### Program at a glance - APSTH 2018 jointly held with the 40th JSTH

**June 28 (Thu.)**

APSTH participants can attend programs in white time slot.

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<tr>
<th>Time</th>
<th>Royton Hall AB (3F) - Room 1</th>
<th>Empress Hall (2F) - Room 3</th>
<th>Regent Hall (2F) - Room 4</th>
<th>Heine's Hall (2F) - Room 7</th>
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**Educational Program with Support of ISTH**

- **Chair**: Claire McLintock, Yukio Ozaki
- **Speaker**: Claire McLintock, Jeffrey Weitz, Walter Ageno, Tatsuya Atsumi, Katsue Suzuki-Inoue

**Educational Program with Support of WFH**

- **Chair**: H. Marijke van den Berg, Akira Yoshioka
- **Speaker**: H. Marijke van den Berg, Midori Shima, Ki-Young Yoo, Yeu-Chin Chen, Kumiko Ono

**Luncheon Symposium (Stago)**

- **New insights in haemostasis laboratory medicine**
- **Moderator**: François Depasse
- **Speaker**: Hideo Wada, Heng Joo Ng

**Afternoon Tea Seminar (Chugai Pharmaceutical Co., Ltd.)**

- **Creation and Clinical Application of emicizumab**
- **Chair**: Renchi Yang, Katsuyuki Fukutake
- **Speaker**: Takehisa Kitazawa, Midori Shima

**Opening Ceremony**
Program at a glance - APSTH 2018 jointly held with the 40th JSTH

APSTH participants can attend programs in white time slot.

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<tr>
<th>Time</th>
<th>Crystal Room A (2F) - Room 5</th>
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<th>Crystal Room C (2F) - Room 8</th>
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APSTH participants can attend programs in white time slot.

June 28 (Thu.)

Educational Program with Support of ISTH
【Chair】
Claire McLintock
Yukio Ozaki
【Speaker】
Claire McLintock
Jeffrey Weitz
Walter Ageno
Tatsuya Atsumi
Katsue Suzuki-Inoue

Educational Program with Support of WFH
【Chair】
H. Marijke van den Berg
Akira Yoshioka
【Speaker】
H. Marijke van den Berg
Midori Shima
Ki-Young Yoo
Yeu-Chin Chen
Kumiko Ono

Opening Ceremony
学術推進委員会(SPC)
シンポジウム 1
第10回 Bayer Thrombosis Seminar
学術奨励賞
受賞講演
開会式
岡本賞
受賞講演
ランチョンセミナー 1
一般演題1
一般演題 3
一般演題 2
一般演題 4
総会
Exhibition / Poster
All APSTH & JSTH participants have access to exhibition room

Luncheon Symposium (Stago)
New insights in haemostasis laboratory medicine
【Moderator】
François Depasse
【Speaker】
Hideo Wada,  Heng Joo Ng

Afternoon Tea Seminar (Chugai Pharmaceutical Co., Ltd.)
Creation and Clinical Application of emicizumab
【Chair】
Renchi Yang,  Katsuyuki Fukutake
【Speaker】
Takehisa Kitazawa,  Midori Shima

12:00 ~ 19:00

12:00 ~ 19:00
Program - June 28 (Thu.)

Heine's Hall (2F)

Educational Program with Support of ISTH  9:00 - 12:00

**Chair:** Claire McLintock  National Women’s Health, Auckland City Hospital, New Zealand
Yukio Ozaki  Fuefuki Central Hospital, Japan

**Management of Women with Inherited Bleeding Disorders in Pregnancy**
Claire McLintock  National Women’s Health, Auckland City Hospital, New Zealand

**Medical Patients From EXCLAIM to MARINER: Who would benefit from extended thromboprophylaxis?**
Jeffrey Weitz  Department of Medicine and Biochemistry and Biomedical Sciences, McMaster University, Canada

**VTE: How We Treat in 2018?**
Walter Ageno  Department of Medicine and Surgery, University of Insubria, Italy

**Management of the Antiphospholipid syndrome**
Tatsuya Atsumi  Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, Japan

**Fundamental knowledge about platelet activation and platelet function tests**
Katsue Suzuki-Inoue  Department of Clinical and Laboratory Medicine, Faculty of Medicine, University of Yamanashi, Japan

Luncheon Symposium (Stago)
New insights in haemostasis laboratory medicine  12:30 - 13:30

**Moderator:** François Depasse  Diagnostica Stago, Asnières sur Seine, France

**Thrombin generation: from research to clinical practice**
François Depasse  Diagnostica Stago, Asnières sur Seine, France

**Elevated fibrin related markers in patients with disseminated intravascular coagulation**
Hideo Wada  Department of Molecular and Laboratory Medicine, Mie University Graduate School of Medicine, Japan

**Practical issues in coagulation testing of patients on direct oral anticoagulants**
Heng Joo Ng  Department of Haematology, Singapore General Hospital, Singapore

Educational Program with Support of WFH  14:00 - 17:00

**Chair:** H. Marijke van den Berg  PedNet Haemophilia Research Foundation, The Netherlands
Akira Yoshioka  Nara Medical University, Japan

**New era for hemophilia, future never looked that bright**
H. Marijke van den Berg  PedNet Haemophilia Research Foundation, The Netherlands

**Current status of hemophilia in Japan**
Midori Shima  Department of Pediatrics, Nara Medical University, Japan

**Incidence of Factor VIII inhibitor in Previously Untreated Hemophilia A patients.**
Ki-Young Yoo  Foundation Clinic, Korea Hemophilia Foundation, Korea

**Obesity and Overweight Impacts on Hemophilic Arthropathy**
Yeu-Chin Chen  Hemophilia Care & Research Center, Tri-Service General Hospital, National Defense Medical Center, Taiwan
Risk of deep Venous thrombosis after total knee arthroplasty in patients with haemophilia A
Kumiko Ono  
Department of Joint Surgery, Research Hospital, The Institute of Medical Science, The University of Tokyo, Japan

Afternoon Tea Seminar (Chugai Pharmaceutical Co., Ltd.)
Creation and Clinical Application of emicizumab 17:20 - 18:20

Chair: Renchi Yang  
Thrombosis and Hemostasis Center, Institute of Hematology and Blood Diseases Hospital, China
Katsuyuki Fukutake  
Laboratory Medicine, Tokyo Medical University, Japan

Creation of emicizumab
Takehisa Kitazawa  
Research Division, Chugai Pharmaceutical Co., Ltd., Japan

Novel Therapeutic Strategy for Patients with Hemophilia A (PwHA) with Inhibitors by emicizumab
Midori Shima  
Department of Pediatrics, Nara Medical University, Japan
Claire McLintock (New Zealand)

Education Background
- MBChB, FRACP, FRCPA

Current Position
- Clinical Director Regional Maternity Services (Obstetric Medicine and Maternal Fetal Medicine)

Management of Women with Inherited Bleeding Disorders in Pregnancy

Claire McLintock
National Women’s Health, Auckland City Hospital, Auckland, New Zealand

Pregnancy and childbirth pose a major haemostatic challenge for all women but in particular for women with inherited bleeding disorders. Some clotting factors such as factor VIII and von Willebrand’s factor increase during pregnancy leading to a normalization of these clotting factors at the time of birth, whereas other such as FIX and FXI do not change in pregnancy and women with low levels of these clotting factors may require treatment to correct the factor deficiency in preparation for birth. Bleeding disorders have different patterns of inheritance so precautions may be required at the time of birth to reduce the risk of bleeding in the infant.

Learning Objectives:
1. Develop an understanding of issues relating to pregnancy and childbirth in women with inherited bleeding disorders and how changes in coagulation factors during pregnancy impact on the risk of bleeding in women and their child.
2. Develop an approach to management of women with inherited bleeding disorders focusing on care during pregnancy, at birth and in the postpartum period taking into account the risks of bleeding and inheritance pattern of specific bleeding disorders.

Conflicts of Interest
None declared
Medical Patients From EXCLAIM to MARINER: Who would benefit from extended thromboprophylaxis?

Jeffrey I. Weitz
Department of Medicine and Biochemistry and Biomedical Sciences, McMaster University, Canada

Venous thromboembolism is responsible for an estimated 900,000 deaths each year in the United States and 543,000 deaths each year in the European Union. Therefore, the burden of disease from venous thromboembolism is substantial.

About 75% of the cases of fatal pulmonary embolism occur in medical patients. To prevent this, current guidelines recommend in-hospital thromboprophylaxis for medical patients at risk, but suggest against extending the duration of thromboprophylaxis beyond the period of hospitalization. However, the shortening length of hospital stay attenuates the benefit of in-hospital thromboprophylaxis. Consequently, studies have evaluated the benefit-risk profile of extended thromboprophylaxis in medically ill patients.

In unselected medical patients, the results of the EXCLAIM, ADOPT and MAGELLAN trials indicate that extended thromboprophylaxis with enoxaparin, apixaban or rivaroxaban reduces the risk of venous thromboembolism. However, this benefit is offset by a 2- to 3-fold increase in the risk of bleeding. Therefore, extended thromboprophylaxis is not beneficial for unselected medical patients.

The APEX and MARINER trials selected high risk medical patients for evaluation of extended thromboprophylaxis. An elevated D-dimer level is an important biomarker to identify high risk medical patients. In such patients, extended thromboprophylaxis with betrixaban resulted in a 1.7% absolute reduction in the risk of venous thromboembolism without a significant increase in the risk of bleeding. Therefore, the number needed to treat with betrixaban to prevent one episode of venous thromboembolism is 59. The results of the MARINER trial will determine whether rivaroxaban offers the same benefit.

In summary, pulmonary embolism is the number one preventable cause of death in hospitalized medical patients. Mandatory assessment for the risk of venous thromboembolism and the provision of in-hospital thromboprophylaxis saves lives. However, high risk medical patients require extended thromboprophylaxis and the APEX and MARINER trials will help us determine which patients benefit the most, and which anticoagulant strategies offer the optimal benefit-risk profiles.
Walter Ageno (Italy)

Education Background
· M.D. University of Pavia School of Medicine, Italy

Current Position
· Associate Professor of Internal Medicine, University of Insubria, Varese, Italy
· Director, Research Center on Thromboembolic Diseases and Antithrombotic Therapies, University of Insubria, Italy
· Director, Short Medical Stay Unit and Thrombosis Center, Ospedale di Circolo, Varese

VTE: How We Treat in 2018?

Walter Ageno
Department of Medicine and Surgery, University of Insubria, Varese, Italy

Venous thromboembolism, comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is a major cause of death and disability worldwide. Traditionally, standard treatment for the majority of patients with acute VTE consisted on parenteral anticoagulation with unfractionated heparin (UFH), low molecular weight heparin (LMWH) or fondaparinux overlapping and followed by vitamin K antagonists (VKA). In the presence of cancer associated thrombosis, LMWH is preferred over VKAs for at least the first 3 to 6 months. Patients with hemodynamically unstable PE also receive thrombolytic therapy before starting anticoagulation. Over the last years, the availability of direct oral anticoagulants (DOACs) has rapidly changed our therapeutic approach to patients with VTE. A substantial proportion of patients now receive a single drug approach with either apixaban or rivaroxaban, while other patients (usually those presenting with PE) are started with LMWH and then switched after 5 to 7 days to dabigatran or edoxaban. This change in treatment patterns is resulting in fewer hospital admission and, for hospitalized patients, in shorter lengths of stay. Recent evidence suggests that DOACs are a valid alternative to LMWH also for patients with cancer associated thrombosis, although some caution is still required in particular for patients with gastrointestinal cancer due to an increased risk of gastrointestinal bleeding. Clinical studies with the DOACs also support extended duration of secondary prophylaxis for patients with unprovoked VTE with a 50% dose reduction after the first 6 months of treatment (apixaban and rivaroxaban). Finally, ongoing research is trying to identify safer reperfusion strategies for patients with hemodynamically stable PE defined at intermediate-high risk of mortality.

Conflicts of Interest

COI Declared
Antiphospholipid syndrome (APS) is characterized by thrombosis and pregnancy morbidity in the presence of antiphospholipid antibodies (aPLs). It is now well-accepted that, despite their name, the majority of aPLs associated with APS are directed against phospholipid-binding proteins, of which beta2-glycoprotein I (b2GPI) and prothrombin are regarded as the most relevant antigenic targets.

Since the first description of APS in 1983, the range of features associated with aPLs has considerably increased. APS may present with heterogeneous clinical symptoms and laboratory manifestations. We analysed the clinical and immunological manifestations of APS in a cohort of Japanese patients recruited in a single centre. All the patients were followed up; the prevalence of APS manifestations and the profile of aPL during the study period were evaluated. High prevalence of arterial thrombosis was noted in Japanese patients with APS.

One of the most difficult factors on APS in daily clinical practice is how to interpret the aPL results. Recently, scoring systems to quantify the probability of antiphospholipid syndrome (APS) have been proposed: the Antiphospholipid Score. The score is derived from the combinations of independent risks for thrombosis particularly focused on antiphospholipid antibodies profiles. These scores, as well as tools for diagnosis, function as index for predicting future thrombosis in autoimmune diseases. On the other hand, exhaustive detection of aPL for diagnosis of APS burdens the laboratory department in clinical practice. In general, sensitive tests are recommended for screening, followed by specific tests for definite diagnosis. However, two non-criterial aPLs have been focused: phosphatidylserine dependent antiprothrombin antibody (aPS/PT) and anti b2GPI domain I IgG antibodies (aDI). To reduce the cost and effort for APS diagnosis, we hypothesized that those two highly specific tests can paradoxically serve as screening procedure.
Katsue Suzuki-Inoue (Japan)

**Education Background**
- M.D., Ph.D., Yamanashi Medical University, School of Medicine, Japan

**Current Position**
- Professor, Department of Clinical and Laboratory Medicine, Faculty of Medicine, University of Yamanashi, Japan
- Chairperson, Department of Clinical and Laboratory, Division of Transfusion Medicine and Cell Therapy, University of Yamanashi Hospital

**Fundamental knowledge about platelet activation and platelet function tests**

Katsue Suzuki-Inoue

Department of Clinical and Laboratory Medicine, Faculty of Medicine, University of Yamanashi, Japan

Platelets play a crucial role in physiological hemostasis and pathological thrombosis. The process of thrombus formation with platelet aggregation are integrated process that involves several platelet receptors and agonists. However, understanding of this process is hampered by its complexity. The first step of arterial thrombus formation is platelet interaction with exposed collagen at the sites of vascular injury. Platelet adhesion and aggregation on collagen fibers and the subsequent stable clot formation are an integrated process that involves several platelet receptors and agonists such as ADP, thromboxane A2 (TxA2), and coagulation factors such as thrombin. One of the major and powerful receptors involved here is a collagen receptor, glycoprotein VI/FcRγ chain complex (GPVI). The signal transduction pathway related to GPVI involves a number of tyrosine kinases, adapter proteins, and lipases including Src, spleen tyrosine kinase (Syk), SH2 domain-containing leukocyte protein of 76 kDa (SLP-76), and phospholipase Cγ2 (PLCγ2). C-type lectin-like receptor 2 (CLEC-2), which belongs to a non-classical C-type lectin also generates activation signals depending on protein tyrosine phosphorylation in a manner similar to GPVI, although a role of CLEC-2 in physiological hemostasis has not been fully elucidated to date. Platelet activation induced by GPVI-collagen interaction stimulates release of secondary mediators, ADP and TxA2, which then interact with their respective G protein-coupled receptors and further activate platelets forming a positive feedback loop. Aspirin and cropidogrel are widely used for the secondary prevention for myocardial infarction, which suggest the critical role of the secondary mediators in thrombus formation. In this Educational Program, I will expound at length on the subject of the mechanisms of thrombus formation with platelet aggregation for beginners.

**Conflicts of Interest**
None Declared