Sessions (Industry Sponsored)

Effects of Plasma Tainted with CJD Still Under Scrutiny in U.K.

About half of the 8,730 people in the United Kingdom who were exposed to plasma tainted with variant Creutzfeldt-Jacob disease have not yet been treated.

Physicians are trying to assess the risk to the patients who received the tainted plasma from 1987 to 1999. **Frank G. H. Hill, MB, ChB, FRCPath, FRCPC**, at Birmingham Children's Hospital NHS Trust and the U.K. Haemophilia Centre Directors Organization, discussed the extent of exposure and risk stratification during a plenary session Monday morning.

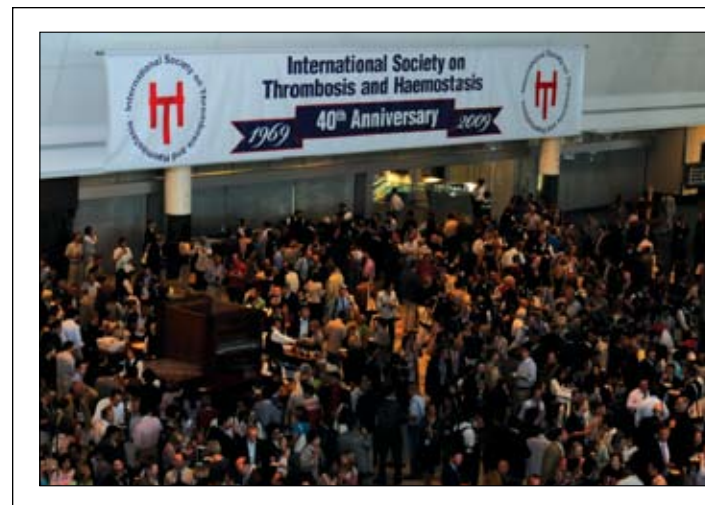
"Information on the National Haemophilia Database shows us we have in excess of 23,000 registered patients; 8,730 of those have been treated," said Hill. "From annual return data, we can identify 4,580 patients who have received U.K. plasma products and therefore are at risk of variant CJD and require public health precautions with certain operative procedures. Of those, 792 have been positively notified as having received an implicated batch," Dr. Hill said.

Among those 792 patients, 1,157 have had treatment or exposure episodes with 12.7 million units of the implicated product. That is about half of the 23 million that have been issued. Sixty-seven percent of this cohort had received only one batch from an implicated donor, "but all have received other batches which may add to their cumulative risk."

Dr. Hill cautioned against making too much of these findings. "There are many uncertainties about this data, and there are questions about the current risk assessment.

"We possibly don't know the full extent of contaminated batches. The patterning incubation of time of variant CJD following exposure to plasma product may well be different even to exposure through cellular product."

Finding answers to these questions may involve better recruitment, post mortem, results of longitudinal studies involving these patients and the development of a blood test.



Opening Ceremony Draws Large, Festive Crowd

Hundreds of delegates gathered Sunday night to celebrate the opening of the XXII ISTH Congress.

PrPSC Detected in Spleen of Adult Hemophilic Patient in U.K.

Analyses of tissues from 17 patients exposed to variant Creutzfeldt-Jacob disease in the United Kingdom showed that one patient with hemophilia had disease-associated prion protein – PrPSC - in his spleen tissues.

It is not yet known whether the patient came in contact with the disease through diet, blood transfusion or pooled clotting factor concentrate. **Dr. James W. Ironside, FRCPath**, director of the U.K.'s National CJD Surveillance

Unit, said Monday that the patient "likely" contracted the disease from an unidentified source.

"Because of the large volume of non-implicated products received, it is likely this could be the source of the infection," he said. "On the relative risk, it is very difficult to discriminate between the implicated and non-implicated



Dr. James W. Ironside, FRCPath

products. All we can say we know for sure is that there was an infected donor in this pool."

Investigators performed prospective and retrospective analyses on tissues collected from biopsies or autopsies, searching for the presence of disease-associated prion protein. All patients had been treated with U.K.-sourced pooled factor concentrates for bleeding disorders from 1980 and 2001. That pool is known to contain tainted plasma from

(Ironside, continued on page 11)

Tuesday, July 14, 6:30 PM – 7:30 PM

Industry Sponsored Technical Sessions

• **Network for Continuing Medical Education (Novo Nordisk)**
Room 107 ABC

• **Rovi**
Room 104 ABC

TIPS OF THE DAY

Add future professional conferences to your calendar after stopping by the Future Events Kiosk.

Stay connected at the Cyber Café & Message Center in the Exhibition Area.

LATE BREAKING TRIAL

ADVANCE-2: Favorable Risk-Benefit Profile With Apixaban

Apixaban for thromboprophylaxis after total knee replacement had better efficacy and safety compared to the current standard of care enoxaparin, according to late-breaking results of ADVANCE-2 presented Monday.

ADVANCE-1 results, presented in December 2008 at the 50th ASH Annual Meeting, showed that apixaban failed to meet one of two prespecified noninferiority criteria margins in reducing rates of VTE but showed

lower major and clinically relevant non-major bleeding rates in patients undergoing total knee replacement. ADVANCE-1 compared apixaban with the North American dosage of enoxaparin 30 mg twice daily.

ADVANCE-2 was a randomized, double blind, multicenter trial com-



Michael Lassen, MD

paring efficacy and safety of 2.5 mg apixaban twice daily for preventing VTE vs. the current European standard of care, 40 mg subcutaneous enoxaparin once daily, said Michael Lassen, MD, of the University of Copenhagen, Hørsholm, Denmark.

Primary efficacy outcome was the composite of DVT by venography, symptomatic objectively confirmed DVT or pulmonary embolism, or death from any cause during treatment. Primary safety outcome was

bleeding (major and clinically relevant nonmajor).

The primary outcome occurred in 15.1% of patients in the apixaban group vs. 24.4% in the enoxaparin group ($P<.001$). Major VTE occurred in 1.1% of apixaban patients treated with apixaban vs. 2.2% of patients treated with enoxaparin, Dr. Lassen said.

Apixaban also conferred a better safety profile compared with apixaban (3.5% vs. 4.8%; respectively; $P=.09$).

LATE BREAKING TRIAL

Four-Week Prophylaxis Better Than One Week After Abdominal, Pelvic Surgery

When compared with a one-week prophylaxis, four weeks with the low molecular weight heparin bemiparin significantly reduced the rate of major venous thromboembolism without increased complications in pa-

tients undergoing cancer abdominal or pelvic surgery.

These results were part of the CANBESURE trial presented Monday by Dr. Vijay V. Kakkar, MD, director of the Thrombosis Research Institute, London, as part of the late-breaking abstracts session.

CANBESURE was a multicenter, randomized, double blind parallel group trial. The study included 703 patients aged 40 or older who were undergoing surgery on the gastrointestinal or genitourinary tract, or female reproductive organs. The safety analysis included data on 625

patients; the efficacy analysis, 488.

Prior to randomization, all patients received 3,500 IU bemiparin starting six hours postsurgery for eight days. They were then randomly assigned 3,500 IU bemiparin once daily or placebo for 20 more days, Dr. Kakkar said.

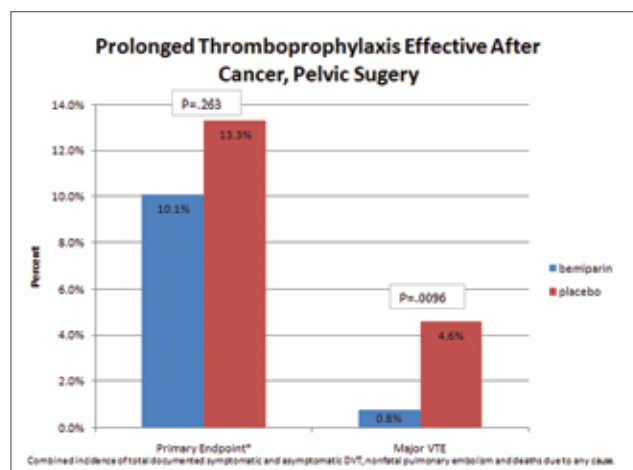
Follow-up was three months. Twenty-eight days after surgery, bilateral ascending venography was performed and examined by five in-

dependent radiologists.

The primary efficacy endpoint was the combined incidence of total documented symptomatic and asymptomatic DVT, nonfatal pulmonary embolism and deaths due to any cause. Primary safety endpoint was major hemorrhage, according to Dr. Kakkar.

Patients assigned bemiparin had a 24.4% relative risk reduction for the primary endpoint and a 82.4% relative risk reduction for incidence of major VTE (see chart).

Rates of major bleeding were similar in both groups (0.6% vs. 0.3%, respectively; $P=.572$).



LATE BREAKING TRIAL

Enoxaparin Effective for VTE Prevention in Advanced Pancreatic Cancer

CONKO 004 trial results suggest that the low molecular weight heparin enoxaparin helped prevent symptomatic venous thromboembolism in patients undergoing chemotherapy for advanced pancreatic cancer.

H.B. Reiss, MD, at the University Medicine in Berlin, presented these late-breaking results on Monday.

Patients with advanced pancreatic cancer are among those with the highest risk for VTE, Dr. Reiss said. To investigate the role of enoxaparin in the prevention of VTE, Reiss and colleagues began the open, prospective, randomized, multicenter

CONKO 004 trial.

In an intent-to-treat analysis, enoxaparin reduced the risk of VTE by 65% with no increased safety complications, Dr. Reiss said.

From April 2004 to January 2009, 312 VTE- and chemotherapy-naive patients with advanced pancreatic cancer were recruited. One hundred sixty patients were assigned chemotherapy plus once-daily 1 mg/kg starting dosage of enoxaparin for the first 12 weeks, after which the dosage was reduced to once-daily 40 mg. The remaining 152 patients were assigned to chemotherapy alone (observation).

(Reiss, continued on page 11)

LATE BREAKING TRIAL

Better Anticoagulant Control With Warfarin

Patients who switched from acenocoumarol to warfarin spent more time within therapeutic ranges than those who switched to phenprocoumon, according to late-breaking results presented Monday. The trial compared warfarin and phenprocoumon in patients who were either initiating anticoagulant treatment or switching from the vitamin K antagonist acenocoumarol to a new therapy.

Yvonne van Leeuwen, MSc, from the department of clinical epidemiology at Leiden University Medical Center, said Monday that the results indicate that, overall, warfarin leads to better anticoagulant control than phenprocoumon.

The researchers recruited 504 patients at Leiden Anticoagulation Clinic from March 2004 to September 2008.

Two hundred and fifty patients

were randomly assigned to warfarin and 254 to phenprocoumon. An equal number of patients initiating and switching therapies were in both groups.


After six months' follow-up, the overall mean percentage of time spent within therapeutic ranges was 74.6% for the warfarin group and 65.3% for the phenprocoumon group (95% CI, 5.8-12.8), she said.

The difference in mean percentage of time spent within therapeutic ranges was more substantial in patients who switched therapies: 78.3% for the warfarin group vs. 57.6% in the phenprocoumon group (95% CI, 16.3-25.1). The researchers observed no difference in mean percentage of time spent within therapeutic ranges for patients initiating therapy.

Excluding the first six weeks of follow-up did not change the results, according to van Leeuwen.



Yvonne van Leeuwen, MSc



Thrombosis—with no apparent link to clinical presentation—should increase your suspicion of PNH.

Add PNH to your hypercoagulation panels for patients with unexplained thrombosis.

- PNH patients are 62 times more likely than the general population to experience venous thromboembolism¹
- This incidence of thromboembolism in PNH is markedly elevated, even when compared to other hypercoagulable states such as AT deficiency, PS deficiency, PC deficiency, PT mutation, and Factor V Leiden¹
- Venous or arterial thromboses account for approximately 40% to 67% of PNH-related deaths²
- First thrombotic event (TE) increases risk for death 5- to 10-fold²
- Incidence of first ever ischemic stroke (FEIS) is elevated in PNH patients; age of FEIS in the PNH population (median age 46) is markedly lower than the general population (median age 72)^{3,4}

→ Visit us at booth #711 to learn about the progressive and destructive nature of PNH, as well as the increased risk of thrombosis, end organ damage, and mortality.

References: 1. De Stefano V, Rossi E, Paciaroni K, Leone G. Screening for inherited thrombophilia: indications and therapeutic implications. *Haematologica*. 2002;87:1096-1108. 2. Hillmen P, Muus P, Duhrsen U, et al. Effect of the complement inhibitor eculizumab on thromboembolism in patients with paroxysmal nocturnal hemoglobinuria. *Blood*. 2007;110:4123-4128. 3. Data on file, Alexion Pharmaceuticals Inc. 4. Gostynski M, Engelter S, Pape S, Ajdacic-Gross V, Gutzwiller F, Lyrer P. Incidence of first-ever ischemic stroke in the Canton Basle-City, Switzerland. *J Neurol*. 2006;253:86-91.



International Society on Thrombosis and Haemostasis

1969

40th Anniversary

2009



The Founding of ISTH: 40 Years Ago

Harold R. Roberts, MD
Gilbert C. White, MD

The history of the International Society on Thrombosis and Haemostasis can be traced back to 1954, with the formation of the International Committee on the Nomenclature of the Blood Clotting Factors. The initial committee was composed of investigators who were all internationally well known for their contributions to modern knowledge of blood coagulation and was funded by the National Heart, Lung, and Blood Institute. There were, however, relatively few members, and as interest grew, it became necessary to enlarge the membership to include all investigators interested in the basic and clinical aspects of blood coagulation, including hemorrhage and thrombosis.

An international society was envisioned as early as 1960. During the planning for the sixth meeting of the committee in Princeton, New Jersey, Dr. Irving Wright wrote to Dr. Kenneth Brinkhous that deliberations of the committee had become constrained by the growing number of scientists, “innumerable well-qualified delegates,” who wished to be included in the committee’s discussions but were turned away because of the committee’s restricted size.

At this point, attendees were invited, and only about 70 could be chosen. These attendees were individually selected based on their internationally recognized expertise and their ability and willingness to contribute to the meeting. (A complete list of the 1960 attendees is available from the ISTH archives.)

At the committee’s business meeting, Dr. Wright reported to the assembled members that “the catalytic effect of [our] few conferences ... has been explosive. It has stirred the imagination and interest of many people who are not members of [this] committee.”

Committee member Dr. Armand Quick raised the possibility of expanding the committee’s purpose and scope, noting that there were three groups that should be considered as constituents: (1) the current committee with a primarily chemical character, that is, those isolating factors, methods for assay and so on; (2) those interpreting results in terms of physiology, that is, hemostasis; and (3) clinicians.

Dr. J. Roskam of the University of

Liege in Belgium made a proposal to the assembled committee, one that he had previously aired at the 7th Congress of the European Society of Hematology, calling for a new entity supporting a broader forum for discussion for hemostasis and thrombosis, as well as nomenclature: He proposed that the committee consider widening its aims. The committee members began discussing the possibilities.

Dr. Wright agreed that Dr. Roskam’s proposal was important and believed that there was no other agency organized at that time that could accomplish such a project. Perhaps the committee should consider it?

Dr. Tage Astrup of Copenhagen observed that such an endeavor would require the reorganization of the committee and would result in taking into membership many more individuals from other disciplines. He suggested that it might be better to form a new organization for this purpose that would be coordinated with the current Committee on the Nomenclature of the Blood Clotting Factors.

In a question that foreshadowed the eventual mission of the new organization, Dr. Wright asked Dr. Roskam for clarification of his intention: “Dr. Roskam ... are you interested in the approach of the committee towards stimulating research and interest [of] more investigators to work in the field [or] attempting to stimulate more new young investigators to work in this field?” The answer being affirmative for both objectives, Dr. Wright reminded the membership that they had avoided enlarging the committee to a point where “we cannot finance it or it becomes too large to function efficiently,” although, “on the other hand, over the years we will bring together many people interested in the big fields of thrombosis and coagulation.”

The problem before the committee was how to accomplish these goals without compromising effectiveness.

Committee member Dr. Louis Jacques said: “Dr. Roskam has raised a point which is our responsibility, arising from what we have already done. If the job we have done [is] too narrow to provide the picture needed by [those with] responsibility for patients, responsibility for teaching students who are going to practice medicine, it means we have not finished our job.”

The consensus was that the committee would go offer membership opportunities to the broader community, including researchers in the field of hemostasis and thrombosis.

Over the next nine years, committee members planned for a new organization that would be open to all interested scientists and clinicians working in the many interrelated fields of blood clotting, hemorrhage, thrombosis and vascular biology. They planned the structure, function, leadership, and mission of this new society.

At the 15th Annual Meeting of the International Committee on Haemostasis and Thrombosis in Bath, England, the new organization finally came to a vote.

The committee unanimously approved establishing a society called the *International Society on Thrombosis and Haemostasis*. Quickly following were the adoption of a constitution and unanimous election of the first officers, council members and honorary members.

The first meeting of the new International Society on Thrombosis and Haemostasis was set for the following year, 1970, in Montreux, Switzerland,

under the direction of Dr. Fritz Koller. This joint meeting of the originating committee and the ISTH was to focus on the theme “Immunology, Thrombosis and Haemostasis.”

Interested readers will find a detailed account of the Society’s organization between 1960 and 1969 in the article, “The Founding of the International Society on Thrombosis and Haemostasis: How It Came About,” by Dr. Sol Sherry (*Thrombosis and Haemostasis*, 1990; 64(2):188-191).

And the rest, as they say, is history.

You are cordially invited to see the ISTH History display in the North Lobby of the Convention Center during this XXII ISTH Congress and 55th Annual Meeting of the Scientific and Standardization Committee. Among the items on display are the roster of founding officers and council members; the original invitation to join the society; a roster of those who accepted the invitation; and several other bits of information that have been donated by members, past and present.

If you have documents or memorabilia of the Society or Committee that you would like to donate to the permanent archives of the Society, kindly contact the executive secretary at ISTH Headquarters.

Risk for VTE Linked to Ethnicity

Accumulating data suggest that genetic risk factors linked to ethnicity may play a large role in risk for venous thromboembolism for some people, according to **Toshiyuki Miyata, PhD**, of the National Cardiovascular Center Research Institute, Osaka, Japan.

In white populations, genetic factors such as Factor V Leiden and G20210A confer greater risk for venous thromboembolism (VTE). Different genetic mutations may increase risk for VTE in Japanese populations.

“In 2006, we identified protein S-K196E as a risk factor for VTE in the Japanese population that is not present in a white population.”

To confirm the role that the protein plays in VTE, a case control study was conducted in 3,500 men and women aged 30 to 79. Protein S-K196E increased the odds of

VTE three- to fourfold in patients with the mutation.

The effect of protein S1K196E in VTE has also been confirmed by two independent Japanese groups. This mutation, referred to as protein SK196E or Protein S Tokushima, is present in the second EGF-like domain of protein S.

Three studies, including Dr. Miyata’s, have also identified the frequency of this mutation in Japanese patients. Overall, 74 heterozygotes have been identified in 4,137 people. The mutant allele frequency was 0.89%, which means that about 10,000 Japanese are heterozygous, said Dr. Miyata.

In addition, the studies found that people heterozygous for the mutant allele had lower plasma protein S activity than wild-type patients (71.9% vs. 87.9%, respectively; $P < .0001$).

Shaping
the future, together



Let's shape the future, together

Share your thoughts. Reach the world.

Stop by the Baxter booth #660 to tell us why you chose to study hematology and partner with Baxter to support fellowship programs that educate the hematologists of the future.

PLUS:

Test your skills on our Wii™ interactive challenges



Learn the latest product information from Baxter



PLENARY LECTURE

TODAY at 9:45 am — 10:30 am: Grand Ballroom

Contribution of Allosteric Disulfide Bonds to Regulation of Hemostasis (Philip Hogg)



The inaugural Oscar Ratnoff Memorial Lecture will be delivered today by Professor **Philip J. Hogg** from the University of South Wales, Sydney, New South Wales, Australia. Professor Hogg will present his novel research on allosteric disulfide bonds, disulfide bonds that control protein function by forming or breaking in a precise way.

Professor Hogg's groundbreaking research in disulfide bonds enabled his discovery of a structural motif that characterizes these allosteric disulfide bonds and distinguishes them from other functional disulfide bonds. Professor Hogg predicts that about one in 15 of all structurally determined disulfides is a potential allosteric bond, implying a significant role for these bonds in controlling protein function. Allosteric disulfide bonds have been studied significantly in important hemostatic proteins, including tis-

sue factor, von Willebrand factor and integrin β_3 , and may be at the heart of how hemostasis is regulated.

Professor Hogg is a National Health and Medical Research Council Senior Principal Research Fellow at the University of South Wales, where he is also founder and director of its Cancer Research Centre. He was a key figure in the establishment of the university's Lowy Cancer Research Institute and will serve at its co-director when it opens in late 2009.

Professor Hogg is the recipient of numerous awards including the Australian Society for Thrombosis and Haemostasis Speywood Medal, the New South Wales Biomedical Sciences Scientist of the Year and most recently the Premiers Award for Outstanding Cancer Researcher of the Year, the highest cancer research honor in New South Wales.

Oscar Ratnoff (1926-2008) was a distinguished physician-scientist who made seminal contributions to our understanding of blood coagulation mechanisms and bleeding disorders. Over a 60-year career at Johns Hopkins and Case Western Reserve Universities, he conducted original studies that revolutionized and advanced the field. His achievements included the proposal of the waterfall sequence of blood coagulation with Earl Davie, the discovery of Factor XII (Hageman factor) and high molecular weight kininogen (Fitzgerald factor), the development of an immunoassay to differentiate Factor VIII deficiency and von Willebrand disease and early recognition of potential danger of contamination with a putative AIDS agent in Factor VIII concentrates. Ratnoff was an outstanding teacher and clinician who trained many fellows who went on to establish their own distinguished careers. The Ratnoff Lectureship was established following his death in 2008. The initial lecture will be given at this Congress.

Best Treatment for Snake Bite Coagulopathy Still in Question

The widely accepted treatment for snake bite coagulopathy prior to 2008 was antivenom until reversal of coagulopathy. However, ongoing research in Australia suggests that delaying the use of fresh frozen plasma until coagulopathy is reversed may be unnecessary.

Geoff Isbister, MD, of the Menzies School of Health Research, Charles Darwin University, Australia, said Saturday that much research has examined toxins and venoms that cause coagulant effects. "But, despite that, we know very little about toxin and venom effects in patients."

Not much is known about how venoms work, according to Dr. Isbister. Traditionally, multiple doses of antivenom were given during the first 24 hours after a snake bite until coagulopathy was reversed.

"However, it will often take as long as 24 hours before you get a blood recording that is normal. Physicians are trying to find out if the antivenom has worked, but whether clotting has recovered does not answer that question," he said.

Currently, the Australian Snakebite Project is conducting prospective studies to determine the efficacy of antivenom, the proper doses and administration. Randomized controlled trials of fresh frozen plasma are also in progress. Together these studies should help develop evidence-based guidelines for the treatment of venom-induced consumption coagulopathy.

"There have been some lab studies that showed that antivenom doesn't work," Dr. Isbister said. "In the test tube, researchers have used 10,000 times the venom you find in

patients, and of course the antivenom doesn't work unless you give 10 times the toxin.

"By knowing the venom concentration in patients, we can do the same tests again with a much lower concentration of antivenom. In those tests, we have shown that one vial [of antivenom] is more than enough."

Therefore, the recommendation in Australia since 2007 is to give only two vials of antivenom.

Fresh frozen plasma

A more controversial question has been when and if to administer fresh frozen plasma.

When Dr. Isbister and colleagues began studies of fresh frozen plasma it was with the recommended practice of using no more than two vials of antivenom.

Because it is not possible to do a placebo controlled trial in snake bites, the study instead used variations of timing and doses of antivenom and fresh frozen plasma. The main outcome measure was time until recovery from venom-induced consumption coagulopathy.

They found that administration of fresh frozen plasma within four hours was the only important determinant of venom-induced consumption coagulopathy. Neither earlier administration of antivenom nor an increased dose of antivenom had any effect on venom-induced consumption coagulopathy.

Dr. Isbister said that his research results may be unique to Australian snakes. He challenged other researchers to examine these findings in snake bite cases in other parts of the world.

The "CSL Behring - Prof. Heimburger Award" to support scientific research in the field of coagulation will be awarded again in 2010. The global grant is sponsored by CSL Behring.

CSL Behring - Prof. Heimburger Award 2010

The global grant is named in honour of Prof. Norbert Heimburger, a pioneer of modern coagulation. One of his major contributions in this area was the development of virus-inactivated products based on pasteurisation. Due to his research efforts, CSL Behring launched the first effectively virus-inactivated FVIII concentrate in 1981.

Eligibility:

CSL Behring will set up 5 start-up grants for the cycle 2010. The grants are targeted at young investigators, who hold an MD degree. Applicants with less than 5 years faculty experience in haemostaseology will be preferred. The grants will be available for pre-clinical and/or clinical research in the area of coagulation.

Grant: € 20,000

Upcoming cycle in 2010
- apply now!

Application forms are available from the following address:

CSL Behring GmbH
Att. Dieter Pluennecke
Commercial Development Coagulation
Emil-von-Behring-Strasse 76
35041 Marburg
Germany
T: +49 6421 394191
E-mail: Heimburger.Award@cslbehring.com
or log onto
www.cslbehring.com/ProfHeimburgerAward
online application available

In addition to the application forms, the applicant's current CV and research proposal (one-pager) should be attached. Please submit application to the address above.

Closing date for applications: 9th of October 2009

Human Genetics Research Offers Clues About CHD Prevention

For the 20th Shirley Johnson Memorial Lecture, **Helen H. Hobbs, MD**, examined the potential future impact of genetics research on cardiovascular disease prevention.

"In human genetics, there are two major approaches to use genetics to try to identify genes and sequence variations that contribute to differences in traits; in this case our focus has been on LDL," Dr. Hobbs said Monday. This research has "shed new insights into LDL metabolism" with implications for public health.

Dr. Hobbs is a Howard Hughes investigator and professor of internal medicine and molecular genetics at the University of Texas Southwestern Medical Center in Dallas. Research by Dr. Hobbs and her colleagues is providing the framework for future development of new cholesterol-lowering drugs.

They began their research by looking at Mendelian disorders to find

genes that contributed to differences in plasma levels of LDL, in particular elevated levels of LDL. All Mendelian forms of severe hypercholesterolemia are associated with premature coronary heart disease, irrespective of the mechanism, she said.

Discovery of PCSK9 gene

The discovery of PCSK9, a gene that causes a dominant form of hypercholesterolemia, led to research in mice that demonstrated that when PCSK9 was expressed in the liver, there was no change in LDL receptor messenger RNA, a dramatic reduction in LDL receptor protein, and the mice became hypercholesterolemic.

"It was here that we became interested in PCSK9. Our thinking was that if a wildtype protein promotes the degradation of the LDL receptors and retards the clearance of a lipoprotein, then if you have a mutation in PCSK9, you would expect there to be an increase in LDL receptor

activity and hypocholesterolemia, and low plasma levels of LDL," Dr. Hobbs said.

A study by Dr. Hobbs and colleagues demonstrated that African Americans have one of two nonsense mutations that do not secrete PCSK9 into the blood. Using an ELISA assay, they determined that people who are heterozygous for nonsense mutations had lower levels of PCSK9 circulating in the blood and lower levels of LDL.

Their next study followed patients with PCSK9 for 15 years. Among the African American patients in the study, 28% lower LDL levels were associated with an 88% reduction in coronary artery disease, even though over half of the population was hypertensive, a third smoked, and almost 20% had diabetes.

She reported similar results in European-Americans: a 15% lower LDL level – the equivalent of a very low dose of statin – resulted in a 46% reduction in coronary artery disease.

The findings have not been replicated in African American but they have been reproduced in European-Americans, she said.

Using PCSK9 to prevent CHD

Major drug companies are currently pursuing PCSK9 as a therapeutic target to lower plasma levels of LDL and prevent coronary heart disease, according to Dr. Hobbs.

"The work with PCSK9 in human populations really drives home work that has come from many directions and many different studies really focusing on the role of LDL in this disease," she said "Also, others have developed other approaches to reducing PCSK9."

Research with PCSK9 also emphasizes the need for CHD prevention, lowering the threshold of treatment, by intervening earlier in life with diet modifications and possibly low doses of drugs that are now available, Dr. Hobbs said.

Pier M. Mannucci Awards

The Pier M. Mannucci Awards is an annual competition for the best articles published in the *Journal of Thrombosis and Haemostasis* that rewards and encourages investigators in the early stages of their careers. Established in honor of Pier Mannucci, founding editor of the journal, the prize is made available through a generous contribution by Bayer Healthcare. This year four prizes were awarded for papers in the following categories: Platelets, Fibrinolysis, Clinical and Vascular Biology.

Dr. Xiaolin Zhang was given a Mannucci award for her paper "Modulation of Immune Response with CTLA4-Ig-Induced Anergic T Cells in Chronic Idiopathic Thrombocytopenic Purpura," which focused on the cytotoxic T-lymphocyte-associated antigen 4 immunoglobulin (CTLA4-Ig)-induced GP-specific anergic T cells and their inhibitory function on GP-reactive T-cell proliferation and antibody production. Using in vitro culture systems, she found that the anergized GP-specific T cells have profound effects on both GP-specific T-cell proliferation and antibody production.

Dr. Zhang was awarded her doctorate in 2007 at Shandong University,

China. While pursuing this degree, she focused on the tolerance induction of autoreactive T cells in idiopathic thrombocytopenic purpura (ITP) and finished her study on the underlying mechanisms of CTLA4-Ig in treating ITP. Her supervisor is Professor Ming Hou. After graduation, she started her clinical training in the Department of Hematology, Qilu Hospital, Shandong University. She hopes to continue her scientific work in immunology of platelets, especially the etiology and new therapies of refractory ITP.

Dr. Adriana F. Paes Leme's paper "Bothrops Protease A, a Unique Highly Glycosylated Serine Proteinase, Is a Potent, Specific Fibrinolytic Agent" earned her a Mannucci award. Bothrops protease A (BPA), the most glycosylated snake venom serine proteinase (SVSP), is a non-coagulant, thermostable enzyme. She has shown that BPA is a potent fibrinolytic agent in vitro and in vivo. She has also studied partially N-deglycosylated BPA (p-N-d-BPA), which has enhanced activity. This investigation identifies a new, thermostable, specific defibrinogenating agent that may have application in preventing thrombus formation.



Adriana F. Paes Leme
FIBRINOLYSIS

In July 2005, Dr. Leme finished her PhD thesis, which was focused on the study of dental biofilm and saliva proteome. After that, she started postdoctoral training with Dr. Solange Serrano at Instituto Butantan, Brazil, where she continued the study of biological fluids, particularly snake venoms. Her studies are mainly aimed at understanding the mechanisms by which snake venom serine proteinases and metalloproteinases disrupt hemostasis upon envenoming. She hopes to identify new molecules that could contribute to our understanding of the coagulation and fibrinolytic systems.

Dr. Michiel Coppens earned a Mannucci award for his paper "Testing for Inherited Thrombophilia Does Not Reduce Recurrence of Venous Thrombosis." Testing for inherited thrombophilia in patients with a first venous thrombosis or pulmonary embolism is controversial. In his nested case-control study, he shows that testing as carried out in clinical practice does not reduce the risk of recurrence of thrombosis. These results add another argument against testing for inherited thrombophilia.

In February 2008, Dr. Coppens finished his PhD thesis entitled "Thrombophilia," from which his paper is derived. After his thesis, he started his training in internal medicine with a subspecialization in vascular medicine, which he

will finish in 2012. Both his thesis and training are at the Departments of Internal and Vascular Medicine of the Academic Medical Center in Amsterdam under supervision of Professors Marcel Levi and Harry R. Büller. He hopes to continue his scientific work in the field of thrombosis and hemostasis with emphasis on clinical studies on risk factors for venous thrombosis and new anticoagulant therapies.

Dr. Jonathan Tardos won a Mannucci award for his paper "SR Proteins ASF/SF2 and SRp55 Participate in Tissue Factor Biosynthesis in Human Monocytic Cells," which shows that exonic splicing enhances interact with binding motifs in the tissue factor gene. These appear to interact with the variable tissue factor exon 5, altering splicing and regulated biosynthesis of the gene in monocytes.

Dr. Tardos is currently finishing his internal medicine residency at Beth Israel Medical Center, New York, with plans to start a cardiovascular fellowship at SUNY Stony Brook University, New York, in July 2010. His career goals are to continue his training with an additional fellowship in electrophysiology cardiology, ultimately working at an academic center to continue translational research identifying risk factors and novel indications for cardiac resynchronization.



Jonathan Tardos
VASCULAR BIOLOGY



Michiel Coppens
CLINICAL

Come test your knowledge of NovoSeven[®] RT at Booth #331



Visit Booth #331 to learn more about NovoSeven[®] RT Room Temperature Stable—and see what else is on the horizon at Novo Nordisk.

Novo Nordisk Inc., 100 College Road West, Princeton, New Jersey 08540 U.S.A.

NovoSeven[®] is a registered trademark of Novo Nordisk Health Care AG.
© 2009 Novo Nordisk Inc. 138380 July 2009



Education Should Reach All Professionals in Thrombosis and Hemostasis Around the World

The Outreach Forum members and the ISTH Council Education Committee members met Saturday to discuss current and future Reach the World programs and to identify the needs for education around the globe.

This year, for the first time, with help from **Drs. Ken Bauer, Bruce and Barbara Furie**, a fully integrated education meeting took place during the SSC sessions of the Congress.

Numerous young and senior investigators or medical doctors who study the science of thrombo-

ISTH improved over the past decade, the education committee organized 20 educational events throughout the world. These events have included standalone symposia, dry and wet laboratory workshops, symposia linked to regional congresses and state-of-the-art seminars.

Following the successful education symposia that were organized at the biennial Thrombosis and Hemostasis Congresses of Latin American countries since 2001, ISTH was decided to organize two educational activities in Latin America every

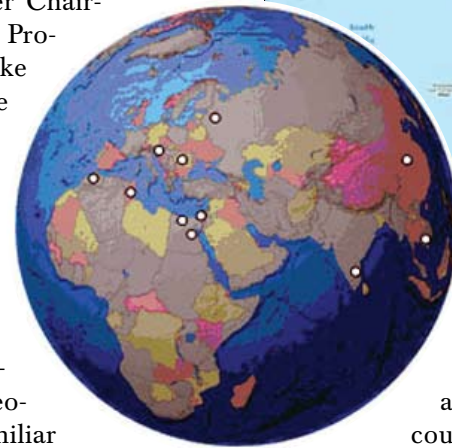
year. The aim is to enable education in the Latin American countries using native language. **Professor Raul Altman** was appointed to lead this mission, and in this

American Thrombosis and Hemostasis Society (CLAHT) were a great success. The half-day dry lab course as well as the two full-day educational course were well received and well attended by physicians, biochemists and students in related medical fields.

In 2007, former Chairman of Council Professor Ian Peake proposed at the Geneva ISTH Congress to substantially increase the budget for education and create a forum in less privileged countries of eminent people who are familiar with the needs for clinical and laboratory education in their respective countries or regions.

An Outreach Forum was formed that includes 25 dedicated individuals from countries that might benefit from educational activities. The aim was to first identify and evaluate the needs for education.

A survey was held among the Outreach Forum members to evaluate the status of thrombosis and hemostasis centers, coagulation laboratories, formal training of physicians and laboratory scientists, national meetings and educational activities. The Outreach Forum also aimed to



provide indications of the priorities of education programs that are needed in the countries or regions.

An analysis of the questionnaire yielded the following information:

- The status of thrombosis and hemostasis is more advanced than was expected.
- In most countries, hematology embraces thrombosis and hemostasis.
- All countries have national meetings with an educational element to which ISTH-sponsored events can be linked.
- Most countries have training programs for hematologists and hematology laboratory technicians, and more than half have PhD students in thrombosis and hematology.
- There is a great need for the three modalities of education we can offer: theoretical courses, dry laboratory and wet laboratory workshops, mainly for physicians and laboratory technicians.
- A visiting professor program could be a "winner."

Future programs of Reach the World will include a fellowship program to enable young professionals to visit for several weeks an advanced center in the field. In addition, a visiting professor program will enable leading physicians and scientists to spend several days in centers around the world to give lectures, seminars, short courses and scientific advice. E-Learning throughout the world is also planned.

Young Investigators Travel Awards were established to assist those who come to the meetings and to promote the involvement of young Society members at the ISTH meetings.



Raul Altman



Orly Katz



Frits Rosendaal

sis and hemostasis, live and work around the world. However, not all of them can acquire advanced, up-to-date skills and knowledge. Some of these professionals do not have the financial means to travel abroad to congresses or attend educational seminars where they could attain additional education. Since its inception, the ISTH has tried to develop educational activities, but with limited resources.

Because the financial status of

role he has been fostering science-related medical education in the areas of problems of thrombosis and hemostasis, standardization of methods of diagnosis, and introduction of appropriate therapy for the prevention and treatment of thrombotic and bleeding disorders.

Working from the course evaluations collected after the educational meetings, Professor Altman reported that the first ISTH courses organized together with the Latin

Select Abstracts Presented Today at Presidential Plenary Abstract Session

Six of the most highly rated abstracts submitted to the ISTH 2009 Congress will be featured in a special Presidential Plenary Abstract Session to be held today at 3:15 p.m. in the Grand Ballroom. These abstracts cover a wide range of topics and were selected both for their quality and for their potential interest among a broad cross-section of delegates.

Congress President Barbara Furie noted: "Abstracts are regularly submitted on seminal work important to our entire field, and we wanted to create a forum where we could showcase these abstracts to a large audience."

Abstracts to be presented include:

- Genome-Wide Scan in Affected Sibling Pairs (Gift Study) Identifies a Novel Susceptibility Region for Venous Thromboembolism
— MARIEKE DE VISSER
- Examination of the Final Stages of Platelet Production
— JONATHAN N. THON

- Feedback Activation of Factor XI by Thrombin Is Essential for Hemostasis In Vivo
— HENRI SPRONK
- Evidence of the First X-Linked Thrombophilia Due to a Novel Mutation in Clotting Factor IX Gene Resulting in Hyperfunctional FIX: Factor IX Arginine 338 Leucine (Factor IX Padua)
— PAOLO SIMIONI
- Kindlin3 in Integrin Activation
— TATIANA V. BYZOVA
- Thrombomodulin Mutations Predispose to Atypical Hemolytic-Uremic Syndrome Via Impaired Complement Regulation
— MIEKE DELVAEYE

The XXII Congress Awards Presentation will take place from 4:00 p.m. to 4:15 p.m. between the third and fourth abstract presentations.

LATE BREAKING TRIAL

Nadroparin Failed to Improve Survival in Patients with Cancer

Preliminary data from the INPACT trials indicate that treating patients with the low molecular weight heparin nadroparin did not improve survival among patients with cancer, according to **Dr. H. Roger Buller, MD**, of the department of vascular medicine, Academic Medical Center, Amsterdam. Researchers conducted the INPACT study to confirm the findings



Dr. H. Roger Buller, MD

from two prior trials that showed that nadroparin prolonged survival in patients with cancer who did not have venous thromboembolism.

The multicenter, randomized, open-label INPACT study included 503 patients with hormone-refractory prostate cancer, locally advanced

pancreatic cancer or stage IIIb non-small-cell lung cancer. The primary outcome was death due to all causes and time to cancer progression, Dr. Buller said.

Patients were randomly assigned to subcutaneous nadroparin once daily for two weeks followed by half

Comparison of Endpoints

Survival	Nadroparin	No nadroparin
Major Bleeding	10 (4.1%)	9 (3.5%)
One major bleed or nonmajor clinically relevant bleeding	22 (9.0%)	21 (8.1%)

therapeutic doses for four weeks, or to a control group. Patients in the treatment arm were then assigned to six cycles of therapeutic-dose nadroparin at two-week intervals every six weeks. The primary endpoint was death from all causes; the secondary endpoint was time to cancer progression; and the safety endpoint was major bleeding.

To date, data indicate that the median survival of nadroparin patients was 12.5 months vs. 11.9 months for patients not assigned the drug ($P=.48$), according to Dr. Buller. The HR adjusted for type of cancer was 0.92, a nonsignificant, nonclinically relevant difference. In addition, the survival difference did not vary over time.

The use of nadroparin was not associated with an increased risk of bleeding (see table).

Shock with Injury Linked to Coagulopathy

Injury, regardless of severity, is not enough to cause coagulopathy, **Karim Brohi, FRCS, FRCA**, said during an educational session on Sunday. Shock is a crucial component of the condition.

The onset of coagulopathy, he noted, is much earlier than previously thought and is often fatal. In a retrospective study of patients who were transported by helicopter to London Royal Hospital, 24% of patients were coagulopathic upon arrival. Mortality was four times greater than normal for those patients.

Dr. Brohi, a surgeon at London Royal Hospital and professor of trauma sciences at Barts and The London School of Medicine and Dentistry, said there is a linear increase in mortality depending on injury severity and the patient's level of shock, but the whole story is more complicated. Neither patients who are only injured nor those who are shocked develop a condition he calls "acute traumatic coagulopathy," characterized by early coagulopathy associated with both injury and shock.

"When you put the two together,

we see the real picture. Patients become coagulopathic when they are both shocked and injured," he said. "A patient can be very injured and never get coagulopathic, and he can be very shocked and never become clinically coagulopathic, but the combination of the two does something that makes patients bleed. It is not clear what is going on in those patients yet, but it is certainly not normal."

Dr. Brohi described acute traumatic coagulopathy as a snowball that rolls downhill to become an avalanche. As patients become coagulopathic, they begin to experience several attendant conditions such as decreased fibrinogen utilization, dropping protein C levels and increased levels of APC.

"In this systemic anticoagulation with fibromyositis and increased fibrinogen utilization, you see this perfect storm of coagulopathy where patients don't use fibrinogen, inhibit TOP formation through APC activa-

tion, and whatever clots that are made are broken down through this fibrinolytic mechanism," Dr. Brohi said.

"Our current model of trauma-induced coagulopathy, the global picture, is that it starts with a snowball, a combination of trauma and shock leading to acute traumatic coagulopathy. Then the avalanche takes over when we start getting the dilution, hypothermia and acidosis."

Mortality from trauma is increasing, Dr. Brohi said, and hemorrhage accounts for about 40% of those deaths. Death from the bleeding is the most preventable cause of mortality in the world.

"All is not dilution, although it certainly does come into play later," he said. "Early on, the beast is something different. If we're going to make an impact on these significant death rates associated with trauma hemorrhage and traumatic coagulopathy, understanding the beast is our first process."

Ironside

(continued from page 1)

asymptomatic donors with variant CJD (Creutzfeldt-Jakob disease).

Dr. Ironside and his colleagues discovered disease-associated prion protein in one-quarter of spleen samples collected from the autopsy of a single patient with hemophilia. There was one evidence of variable levels of the disease-associated prion protein in frozen tissue. All other samples including brain and other lymphoid tissues were negative.

The patient had received more than 8,000 units of variant CJD-implicated Factor XIII; however, he had

also received very large quantities, 400,000 units, of UK Factor XIII not known to be implicated.

"In addition, the patient had been transfused with 14 units of red blood cells in the past and undergone multiple surgical and endoscopic procedures, all of which are potential risk factors," Dr. Ironside said.

There is a genetic susceptibility associated with variant CJD. All patients who had the MM genotype at position 129 in the prion protein have developed the disease, he said. In comparison, 38% of the normal population in the West have the MM genotype, and 50% have the MV genotype. The patient in this study with

Reiss

(continued from page 2)

The primary endpoint was symptomatic VTE at three months.

The incidence rate for VTE was 9.9% in the observation group, which was reduced to 1.3% in the enoxaparin group ($P<.01$). This was an absolute risk reduction of 8.6% and a relative risk reduction of about 90%.

The incidence of bleeding at three months was 3.75% in the enoxaparin group vs. 2.63% in the observation group, according to Dr. Reiss.

Although the rate of VTE and bleeding events increased at 30 weeks compared with three months, patients assigned enoxaparin still had reduced rates of both compared to observation. Data on response rate, progression-free survival and overall survival will be analyzed after a longer follow-up.

disease-associated prion protein in his spleen had the MV genotype.

"This raises questions whether the other two unit types will eventually have clinical cases because we know that they can suffer from sporadic CJD," Dr. Ironside said. "This is one of the great uncertainties."

He added that as many as one in 10,000 people in the U.K. could be infected without showing signs of the disease. "The other uncertainty is whether the number of patients so far who have died from the disease represent merely the tip of an iceberg – the iceberg beneath the water representing the number of patients who are infected but so far asymptomatic."



ISTH 2009 DAILY

ISTH 2009 Daily is published four times during the XXII Congress International Society on Thrombosis and Haemostasis



Publishers of HemOnc Today

SLACK Incorporated, 6900 Grove Road, Thorofare, NJ 08086; Phone 856-848-1000

Forum Provides Online Access to Experts and More

Created at the beginning of 2009 and unveiled at this year's Congress, ISTH is pleased to introduce you to the newest opportunity to communicate with fellow Society members and international experts.

What Is ISTH Forum?

ISTH Forum is an evolution of *The Haemostasis Forum*, an online resource that provided a medium for discussion of clinical questions posed by registered members. The original forum was created in 1996 by Dr. Harold R. Roberts and was supported by an unrestricted educational grant by Novo Nordisk. At the end of 2008, Novo Nordisk transferred ownership of the forum (and its archive of information) to the Society.

The new ISTH Forum, in keeping with the spirit of the original Haemostasis Forum, will continue to allow members to post questions and reply to fellow members on topics ranging from research queries to clinical diagnostic and treatment dilemmas in thrombosis and hemostasis.

The enhanced ISTH Forum also allows members to conduct polls, announce new registries, organize and discuss research collaborations, and post job openings. The ISTH Forum can be used to inform members about future conferences or to facilitate meetings with colleagues in advance of an upcoming conference. The ISTH Forum can also be used to support the work of the subcommittees of the Scientific and Standardization Committee during the year. If you have a question for the SSC or simply want to become involved in SSC work, the ISTH Forum offers the perfect opportunity to post a

question to the relevant subcommittee chair.

Speakers' Forum: Open to All Congress Attendees

The XXII Congress is the first ISTH Congress to use an online forum to promote interaction between delegates and featured speakers. A section of the forum (entitled "ISTH 2009") is open to all attendees for an extended plenary session question and answer period.

We thank the following speakers who have agreed to answer questions on the ISTH Forum for one week after the Congress:

Plenary Speakers

Helen Hobbs: Protection from Cardiovascular Disease: Getting to the Heart of the Matter

William Geerts: Thromboprophylaxis as a Key Patient Safety Priority: Current Approaches and Future Directions

Philip Hogg: Contribution of Allosteric Disulfide Bonds to Regulation of Hemostasis

Shaun Jackson: Modern Concepts of Platelet Activation During Thrombus Development

Evan Sadler: von Willebrand Assembly and Secretion

Rudolf Jaenisch: Stem Cells, Pluripotency, and Nuclear Reprogramming

Presidential Plenary Abstract Presenters

Marieke de Visser: Genome-wide Scan in Affected Sibling Pairs (Gift Study) Identifies a Novel Susceptibility Region for Venous Thromboembolism

Jonathan N. Thon: Examination of the Final Stages of Platelet Production

Henri Spronk: Feedback Activa-

tion of Factor XI by Thrombin Is Essential for Hemostasis In Vivo

Paolo Simioni: Evidence of the First X-Linked Thrombophilia Due to a Novel Mutation in Clotting Factor IX Gene Resulting in Hyperfunctional FIX: Factor IX Arginine 338 Leucine (Factor IX Padua)

Tatiana V. Byzova: Kindlin3 in Integrin Activation

Mieke Delvaeye: Thrombomodulin Mutations Predispose to Atypical Hemolytic-Uremic Syndrome Via Impaired Complement Regulation

How to Use ISTH Forum

ISTH Forum is located on the Society's website. Go to <http://www.isth.org> and click on "ISTH Forum" (<http://www.isth.org/ISTHForum/tabid/60/Default.aspx>). Go to "ISTH 2009" to post Congress-related questions. To ask a specific question on a plenary or presidential plenary

abstract session that you attended, look for the speaker's name and title of the lecture. Attendees may post questions to the ISTH Forum via the Congress Internet Cafe or at the Society's booth (#161) located in the Exhibition Area. Questions to the speakers must be submitted no later than July 22, 2009.

Reminders on how and where to post questions will be shown during participating sessions, and instructions are located on the ISTH Forum. We hope you find the enhanced online dialogue informative and easy to use.

Please experience the ISTH Forum for yourself. Post a question, poll the membership, add your expertise to the discussion or simply connect with members around the world. We hope that you have a great week connecting with your colleagues in Boston; now go to the ISTH Forum to continue the conversation!

All Congress Party Features Something for Everyone

The All Congress Party Thursday evening from 6:30 p.m. to 11:00 p.m. will feature food from Boston's many neighborhoods, a special performance by the renowned conductor Keith Lockhart and the Boston Pops Esplanade Orchestra, and activities for guests of all ages.

Guests will stroll among Boston's "neighborhoods," with each offering its own characteristic food and entertainment. Get a hot dog and have a souvenir baseball photo taken at the famous "Green Monster" left field wall of Fenway Park, home of the Boston Red Sox. Visit the Cheers bar and pose for a caricaturist while toasting your colleagues. Authentic Chinese lion dancers will entertain the tasters at the Chinatown neighborhood, and a vocal and accordion duo will serenade the samplers of a little taste of Italy from Boston's North End. From the waterfront to Beacon Hill, Boston's neighborhoods have something for everyone.

In a special program for ISTH 2009, the Boston Pops Esplanade Orchestra will highlight music by composers with ties to Boston, as well as music that is so well known that the audience will be asked to sing along. Afterward, dessert will be served and an All Congress Party DJ will keep the music going. Regular bus service will take guests back to Congress hotels.

Advance reservations are required for the All Congress Party, but there is still time to purchase tickets if you have not already done so. Please inquire at the Registration Desk.



Bank of America Pavilion, a Live Nation Amphitheater, just a short walk from the BCEC, is the site of the All Congress Party to be held Thursday evening from 6:30 p.m. to 11:00 p.m.

Important Announcement

The ISTH XXII General Membership Assembly will take place today, July 14, in the Grand Ballroom from 3 p.m. to 3:15 p.m.

Members will receive reports from the Society's leaders:

- Congress Presidents **Drs. Bruce and Barbara Furie** on the organization of the XXII Congress.
- ISTH Council Chairman **Dr. Frits Rosendaal** reporting to the membership on actions of Council taken at this year's business meeting.
- ISTH Executive Director **Dr. Gilbert C. White II** summarizing the state of the Society over the past year and to date.

The ISTH is an individual membership association and exists for and by the will of all members as an interna-

tional nongovernmental organization.

Programs and activities of ISTH and the Scientific and Standardization Committee (SSC) are entirely member-driven and include:

- *The Journal of Thrombosis and Haemostasis: JTH*
- Congresses and SSC annual meetings
- SSC scientific subcommittees
- ISTH programs, such as the Reach the World Initiative with its education and outreach components and the new ISTH Forum

ISTH members are encouraged to attend this brief meeting and to raise questions or make remarks. This is the membership's opportunity to hear from leadership, and this is the leadership's opportunity to hear from you.