

Working Group on Women's Health Issues
July 20, 2002
08:00 to 12:00
Whittier Room
Boston Park Plaza Hotel

Chair: M. J. Manco-Johnson, USA

This was the first open working party meeting on coagulation issues of women. There were 40-50 persons attending and participation was active.

- I. Organization of the Working Party, scope of activities, composition of the working group, method of approach and anticipated products.

Time was devoted to discussing and planning the above issues. This working party will be focused on coagulation values and clinical syndromes that are influenced by hormones. The working party will evaluate existing data, determine issues for which data is missing or deficient, identify areas of controversy and pressing clinical need and discuss methodologic approaches to answer questions raised. The working group may suggest or organize future collaborative studies as a result of these activities. The working group will incorporate laboratory scientists, epidemiologists, hematologists, high-risk obstetricians and gynecologists. All interested parties are encouraged to join an e-mail tree through marilyn.manco-johnson@uchsc.edu. The e-mail tree will be used to further discussions and continue active collaborations throughout the year.

Bleeding Disorders in women:

Anne Dilley, CDC, Atlanta, USA, discussed screening for von Willebrand's disease and other genetic bleeding disorders in women with menorrhagia. The use and limits of existing screening tools for menorrhagia were reviewed. Difficulties in the diagnosis of vWD were discussed including cost, timing and number of evaluations, use of reference laboratories, and high prevalence of the trait. Current challenges include validation of a screening questionnaire for menorrhagia, exploration of screening tests, including whole blood and thrombin generation assays, for vWD, platelet dysfunction and other bleeding disorders.

Peter Kouides, Rochester, USA, addressed efficacy of various therapies (OCPs, DDAVP, tranexemic acid, etc.) for menorrhagia. He raised the issue of safety of intrapartum DDAVP, endometrial ablation, Mirena pretestational ring, use of DDAVP for sports, and safety of hormonal therapies in menopausal women. Limitations of efficacy and adherence with various vWD therapies were reviewed. Dr. Kouides suggested an ISTH survey on DDAVP use, guidelines for screening vWD, guidelines for management, and a survey on the diagnosis of vWD while using OCPs.

James Bussel, New York, USA, reviewed current updating of the Platelet Immunology Subcommittee recommendations for the evaluation and management of neonatal alloimmune thrombocytopenia. Dr. Bussel discussed advances in platelet antigen typing, serologic testing, and antenatal treatment. Revisions to recommendations for fetal testing were discussed. Current in-process studies of combined use of IVIG and steroids prenatally were presented. New recommendations stratified by fetal risk were discussed.

II. Influence of hormones on coagulation values in women.

Dr. Margareta Blombäck presented data for coagulation proteins relative to the menstrual cycle, trimesters of pregnancy and hormonal therapies, including oral and topical administration of HRT during menopause. Professor Blombäck advised that data are lacking primarily for hormonal effects on fibrinolysis overall, and that data are weak for the three generations of contraceptive agents. The recommendation was made to explore global assays of thrombin generation, coagulation potential and fibrinolytic potential and apply these to the various hormonally influenced states noted above.

III. Risk factors for thrombosis and adverse outcome in pregnant women.

Dr. Ian Greer, Glasgow, UK, discussed risk factors for thrombosis during pregnancy. He stressed the gap between knowledge of risk factors (obesity, age, caesarean section, prior venous thrombosis, personal and family history of thrombosis) and appropriate application of diagnosis and interventions in pregnancy. Prof. Greer reviewed evidence for thrombosis and thrombosis recurrence during pregnancy, safety of prophylaxis with LMWH and cost of screening and complications. Suggestions were made to collaborate the study cost/efficacy of targeted screening as well as the use of aspirin and compression stockings for prevention.

Dr. Jacqueline Conard gave an elegant presentation of venous thromboembolism in pregnancy complicated by genetic antithrombin deficiency. Thrombosis risk was delineated by propositus vs relative for antithrombin presentation, history of previous thrombosis, history of previous pregnancy-associated thrombosis, anticoagulation prophylaxis and antithrombin concentrate prophylaxis. Recommendations were made to proceed with similar data construction for all known thrombophilic traits.

Dr. Marilyn Manco-Johnson presented evidence for the role of thrombophilic genes in adverse pregnancy outcomes including preeclampsia, abruption, intrauterine growth retardation, recurrent miscarriage and fetal demise. General trends support the role of thrombophilic genes to increase the risk of adverse pregnancy outcome and to worsen existent disorders. There is a wide variation in presence and strength of these effects, diluting the power of meta-analyses secondary to methodologic differences in case definition, sample size, referral patterns, eligibility criteria, and other genetic and environmental variations in the study populations. Examples include divergent results regarding the role of antiphospholipid antibodies in adverse pregnancy outcome. Two large studies of more than 1000 cases failed to support a relationship of adverse pregnancy outcome to factor V Leiden. Suggestions were made for prospective, multi-center studies with large numbers, standardized case definitions and outcome determinations.

IV. New Business

Future efforts will address HRT effects on coagulation and thrombosis risk, oral contraceptives and HELLP syndrome. The e-mail tree will be used to continue these discussions, identify new members and prepare for an open meeting next year.

Working Group on Women's Health Issues
July 12, 2003
09:00 to 13:00
Hall 10
The International Convention Center, Birmingham

Chair: M. J. Manco-Johnson, USA
To contact; email marilyn.manco-johnson@uchsc.edu

This was the first open meeting of the Working Group on Women's Health Issues. Over the past year, the Women's Group has worked to define issues appropriate to this working group and develop approaches for the working group.

- I. Issues of Standardization of Coagulation Assays to detect effects of hormones, including the menstrual cycle, pregnancy and hormone replacement therapy.

Speakers included: Dr. He discussed the OHP (overall hemostatic potential) applied to the normal pregnancy, pregnancy complications and hormone replacement therapy; Dr. Hellgren discussed the TEG (thromboelastogram) and the Sonoclot applied to pregnancy; and Dr. Eichinger discussed application of activation markers to predict TE events during pregnancy. There is a need for a screening assay(s) to predict bleeding or thrombotic events and, potentially, to predict adverse pregnancy outcomes.

The evidence presented demonstrated a good ability of all global assays to discriminate populations, including normal pregnant women from non-pregnant control women, as well as women with complicated pregnancy from uncomplicated. However, individual data points showed substantial overlap, and the sensitivity and specificity of these assays to predict clinical events, as well as the comparability of various assays, is of yet unknown.

ACTION STEPS: There was agreement regarding a need to determine the usefulness of global assays by validation and application. Various approaches were discussed including comparison studies utilizing a specific global assay in various laboratories and patient groups, collaborative studies with assays performed in one central lab or direct comparison of more than one global assay in a single population. The goal is to develop an experimental approach with implementation ongoing prior to next year's meeting. Working group members are encouraged to participate in the development and execution of these validation studies by e-mailing directly to the following people:

Shu He	he_shu@yahoo.com
Katarina Bremme	katarina.bremme@ks.se
Margareta Hellgren	margareta.hellgren@vgregion.se
Margareta Blombäck	margareta.blomback@ks.se
Sabine Eichinger	sabine.eichinger@akh-wien.ac.at

Dr. Blombäck discussed standardization of patient and laboratory conditions for determination of coagulation factors in women. For example, factor assays, especially factor VIII and vWF should be drawn during days 1-4 of the menses. Women should be off OCPs for a minimal period (e.g. 2 months) prior to baseline testing or on HRT for a minimal period to determine

hormonal effects. Women should be encouraged to have blood drawn in the morning prior to any vigorous exercise or stress, after sitting for 20 minutes.

ACTION STEP: It was agreed that there are many conditions specific to accurate laboratory determination of hormonal effects on coagulation. A short recommendation paper will be written to suggest such clinical methodologies to be used for all published reports. Dr. Blomback will draft the report and copies, comments and collaborations can be made by e-mail to her (see address above). Input from other relevant subcommittees including vWF committee will be solicited. This project should be completed within six months and the results available for clinical protocols related to the global assay validation described above.

II. Issues in thrombophilia relative to pregnancy: assays and normal values.

Risk factors for thrombosis during pregnancy were reviewed by Dr. B. Brenner. Discrepancies in the literature were highlighted and the suggestion was made that differing risk assessments result from differences in eligibility criteria of women studied as well as laboratory assays performed. Specifically, the relationship between thrombophilia and pregnancy outcome is predicted to be strongest when pregnancy complications (such as pre-eclampsia or intrauterine growth retardation) are severe in nature and thrombophilia risk (e.g. lupus anticoagulant, antithrombin deficiency or multiple trait thrombophilia) is also severe.

ACTION STEP: A recommendation paper has been developed in conjunction with the perinatal and pediatric subcommittee regarding thrombotic risk during pregnancy and will be submitted for review and recommendation for publication in JTH. This will be accomplished within the next month.

ACTION STEP: A recommendation paper will be developed proposing definitions to standardize severity of pregnancy complications as well as thrombophilia severity to be used in future studies of maternal outcome relative to thrombophilia. This objective should be accomplished within the next six months. To participate please contact: Dr. Benjamin Brenner: s_kamenetsky@rambam.health.gov.il

Dr. Saskia Middeldorp discussed indications for anticoagulation in women with a history of pregnancy loss.

Dr. Barbara Konkle introduced the issue of thrombosis associated with the ovarian hyperstimulation syndrome (OHSS), seen particularly in women with polycystic ovary syndrome. The contribution of endogenous androgens and thrombophilia to clinical VTE events is unknown.

ACTION STEP: Dr. Konkle will establish a registry structured to collect data regarding OHSS, thrombophilia, clinical and/or biochemical evidence of androgen excess and clinical VTE events. Input into registry data collection form development is welcome. The registry should be established by the next meeting. Contact Dr. Konkle for registry development and data collection: Barbara Konkle: barbara.konkle@uphs.upenn.edu

Dr. Jacqui Conard presented existing data on pregnancy-associated VTE in antithrombin deficient women with provocative evidence that prognosis may differ in AT deficient women detected with family studies, regardless of history of prior thrombosis. AT deficiency is rare and has been considered to convey a high risk of pregnancy-associated VTE in all affected women. To further determine the magnitude of differential risk, Dr. Conard will establish a registry. The registry will be established and running by next year's meeting. Please contact her:

Dr. Jacqueline Conard jacqueline.conard@htd.ap-hop-paris.fr

Dr. Andra James presented data regarding the poor prognosis of pregnancy in women with mechanical heart valves affected both mother and fetus. Recommendations regarding anticoagulation in pregnant women with mechanical heart valves are considered a very high priority need. To collect preliminary data, a registry will be established. To participate in registry development, contact her: Dr. Andy James andra.james@duke.edu

III. Issues in thrombophilia relative to hormonal therapies.

Reports were made by : 1) Dr. James. Douketis on the effects of prothrombotic factors on DVT risk in women using hormone replacement therapy (HRT); 2) Dr. Leo Zacharski on the role of iron accumulation in cardiovascular risk in postmenopausal women; and 3) Dr. Kluft on the results of a European Consensus Conference on sex steroids and cardiovascular disease in women. Recent data was discussed that suggests cardiovascular event risk is higher in women using combined estrogen/progesterone HRT as compared with estrogen alone. This is of concern as gestational agents alone have been prescribed to women with thrombophilia.

ACTION STEPS: In order to determine the safety of progestational-only agents in DVT risk, a registry will be developed to record the outcome of women with thrombophilia who have been treated with progestins only including women with asymptomatic thrombophilia as well as women with thrombophilia and previous symptomatic VTE. To review the draft registry, comment and record data, contact: Dr. J. Douketis jdouket@mcmaster.ca

IV. Hormonal influences in bleeding disorders of women.

Dr. Peter Kouides presented recommendations for screening, laboratory assays and treatment algorithm for women with menorrhagia on behalf of himself, Anne Dilley, Connie Miller, Christine Lee and the working party following 2 years of developmental work.

ACTION STEP: The recommendations will be submitted to the Chair for proposal as a recommendation paper in JTH on behalf of the working party in collaboration with the vWF Subcommittee. This goal should be completed within 3 months. To comment, please contact: Dr. Peter Kouides peter.kouides@vianethealth.org

Dr. James Bussel discussed issues in ITP during pregnancy including inadequate data regarding minimal platelet numbers during normal pregnancy, and hemostatic levels of platelets for procedures during pregnancy, such as amniocentesis or epidural anaesthesia. Further discussion

of this issues will be conducted in conjunction with the perinatal and platelet subcommittees. To contribute to this issue contact: Dr. James Bussel jbussel@med.cornell.edu

V. New Business

The creation of a standing subcommittee from the working party was discussed. This concept was approved by the attendees of the meeting and a request will be forwarded to the SSC for consideration.

Women's Health Issues

June 19, 2004

8:30 to 12:30

**Piccolo Teatro Room
Fondazione Giorgio Cini**

Chairman: M. Manco-Johnson, USA

There were approximately 50 persons present at the subcommittee meeting.

Recommendations:

Several activities have been completed and recommendations were forwarded at the meeting.

1. Radiologic exposure during pregnancy: Dr. M. Nijkeuter reported on fetal x-ray exposure from either CT or VQ scanning performed to exclude pulmonary embolus in high-risk pregnant women. It was concluded that fetal exposure is less than background (environmental) radiation from helical CT chest scanning and less than that of VQ scanning. It was recommended that testing for pulmonary embolus not be avoided during pregnancy and that CT is the preferred technique. A recommendations paper was completed and will be submitted within a month following circulation to other committee members for approval.
2. Value of thrombophilia testing for VTE related to pregnancy, oral contraceptive or hormone replacement therapy as well as following various adverse pregnancy outcomes. Dr. I. Greer reviewed data that conclusively implicates thrombophilia in the predisposition of women to thrombosis during pregnancy and hormone therapies. In addition, convincing evidence was presented that thrombophilia predisposes to adverse pregnancy outcomes of preeclampsia, low birth weight, abruption and fetal loss. However, analyses of several studies did not support that diagnosis of thrombophilia would alter management, nor that prevention of first episodes of venous thrombosis by either universal or selective screening programs would be cost effective. Thus, thrombophilia studies have been important to determine the pathophysiology of these disorders, but not to manage pregnant women. A recommendation manuscript has been developed and will be submitted for publication following circulation for review.
3. Coagulation testing and treatment for women with menorrhagia. This was presented by Dr. C. Phillip. Evidence exists that menorrhagia is an important clinical problem of women, that bleeding disorders are increased in women with menorrhagia, that racial differences exist in the etiology of bleeding disorders of women and that testing is difficult and expensive. A recommendation paper summarizing the state of knowledge and calling for careful studies of coagulation and platelet function in women with menorrhagia, the effectiveness of current coagulation evaluations to determine the etiology of menorrhagia and the efficacy of therapy and cost-

effectiveness of screening will be submitted within the next two months following further review and refinement of the initial paper.

4. Scoring systems for severity of thrombophilia and pregnancy complications. The existing literature regarding the contribution of thrombophilia to adverse pregnancy outcome is difficult to interpret due to the lack of standard definitions for pregnancy outcomes as well as thrombophilic disorders. Dr. B. Brenner reviewed the existing literature and developed an innovative system of scoring maternal, fetal, gestational, and genetic factors for application to future studies. A paper describing the rationale and proposed scoring system will be submitted within the next three months and applied to individual and group activities. Next year's meeting will describe experience using the scoring system.
5. Conditions for drawing blood samples to determine hormonal effects on coagulation in women. Dr. M. Blomback has reported on this project for the past two meetings. Her recommendations have been finalized. The initial recommendations paper will be rewritten and submitted for publication within the next three months.

Registries:

1. Pregnancy complications in women with prosthetic heart valves. Dr. A. James presented the finalized version of the registry which will be put on the ISTH web page for a committee activity this year.
2. Ovarian hyperstimulation syndrome. Dr. B Konkle presented the finalized version of the registry data forms for the incidence of the ovarian hyperstimulation syndrome and rate and outcome of thrombosis caused by hormonal stimulation for infertility. This registry will be put on the ISTH web page and entered as a committee group activity.
3. Pregnancy outcome in antithrombin deficient women. Dr. J Conard presented the final version of this registry which she piloted in France during the last year. This registry will also be posted on the ISTH web page for use this year.

Global assays for screening of hormonal effects in women.

Various global assays were presented by Drs. Antovic, Hellgren and He of Sweden including thrombin generation assays, variations of the thromboelastogram and the overall haemostatic potential. A plan was made to conduct a validation study. Dr. Manco-Johnson will prepare aliquots of unknown plasmas and distribute them to participating laboratories for local performance. The analysis will assess the sensitivity of the assays to bleeding and clotting disorders.

Gender-influenced recurrence risk for venous thrombosis.

Dr. Eichinger presented intriguing evidence that women have a lower risk for recurrence of venous thromboembolism that is not influenced by use of oral contraceptives at the time of initial clot onset. Younger women exhibit a lower recurrence rate than women beyond the age of 45 years. A discussion of protective effects of hormones on recurrence risk for venous thromboembolism will be continued next year.

The meeting was concluded at 12:35.

Respectfully submitted,
Marilyn J. Manco-Johnson

Women's Health Issues in Thrombosis and Haemostasis

August 7, 2005

08:30 to 12:00

Sydney Convention Centre

Chairman: M. M. Manco-Johnson

Co-chairs: M. Blomback, Sweden, B. Brenner, Israel, J Conard, France, S. Eichinger, Austria, I. Greer, UK, A. James, USA, B. Konkle, USA.

Approximately 150 people attended the SSC meeting on Women's Issues.

Thrombophilia Issues in Pregnancy

Ian Greer presented a systematic review of thrombophilia in relationship to pregnancy outcomes. He emphasized important variables in screening that the health problem be significant, with a known natural history and identifiable before onset of disease; that the predictive test be safe and acceptable; and finally that an effective intervention be available. It was noted that we are at a time of fragile equipoise regarding attitudes toward anticoagulant prophylaxis during high-risk pregnancies, and that women are not willing, in some circumstances to allow randomization to placebo or no treatment. B. Eni Brenner presented his scoring system for severity of thrombophilia syndromes and severity of pregnancy outcomes. The scoring system is intended to predict potential outcome of pregnancy based upon personal and family history of thrombosis, past pregnancy outcome and thrombophilic traits identified. S. Eichinger presented data regarding factor V Leiden and thrombosis outcomes, concentrating on oral contraceptives.

The Scoring System of Dr. Brenner will be compiled to be submitted from this Subcommittee publication in JTH. A collaborative activity will be developed to apply the scoring system prospectively to pregnancy, as an observational study, with or without clinically ordered intervention, in order to validate the scoring system. In particular the strength of a previous history of thrombophilia-related thrombosis in predicting thrombophilia-related non-thrombotic complications of pregnancy needs to be analyzed. S. Eichinger will develop a scoring system for thrombophilia and OCP outcomes modeled on the thrombophilia/pregnancy outcome scoring system. Recommendations regarding issues for women with FVL around oral contraceptive and hormone replacement therapy will be developed. If appropriate, the OCP, HRT and thrombophilia risk scoring system would be later extended beyond FVL to other thrombophilias.

Dr. M. Nijkeuter is continuing to organize the project on diagnosis of pulmonary emboli during pregnancy. This will be reported at the Oslo meeting, next year.

Reports on Registries

Pregnancy Outcomes in Women with Prosthetic Heart Valves : Andra James This registry is developed and three patients have been enrolled. The data base will reside at Duke University, Durham, US. The protocol, consent and data forms will be listed on the ISTH SSC website along with Dr. James contact information.

Thrombotic Outcomes in Women Undergoing Ovarian Stimulation : Barbara Konkle has established this registry on the ISTH SSC website.

Pregnancy Outcomes in Women with Antithrombin Deficiency : J. Conard has developed this registry. It will be expanded to include women with deficiencies of protein C or protein S. Forms, consents and contact information will be included. Dr. Conard can be reached by email: jacqueline.conard@htd.ap-hop-paris.fr

New Business:

Validation of the usefulness of global assays to detect hormonally-related alterations in coagulation. This project is in development. The Women's Subcommittee will collaborate with the Thrombin Generation Questionnaire that has been developed by the SSC on Plasma Coagulation Inhibitors. All interested potential participants employing global hemostasis assays are encouraged to participate. Contact marilyn.manco-johnson@uchsc.edu.

Position Papers:

Evaluation of Women with Menorrhagia, Claire Phillip, 1st author : This paper has been developed and has been circulated among SSC Subcommittee members. It will be forwarded to the ISTH Council shortly.

Pre-analytic variables affecting testing of hormonally-affected coagulation proteins. Margareta Blomback, 1st author: This paper has been completed and is receiving comments from co-chairs.

Scoring system for thrombophilia and pregnancy outcomes, Benjamin Brenner, 1st author: This paper has been developed and will be circulated among subcommittee members promptly.

Women's Issues in Haemostasis and Thrombosis

Chair: Marilyn Manco-Johnson

Co-Chairs: M Blömbäck, Sweden, B Brenner, Israel, J Conard, France, S Eichinger, Austria, I Greer, UK, A James, US, B Konkle US, C Philips, US

Attendance: approximately 80 people attended the meeting

Manuscripts:

Recommendations for testing women for hemostasis: awaiting reviews and approvals

Proposal for a scoring system for thrombophilia and pregnancy outcome in women to be applied to prospective outcome studies

Dr. Brenner will submit his analysis of the scale derivation in 94 Israeli women to JTH as an independent manuscript. The scale will then be placed on the web as a WP project for validation in a multinational study. The strong predictive value of previous thrombosis which is incorporated in this scale was supported by evidence presented by Dr. Conard in women with AT deficiency. The collaborative multicenter study validating the obstetrical scoring system will hopefully be submitted as a recommendation paper from this subcommittee.

Dr. Blombäck presented data on correlates of recurrent miscarriage in women. She determined overweight body habitus and obesity predisposing to secondary miscarriage, and certain thrombophilias predisposing to primary miscarriage. The inclusion of recurrent early miscarriage in a scale of maternal risk factors was agreed upon.

Recommendations for evaluation and management of menorrhagia in women.

This manuscript will be reviewed for submission as an SSC publication.

It was discussed that a detailed descriptive study of women with bleeding disorders is currently funded by the US CDC and preliminary data will be presented to this Subcommittee next year. The US data will characterize women with bleeding disorders who are referred to a hemostasis center.

Dr. Shoshana Revel-Vilk will develop a community-based study of adolescents with menorrhagia in order to determine whether predictors for a bleeding disorder can be applied to an adolescent population to increase the yield of coagulation screening. She can be contacted at shoshanav@hadassah.org.il.

Registries:

Pregnancy in women with mechanical heart valves. **A James, USA**

Dr. James presented a literature review of pregnancy outcome in 76 women with mechanical heart valves as a background to the current registry. Her review is currently in press (J Mat Fetal and Neonatal Med, 2006). The prospective registry is up and running. There have been three case entries and several other centers are in the process of obtaining ethics approvals. It is anticipated that results will be presented to the Geneva SSC meeting.

Pregnancy in women with genetic antithrombin deficiency. **J Conard, France**

This registry is on the web and now includes 51 women from several centers in France and one other country. Participants were urged to join the registry. An update will be presented in Geneva. Dr. Conard may be contacted at jacqueline.conard@htd.ap-hop-paris.fr

Outcome of ovarian hyperstimulation syndrome. **B Konkle, USA.**

This registry is near completion and will be on the ISTH website along with sample protocol and ethics consent forms in the near future.

New Business

Diagnosis of Pulmonary embolism in pregnancy: **Matilde Nijkeuter, The Netherlands**

In this proposal pregnant women with clinically suspected pulmonary emboli will be studied with helical CT and if the study is negative, anticoagulation will be withheld and the woman will be followed for three months in order to determine the safety of the approach. This multicenter study has been initiated in the Netherlands and has enrolled 20 cases. From 100 to 400 cases will be needed to determine the safety of withholding anticoagulation from pregnant women with normal findings on helical CT, based upon an expected rate of positive PE ranging from 5 to 20%. There was some controversy expressed regarding the use of CT in pregnancy and the difficulty to enroll adequate numbers. Nonetheless, the study is endorsed by the subcommittee and potential participants are encouraged to contact Dr. Nijkeuter at Matilde.nijkeuter@lumc.nl.

Proposal for a registry on Mirena IUD in women with menorrhagia: **Rezan Kadir, UK**

Dr. Kadir presented data regarding use of the Mirena IUD to control menorrhagia in women as a whole, and in subsets of women with confirmed bleeding disorders. While the Mirena IUD has been generally effective and safe, its use in women with bleeding disorders may be accompanied by a higher rate of break-through bleeding and side effects resulting in discontinuation. Response to the registry was positive and it will be posted on the ISTH website. Dr. Kadir may be contacted at rezan.abdul-kadir@royalfree.nhs.uk.

There was a lively discussion provoked by Dr. James presentation on pregnancy in women with mechanical valves relating to the use and requirements for monitoring LMWH during pregnancy. It was decided to form a WP on anti-Xa activity monitoring during pregnancy. Dr. Charlie Hay of the UK, Dr. Aima of Greece and Dr. Sandy Duncan of the US volunteered to organize the WP. They may be contacted at: haemophilia@man.ac.uk; aima09@hippocratio.gr; and aduncan@emory.edu.

Dr. Manco-Johnson suggested that the current recommendation not to test asymptomatic women prior to use of oral contraceptives or hormonal replacements may be modified if there were a way of improving risk prediction for hormonal-related DVT. Dr. Brenner proposed a study using global assays to predict risk of thrombosis in asymptomatic women presenting for oral contraception or hormone replacement therapy. A lively discussion ensued and it was decided to invite Dr. Rossing and others to speak further on this at the Geneva meeting.

Dr. Manco-Johnson suggested inclusion of neonatal thrombotic disorders including neonatal stroke in the registry of Dr. Brenner to expand detection of potential perinatal risks conferred by thrombophilia or maternal thrombosis. It was decided to embark on this as a joint activity with the Perinatal and Pediatric Subcommittee with Dr. Manco-Johnson acting as a liaison with Dr. Gili Kenet of Israel. Dr. Manco-Johnson can be contacted at marilyn.manco-johnson@uchsc.edu.

Women's Health in Thrombosis & Haemostasis

Chair: Andra H. James (USA)

Co-Chairs: Margareta Blombäck (Sweden), Benjamin Brenner (Israel), Jacqueline Conard (France), Sabine Eichinger (Austria), Ian Greer (UK), Barbara Konkle (USA), Claire Philip (USA)

Minutes:

Introduction and Overview:

In the introduction and overview Dr. Andra James presented the

- Purpose and function of the scientific subcommittees
 - to develop standards, methods, nomenclature
 - to address issues of practical importance to the research community
 - to complete a specific program of work
 - to create international collaborations for the purpose of planning, executing and completing projects of benefit to the international community
 - to generate, publish and distribute reports, recommendations and other documents concerning the above
- Route to publication of SSC reports, recommendations and documents
 - development
 - approval by a “vote” of international experts within and possibly outside of the SSC
 - approval by 2 external reviewers
 - approval by the chair of the scientific subcommittee who forwards the document to the Chair of the SSC and ISTH headquarters
 - approval by the Chair of the SSC and the ISTH
- Options for publication
 - on the ISTH Website
 - in the Journal of Thrombosis and Haemostasis
 - short communication (1 ½ pages) – usual route for SSC publication – requires approval by editors of JTH
 - full-length article – requires usual peer review and approval by editors of JTH (official SSC documents may not be published elsewhere.)
- Development of standards (similar process to development of document)
 - After approval by ISTH, a recommendation is forwarded to the Expert Committee on Biological Standardization (ECSB) of the World Health Organization (WHO)

Dr. Marilyn Manco-Johnson presented an overview of the history of the Women's Health in Thrombosis and Haemostasis including its origins and accomplishments.

Educational Activities

Dr. Benjamin Brenner reported on the successful 2nd Symposium on Women's Issues in Thrombosis and Hemostasis held in Vienna the first week of February 2007 and announced the next symposium to be held February 6-8, 2009.

Report on the Women's Health in Thrombosis & Haemostasis Subcommittee Inspired or Sponsored Publications

Dr. Brenner reported on a Scoring System for Pregnancy Outcomes. Application of this scoring system to patients at his institution has shown a strong correlation between the score and the level of anticoagulation required during pregnancy. Publication of these results will emanate from his institution. Future directions include, possibly, application to women who have and have not received anticoagulation and an international, multi-center validation of the study.

Dr. Margareta Blomback summarized the Women's Issues SSC publication, Blomback et al, Preanalytical conditions that affect coagulation testing, including hormonal status and therapy. JTH 2007; 5 (4), 855–858.

Report from the 8th American College of Chest Physicians' Conference on Antithrombotic and Thrombolytic Therapy

Dr. Shannon Bates summarized her group's recommendations for the chapter, "Use of antithrombotic agents during pregnancy," and highlighted the differences from the last version published in 2004. Of interest to the audience were expanded options for the management of women with mechanical heart valves and the absence of a recommendation to screen women with a history of poor pregnancy outcome for thrombophilia. The reasons cited for the latter were weak associations between thrombophilia and poor pregnancy outcome and limited data on the benefits of anticoagulation in these women.

Update on Registries

Pregnancy outcome in women with antithrombin deficiency:

Dr. Jacqueline Conard presented a summary of the incidence of thrombosis during pregnancy among women with antithrombin deficiency. The only contributors to the registry have been from France.

Pregnancy outcome in women with mechanical heart valves:

Dr. James reported that only one subject has been added to the registry this year. Dr. Claire McLintock has been recruited to assist with enrollment. Dr. McLintock reported on 15 cases from New Zealand that she expects will be added to the registry.

Thrombosis and thrombotic risk in women receiving ovarian stimulation for pregnancy:

Dr. Barbara Konkle reported that to date no subjects have been enrolled in this registry and it will be withdrawn.

Update on New and Proposed Registries:

Mirena IUD for menorrhagia in women with bleeding disorders:

Dr. Rezan Kadir reported that she and Dr. Peter Kouides have completed a questionnaire that can be used to gather data about women with bleeding disorders and their experience with the Mirena IUD. The questionnaire is ready to be added to the website.

Application of pregnancy scoring system to neonatal thrombosis – joint activity with the Perinatal/Pediatric Scientific Subcommittee

Dr. Manco-Johnson reported that the concept for this study is evolving into a case-control study. The study will likely not take the form of a registry.

Update on Other New and Proposed Projects:

Monitoring anti-Xa activity during pregnancy:

Dr. Sandy Duncan spoke to the benefits of monitoring anti-factor Xa levels in pregnancy. In the ensuing discussion, questions were raised about the methodological problems in trying to answer the relevant research questions using a registry. An outcome of the discussion was the recognition of the need for a registry for women who have received fondaparinux during pregnancy. Dr. James will pursue the establishment of such a registry with Dr. Duncan.

New Opportunities for Collaboration: Studies of Reproductive Tract Bleeding in Women with Bleeding Disorders:

Dr. Althea Grant summarized the past and current research on women with bleeding and clotting disorders being conducted at the United States Centers for Disease Control and Prevention. Her presentation was followed by a presentation by Dr. Flora Peyvandi on her group's proposal of a study on menorrhagia in women affected by bleeding disorders. Data would be collected from multiple international sites. There was general consensus regarding the merits of the study and the feasibility of an international collaboration.

Future Meetings:

There was support for the new congress meeting structure that will include educational sessions. The Women's Health SCC will propose that 1 to 1.5 hours at their next meeting be devoted to education. The two topics that will be proffered are, "Anticoagulation during Pregnancy," and "Reproductive Tract Bleeding in Women with Bleeding Disorders."

There were approximately 100 persons in attendance.

Women's Health in Thrombosis and Haemostasis

4 July 2008
Vienna, Austria

Chair: *Andra James, USA*

Co-Chairs: *Margareta Blomback, Sweden; Benjamin Brenner, Israel; Jacqueline Conard, France; Sabine Eichinger, Austria; Barbara A. Konkle, USA; Claire McLintock, New Zealand; Claire S. Philipp, USA*

Introduction and Overview – Andra H. James, MD, MPH

- Purpose and function of SCCs
- What constitutes issues in women's health in thrombosis and haemostasis –
- Introduction of co-chairs

Educational Activities Overview of the 2009 ISTH meeting and proposed educational sessions

- Next year there will be general sessions that address women's issues **plus** we will need to come up with **three** educational sessions (30 minutes each) for inclusion in our 4 hour meeting time (90 minutes of educational sessions, 150 minutes of meeting time). We don't know yet what the general sessions will be, but when we find out, we will need to make sure that the topics we select to present during our SSC meeting will be complementary.
- Topics that have already been suggested for educational sessions within our SSC meeting next year-
Anticoagulants in pregnancy
Reproductive tract bleeding in women with bleeding disorders
- Other topics that were suggested at the July 4, 2008 meeting:
Diagnosis of pulmonary embolism during pregnancy
Hormone therapy: contraception (J. Conard)
Hormone therapy: postmenopausal

Next International Symposium on Women's Health Issues in Thrombosis and Haemostasis will be February 6-8, 2009 in Prague - Benjamin Brenner MD

Report on the Women's Health in Thrombosis & Haemostasis Scientific Subcommittee (SSC) Inspired or Sponsored Publications – Claire Phillip, MD

- A screening tool for identifying women with menorrhagia for hemostatic evaluation – published this year in the Am J of Obstet Gynecol
- A multi-site, prospective cross-over study of intranasal desmopressin and oral tranexamic acid in women with menorrhagia and abnormal laboratory hemostasis – presented on behalf of her co-investigators – manuscript in preparation

Update on Registries

- Pregnancy outcome in women with mechanical heart valves – presentation of large series of cases by Claire McClintock, MD – manuscript in preparation – proposal for data management by MedSciNet with funding from an unrestricted grant to ISTH
- Mirena IUD for menorrhagia in women with bleeding disorders – registry is now on the ISTH website. Andra James reporting for Rezan Kadir, MD

Update on Ongoing international collaborations

- Menorrhagia in women affected by bleeding disorders – an international study – Flora Peyvandi MD presented an overview of the study. ISTH members are encouraged to participate. More information can be found at www.wrbd.org

New registry:

- Corpus luteum bleeding in women with bleeding disorders – a summary and a proposed registry was presented by Ron Hoffman MD. The data collection form is ready to go and we will get it posted to the ISTH website.

Presentation on haemostatic disturbances in women undergoing in vitro fertilization (IVF) – Eli Westerlund, MD

Topics suggested for inclusion in next year's SSC meeting (besides the educational sessions):

- Update on Mirena registry - R. Kadir, MD
- Update on mechanical valves registry – C. McLintock, MD
- Data on fondaparinux in pregnancy – S. Duncan, MD
- Update on the international study - Menorrhagia in women affected by bleeding disorders – F. Peyvandi MD
- Update on registry of corpus luteum bleeding – R Hoffman, MD
- Predictive scores for thromboprophylaxis in pregnancy – TBA
- D-dimer levels in pregnancy – R Alkier, MD
- Thrombin generation testing in pregnancy
- Preliminary results of multicenter study of VWD levels in pregnancy – B Konkle, MD
- Update in antithrombin registry – J Conard, MD
- Proposed registry of women with thrombocythemia in pregnancy –

Submitted by A. James