



# THE CONGRESS DAILY

THE OFFICIAL NEWSPAPER OF THE WFH 2016 WORLD CONGRESS

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/ WFH President Alain Weill

## WFH PRESIDENT: EDUCATION IS THE OTHER SIDE OF THE TREATMENT FOR ALL

In 1942, *The Little Prince* author Antoine de Saint Exupery wrote to a friend: “Far from hurting you, being different enriches you.”

Nearly 75 years later, it's still important for everyone in the bleeding disorders community to reflect on that truism, said Alain Weill, WFH president, during the Monday morning plenary “Treatment for All: Another Side of the Equation.”

While much has been accomplished in bleeding disorders awareness and treatment, Weill said much remains to be done.

Recent accomplishments include the expansion of the WFH Humanitarian Aid Program. Between 1996, when the WFH started the program, and 2011, the yearly average volume of international units (IUs) of clotting factor donated to developing countries was 10.5 million. Between 2012 and 2014, factor donations increased to 25.5 million IUs per year, and they skyrocketed to 116 IUs during the last 12 months.

Along with providing more treatment options, Weill said that another objective is to use the WFH Humanitarian Aid Program as leverage to demonstrate to government officials how proper treatment enables people with hemophilia to live a normal life and actively participate in the social and economic activities of their country.

This is crucial because too many people in the global hemophilia community still face frustration, discrimination and intolerance. “This inequity drives my passion for continued advocacy,” Weill said. “We must eliminate the stigma associated with having a bleeding disorder and we should not accept anything else.”

Even in developed countries, it can feel like society is at odds with people with bleeding disorders and their families, Weill said. Factor costs can be prohibitive.

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## NEW EXCITING ASPECT OF THE COAGULATION SYSTEM

All the players in the coagulation system are known—or are they? Thrombin is a key enzyme in the system that controls clot formation; too much or too little can lead to either hemorrhage or thrombosis. At the medical plenary “Rethinking Events in the Hemostatic Process: Role of factor V and TFPI,” Rodney Camire, Philadelphia, Pennsylvania, USA, explained that extrinsic Xase, intrinsic Xase and prothrombinase are regulators of thrombin. “By dampening inhibitors you can control thrombin,” he said.

Camire shared his expertise with hundreds of attendees Monday morning. “FV is very similar to FVIII in some ways and needs to be processed at specific sites,” he said, pointing out however, that FV is a procofactor requiring proteolytic activation in the B domain. The role of the B domain is to keep the molecule active. By looking at sequences for the alignment of FV B domain, Camire and his research team experimented with how both the basic region (BR) and the acidic regions (AR) contribute to keeping the molecule active.



/Rodney Camire

Camire stated that the FV BR fragment and FXa compete for FV-810 binding. There is a discrete segment of the B domain that serves an essential autoinhibitory function to maintain FV as a procofactor. “Disseminating this region is the driving force to unveil a high affinity binding site for FVa,” he explained.

He pointed out that an important step in thrombin generation is the activation of FV to FVa. Mr. Camire said that certain Australian snakes have a unique form of FV in their venom with these inhibitory sequences removed, thereby creating an active procoagulant cofactor.

Tissue factor pathway inhibitor (TFPI) naturally forms in the blood. TFPI binds FV in plasma, but shows no affinity to FVa. “There are two to three different forms of FVa that are generated during the initiation of coagulation that are sensitive to TFPI alpha (TFPIα),” said Camire.

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Speakers share cutting-edge information on clotting issues.

### TODAY

09:30 – 10:00

Medical Plenary – Hemophilia Treatment in 2030 (Hall A4)

14:15 – 15:45

Health Technology Assessment (Room 206)

**Remember to stop by the WFH Resource Center.**

# WFH HUMANITARIAN AID PROGRAM: LASTING CHANGE FOR THOSE MOST IN NEED

The success of the WFH Humanitarian Aid Program firmly rests on ensuring a sustainable and predictable supply of treatment products. Evidence of this success was illustrated during the session “Humanitarian Aid: Treatment for all is The Vision of All” on Tuesday morning.

Dr. Assad Haffar, WFH Humanitarian Aid Director, chaired and opened the session highlighting the reality for many around the world living with a bleeding disorder. In numerous developing countries, the lack of access to treatment is an urgent need and an important public health challenge. Since 1996, 322 million IUs have been donated to 90 countries, directly helping over 100,000 people who are in urgent need. The expansion of the WFH Humanitarian Aid Program will now include over 500 million donated IUs in a five year period, providing a predictable supply and permitting planning and forecasting for the first time for the WFH.

Megan Adediran, Executive Director of the Haemophilia Foundation of Nigeria (HFN), began her talk explaining how her organization was created. It was the first treatment donation from the WFH that spurred her to create HFN. As diagnosis rates within Nigeria have increased, so has the need for access to treatment products. The expansion of the WFH Humanitarian Program has also impacted the bleeding disorders community significantly beyond providing lifesaving treatment. Before the expansion began in 2015, only 178 patients were diagnosed. One year later that number



/Assad Haffar opens the Humanitarian Aid session.

increased to 271 patients as word has spread that predictable treatment is now available. “The WFH Humanitarian Aid Program has given hope to families,” said Adediran. “That’s what this program has been able to do for the people of Nigeria.”

Each speaker during this session outlined how improving and sustaining care for those most in need is imperative. Thomas Sannié, President, the Association française des hémophiles (AFH), spoke about how the AFH is working together with the WFH to improve the situation in French speaking countries in sub-Saharan Africa through the French

African Alliance for the Treatment of Hemophilia (AFATH). “What motivates us to act is a vision shared with all our partners to bring treatment to all sufferers of bleeding disorders,” said Sannié.

Dr. Kibet Shikuku, Chairman of the Kenya Haemophilia Association, further illustrated the need for the WFH Humanitarian Aid Program. He emphasized that education and

The expansion of the WFH Humanitarian Aid Program will now include over 500 million donated IUs in a five year period, providing a predictable supply and permitting planning and forecasting for the first time for the WFH.

research needs to go along with these donations.

As Ahmed Naseer was unable to speak at this session, his hematologist Dr. Shasahi Apte described Naseer’s journey to receive knee replacement surgery. It was only through donations from the WFH that his surgery was made possible, further demonstrating the impact of support for those most in need.

The session concluded with a final thought from Haffar, “Together, we can make the impossible possible.” To learn more about the WFH Humanitarian Aid Program, visit [www.treatmentforall.org](http://www.treatmentforall.org).

## FIVE AMAZING FACTS ABOUT EPCOT

For those who enjoy a healthy dose of excitement, today’s social program at Epcot is sure to please. We won’t give away too many details—but expect a fantastic show that will surely enthrall your senses.

- 1. 7,257,500 kg** (16 million pounds): the weight of the iconic Spaceship Earth at Epcot
- 2. 1.5 million cubic metres** (54 million cubic feet): the amount of dirt that was excavated to build Epcot Park
- 3. 158,800 kg** (350,000 pounds): the weight of the Illuminations: Reflections of Earth Globe
- 4. 1,500 litres** (400 gallons): the amount of propane used by the Illuminations: Reflections of Earth Inferno Barge every night
- 5. 30,500 kg** (67,200 pounds): the weight of the fruits and vegetables grown in the pavilion every year

If you’re planning on attending the event this evening, be sure to wear casual, comfortable shoes, and be at the **Orange County Convention Center (Level 1 Bus loading West Concourse) at 18:00.**

Source: [www.themeparktourist.com](http://www.themeparktourist.com)



/Jeanne White-Ginder shares her experiences being a spokesperson for AIDS. Her son Ryan White—who died in 1990 at age 18—successfully fought discrimination in his community and at his school when he was diagnosed with AIDS following a transfusion of tainted clotting factor.

**The Congress Daily** is the official newspaper of the WFH 2016 World Congress.  
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# THE FACE OF INHIBITORS: PATIENTS, FAMILIES AND CAREGIVERS SHARE THEIR STORIES

Inhibitors affect between 20 to 40 percent of people with severe hemophilia A. In a Monday morning panel discussion, patients, families and caregivers impacted by this rare condition put a face on their trials and triumphs.

Kari Atkinson, with her 13-year-old son Beau by her side, gave a moving presentation on what life has been like for her, Beau, her husband Craig and daughter Jordan since Beau was diagnosed with hemophilia and an inhibitor.

When Beau was only 6 months old, he was diagnosed with severe hemophilia A. Kari and Craig were shocked because there was no known history of hemophilia in their family. But they had no idea it was about to get worse.

When Beau had a routine blood test at age 18 months, the doctors discovered an inhibitor. “That inhibitor detection literally rocked our world,” Kari said. “It is so different from normal hemophilia. We prayed every night that we could just have normal hemophilia.”

Beau’s inhibitor affects the whole family, Kari said. “For anyone in this room, you know the number of tears and sleepless nights.” The inhibitor started low, and the first treatment lasted four years. But the next treatment only lasted a year, and since 2012, Beau, his family and caregivers have been struggling with managing his inhibitor. They’ve tried different factor treatments and inserted two ports.

“The cost of care went from \$250,000 annually with hemophilia to \$1 million to \$1.5 million per year with the inhibitor, depending on the number of bleeds,” Kari said.

Managing Beau’s hemophilia and inhibitor is a true family commitment, Kari said. “We have to be on high alert at all times. [When a bleed occurs], minutes is our reality between walking, crutches and wheelchair. It doesn’t matter if we’re in the car, at the amusement park—we infuse.”

At school, Beau stands at the back of the line so he won’t be jostled. He can’t participate in recess. But his friends are very supportive. And, “Other inhibitor patients are like a family beyond a family beyond a family,” Kari said.

“It takes a village to raise a child with hemophilia and an even larger village to raise a child with an inhibitor.”

But there are plenty of positives, Kari said, as Beau smiled beside her. Beau is currently treated every other day for immune tolerance with long-lasting factor. His Inhibitor levels did spike but now are steady.

Zoe McGough, a 16-year-old girl from Mirfield, UK, spoke about her factor VII deficiency with an inhibitor. After a childhood of being easily bruised but still having normal blood tests, she was diagnosed at age 7 with hemophilia. “The doctors said I would only need treatment if I had a serious accident,” she said. “But the reality was quite different.”

She had multiple bleeds and began factor treatment, but developed allergies and more bruising. A couple of months later, she was diagnosed with an inhibitor. She was given immune tolerance and factor twice a day, but all that did was give her a needle intolerance, so a port was added.



/Beau Atkinson watches as his mother Kari discusses how the family copes with his severe hemophilia A, compounded by an inhibitor.

To make matters worse, in the mornings, Zoe would wake up with terrible bruising. She was eventually diagnosed with a type of facitis that causes the tissue under the skin to become inflamed.

“At one point I asked my mum, ‘How can people get new arms and legs but they can’t figure out what is wrong with me?’” she said. “I just wanted to enjoy myself and play with my friends, and I couldn’t.”

At age 10, a dose of steroids knocked Zoe’s inhibitor to the lowest it had ever been. And it helped prevent bleeds. Six years later, her inhibitor is still in check, allowing Zoe to live a relatively normal life—considering that she’s a girl with hemophilia.

“Even though I have these issues, I haven’t let them hold me back,” she said. “I do most of

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## THE WFH ELEARNING PLATFORM LAUNCHES: ONE STOP FOR EASY ACCESS TO ALL BLEEDING DISORDER RESOURCES

The WFH is proud to announce the launch of a major advance in its educational resources for the bleeding disorders community: the WFH eLearning Platform. Designed to support education worldwide, the portal puts content and tools at the fingertips of anyone with a computer or mobile device and an internet connection.

The WFH eLearning Platform facilitates filtered search queries of the hundreds of resources in its collection. Searches can be narrowed down by category (article, book, fact sheet, etc.), resource type (webinar, ePoster, video, etc.), author, or language. And of course, Google-like keyword searching is just a few keystrokes away. Users can also make use of a powerful interactive resource navigation tool that lets them explore content through the six pillars of the WFH Comprehensive Development Model: government support, care delivery, medical expertise (including multidisciplinary), treatment products, patient organizations, and data collection and outcomes research. What’s more, the platform lets users know about recently added material, and even gives them a glimpse into what information is most frequently consulted by other users.

“The WFH is committed to supporting the bleeding disorders community internationally,”



/Congress attendee explores the WFH eLearning Platform.

explained Alain Weill, WFH President. “And one of the best ways to provide that support is by providing easy access to educational resources, whether that’s illustrated explanations for a recently diagnosed child, technical demonstrations that help a laboratory

scientist efficiently perform a diagnostic assay, or an interactive module that brings the complex content of the Treatment Guidelines to life for patient advocates and healthcare professionals. The new WFH eLearning Platform does all of this by making our

bleeding disorders educational resources easily available to anyone and everyone.”

Available tools cover nearly everything someone involved in the field of bleeding disorders could need, including interactive modules presenting the WFH Guidelines for the Management of Hemophilia, a laboratory manual, an online registry of clotting factor concentrates, a pictorial introduction to hemophilia and a compendium of assessment tools.

Once a user has found educational content to explore, the eLearning Platform offers them powerful functionality to help them access exactly what they’re looking for, quickly and easily. For example, lab manual demonstration videos are complemented by complete searchable transcripts and even the ability to instantly jump to specific sections of the video corresponding to keywords of interest.

The WFH eLearning Platform officially launches at the Congress—so drop by the WFH Resource Center to take it for a spin! There are already hundreds of educational documents available and new content will be added regularly. You can also visit eLearning, [wfh.org](http://wfh.org) to take a look for yourself right now, and learn more about the bleeding disorder topics of interest to you.



## DATA COLLECTION AT THE WFH RESOURCE CENTRE

The Resource Centre at Congress is your chance to learn about the data collection initiatives at the WFH. Stop by to speak with someone from the Research & Public Policy team and test out the many different programs that are available on our computer pods.

For the very first time, the World Bleeding Disorder Registry (WBDR) will be on display. This newly-designed web-based registry is the key focus of the WFH Epidemiological Research Program. The database will collect high quality, observational data on a large population of patients with hemophilia. The WBDR is currently in a pilot phase of implementation with 31 hemophilia treatment centres across the world participating. The WFH Resource Center is your chance to have a very first look at the WBDR.

The Annual Global Survey will also be showcased at the WFH Resource Center. This is your opportunity to ask questions, receive useful tips on the online platform and learn about updates in the 2015 survey. The 2014 Report on the Annual Global Survey is available if you want to take a hard copy home. If you are an Annual Global Survey data respondent who has a question about your 2015 submission, please drop by for a chat. The interactive public graphs—using Annual Global Survey data—are also on display if you are interested in boosting your evidence-based advocacy efforts. The interactive public graphs offer customizable queries on 15 years of Annual Global Survey data.

We look forward to showing you how you can benefit from the WFH data!

*WFH Resource Center, Exhibit Hall*

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## FUTURE TREATMENTS FOR HEMOPHILIA

Scientific research and technology have vastly increased our knowledge of bleeding disorders in the last few decades. But still, not everyone is treated successfully. The development of long acting concentrates, by-pass therapy, gene therapy, modifications of activation and control of the clotting system has brought increasing knowledge of clotting factor immunogenicity so that we have the potential to meet the needs of every patient by 2030.

Erik Berntorp, Malmö Centre for Thrombosis and Haemostasis, is the principal investigator for several

multinational studies and a reviewer of numerous scientific journals such as *Blood*, *Journal of Thrombosis and Hemostasis* and *Hemophilia*. He has published over 300 papers in peer-reviewed journals and has been the editor for a number of major textbooks including *Textbook of Hemophilia and von Willebrand Disease – Basic and Clinical Aspects*.

Berntorp will share his knowledge at the Medical Plenary Session on Tuesday from 09:30-10:00, Hall A4, during “Hemophilia Treatment in 2030.”

*0930–1000, Hall A4*

## APPROACHES TO HTA IN EUROPE, THE USA, AND ELSEWHERE

### IMPLICATIONS FOR PATIENT ACCESS TO CURRENT AND FUTURE HEMOPHILIA TREATMENTS

Traditionally, the choice of drugs in developed countries has been driven by the views of patients and clinicians on the relative value of the available drugs. But increasingly, higher prices for novel and breakthrough drugs are focusing greater attention on determining the value for money spent, and health care systems, insurers and governments have all started to consider the affordability of drugs in their decision making.

In this afternoon’s “Medical: Health Technology Assessment” session, participants will see how health technology assessments

(HTA) are the mechanism governments use to inform their decisions of whether to invest in or pay for a new drug or technology. While the pace of drug development for those living with bleeding disorders is accelerating, the use of HTAs is expanding globally a well. That means there is an increasingly urgent need to understand how HTAs work and how we as a community should be adjusting to these developments.

The interactive panel discussion will present both US and global perspectives on how HTAs operate and provide insights to inform us on what we should be preparing today to address future access and reimbursement challenges. It will also offer insight on current trends in health care and drug development that people involved in the community should be watching.

*14:15–15:45, Room 206*



/Attendees fill the Exhibit Hall Monday afternoon.



# TOLERANCE INDUCTION RESEARCH SHOWS SUCCESS

Exciting news infused the room Monday afternoon as attendees of “Medical: Innovating Immune Tolerance Induction for Hemophilia” learned what is on the horizon for tolerance induction. Shannon Meeks, Atlanta, Georgia, USA; Roland Herzog, Gainesville, Florida, USA and Sebastien Lacroix-Desmazes, Paris, France, comprised a panel presenting their research in this field.

Meeks provided a quick overview of the immune response to FVIII. “Most FVIII is released into the circulation as a set of heterodimeric proteins and is made up of a heavy and a light chain,” said Meeks. “VWF inhibits FVIII binding to phospholipids.”

She reminded the audience that most inhibitors—IgG antibodies directed against the missing FVIII—are developed in the first 10 to 20 exposure days. In those with severe hemophilia A, 20 percent to 30 percent develop inhibitors. In research with mice, she noted the following conclusions:

- There is no statistical difference in titers between inactive construct and FVIII
- Thrombin generated by FVIII is not necessary for immune response
- FVIII thrombin generation does not account for immunogenicity of FVIII
- Patients with point mutations have more limited spectrum of potential immunogenicity peptides

“More research is needed on if it is possible to engineer less immunogenic FVIII and also on the impact of whether the VWF presence or absence makes a difference,” Shannon Meeks concluded.

Based on the premise that we tend to be tolerant to things we eat and that we activate regulatory T cells in this manner, Herzog introduced the concept of oral tolerance induction using transgenic plants. Traditionally oral agents were hampered by cost and may no longer be useful by the time they get to the small intestine. “Plants have cell walls that protect the proteins inside,” said Herzog.

The first plant-based oral tolerance experiment for hemophilia involved tobacco plants and mice. The results showed suppressed inhibitor formation against FIX in hemophilia B mice. “This also protected them from anaphylaxis,” said Herzog. “While our control mice were dying, the ones eating the infused plants were protected.” This works as the plant cell protects the protein until it gets to the small intestine and then the antigen is released. The epithelial cells in the small intestine then deliver it to the immune system.

Since Herzog and his team felt it might not be ethical to feed tobacco plants to children, they concentrated their next efforts on lettuce. “Lettuce appears to remain stable,” he stated.

The research was then scaled up to include dogs. “Of course we had to trick the dogs into eating lettuce and we wondered if dogs would have the enzymes in their guts they needed. Not only was the oral administration of chloroplast transgenic leaf cells expressing CTB fusion proteins efficient in prevention, and to some extent reversal of antibody responses to FVIII and FIX in hemophilic mice, the first successful oral tolerance studies in hemophilic dogs were carried out



/Roland Herzog presents his research.

indicating that the approach is applicable to the nonrodent immune system.”

Lacroix-Desmazes addressed tolerance induction through transplacental delivery. “We know that maternal IgG is transferred in the third trimester, so that the infant has some protection when born,” he said. “We wanted to see if we can transfer FVIII to induce tolerance in utero when we know the baby is to be born with hemophilia A.”

In certain experimental mice models transplacental transfer has been successful with specific T cell receptors. “There are issues, however,” he said. “Would mothers-to-be of hemophilic babies accept this treatment? Would the VWF protein be too large to cross the placenta? And would humans behave as mice in coagulation and immunogenicity?”

In order to answer these questions, more research in this area will need to be done.



/Shannon Meeks provides coagulation overview.

## Medical

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Camire also said that there are new physiologic forms of FV. Citing research from east Texas (USA), individuals have been found that have a mutation in exon 13 of FV, which causes a spliced transcript. Thus, there are forms of FV that are B domainless, that lack the BR, but harbor in the acidic region. Known as FV short, this binds to TFPIa.

These patients were shown to have 10 times the level of TFPIa. TFPIa via the BR can block FVa function. This is currently a therapeutic target for hemophilia treatment.

In summary he said blocking TFPI function will enhance coagulation. “Antibodies targeting TFPI are in clinical trials. Specific B domain sequences are key autoinhibitory elements responsible for keeping FV as a procofactor. Dismantling these sequences drives FV activation. These mutations change a weak splice site into a strong splice site.”



WORLD FEDERATION OF HEMOPHILIA  
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE  
FEDERACIÓN MUNDIAL DE HEMOFILIA



# CUTTING-EDGE RESEARCH EXAMINES INHIBITORS, MEASUREMENT DISCREPANCIES AND MORE

## RESEARCHERS PRESENTED SIX NEW STUDIES ON HEMOPHILIA DURING A MONDAY AFTERNOON SESSION. PRESENTATIONS INCLUDED:

### Generation of IPS Cell Lines from Haemophilia A patients

Author Heike Singer said this study focused on nonsense mutations versus inhibitor risk. Noting that there's a higher inhibitor risk in the light chains of proteins versus heavy chains, the research team posed the following questions: Why do different nonsense mutations have a higher risk of inhibitors? Does this have to do with cross-reactive material status? RNA? Protein?

The research team generated induced pluripotent stem cells (iPSCs) from a hemophilia A patient. They then reprogramed

the cells and differentiated them into endothelial cells. "This cellular system will help us to further study the mutation-specific effect on FVIII formation," Singer said.

### Macrovascular and Microvascular Endothelial Function in Adult Males with Hemophilia

Author Shannon Jackson said several studies have shown that hemophilia is associated with a lower cardiovascular mortality compared to the general population. This may have to do with atherosclerotic plaque formation.

In a study of 1,600 healthy firemen, microvascular endothelial function (EF)—but not macrovascular EF—was identified as an independent predictor of cardiovascular risk.

In the first similar study on hemophilia patients, Jackson and her team gathered 81 males with all severities of hemophilia A and B, along with controls from the firemen study. The researchers measured macrovascular and microvascular EF functions in all subjects. They found similar macrovascular EF between hemophilia patients and controls, but significantly lower microvascular EF.

### Non-Neutralizing Antibodies Against Factor VIII and the Risk of Inhibitor Development in Untreated and Minimally Treated Patients with Severe Hemophilia A (SIPPET Study)

Manuel Carcao said the choice of factor may affect inhibitor development in young children with hemophilia A. The Study on Inhibitors in Plasma-Product Exposed Toddlers (SIPPET) was designed to measure whether there is more inhibitor development with recombinant FVIII versus plasma-derived FVIII.

The study involved 42 centres in 14 countries, and included 251 males age 6 or younger with severe hemophilia A, randomized to recombinant or plasma-derived FVIII groups.

Results showed that 73.3 percent of the plasma VIII group did not develop an inhibitor, compared to 55.5 percent for the recombinant group. The recombinant group also had a 1.87 percent higher incidence of developing an inhibitor compared to the plasma-derived group. The high-titer rate was 1.69.

For both products, Carcao said 90 percent of inhibitor development occurred in the first 58 exposure days. No individual country results changed the hazard ratio. Overall, Carcao said toddlers given recombinant FVIII had an 87 percent higher risk of developing all inhibitors, and a 69 percent higher risk of developing high-titer inhibitors.

Manufacturers should investigate what it is about plasma product that makes it less immunogenic, and incorporate those discoveries into recombinant product, Carcao said.

### Inhibitor Neutralizing Capacity of FVIII Therapeutic Concentrates Depends on VWF-Natural FVIII/VWF Complex Versus Isolated FVIII. Study of Eleven Products

Author Juan Ignacio Jorquera said many plasma FVIII concentrates contain natural FVIII/VWF complexes. These concentrates may have some benefits for immunogenic response.

His team's in vitro study was designed to analyze the VWF role on FVIII. The researchers used both a hemophilia-mimic case and a pre-mixture case. Both cases behaved similarly to plasma in the in vitro assay. But concentrates of FVIII with low VWF or without VWF showed higher inhibitor titers, even when pre-mixed with VWF for the assay.

"Is it possible that what people with hemophilia lack is not only FVIII, but FVIII with VWF?" Jorquera asked.

### Discrepancies Between the One-Stage Clotting Assay and the Chromogenic Assay in Haemophilia B

Author Jan Astermark discussed this study dealing with discrepancies in the measurement of FIX:C in hemophilia B patients.

Plasma samples from 32 patients with mild and moderate hemophilia B were analyzed by both one-stage assay and chromogenic assay. The assays measured the patients' mean FIX levels. Fourteen samples from seven patients showed a twofold or greater difference between the results of the two methods, with the chromogenic method presenting the higher value.

Mutation at the N-terminal site of the activation peptide at Arg191 was associated with a higher FIX:C activity measured by chromogenic rather than one-stage assay. The bleeding phenotype may correlate better to the activity defined by the chromogenic assay, Astermark said.

### Platelet Function Measured Using the Multiplate (R) Analyzer in Pediatric Patients with Severe Hemophilia A (SHA)

Author Margaret Rand said this study of pediatric patients with severe hemophilia A in two Canadian centres found dose-response curves in ADP, collagen, arachidonic acid and thrombin receptor active peptide (TRAP), as measured by the Multiplate® analyzer.

The patients were then compared to healthy male adult controls. There was no significant difference in measurements between the two groups at site 1. At site 2, the aggregation responses were increased in patients versus the controls. But when both sites were combined, there was no significant difference in responses between controls and patients. Rand said the same results occurred in overall platelet aggregation responses between sites.

## DID YOU KNOW THAT...

The famous beat writer Jack Kerouac wrote "On the Road" in Orlando in 1957?

## THE WFH HELPS YOU SAVE

The WFH has set up two programs to help you get more value for your money at this year's congress.

### • Discount attraction tickets.

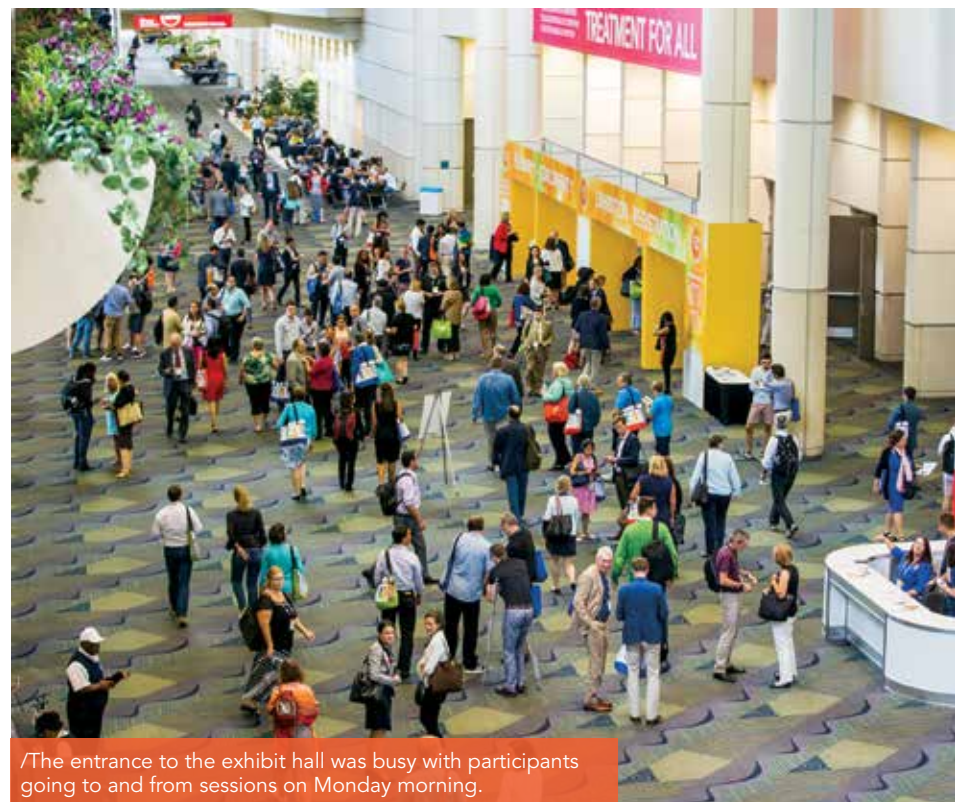
Visit Orlando offers specially discounted attraction tickets specifically for convention delegates. See everything Orlando has to offer at attractively discounted rates.



### • Show your badge and save.

Show your convention badge to a participating "Show Your Badge" restaurant during the dates of your event to take advantage of a great dining offer. Eat well and save!

To find out more about the many offers available to attendees, please visit our Discounts & Tickets page: <http://wfh2016.orlandomeetinginfo.com/discounts-and-tickets/>

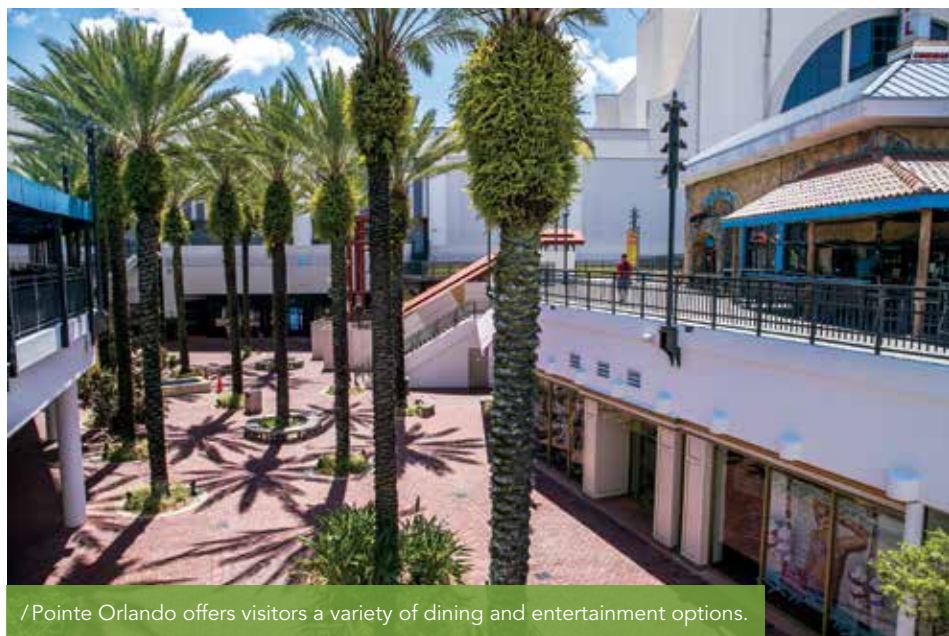


/The entrance to the exhibit hall was busy with participants going to and from sessions on Monday morning.



## UNWIND IN POINTE ORLANDO

If you're looking to unwind after a big day at the Congress, Pointe Orlando may be the place for you. Located just 5 minutes from the Orange County Convention Center by taxi, Pointe Orlando is a pedestrian-friendly mall that offers visitors myriad dining, shopping and entertainment options. Foodies can enjoy anything from pub grub to BBQ, to sushi, while shoppers can stroll into well-known stores like Tommy Hilfiger, Hollister Co and A|X Armani Exchange. And for those looking for entertainment, there's improv comedy, blues, a nightclub and even IMAX. Visit [www.pointeorlando.com](http://www.pointeorlando.com) to find out more.



/Pointe Orlando offers visitors a variety of dining and entertainment options.

## Inhibitors

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the things teenagers do. I go dancing three times a week. I've traveled around the world many times—all we do is bring an extra suitcase for my medication and I am fine."

"I've learned that as long as I have my factor, I can do what I like. I have even swum with dolphins," she said proudly.

Augustus Nedzinkas, a 29-year-old Lithuanian, was diagnosed with hemophilia A with an inhibitor when he was 14 months old. Hemophilia treatment was rudimentary in Lithuania at the time, and "Sometimes the bleeding wouldn't stop until the joint had expanded to the max," he said.

Nevertheless, he was still able to attend public school, graduate from university, get a full-time job and even scuba dive.

Augustus had low inhibitor levels for several years, so in 2012, his doctors decided to try a high-dose immune tolerance treatment of 100 IU/kg twice daily. This type of treatment had never been used before in Lithuania, but it was a success. Augustus' inhibitor dropped below zero in the first month.

"Then they prescribed daily prophylaxis and that made my life very happy," he said. "The first thing I did was go spear fishing and get my trophy fish. I changed my car's gear box from an automatic to a manual. And I got married." He has a knee replacement scheduled for next year. "Now I can plan things and expect my health won't be an issue—all I have to do is infuse myself every morning," he said.

Kuixing Li, a nurse at Peking Union Medical College Hospital in China, talked about inhibitors from a caregivers' standpoint.

One of her patients was a 9-year-old boy with an inhibitor. "He was in a wheelchair, and he often lost his temper and was always angry," Kuixing said. "Sometimes he wanted to give up his treatment." His family couldn't afford factor and had to use prothrombin complex concentrates (PCC) instead.

The boy eventually left the hospital after suffering a brain bleed. One day, Kuixing called his grandmother to see how he was doing. "This is not a good story," she said, her voice breaking. "I found out he died—they could not stop his bleeding."

This is not an unusual occurrence in China, which is home to an estimated 100,000 to 150,000 hemophilia patients. "Sometimes I think if the WFH wants to establish their goal of Treatment for All, they should move their office to China," Kuixing said with a laugh.

In 2015, there were only 31 hemophilia treatment centres throughout China—but that's a notable increase from the six centres in 2007. There are also only about 20,000 patients in the national registry.

After a national program in 2008 to 2011 to screen people with inhibitors, Kuixing said the Chinese developed an inhibitor management plan that includes PCC infusion after bleeding and low-dose prophylaxis. It works for about 50 percent of patients, she said. Meanwhile, Chinese chat rooms are full of inhibitor patients who can't afford factor treatment, so they opt for dangerously high doses of PCC.

"It's a big challenge for caregivers to give good care for hemophilia patients in China," Kuixing said.

## WFH RESOURCE CENTRE: 20,000 FREE PRINTED RESOURCES

The World Federation of Hemophilia (WFH) Resource Centre in the exhibit hall is a great place to drop by and get information related to bleeding disorders. If you're looking for our interactive Global Map, the WFH eLearning Platform, information on the many

fundraising activities the WFH offers, the World Bleeding Disorder Registry, the Registry of Clotting Factor Concentrates (CFC registry), the WFH Annual Global Survey or the World Bleeding Disorders Registry (WBDR)—the WFH Resource Centre is the place to go.

The Resource Centre also has a wealth of free content that you're welcome to bring home with you. We've brought over 20,000 printed resources weighing over 2,000 kg (4,400 pounds) to Orlando this year, and we encourage you to take whatever you need home for yourself, or for someone you feel would benefit from our publications. You'll find articles, patient information booklets, guides, illustrated handouts, books, binders, and reports. Most publications are available in multiple languages—and everything is free. Note: if you're interested in bulk copies of a publication, please speak with a WFH Resource Centre attendant.

## DONORS OF CONGRESS: LAURA-JEAN SIGGENS

Ms. Laura-Jean Siggins of Ann Arbor, Michigan, USA was our very first Donor of Congress for the WFH 2016 World Congress. The WFH Philanthropy Resource Team was happy to welcome this grandmother of seven to the Resource Center shortly after the exhibition hall opened. This is Laura-Jean's first Congress and she supports the WFH Humanitarian Aid Program as she is "Sad to know people are suffering and happy that companies and the WFH are taking a step forward to help." The Philanthropy and Resource Department team wholeheartedly agrees. Thank you Laura-Jean! Join Ms. Siggins and our growing list of supporters at [www.wfh.org/donateusa](http://www.wfh.org/donateusa) today!

/Ms. Laura-Jean Siggins and Paula Curtis, WFH Director Philanthropy and Resource Department



## President

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Employment opportunities can be limited. In some countries, a person with a disability can't get a bank loan. And in numerous countries, it's not unusual for hemophilia patients to be denied services from fearful care providers.

Children with bleeding disorders continue to face discrimination, Weill said. In a significant amount of countries, when a child is diagnosed with a bleeding disorder, many families experience devastating hardships. In some cases, when a child with hemophilia reaches school age, some misguided teachers believe bleeding disorders are communicable and ban the child from their classroom. "Already having to deal with their clotting deficiency, many children find themselves confronted with anxiety, depression and isolation," said Weill.

But there are steps members of the bleeding disorders community can take to fight this discrimination and intolerance. One way is to educate government and other leaders of existing legislation and regulations protecting people with disabilities. These include the

Universal Declaration of Human Rights Article 1, adopted in 1948, and the United Nations Convention's Rights of Persons with Disabilities, which was approved in 2006.

In addition, the WFH has recently committed to the WFH Transform 2016 action plan, which increases the number of regional program managers around the world to assess regional situations and offer solutions.

The WFH will also become a member of Rare Diseases International, which has the prime objective of convincing the United Nations to make rare diseases an international health priority.

Weill urged each member of the bleeding disorders community to also think locally when it comes to education. "As you go through the congress experience, gather the tools that you can take back to your own communities that can help to educate and make a difference," he said.

"For when we educate people to see that being a patient of a rare bleeding disorder does not define who that individual is, and instead see them as an active member of society who enriches their community, we will show that it is indeed true that the highest result of education is tolerance."

# Friend\*

\*Humanitarian Aid Required

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Centre for more information  
on how you can help.

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