



# **EHC NEWSLETTER**

SEPTEMBER 2016

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# EHC Newsletter September 2016

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## President and CEO report

Welcome back from the summer and into the tail end of the year. Here's a short update on the work of the European Haemophilia Consortium (EHC) since May and a look ahead towards the remainder of 2016.

### Leadership Conference



*Brian O'Mahony is the EHC President. Amanda Bok is the EHC CEO.*

The EHC went into the summer with community engagement in mind. In June we held our first stand-alone Leadership Conference in Brussels where we brought together some 70 participants from 23 National Member Organisations (NMOs) for a highly interactive and engaging programme – see pg 10. At the end of the conference, we immediately polled participants on their desired future iteration of this training and were delighted to

see them unanimously confirm conference's utility and vote to make it an annual mainstay of the EHC's work.

### Round Table on hepatitis C

A few days after the Leadership Conference, we held an extra-ordinary Round Table in the European Parliament (on top of our normal set of three Round Tables per year) on access to hepatitis C treatment for people with haemophilia – see pg 7 – as part of the EHC's 2016 focus on improving the access of infected people with haemophilia to the new hepatitis C products.

### WFH Congress

In July, the EHC and much of its European membership met in Orlando, Florida, during the Global NMO Training and the World Congress of the World Federation of Hemophilia (WFH). The EHC had a conference stand for the first time at a World Congress, which was so popular we ran out of some materials in the first days, and also held a European meeting. We congratulate both the WFH on a successful congress as well as the many talented European chairs, speakers and panellists who played a prominent role.





### **EHC Conference: Stavanger**

Now our sights are directed north as the countdown has begun to our own EHC Conference. Stavanger offers many things to look forward to: a strong scientific programme (see pg 60), traditional and new debates and interactive discussions, a spotlight on care in Nordic countries – including of course Norway – and a warm welcome and social programme by the Norwegian NMO.

Programme sessions will cover a range of rare bleeding disorders, with a particular focus on von Willebrand Disease this year, and comprehensive care, with a special focus on dental care this time. Current and future aspects of haemophilia treatment and care, including updates on new developments such as gene therapy, bi-specific antibodies, antithrombin and other novel technologies, will be presented, but there will also be a series of clinician debates on these and other fields of investigation in order to pursue a deeper dialogue and understanding of these new therapeutic developments.

Inhibitors will also be covered prominently in the programme with presentations focusing not only on the Survey of Inhibitors in Plasma-Product Exposed Toddlers (SIPPET) and previously untreated patients, mild haemophilia and acquired haemophilia, but also on the views of experts during a panel discussion.

Last on the programme, the conference will also spotlight patient-reported outcome data and its various uses, including the EHC's own surveys, the CHES and PROBE studies and the use of national registries.

Finally, with two additional symposia slots – six instead of four – there will be something for everyone. Two of these slots belong to the EHC and we humbly encourage you not to miss them! The first one will take place on Friday evening and feature our traditional youth vs. clinician debate (we're rooting for our youth!), which is always an entertaining, engaging but also very insightful session. The second will be held on Sunday morning and focus on hepatitis C and haemophilia, as we continue to pursue our focus area and push all stakeholders to seek and ensure access to the new treatments available!

### **Elections, elections**

Before all of this happens at our conference, we'll have our General Assembly (GA), which has moved to Friday morning, where all four lay positions of the Steering Committee will be up for election for a new three-year term. We invite all of our NMOs to study candidates' bios carefully and advise NMO representatives attending the GA meeting to arrive in Stavanger early (in time for Thursday evening's dinner or Friday's breakfast if possible) to ask candidates any questions you may have. NMOs will also be voting for the host of the 2018 EHC Conference.

### **Blood relatives**

Finally, don't forget to sign up to join our Dutch cyclist friends for the last leg of their over 1,300 km bike ride from Utrecht to Stavanger! The cycling team composed of nine volunteers left Utrecht on September 21<sup>st</sup> and will arrive in Stavanger early on the Friday morning after having cycled a collective 10,000 km!. For anyone wishing to welcome them at the harbour and cycle with them in their last leg to the Conference location, please visit their [website](#) and [Facebook page](#).



*Bloedverwanten (bloodrelatives) is a group of Dutch volunteers cycling 1,300 km to raise awareness about bleeding disorders. They will end their journey in Stavanger on the first day of our Annual Conference.*

**Autumn programme**

In addition to the above we look forward to starting our new three-year cycle of economics workshops, this time focusing on ‘Tenders and Procurement.’ We started it with a workshop for Russian-speaking countries that took place in Baku, Azerbaijan, on 9-11 September 2016.

November will then host two additional events. Our New Technologies workshop will be held in Berlin, Germany, from 18-20 November – registration is closing soon (at the end of September) so if you haven’t registered already, we encourage you to do so promptly (by writing to [laura.savini@ehc.eu](mailto:laura.savini@ehc.eu))! Later that month, our last Round Table of the year will take place on Monday, November 28<sup>th</sup> and focus on Outcome Measures.

Finally, in December we plan to go out with a bang: our newest and most exciting event, the first face-to-face Summit of the European Inhibitor Network, will take place from 1-4 December in Barretstown, Ireland (see pg 17). We’ve worked a long time to prepare this look forward to seeing many new faces there!

meeting and very much some familiar but many,



**EUROPEAN  
INHIBITOR  
NETWORK**

# EHC News

## Comprehensive care in haemophilia: Orthopaedics

*Dr Luigi Solimeno\* interviewed by Laura Savini\*\**

*For this edition of comprehensive care and haemophilia, we speak to Dr Luigi Solimeno about the role of orthopaedics in the treatment of haemophilia. Dr Solimeno is the Director of the Department of Orthopaedics and Traumatology at the Fondazione IRCCS Ca' Grande Ospedale Maggiore Policlinico in Milan, Italy. He is also a member of the World Federation of Hemophilia (WFH) Musculoskeletal (MSK) Committee.*

*On orthopaedics and haemophilia*

“For a haematologist, haemophilia is a bleeding disorder with an orthopaedic complication, however for an orthopaedic surgeon, haemophilia is an orthopaedic disorder with a bleeding complication.” This is how Dr Solimeno describes why orthopaedics play an integral role in the comprehensive care of haemophilia and why a multidisciplinary approach is needed.

*On orthopaedics and rheumatology*

Besides orthopaedics, rheumatology also plays an important role in the treatment of haemophilia, however the difference between these two disciplines is often hard to discern for a non-expert. In orthopaedics a greater emphasis is placed on surgery while rheumatology will have a greater focus on conservative treatments, such as physiotherapy and exercise. Both specialties are needed by people with haemophilia as they are more likely to develop complications related to osteoporosis<sup>1</sup> caused by a less frequent use of the joints (e.g. target joints), which in turn will result in different bone quality.

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*Pain is certainly the main problem faced by patients suffering from joint damage*

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*On how haemophilia impacts the musculoskeletal system and prevention*

As mentioned above, haemophilia is a disorder that impacts joints and in particular knees, ankles and elbows, although it is not clear why these particular joints are most affected. These joints are damaged due to the corrosive effect of blood in the joint, which will result in synovitis<sup>2</sup>, cartilage defect and arthropathy. Obviously, the most important way to avoid these problems is prophylactic treatment with coagulation factor concentrates, which will prevent recurring bleeds in the joints. However, nowadays, prophylaxis is not enough to prevent joint damage, and safe practice of sports, a healthy lifestyle (such as the maintenance of a balanced weight) and rehabilitation play an important role in joint preservation.

*On pain management*

Pain is certainly the main problem faced by patients suffering from joint damage. The pain can be related to a bleed, synovitis, advanced arthropathy or surgery. Regardless of the cause, the role

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<sup>1</sup> Osteoporosis is a disease that causes bones to become weak and brittle resulting in the bones becoming more prone to fractures due to falls or stress.

<sup>2</sup> Synovitis is an inflammation of the synovial membrane, a tissue that lines joint cavities, and is extremely painful.

of an orthopaedic surgeon is also to manage pain by using painkillers, rehabilitation, surgery and, if necessary, joint replacement.

#### *On the role of an orthopaedic surgeon*

As the name indicates, the role of an orthopaedic surgeon will be primarily to conduct surgery and carry out proper follow-up of patients, especially in the case of complications. This professional will also be involved in research through conducting clinical trials together with haematologists, for example.

#### *On working with other healthcare professionals*

Orthopaedic surgeons are in close contact with haematologists, physiotherapists and nurses and this comprehensive approach is quite important to have a global overview of the patient. In Dr Solimeno's hospital, for example, each patient will be able to meet jointly with a haematologist, an orthopaedic surgeon and a physiotherapist to talk about his problems and gain a better understanding of his situation. Additionally, this will help to determine the most appropriate course of action. In Dr Solimeno's opinion, nowadays it is unthinkable to manage haemophilia without a multidisciplinary approach.



*Dr Solimeno spoke at the EHC Annual Conference in Belgrade in 2015*

#### *On orthopaedics and haemophilia in Italy and in Europe*

Dr Solimeno describes the situation for people with haemophilia in Italy as being very good. He also notes that this is currently the case for countries in Europe that have access to higher quantities of factor concentrate as, noted above, prophylactic treatment is not only key in preventing joint damage but also to carry out proper surgery. In fact patients need to receive infusions to bring up their level of coagulation factor prior to the surgery.

In Italy, orthopaedic services for people with haemophilia have been concentrated in two key centres where patients can access specialist services for surgery. However rehabilitation is carried out locally and this is thanks to the education programme carried out by these specialist centres that give training to local physiotherapists on how to manage people with haemophilia who have recently undergone surgery and who need more regular follow-up.

#### *On professional training*

A specialised training is definitely needed for orthopaedic surgeons wanting to work with people with haemophilia. Dr Solimeno's hospital provides trainings in this area for orthopaedic surgeons from across the world. Even the most common surgeries such as knee or ankle replacements will have to be performed differently so specialised training is key.

#### *On professional societies*

Currently the only place for orthopaedic surgeons working with people with haemophilia to meet is the WFH MSK committee, which meets and organises a conference every other year (the next meeting will be held in Seoul, South Korea in 2017). This group is comprised of approximately 300

professionals from all over the world and it is an important group as it helps to share knowledge and develop a network of professionals working in the same area.

#### *On current and upcoming challenges in orthopaedics and haemophilia*

For Dr Solimeno the main issue in orthopaedics and haemophilia at the moment is related to the timing and indication of surgeries. Until now, there has been a trend to discourage young people from undergoing surgery to fix a problem in the joints, advising them instead to pursue conservative options until there is no other option but surgery. In Dr Solimeno's opinion, surgery should be done at the right time (irrespective of the patient's age), meaning it should be done when the patient can gain the greatest benefits from the procedure. If one waits too long to undertake surgery it may be too late to fully benefit from the results of the procedure and surgery will only give partial results. From Dr Solimeno's perspective this is a mistake and he strongly encourages patients to take advantage of the benefits of orthopaedic surgeries by doing them at the right time for their particular situation.

*\*Dr Luigi Solimeno is the Director of the Department of Orthopaedics and Traumatology at the Fondazione IRCCS Ca' Grande Ospedale Maggiore Policlinico in Milan, Italy.*

*\*\*Ms Laura Savini is the EHC Communications and Public Policy Officer.*

## HCV and haemophilia

*By Kit Greenop, Consultant RPP Group*

*In 2016 the activities of the EHC heavily focused on raising awareness about the need for access to novel HCV treatment for people with haemophilia. Kit Greenop, a policy consultant working for the EHC, outlines how the efforts of the EHC carried out so far and how they fit in a larger European environment.*

In 2016 the European Haemophilia Consortium (EHC) has turned its advocacy efforts with the European Institutions towards one of the most controversial and pressing issues of health policy across Europe: the excitement of, and challenges posed by, new treatments for viral Hepatitis C (HCV). The haemophilia community needs no reminder of the tragedies surrounding blood contamination and the need to eradicate HCV, but the patient voice from the haemophilia community is one that needs amplification in a debate that has transformed the attitude towards health policy, particularly in the European Parliament. To appreciate the importance of the patient voice in this debate, it is crucial to recognize the paradigm shift in policy that the new generation of direct acting antivirals (DAA's) for HCV treatment has brought.



*Participants during the EHC June Round Table of Stakeholders on Haemophilia and HCV*

### ***The debate – a historical re-cap***

In January 2014 Sovaldi (sofosbuvir), a Direct Acting Antiviral (DAA) for the treatment of HCV, received marketing authorization from the European Medicines Agency offering hope to patients across the world with projected 95 per cent undetectable viral load after 12 weeks (SVR12). Quickly this treatment, and others that followed, gained enormous attention from policy makers. Contrary to popular belief at first the price tag that accompanied this product was not the source of controversy, nor was it a novel amount for a company to charge for a medicinal product. The novelty was how good the product was, and the challenges that this brought to 21<sup>st</sup> century healthcare decision making. Many sources will point to the 1990's as the height of blockbuster drugs and, while research spending by pharmaceutical companies has sky-rocketed since then, treatments have followed a more standard scientific mechanism - making continuous advancements, gradually improving patient outcomes. While medicines in the 2000's have had high price tags, the notion of 'me-too' products have enhanced the bargaining power of countries in price discussions. The era of DAA's bucked that trend by being a true block buster and attaching high prices to products with irrefutable clinical evidence showing that these medicines would definitively change millions of lives. With a blockbuster treatment, and ever more constrained health budgets, policy makers were set a challenge in 2014 that was unprecedented in magnitude and profile.

The result at European level was an outcry from politicians, resulting in over 40 parliamentary questions on HCV since 2014, and the launch of debates on access to medicines in relation to price that have clear links to their own initiative report currently being developed in the European Parliament. Whether it was the lack of transparency over how the price was derived, or a lack of engagement in the stakeholder community beforehand, DAA's gained a stigma as the face of bad-pharma – something that surely could not have been envisaged when the first clinical data was published on these products.

The haemophilia community was not only attached to these discussions by the infections of the 70's and 80's but the haemophilia community has also been involved in similar discussions, if on a smaller scale, around the cost of prophylaxis and the long-term value to patients.



*Members of the European Parliament Mr Andrey Kovatchev (centre left in the picture) and Mr Cristian Busoi (centre right in the picture) chaired the EHC June Round Table of Stakeholders on Haemophilia and HCV*

### ***Haemophilia Community's response and involvement***

In 2015 and 2016 it became clear that, where a strong compromise cannot be found, this tragedy will continue to impact haemophilia patients. To this effect, the EHC embarked on a sustained approach to dealing with haemophilia and HCV, through actions on World Haemophilia Day and in the June Round Table on haemophilia and HCV. These events brought together patients, scientists, physicians, policy makers and industry from both sectors to discuss the challenges they faced together.

What this approach has accomplished is threefold:

- 1) The haemophilia community has joined the wider patient community demanding policy makers to implement comprehensive strategies for eradication of HCV,
- 2) The haemophilia community has presented policy makers with the first example of a contained population, which could show eradication in the short term with effective policy,
- 3) Policy makers have understood that in many cases, effective management of HCV would represent compensation for the blood contamination scandal, which many patients never received.



*Participants during the EHC June Round Table of Stakeholders on Haemophilia and HCV*

The haemophilia community has a huge experience to share with the wider HCV community, which is the long history of available treatments, but the constant challenge is to give all access to the best treatments, at the earliest time. Throughout both events, it was stressed that earlier and more proactive use of DAA's was crucial and the haemophilia community have a good experience in working to get access to treatment quickly and effectively.

The involvement of the haemophilia community in HCV discussions highlights further the comparative successes of haemophilia advocacy in defining largely common approaches from all stakeholders and guaranteeing good access to treatment and good care guidelines across a large amount of the EU. Contrastingly, the relationship between stakeholders in the HCV field remains somewhat unaligned and at times, strained. The question then emerges, how does the haemophilia community contribute to the debate, and how does this sustained approach look to benefit the patient community.

It has been said by haemophilia patients in each of the above-mentioned events this year that haemophilia patients are more prepared to deal with HCV than other groups of patients because of the resilience that the community has had to show in light of tragedies over the last 40 years. In this sense, the haemophilia community has a great role to play in the discussions surrounding access to new DAA's. Eradication of HCV in the haemophilia community would give the wider patient community a template from which to work and is a strong goal to work towards moving forwards. It also would show how the historically strong links between haemophilia patients and policy makers, scientists, healthcare professionals and industry is the gold standard in achieving

good patient outcomes. Already, thanks to the events this year, policy makers who have worked on rare bleeding disorders are more aware of the need to deal with infection and are committed to bridging the gap between good blood safety policy and good care for patients with HCV. It is clear that the EHC's entry into this debate is timely, important and must be continued to ensure European policy makers implement good eradication strategies and that the huge breakthrough of DAA's are the denouement to a story of infection that haemophilia patients continue to grapple with through.

## The second edition of the EHC Leadership Conference: Building a cross-border community!

*Kristine Jansone\* interviews Moran Ofek,\*\* Nurbek Orozaliev\*\*\* and Stefan Radovanovic\*\*\*\**

*"A community is like a ship, everyone ought to be prepared to take the helm." - Henrik Ibsen*



*Participants of the EHC 2<sup>nd</sup> Leadership Conference*

*In June 2016, the European Haemophilia Consortium (EHC) held the second edition of its Leadership Conference (LC) in Brussels, Belgium. This event brought together over 70 participants representing the leadership, staff and youth volunteers of 23 EHC National Member Organisations (NMOs), hence creating a unique atmosphere of exchange and mutual learning. The programme of this year's LC focused on various aspects of communications, such as IT tools, social media and external relations with industry, policy-makers and regulators. During the event a great deal of time was allocated for participants to share the experiences and practices within their NMOs.*

*The EHC would like to thank all the participants, facilitators and speakers who made this incredible experience possible and is already looking forward to developing the programme for the 2017 LC!*

Below you can read a Q&A between Kristine Jansone (EHC office), Nurbek Orozaliev (Kyrgyz NMO), Stefan Radovanovic (Serbian NMO) and Moran Ofek (Israeli NMO) about the LC and its value for participants and NMOs.

**Kristine Jansone (KJ): Moran, this was your first experience with the EHC LC. How did you experience the EHC community during this event?**

**Moran Ofek (MO):** Even though much information came from experts' presentations, in my opinion the most valuable learnings came from the field, i.e. from other NMOs. The sessions enabled us to a large extent to learn from one another through a very open and supportive dialogue. This made the LC a very enriching and empowering experience.



*Moran (in the centre) is a board member of the EHC Israeli NMO*

The life of all haemophilia patients depends on a web of very complex socioeconomic elements in which two giant players, the pharmaceutical industry and governments, operate. The patient community must work hard to gain power to influence their own conditions. On a micro level we can achieve a lot as individuals, for every one of us can impact our own life but on the macro level our NMOs play a very important role. A patient alone could never achieve the same rights and services that can be achieved by all patients in a particular country. The same logic works when you zoom out: a local NMO cannot achieve the changes that a consortium of 45 NMOs can. We at עלה – לחולי עמותה – המופיליה, the Israeli NMO, can learn a lot from the knowledge and experience of bigger and more experienced NMOs, and I am sure that even the stronger and more experienced NMOs can learn something new to improve their work and the condition of their members from the kind of exchanges we had during the LC.

**KJ: Nurbek and Stefan, this was the second time that you both attended the EHC LC. What was different this time in comparison to last year?**

**Nurbek Orozaliev (NO):** For me the organisation of the conference was different, there were many more practical exercises, which I enjoyed very much.

**Stefan Radovanovic (SR):** It was different. In a way we were working on themes that are much more present in the everyday work of our NMO. The topic of communication was, for example, looked at more in-depth. Furthermore, I am now more familiar with the concept of this conference and therefore it was easier for me to engage in the discussions from the very beginning.

**KJ: Moran, what was the most valuable insight that you gained from being a participant for the first time?**

**MO:** I was really happy to take part in the EHC LC and it was a very interesting and important experience! For me the LC was valuable in two ways. On the one hand for the learning and empowerment of patients as I received new information about treatment and services that patients are accessing in different parts of Europe. On the other hand, I gained new ideas from hearing about the goals that NMOs are setting for themselves, as well as the methods they use to reach those goals. This really gave me a new perspectives about the level of treatment in Europe

and the role played by the EHC NMOs in getting better access to treatment for their community in each country.

**KJ: Nurbek, you come from the eastern-most country in the EHC membership, Kyrgyzstan, a country also outside the European Union with a very different socio-economic landscape. As such, what was for you the most valuable lesson gained from the LC?**

**NO:** I discovered some IT technologies that I think will enhance the work of our NMO. But also, it



*Nurbek (on the right side of the picture) took part in the EHC 2<sup>nd</sup> Leadership Conference*

would be great to see more fellow NMOs from other CIS<sup>3</sup> countries taking part in this type of event. In this way we would all have a chance to share our great variety of experiences.

**KJ: Stefan, how was your experience of the LC from the perspective of youth? What was the most valuable insight that you gained?**

**SR:** The LC made me realise that many NMOs out there still have major challenges when it comes to communicating with their members and engaging with youth by, for example, forming a youth committee (YC). Many NMO representatives do

not understand the concept of YC and have the wrong impression that setting up a YC will result in youth distancing itself from their NMO. But I believe that this is incorrect. In Serbia, for example, we see the YC bringing together young volunteers with the rest of the NMO membership. In this way the NMO can understand their issues and challenges and be better prepared not only to help them but also to engage with them. In my country this approach has proven to attract younger, more active and motivated youth members.

**KJ: Finally, a question for all three of you. What would you say to the potential participants of the next LC, why is it worth taking part?**

**NO:** It is essential to take part in this kind of activity as it provides a great space for interaction between different NMOs. Also, make sure to bring with you volunteers from your NMO as it is a great motivation for them to attend this sort of meeting and they will be an even bigger asset for your organisation.

**MO:** It is important to take part because through this exchange the NMOs will learn some important lessons and know-how on better access to treatment as well as information on how to be a more effective organisation. Some topics that particularly marked me were the treatment options for adults, the rights and treatment options of women with bleeding disorders and carriers, the importance of democracy within the NMO and how to more effectively engage and

<sup>3</sup> CIS stands for Commonwealth of Independent States, a regional organisation made up of nine out of 15 former Soviet Republics. Members include Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan and Uzbekistan.

retain volunteers. These were just some of the issues that we brought back home along with more understanding, ideas and tools on how to pursue them.

**SR:** I would tell them that you will access a lot of new information and experiences from other NMOs, which will be valuable in the work of your own NMO. You will also be able to exchange with members from other NMOs from all over Europe and for me this is the most important thing. You will make new friends and maybe even find some solution to a problem you couldn't solve. There is nothing like meeting people in the same situation as you with the same problems, conditions and goals and yet a completely different perspective on things. For



*Stefan (on the right hand side of the picture) attended the LC on behalf of the EHC Serbian NMO*

me sharing ideas and experiences is crucial to achieve something as important as haemophilia treatment for all. This is why I would say to NMOs that have not yet attended that if you want capable and trained volunteers and staff members you must send them to the EHC LC because there is no better place for them to learn about the haemophilia community in Europe.

*\* Kristine Jansone is the EHC Inhibitor Programme Officer*

*\*\* Moran Ofek is a Board member of עלה – עמותת המופיליה לחולי עמותה, the EHC Israeli NMO*

*\*\*\* Nurbek Orozaliev is the President of Kyrgyz Haemophilia Society "Community of handicapped – haemophiliacs," the EHC Kyrgyz NMO*

*\*\*\*\* Stefan Radovanovic is a member of Udruženje hemofiličara Srbije, the EHC Serbian NMO*

*The EHC LC was made possible thanks to educational grants from Baxalta (now part of Shire), Pfizer and Sobi.*

## **EHC - EAHAD Meeting of Clinicians: Quality and standards of inhibitor care in Europe**

*By Mirko Jokic, member of the EHC Inhibitor Working Group and member of the Udruženje hemofiličara Srbije, the Serbian NMO*

*On 20<sup>th</sup> July 2016, the European Haemophilia Consortium (EHC) and the European Association for Haemophilia and Allied Disorders (EAHAD) held a meeting in Brussels, Belgium, about quality and standards of inhibitor care in Europe. Mirko Jokic reports on the outcomes of this first meeting.*

It's important to note that this was the first official and high-level meeting between these two organisations on the topic of inhibitors, even though they work regularly together.

The event kicked off with a welcome address by Kristine Jansone, EHC Inhibitor Programme Officer. She then presented to participants the concept of the European Inhibitor Network (EIN), its objectives and programme elements as well as the EHC Inhibitor Working Group (IWG) and its



*Mirko is a member of the EHC Inhibitor Working Group*

work objectives concerning community-building. One of the programme's elements is to reach out to and work together with healthcare professionals towards a framework for treatment and care of people with haemophilia and inhibitors (PWI) in Europe. These objectives were also echoed by Prof Paul Giangrande, Chair of the EHC IWG and EHC Medical Advisory Committee (MAG).

#### *Where are we now*

Once all parties were clear on the objectives, it was important to provide an overview of what the current situation with regard to access to treatment for PWI looks like right now in Europe. To do so, participants were presented with data from three surveys conducted by the EHC targeting patients, their caregivers and families as well as haemophilia centres in

Europe. Additionally, Mr Brian O'Mahony, EHC President, also presented some preliminary results from the EHC 2015 survey on the state of haemophilia care concerning inhibitor treatment in Europe.

Discussions were fruitful and soon there was an understanding in the room that a framework for the treatment of PWI should go beyond treatment regimens. For example, PWI should have access to expert healthcare professionals at national level who could help them develop a treatment plan to be implemented locally. There was also a suggestion to set up a database with contacts of specialised healthcare professionals. Dr Roseline d'Oiron, EAHAD board member (see pg 42) presented an example from France where national-level teleconferences among clinicians are held on a regular basis to discuss problematic cases. This is especially helpful for smaller centres. Participants agreed that this kind of model could be promoted.

#### *Needs of patients with inhibitors and importance of comprehensive care*

Miguel Crato (Portuguese NMO – see pg 33), who is also a member of the IWG and I provided an overview of PWI's needs and the importance of comprehensive care. Obviously one of its most important aspects is the access to immune tolerance induction (ITI) as well as the availability of by-passing agents. Nonetheless, access to medicinal products is not the only important aspect for the treatment and care of PWI. In fact, other medical specialties play an equally important role. For instance, access to physiotherapy is essential to preserve joints and to protect them from future bleeds and injuries. Other important medical areas are specialised surgery for joint replacement (see pg 5) as well as specialised laboratories (see EHC Newsletter May 2015) to perform the assessment of thrombin generation before any surgery. Finally, psychosocial support for patients, families and caregivers is also important to help them overcome any emotional problems and cope with the disorder. It is also extremely important for patients to be able to access information regarding the latest treatments and ongoing research that will impact the future of haemophilia care.

Other points that were taken into account during the discussions included the importance of access to treatment for children and in particular infants. Parents should be given all necessary

information about this condition and early access to treatment will ensure a better outcome for the child. Nonetheless it was recalled that unfortunately inhibitor treatment is not always a success story and that due to its high cost, many patients are not able to have adequate access to medicinal products. This is an important issue that requires much political work in terms of advocacy. Participants were reminded that PWI's quality of life is much similar to that of people with haemophilia in the 1960s and 1970s prior to the advent of coagulation factor concentrates. Additionally, quality of life greatly varies from country to country so it is important to develop standards of care.

#### *Report from the Wildbad Kreuth IV meeting*

Prof Paul Giangrande reported on the meeting organised by the European Directorate for the Quality of Medicines and Healthcare (EDQM), a body part of the Council of Europe, the University of Munich and Rudolf Marx Foundation on the optimal use of coagulation factor concentrates.



*Prof Paul Giangrande is the Chair of the EHC Inhibitor Working Group*

Although the proceedings of the meeting are yet to be published, he informed participants that several recommendations were adopted during the meeting, some of which are expected to have a positive impact for PWI, notably regarding haemophilia centres designations, access to ITI, access to elective surgery and access to treatment choice in order to minimise the risk of inhibitors.

#### *Desirable standards*

Participants continued the discussions and evaluated aspects of care for which it will be desirable to develop standards. Participants agreed that medical treatment of inhibitors, laboratory analysis, physiotherapy and nursing should be considered for standards development.

#### *Medical treatment of inhibitors*

Prof Cedric Hermans, EAHAD President, underlined that bypassing therapy is used to such a big extent in some centres, that ITI is often not even initiated. In his opinion, it is important that the first line of treatment for inhibitor management is ITI and then bypassing agents' therapy. However, he noted that bypassing agents could be used during ITI in order to preserve joints.

There were some further discussions regarding the set-up of a registry for PWI, however this topic also raised some problematic issues that would have to be addressed such as the maintenance of the registry, data ownership, access to data of patients enrolled in clinical trials and the standardisation of the data provided.

Finally, participants agreed that the best practice would be to gather data at a national level and pool it when necessary. This should be introduced as a basic clinical practice.

Furthermore, participants noted the lack of treatment available in Europe with an official indication for prophylactic treatment of inhibitors, which often leads to a lack of reimbursement.

### *Laboratory aspects*

Prof Jan Astermark, EAHAD Board Member, presented a short overview of the need for laboratory standardisation in Europe, in particular with regard to the specialisation of both laboratories and training for laboratory scientists as well as external audits and assays.

Participants suggested that there should be one reference laboratory per country that should accept to test samples, free of charge, to verify and/or detect low titre inhibitors. Furthermore, it would be good to organise a European workshop to further train laboratory scientists. Finally, a standard should be created so that both European haemophilia comprehensive care centres (EHCCCs) and European haemophilia treatment centres (EHTCs) could be able to detect inhibitors. This could be included in the accreditation requirements of the European Haemophilia Network (EUHANET).

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*As a conclusion of this meeting participants agreed that ten sub-principles should be developed expanding on point nine, i.e. on the management of inhibitors, of the European Principles of Haemophilia Care.*

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### *On physiotherapy*

Mr Piet de Kleijn, Chair of the EAHAD Physiotherapy Committee, gave an overview on the role of physiotherapy in haemophilia with a focus on inhibitors. The difficulty is that there is no evidence showing the efficacy and cost-effectiveness of physiotherapy, although it is widely recognised amongst healthcare professionals (see EHC Newsletter December 2015) and therefore it is difficult in many countries to receive recognition and funding for this specialty. Additionally, physiotherapy should not only be used for function recovery, for example after a bleed, but it should be administered long term, which will further strain available resources as, for example, a child with haemophilia and inhibitors may need physiotherapy on a daily basis.

As with other medical specialties, it would be good to establish a network of specialised healthcare professionals such as physiotherapists who could work together with parents and caregivers to provide training and information on optimal level of care. Mr de Kleijn stressed some important actions that should be taken to improve the current situation, such as to provide education to non-specialist physiotherapists, support and empower patients to access physiotherapy daily, ensure that each EHCCC and EHTC has a specialised physiotherapist that can work with PWI, ensure collaboration between physiotherapists and haematologists to develop personalised treatment regimens for each patient and finally, develop some educational guidelines and DO's and DON'Ts when working with people with haemophilia and PWIs that could be paired with a physiotherapy helpline. These guidelines should be translated into national languages so that each patient can share these with their physiotherapist.

### *On nursing*

Mr Martin Bedford, Chair of the EAHAD Nurses Committee, presented the key aspects of nursing care in inhibitor management.

He pointed out that the education and training of nurses is essential for a better understanding of the specificities of haemophilia and patient education.

Furthermore, additional involvement of nurses within the activities of the EHC would be welcome. Finally, proper and validated training courses for nurses working with PWI should be developed. This is something that the EAHAD Nurses Committee is currently working on.

#### *Role of the EHC and EAHAD in promoting the standards developed*

Prof Cedric Herman noted the importance of both EAHAD and EHC in terms of promoting standards for inhibitor care. In his opinion, this can be achieved by first developing standards in a lay language so that they can be easily understood by a wider number of patients and non-specialists as well as by auditing EHCCC and EHTC.

#### *Conclusion and further steps*

As a conclusion of this meeting participants agreed that ten sub-principles should be developed expanding on point nine, i.e. on the management of inhibitors, of the [European Principles of Haemophilia Care](#). The EHC and EAHAD will further meet to expand their activity and to prepare recommendations for inhibitor care.

This meeting was a very good starting point where some general facts and objectives were presented as a basis for further work to establish specialised standards for inhibitor treatment in Europe.

## **The first highlight of the EHC Inhibitor Programme expected in December 2016\***

*By Kristine Jansone, EHC Inhibitor Programme Officer*

*In December the EHC will hold its first Inhibitor Summit, Kristine Jansone tells us more about this event.*

In July 2015, the EHC launched the European Inhibitor Network, a programme focusing on the needs of people with haemophilia who have inhibitors (PWI). This programme has been steadily progressing throughout the year, creating more and more interest among the EHC membership. All the different elements of this programme, such as the establishment of the Inhibitor Working Group, developing needs assessment surveys, conducting research of the resources and developing informative materials, are aimed at empowering and supporting PWI, a part of the EHC community, which is usually more isolated and fragile.

In order to bring the community building process still further, the EHC is organising its first Inhibitor Summit, a meeting that will offer a special time and space for PWI, their family members and caregivers.

The event will take place from 1-4 December 2016 in Barretstown, Ireland, a facility founded by the American actor Paul Newman as a place designed for children living with a serious illness and their families. It offers 24-hour on-site medical and nursing care and complete disability access throughout its property. But most importantly, it offers tailored activities that all children and



adults with a serious illness or disability can participate in as well as excellent and experienced support staff onsite.

The EHC staff and the Inhibitor Working group members are very excited to welcome more than 80 participants, both children and adults, to this event! The programme of the event will be built in a way that all the age groups present will benefit greatly from both practical and informative elements. However, the most important part will be dedicated to peer-to-peer sessions and exchange between the participants. This will help to build long-lasting friendships and find people in similar situation to talk to! Being part of the community and overcoming the sensation of isolation is valued greatly in the EHC community in general, but is even more important for PWI!

*\* The EIN was made possible by educational grants from Baxalta (now part of Shire).*

## Meet the EHC Inhibitor Working Group

*By Kristine Jansone, EHC Inhibitor Programme Officer*

*Kristine Jansone introduces the members of the EHC Inhibitor Working Group together with their hopes for this group and what challenges are faced by people with haemophilia and inhibitors in Europe.*

In July 2015, the European Haemophilia Consortium (EHC) launched the European Inhibitor Network (EIN – see pg 17), a programme dedicated to serve the most isolated group within the EHC membership. Until the end of 2017 the EHC aims to establish a solid and well-functioning network to strengthen this often isolated group of patients as well as to improve their quality of life. The programme will run for three years initially, being constructed of several programme elements to meet an equal number of needs. All these programme elements will be made maximally accessible through translations and different formats.

An initial working group was set up to make initial preparations for the programme and lay the groundwork until the Inhibitor Working Group (IWG) was established in the late fall of 2015. An active involvement from various stakeholders including people with haemophilia who have inhibitors (PWI), their families and caregivers as well as several healthcare professionals was shown in the work of the IWG and in the implementation of this project.

It is the EHC's pleasure to introduce the members of the IWG.



*Members of the EHC Inhibitor Working Group at their first meeting in February*

**Mirko Jokic** is an active member of Udruženje hemofiličara Srbije, the Serbian National Member Organisation (NMO) with a special interest in inhibitors. In fact, he was one of the founding members and is currently the coordinator of the Serbian NMO Inhibitor Working Group, which deals with inhibitor-related topics and events. In addition, he is responsible for the online activities of the Serbian NMO to raise awareness about haemophilia.

Mirko joined the IWG because he wanted to devote more time to volunteering and believes he can do more for PWI not only in his home country, Serbia, but at a European level. Mirko himself is a PWI and therefore fully understands the concerns and issues related to living with an inhibitor. Mirko thinks that the EHC IWG has the potential to achieve better social and health conditions for PWI and more integration in the life of the community.

In Mirko's opinion both the work carried out on the recommendations on inhibitor treatment and the upcoming Inhibitor Summit are extremely important. However the Inhibitor Summit is perhaps the most important event because for the first time PWI will be able to meet at a European level and share experiences and learn from each other.

**Hannele Kareranta** is a 66-years-old eye doctor from Finland, who was diagnosed with von Willebrand disease type III when she was six years old. At 17, she developed an inhibitor but thanks to medical advances and treatment options in her country, she has led a relatively healthy life and was able to have two children with minimal complications. For Hannele 'bad joints' are the biggest problem and she has herself undergone surgery to replace three of them, which has been of great help.



*(From left to right) Mirko, Miguel, Kristine and Christina are part of the EHC Inhibitor Working Group*

Hannele decided to join the EHC IWG to meet others who suffer from an inhibitor. In fact, in her lifetime, she only met very few people who suffered from the same ailment as she did. Hannele was a Board Member of Suomen Hemofiliyhdistys (SHY), the EHC Finnish NMO, and through her involvement in the EHC IWG she hopes to not only bring her personal experience but also to gain more knowledge and know-how to help other patients with inhibitors. In fact, in only a few months of volunteer work with the EHC, Hannele discovered that the needs of those with inhibitors are as many and diverse as are the forms of inhibitors affecting people with bleeding disorders. Hannele is very excited to be on board the EHC IWG and feels very inspired by other members.

**Christina Burgess** is the Head of Membership and Planning at the Haemophilia Society UK, the EHC UK NMO, and as such she supports UK PWI of all ages within her NMO. Through her current role she has already gained a deep understanding of PWI's needs and by joining the EHC IWG she

hopes to not only bring new knowledge to her community but also share experiences from the UK with other countries and particularly with those with lesser access to treatment and support services.

As she saw it, inhibitors are often the last hurdle when it comes to the care and lives of PWI and their families are often a roller-coaster of uncertainty. Christina believes that with the collaboration and expertise that each NMO brings to this much-needed project we can develop additional, improved support, whether sharing knowledge of treatment options on the horizon, or physical and psychological tools for coping.

For Christina, being part of the IWG is hugely stimulating, particularly the collaboration with the colleagues from other NMOs and the healthcare experts from across Europe brought in to share advances being made.

**Miguel Crato** has a severe haemophilia A and developed inhibitors in his youth. Currently he is the president of APH – Associação Portuguesa de Hemofilia e de outras Coagulopatias Congénitas, the EHC Portuguese NMO.

According to Miguel, the IWG is a very important step to achieve better communicating with PWI and to evaluate their real needs. This network will also provide good examples and useful tools for the EHC NMOs to better integrate PWI in their activities.

For Miguel, the work of the EHC IWG is very challenging but he has high hopes that it will lead to better integration and care for all PWI in Europe.

The other three members of the Inhibitor Working group are Elisabeth Olesen from Denmark, a mother of a boy with inhibitors, Carl Fredrik Gustavsson a young man with inhibitors from Sweden, and Dr Oleksandra Stasyshin, a haematologist from Ukraine.

The Inhibitor working group is chaired by Prof Paul Giangrande, Chair of the EHC Medical Advisory Group (MAG) and supported by Prof Flora Peyvandi (EHC MAG) and Radoslaw Kaczmarek from the EHC Steering Committee.

The EHC is delighted to formally welcome these volunteers to its Inhibitor Working Group and looks forward to continue working together!

## EHC staff and volunteers update: Welcoming new recruits and changing roles within the EHC

*By Laura Savini, EHC Communications and Public Policy Officer*

*In the last quarter there have been a few changes within the European Haemophilia Consortium (EHC) and we would like to introduce you to new staff and volunteers contributing to our work.*

### **Russian translations**

The EHC strives to serve all of its members and realises that for many of its National Member Organisations (NMOs), Russian is their preferred second (or sometimes even first) language. This is why the EHC has some live Russian interpretation during its Annual Conferences and selected events provided by our fantastic Russian interpreters Mrs Olga Miniuk and Mrs Julia Krivkina. In the past Ms Katja Krichkevitch from Belarus helped the EHC with the Russian translation of some of its communication and advocacy material such as, for example, position papers and our website. Unfortunately Katja had to discontinue her work for the EHC because of a new career opportunity. The EHC wishes to thank Katja for her support with our Russian translations and we also wish her much success in her new professional endeavours.

Following these changes, we are delighted to announce that Mr Sergiy Shemet from Всеукраїнське товариство Гемофілії, the EHC Ukrainian NMO is taking over the role of Katja to help the EHC staff with Russian translations as needed. We are also delighted to announce that the EHC is also looking at translating its newsletters into Russian. With the support of Sergiy, we are also hoping to be timelier in translating our website material. Unfortunately these translations are quite time-consuming, so if there is any material from the EHC that our EHC NMOs wish to see translated into Russian for immediate use, please get in touch with me ([laura.savini@ehc.eu](mailto:laura.savini@ehc.eu)).

### About Sergiy:

*Tell us about yourself*

I am 37 years old and I graduated from Dnipro National University (DNU) in 2001 with a Master's degree in biology. In parallel, I completed an English course and received a certificate of translator in technical disciplines. In 2004, I completed my PhD and worked as a research scientist at DNU for ten years (2004–2014), studying plant adaptation to environmental stresses using mathematical modelling. I published 113 scientific papers, including 15 peer-reviewed articles and registered nine patents. In 2014 I left academic life to run a small translation company specialising in technical topics related to biotech and life sciences.



*Sergiy is a volunteer supporting the EHC Russian translations*

*What is your relation with the haemophilia community?*

I have severe haemophilia A and as a result I have been involved in the work of the EHC Ukrainian NMO since its creation in 2004. Currently, I am the Head of Dnipro Regional Chapter and a member of the Board.

*Tell us about one exciting thing that you are looking forward to in your new role?*

Surprisingly, I found that being a volunteer translator is exceptionally rewarding. First, I mastered my English skills. Secondly, I developed invaluable expertise in business correspondence and more in general in 'troubleshooting' through communication, as I discovered the work of the Ukrainian NMO is

nothing but continuous troubleshooting. Thirdly, being a volunteer translator allowed me to meet friends in many countries who are outstanding and highly motivated individuals putting lots of efforts to make the life of people with bleeding disorders happier. Lastly but most importantly, it is my hope that my work will help unite people within the EHC to work in an even more coordinated and efficient manner.

*Tell us one fact about you that might surprise us?*

Usually, the translation of any article in the field of life sciences is rather easy for me. However, I find it most challenging is to translate names and family names. That is because if you just read an article or any other document, you never really focus on the names. But during translation I noticed that most of the EHC authors have absolutely outstanding names, and their pronunciation can vary from country to country, reflecting the diversity of the cultures. So I usually try to contact the person and find out the correct transliteration.

*When can our members meet you?*

Unfortunately, I will not be at the EHC Annual Conference in Stavanger, but anyone who would like to get in touch regarding translations or any other matters, should feel free to do so by e-mail at [s.shemet@gmail.com](mailto:s.shemet@gmail.com).

### ***EHC Membership***

Most of our readers will know Jo Eerens, the EHC's first and longest-standing staff member who single-handedly managed the EHC office for three years (from 2010 to 2013). From 2013 onwards, Jo has been working part-time (generally Monday, Tuesday and Thursday mornings) providing administrative support to the EHC team and board and, although Jo will be missed in his previous role, we are delighted to inform you that he will now be the EHC's first membership officer! In this position, Jo will be the main liaison person with our NMOs for all matters concerning EHC membership processes and General Assembly-related matters (e.g. election of board members and bidding for conferences) but also general liaison with NMOs. Jo will also be the first contact point for when NMOs have changes within their structures such as changes within the boards and staff but also when NMOs need particular support or have events or activities of interest to others, which they want to share and advertise. In the long-term, we hope that NMOs will also increasingly share information about their activities with the EHC so that we can better learn

about their needs and if appropriate put NMOs with similar issues and activities in touch. As this is a new role, it will certainly still adapt in the future but for now please keep this in mind whenever communicating to the EHC regarding your EHC membership.

About Jo:

*Tell us about yourself*

I was born in Brussels in 1954 and I started to work part-time for the EHC in 2010. I have a Bachelor's degree in philosophy and a Master's in Theology and I did a lot of different jobs until 2007 when I joined AHVH – Hemofilievereniging – Association de l'Hémophilie, the EHC Belgian NMO as its Director.

*What is your relation with the haemophilia community?*

I have mild haemophilia A and as a result I only need to receive clotting factors treatment during surgery or if I am injured, which, as you can imagine has happened in the course of my lifetime. So, luckily I wasn't infected with HIV, although I was infected with hepatitis C (HCV), which I am very happy to announce I have recently cleared!



*Jo is the new EHC Membership Officer*

*Tell us about one exciting thing that you are looking forward to in your new role?*

In my professional career, I have always worked with volunteers and I have always been surprised by how volunteers were able to organise themselves and achieve amazing things. Volunteers need someone to support their efforts, without doing the job for them, and to keep them on track with the broader objectives of their actions. Therefore I am looking forward to being that support person that will encourage them, create connections and broaden their perspectives.

In my experience people in the haemophilia community, because of their history, tend to often have individualist views and are busy with their own issues. They often don't dare to share about themselves because they were told to keep quiet about their disorder. This is one of the challenges that I see in my new role, to bring volunteers together, to share information about projects and issues and to keep in touch with EHC's less active members so that we can ensure that they are well served and represented.

I'm very excited to be the first EHC membership officer and, although the job role has been set out, it is an innovative job within the EHC. And I like very much that challenge!

*Tell us one fact about you that might surprise us?*

Some people don't know, but I'm fascinated by the new technologies of cars, especially the new inventions on engines: engines on magnets, compressed or liquid air, the application of the Tesla-turbine on the engine of a car. Therefore it shouldn't come as a surprise that I am a part-time driving instructor. I teach both practice and theory.

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*"In my professional career, I have always worked with volunteers and I have always been surprised by how volunteers were able to organise themselves and achieve amazing things. Volunteers need someone to support their efforts, without doing the job for them, and to keep them on track with the broader objectives of their actions," says Jo Eerens EHC new Membership Officer who will be the new EHC liaison with volunteers and NMOs.*

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*When can our members meet you next?*

I will be attending the EHC Conference and you can come and meet me at the EHC stand. I will certainly try to reach out to as many NMOs as possible to discuss the work they are currently carrying out, whether there have been any organisational changes and what the main issues are that they are dealing with. But mainly it will be about further developing relationships.

*NMOs should get in touch with you if they want to:*

- Get some help to reach out to another NMO,
- Share a message with the wider EHC membership,
- Put a request for information on a particular topic/issue or if they want to learn how other NMOs are dealing with said topic or issue,
- Share information regarding changes within their board or staff and in particular if there are changes for the EHC contact person within their NMO,

- Share information about events they are organising, and if/where EHC could support them.

### ***EHC administration***

Finally, the EHC is delighted to inform you that Saskia Pfeiffer joined us over the summer to take over Jo's former role and to provide support to the EHC team and board on all administrative and logistical issues.



*Saskia recently joined the EHC to provide administrative support*

About Saskia:

*Tell us about yourself*

I am originally from the Netherlands, but have been living in Belgium for the past 12 years, and have two children. After completing my European studies I worked for more than ten years in the field of women's rights and health. In my private time I love photography and graphic design

*How did you come to work to the EHC?*

After working in the field of women's health and development for ten years, I was looking for a new challenge and a new field to share my experience and develop new knowledge. The haemophilia community is quite new to me, but I am confident that my past experience working for a membership-based organisation will be relevant to the EHC and also it will allow me to continue to pursue my interest in working for an NGO.

*Tell us about one exciting thing that you are looking forward to in your new role?*

I am really looking forward to learning about a new field as well as meeting people in the community. I love to work towards the efficient running of the administrative side of an office and organising events. I am really looking forward to doing both of these things with a new team.

*When can our members meet you next?*

I will be at the next EHC Conference in Stavanger, Norway.

*NMOs should get in touch with you if they want to:*

- Get reimbursement for travel expenses
- Have any information on an administrative question related to events organised by the EHC.

My role is still new but I am sure that much more will be added to this list over time!

*The EHC is delighted to welcome Sergiy and Saskia to its team and to have Jo taking new challenges on board! Please join us in welcoming them and wishing them a successful time and new role within the EHC.*

## NMO News

### NMO profile: Situation in Kyrgyz Republic regarding haemophilia treatment and care

*By Nurbek Orozaliev, President of the EHC Kyrgyz NMO*

*Nurbek Orozaliev gives us an overview of the activities carried out by the Kyrgyz NMO and the status of haemophilia care in Kyrgyzstan.*

The Kyrgyz National Member Organisation (NMO) of the European Haemophilia Consortium (EHC) was established in 2007, and since then a lot of work has been done to strengthen the society and build its capacity. Unofficial data shows that some 350 people with haemophilia live in Kyrgyzstan, a country with a total population estimated to over five and a half million people. Amongst the known patient population, it is estimated that there are some 125 children (up to 18 years of age) and 225 adults. The ratio of haemophilia A to haemophilia B is 80 to 20 per cent.



*Nurbek (centre) during the Kyrgyz NMO children's summer camp (photo courtesy of the Kyrgyz NMO)*

#### **What has been done so far**

From 2007 onwards, much work has been carried out by the NMO. One of our main activities has been to raise awareness about haemophilia and other bleeding disorders with the general public, public media and on social networks. Furthermore, since 2007, coagulation factor concentrates have also been included on the essential medicines list of the country. Finally, patients and the Kyrgyz Ministry of Health (MoH) have been able to reach an understanding about the needs of people with bleeding disorders, which led to the approval of decree 160 ensuring the treatment for children with haemophilia under the governmental programme of 'State Guarantee.' This legislation was approved in April 2008 and has resulted in the purchase of 6,500 international

units (IUs) of both factor VIII (FVIII) and factor IX (FIX) per child with haemophilia under the age of 16 through the resources of the government's compulsory health insurance fund.

2008 was also marked by the Kyrgyz NMO becoming a member of the World Federation of Hemophilia (WFH). Thanks to this, the haemophilia treatment centre in Bishkek (the capital city of Kyrgyzstan) took part, between 2010 and 2014, in a twinning programme with the Mary M. Gooley Hemophilia Centre in Rochester, New York, USA. The participation in this programme ensured further training and education for healthcare professionals in Kyrgyzstan such as haematologists, physiotherapists, laboratory scientists and dentists. This collaboration also led to the organisation of a haemophilia conference 'The 2nd National Haemophilia Symposium' in Kyrgyzstan with the support from the staff of the Rochester haemophilia centre.

In 2014, a specialised training seminar on modern methods for the diagnosis and treatment of haemophilia was also organised. During this meeting we were able to distribute and raise awareness on clinical guidelines for the diagnosis and treatment of haemophilia as primary care. The same year we also launched our website: [www.hemophilia.go.kg](http://www.hemophilia.go.kg).

In cooperation with the Kyrgyz Scientific Haemophilia Centre and haematologists, we organised trainings on haemophilia for patients, family members and caregivers.

In 2015, the Kyrgyz NMO became a member of the EHC (see EHC Newsletter December 2015) and the same year we were also awarded another twinning programme with the haemophilia centre in Istanbul, Turkey. This twinning will be running from 2016 to 2020. That same year we organised for the first time a summer camp for children under 16. The event was held on the shores of the beautiful lake Issyk-Kul, the largest lake in the world. At the end of 2015, we also organised a training for our volunteers to strengthen our society.



*Members of the Kyrgyz NMO during celebrations of World Haemophilia Day (photo courtesy of the Kyrgyz NMO)*

### **The challenges**

Although it has been a step forward, the current amount of clotting factors (6,500 IUs/ per child/ per year) is not enough to satisfy the needs of people with severe and moderate haemophilia A and B for even a month. Furthermore, adult patients have no access to modern haemophilia treatment whatsoever, which very often puts our members at risk of death and disability.

Currently our patients only receive transfusions of blood components such as fresh frozen plasma and cryoprecipitate, which puts them at risk of blood borne infections such as hepatitis B and C as well as HIV.

**The future**

It is clear that much work remains to be done in our country to provide our members with a decent level of treatment and to achieve this we need a stronger than ever NMO. This is why we are currently trying to establish NMO representatives in every region of the country. Additionally, we are promoting the creation of a national registry to gain better knowledge about the state of haemophilia care and what needs to be done. Finally, our advocacy efforts towards the MoH, other ministries and key organisations will continue in order to inform them of the needs of our community and promote access to better treatment.

We are hoping that all of these actions will help us in improving levels of treatment with the purchase of additional coagulation factor concentrates but also with additional funding to support healthcare services and provide psychosocial support of our members.

Finally, we want to strengthen our cooperation with international organisations such as the WFH, the EHC and the Russian NMO as we believe that this is crucial in order to achieve our objectives.



*The Kyrgyz NMO is set to increase its advocacy efforts for better access to treatment and care (photo courtesy of the Kyrgyz NMO)*

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Ситуация по гемофилии у нас в республике: Общество гемофилии в Кыргызской Республике было создано в 2007 году и начиная с того года ведется работа по укреплению общества. По неуточненным данным всего зарегистрировано 350 больных гемофилией. Из них: Детей до 18 лет -125. Взрослых-225. Гемофилия А-80%. Гемофилия В-20%. Что сделано С 2007 года ведется работа по информированию общественности в СМИ Антигемофильные факторы включены в ПЖВЛС (Перечень жизненно важных лекарственных средств). Достигнуто понимание проблем больных гемофилией со стороны Минздрава: Издан приказ №160 от 16.04.08.«О лекарственном обеспечении детей больных гемофилией по Программе Государственных гарантий». Закуплены факторы VIII и IX на средства ФОМС при Правительстве Кыргызской Республики, для больных до 16 лет в количестве 6,500 МЕ на одного больного в год. С 2008 года наше общество является членом ВФГ. В рамках сотрудничества с ВФГ, был организован проект твиннинг программа «Бишкек-Рочестер» с 2010 по 2014. И были проведены курсы обучения специалистов: гематологов,

физиотерапевта, врача лаборанта, стоматолога. Организована конференция по гемофилии «2-й национальный симпозиум по гемофилии» совместно с Американским центром гемофилии имени Mary M.Gooley, Rochester NY USA, который проходил 22-23 октября 2013 года на базе КНЦГ МЗ КР. Был проведен семинар тренинг по современным методам диагностики и лечения больных гемофилией (РЦЗ МЗ КР, 25-27 июня 2014) где были розданы клиническое руководство «Диагностика и лечение гемофилии на первичном уровне здравоохранения». Был создан официальный сайт общества гемофилии в интернете (адрес сайта: [www.hemophilia.go.kg](http://www.hemophilia.go.kg)). На базе КНЦГ, при участии врачей гематологов проводятся образовательные мероприятия для пациентов и их родственников – «Школа гемофилии». С 2015 года стали членами в ЭКГ. Было подписано двустороннее соглашение о твиннинг программе с Стамбульским центром гемофилии и нашим обществом начало с 2016 года по 2020 год. Впервые в 2015 году был организован летний лагерь для детей до 16 лет на берегу озера Иссык-Куль. В конце 2015 года были обучены активисты для работы и укрепления общества гемофилии. Проблемы Препараты факторов свертывания крови для детей до 16 лет в дозировке 6500 МЕ в год на одного больного, не могут обеспечить даже одномесячную потребность больных со средне-тяжелым и тяжелым течением гемофилии А или В. Взрослые больные не имеют доступа к антигемофильным препаратам, которые жизненно необходимы данной категории больных. До настоящего времени активно используется компоненты крови, т.е. переливание донорской свежезамороженной плазмы (СЗП) и криопреципитата. Через компоненты крови: СЗП и криопреципитат, высокая вероятность заражения гемотрансмиссивными инфекциями (вирусные гепатиты В,С и ВИЧ). Наши планы Укрепление общества, создание региональных представителей по всем регионам республики. Создание единого национального регистра больных. Лоббирование интересов общества в различных министерствах ведомствах учреждениях организациях. Увеличение закупки препаратов свертывания крови от Министерства Здравоохранения. Международное сотрудничество (ВФГ, ВОГ, ЕКГ и т.д.) Улучшение медицинской и социальной реабилитации больных.

Материал подготовил: Нурбек Орозалиев президент общества гемофилии Кыргызстана.

## Outsourcing the purchase of coagulation factor concentrates to the United Nations Development Programme: An Ukrainian experiment

*By Sergiy Shemet and Oleksandr Shmilo from Всеукраїнське товариство Гемофілії, the EHC Ukrainian NMO*

*Access to treatment for haemophilia in the Ukraine has been a struggle in the past few years due to the civil unrest and difficulties in the purchase of products. The Ukrainian NMO offers an overview of the situation and suggestions for improving the status quo.*

In Ukraine our government budget for the purchase of all medicinal products is worth about USD160 millions. Although, it is generally estimated that before the Revolution of Dignity<sup>4</sup>, about 40 per cent of this budget was lost to corruption within our Ministry of Health (MoH). To address this issue, in 2015 the Ukrainian Government decided to transfer the tendering process for medical products to recognised international organisations, such as the United Nations

<sup>4</sup> The civil unrest that took place in Ukraine in February 2014.

Development Programme (UNDP), the United Nations Children's Fund (UNICEF) and Crown Agents. In 2015, the procurement of clotting factor concentrates (CFCs) for children was organised by UNDP while the procurement of CFCs for adult patients was organised, for the last time, by our MoH. In fact it was agreed that as of 2016, all CFCs purchases will be held by international organisations. This gave us a unique opportunity to compare the efficiency, in terms of prices and delivery, of UNDP methods compared to those of our own government before all CFCs purchases will be handed over to international organisations.

In order for the UNDP to be able to carry out this new mission many changes were required in our national legislation, something that considerably delayed the 2015 call for tender for CFCs. In fact the 2015 UNDP tender ended up only being announced in January 2016 and closed in May 2016. Another reason for such an extensive delay was that the UNDP had never before dealt with the purchase of CFCs. Our NMO immediately put in many efforts to try to be involved in this process as an expert observer and finally, in the middle of the bid evaluation process, the UNDP reached out to us to ask for European reference prices for CFCs. With the help of international patient organisations such as the European Haemophilia Consortium (EHC) and the World Federation of Hemophilia (WFH), we were able to provide them with this information. We must say that we really appreciated the help from these two organisations as it allowed the UNDP to engage in a more proactive negotiation strategy with the bidders then simply opening the envelopes of the bid offers.

Here we look at the changes brought in by the change of situation. With regard to plasma-derived FVIII (pdFVIII) we note that the price per unit purchased by UNDP for paediatric use decreased by 26 per cent. However, it is important to keep in mind that UNDP also charges about five per cent fees for their general management services and one point seven per cent fees for logistical costs<sup>5</sup>. Despite these additional costs, the final price of pdFVIII for paediatric use was still 20 per cent lower than when purchased by the MoH in 2014.

However we can also see that when the Ukrainian MoH held a tender at the end of 2015, it was also able to achieve a ten per cent price decrease for the purchase of pdFVIII for adult use, compared to its 2014 tender.

With regard to recombinant factor VIII (rFVIII) for paediatric use purchased by the UNDP the price decreased by a striking 30 per cent when compared to rFVIII purchased by the MoH in its 2014 tender process. At the moment we do not have any governmental figures for the MoH 2015 tender to compare this price with, as the government did not purchase rFVIII for adult use.

In addition to *conventional* pdFVIII our government also purchased von Willebrand Factor (VWF) for the prophylactic treatment of severe forms of von Willebrand Disease (VWD). However the purchase process for these products has proven extremely complicated due to the fact that our government sets very specific ratios of VWF to pdFVIII, for e.g. no less than 0.75 IU and 1 IU of pdFVIII present in the product. Furthermore our government can modify these ratios of pdFVIII to VWF in the official medicines list at any time as well as adding any other specific parameters, such as unique dosage of vials and so on.

Such a situation has made it particularly difficult for pharmaceutical companies to engage in the tender process for VWF and make competitive offers. This was demonstrated by the high price increase in price (two fold) of these products compared to the price decreases noted for both pdFVIII and rFVIII. At the moment, the price of VWF is almost twice as high as that of pdFVIII and

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<sup>5</sup> <http://procurement-notice.undp.org/search.cfm>

higher than the price of rFVIII. Another downside of this situation is that, right now, the purchase of VWF is the largest expense in our haemophilia treatment budget and yet children with severe haemophilia A have no access to prophylactic treatment.

When looking at the prices of factor IX (FIX), we note that the Ukrainian MoH has achieved a higher price decrease compared to UNDP. This is most likely due to the fact that our MoH purchased plasma derived FIX (pdFIX). However, the differentiation between plasma derived or recombinant concentrates was not present in either the MoH or in the UNDP tender nomenclature.

With regard to inhibitor treatment, UNDP achieved a reduction of five per cent in price for anti-inhibitor coagulant complex compared to when purchased by the Ukrainian MoH. A ten per cent drop in price compared to 2014.

Both tenders also achieved a price reduction of 30 per cent for the purchase of recombinant factor VIIa (rFVIIa) compared to 2014.

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*In 2015 the Ukrainian Government decided to transfer the tendering process for medical products to recognised international organisations, such as the United Nations Development Programme (UNDP), the United Nations Children's Fund (UNICEF) and Crown Agents.*

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Besides the prices, it is also worth taking into consideration the timelines of the bidding process. The Ukrainian MoH managed to finalise the tenders in only three months (from October to December 2015) and was able to start distributing products in the various Ukrainian regions as of the beginning of 2016. On the contrary UNDP, due to its slow bid evaluation process along with uncompleted changes in Ukrainian legislation, began providing the first supplies of FVIII in June 2016 for factor concentrates intended to be purchased in 2015. This caused a catastrophic situation for children, as they experienced a one-year gap in the CFC supply.

With this analysis in mind, we can draw several preliminary conclusions and also offer some recommendations for the improvement of this process:

#### ***Increase competition for VWD treatment***

Only one product containing VWD and no less than one per cent of pdFVIII is currently available in Ukraine and it results in this product being the most expensive factor concentrate with a price 160 per cent higher than the current price of rFVIII.

Seeing that currently the expenditure for VWF is the biggest expense in our haemophilia treatment budget, we believe that changes are needed in the tendering process to purchase product at more competitive prices.

#### ***Prefer national vs regional tenders***

With larger quantities of coagulation factors purchased through the national tender, it was possible to achieve better prices as showed for the purchase of pd and rFVIII. This was also true when compared to regional tenders, which resulted in higher prices for both FVIII and FIX products. In addition, it is our opinion that patients' involvement in the tender process is exceptionally important. In fact, in some regional tenders, the Ukrainian NMO was able to interrupt the tender process and have restrictions for bidders removed, which allowed a price

decrease of 40 per cent. This was in line with the percentage of the medicines budget thought to end up in corruption schemes.

***Directly purchase from pharmaceutical companies instead of distributors***

We believe that coagulation factors costs could be further brought down by proposing some simple measures to both the MoH and UNDP. To begin with, both UNDP and our MoH should consider purchasing directly from pharmaceutical manufacturers instead of distributors. In fact, we estimate that costs for coagulation factors increase by 40 per cent through the work carried out by these distributors who have been adding fees to the retail price for services such as the registration of the product, its marketing, the participation to the national bids and transport of the products to the hospitals.

We believe that such high prices are also caused by the fact that only a handful of distributors operate in Ukraine and that opening the market to more fair competition could achieve better prices. In 2016 UNDP made one direct contract with a pharmaceutical company and we believe that continuing this practice and reaching out to more companies could further lower prices.

***Ensure a timely announcement of tenders***

We would also like to see tenders announced well ahead of time in order to enable pharmaceutical companies to plan for the long production cycle of plasma-derived factor concentrates. In fact, both in 2015 and in 2016 the tenders were announced so late that manufacturers were unable to plan production properly, which led to higher prices. In this instance, we attribute this problem to our MoH.

***Ensure safety of purchased factors***

We would also like to emphasise that mechanisms should be implemented to ensure that the products purchased are safe. Although the UNDP was able to obtain lower prices with their call for bids, those CFCs were not certified by international regulatory bodies, and were rejected by UNDP

***Hold joint bids for product for adult and paediatric use***

Combining the bids for treatment of both children and adult patients could create a basis for an even further decrease in price thanks to the larger quantities purchased. However, in order for this to happen, our government would need to consider a strict harmonisation between the nomenclature on the medicines lists for each category of patients (i.e. paediatric and adult).

***A final word***

In conclusion it was a great surprise for all of us to find that UNDP was able to achieve only minor price reductions for CFCs compared to other types of medicinal products it usually purchases such as hepatitis treatment, medicines for tuberculosis and vaccines. We believe that this is due to the specificity of haemophilia treatment products but also due to the fact that the market in Ukraine for haemophilia treatment is still quite a closed one, with only a handful of companies operating.

We are pleased to report that the Ukrainian government has already taken some steps to address this issue. In fact, it started to work on new legislation with simplified requirements for marketing authorisation for novel treatments, which are already registered in countries complying with requirements from either the European Medicines Agency or the US Food and Drug

Administration. These amendments were adopted by the Ukrainian Parliament and entered into force on 16 June 2016, shortening the registration period for new products to ten days<sup>6</sup>.

In recent days the draft State Budget for 2017 was announced by the Government of Ukraine. The budget for the purchase of coagulation factor concentrates for adult haemophilia patients was increased by 167 per cent. The budget for the treatment of children with haemophilia was also increased by 68 per cent. Taking into account our goal of reaching two IUs in two years (see EHC Newsletter of May 2016) this could stimulate more manufacturers to enter Ukrainian market right now, when this market is in its phase of active development, which could be considered as good investment into the future success.

## Portuguese National Haemophilia Commission created

*By Miguel Crato, President of the Associação Portuguesa de Hemofilia e de outras Coagulopatias Congénitas, the EHC Portuguese NMO*

*Portugal recently created a national haemophilia council, Miguel Crato, President of the Portuguese NMO explains why this is a milestone for haemophilia care in Portugal.*

7 July 2016 was a very important day for the Associação Portuguesa de Hemofilia e de outras Coagulopatias Congénitas, the Portuguese National Member Organisation (NMO) of the European Haemophilia Consortium (EHC) because it was the day that a bill was published to create the Portuguese National Haemophilia Commission.

The creation of this commission, for which the Portuguese NMO strongly pushed in the last few years, was the fulfilment of a serious gap that existed in our country in terms of management of haemophilia.

We now see that in Europe a majority of countries organising the treatment of haemophilia in a comprehensive and rational way have some form of haemophilia council or commission, so it was imperative that this type of body should be established in Portugal.

The Portuguese NMO presented to the Portuguese health authorities the good practices and good examples from across Europe on the organisation of haemophilia care and, in this regard, the information provided by the EHC was crucial. These elements were included in the dossier presented to our Ministry of Health (MoH) and Secretary of Health who finally recognised the importance of a National Haemophilia Commission.

Careful management of the disease, in terms of treatment and inclusiveness of patients as well as the optimisation of cost-effectiveness were part of the rationale that prompted the establishment of this organism.

The responsibilities of this commission are many and include:

- the establishment of a national registry for bleeding disorders,
- the evaluation of the effectiveness of the rare disease card adopted by people with rare bleeding disorders,
- the development of criteria to create comprehensive treatment centres for congenital bleeding disorders, which are not yet formalised,

<sup>6</sup> <http://zakon5.rada.gov.ua/laws/show/1396-19/paran2#n2>

- the implementation of a working model between the comprehensive treatment centres and affiliated centres around the country and their evaluation,
- the set-up of a referral criteria for emergency routing of patients with rare bleeding disorders,
- the analysis and recommendations of novel treatments,
- the development and update of clinical standards issued by the Portuguese General Health Directorate;
- the development of formal advice for tenders of medicinal products,
- the monitoring of clinical trials for novel therapies.

As you can see, the work of this commission covers all the essential matters related to the treatment of haemophilia and other congenital bleeding disorders that need to be developed in Portugal.

The Portuguese Haemophilia Commission will be composed of a representative of the Portuguese NMO, three haematologists who work closely with people with haemophilia, a representative of the Central Administration of the Health System (i.e. the paying health authority) and a representative of Infarmed, the Portuguese agency for medicinal products.



*Members of the newly established Portuguese Haemophilia Council  
(photo courtesy of the Portuguese NMO)*

We are delighted that such a commission was created and are committed to collaborating and creating a dialogue between all interested parties as well as to provide this commission with the perspective of people with bleeding disorders. We will take every step necessary to fulfil the objectives of this commission and lead haemophilia care in Portugal in the right direction.

## Danish telemedicine initiative: An update

By Bløderforening, the Danish NMO

In the fall of 2015, Bløderforening, the Danish National Member Organisation (NMO) of the European Haemophilia Consortium (EHC), initiated a project about telemedicine (see EHC December 2015 Newsletter). In this article the NMO reports on the project's progress.



*Naja Skouw-Rasmussen (left) is a board member of the Danish NMO and Terkel Andersen (right) is the President of the Danish NMO. (Photo courtesy of the Danish NMO)*

To ensure the progress and national anchoring of the telemedicine project, the Danish NMO established a project committee composed of representatives from haemophilia treatment centres and the Centre for Telemedicine and Tele-healthcare from two regional administrative units in Denmark.

Recently the project won a prize for “Best initiative” among patient organisations in Denmark, thanks to its patients’ lead and involvement. Furthermore, the project was praised for being innovative and the Danish NMO received, along with the prize, a donation worth €1,300 euros.

The first phase of the project is ending and it has resulted in two analysis: a needs’ assessment of people with bleeding disorders, their relatives and healthcare professionals, as well as an assessment of the economic potential achievable by introducing telemedicine in the haemophilia treatment model. With regard to the economic assessment, it has been shown that savings of €1.6 million can be achieved in a period of five years by having patients electronically recording their treatment intake. This is because, it is estimated that it will improve patients’ adherence to their treatment and reduce waste of medicinal products by avoiding medicines reaching their expiry date. Additionally, both analyses show a current demand and need for telemedicine solutions in haemophilia treatment among Danish patients, their relatives and health care professionals.

The project committee is continuously working towards the promotion of the project among relevant parties, to ensure interest, acknowledgement and endorsement so that the project can continue into the next development, testing and implementation phases for novel telemedicine solutions.

*The Danish NMO would like to thank the following organisations that have supported this project: the Health Foundation, the Obel Family Fund and the Jascha Foundation as well as Sobi and Baxalta (now part of Shire).*

## 25 years of rehabilitation camps for patients with haemophilia and other inherited bleeding disorders in Slovakia

*By Martin Sedmina, member of Slovenské hemofilické združenie, the EHC Slovakian NMO*

*Slovenské hemofilické združenie, the Slovakian National Member Organisation (NMO) of the European Haemophilia Consortium (EHC) marks its 25<sup>th</sup> year of holding summer camps and shares with us how these events positively impact and support the NMO community.*



*Martin Sedmina is helping a summer camp participant learning how to infuse (photo courtesy of the Slovakian NMO)*

Slovakia is a fairly young country located in central Europe with an estimated population of five and a half million inhabitants. As a result, the Slovakian NMO, Slovenské hemofilické združenie, is an equally young NMO having been established only in 1990 in what was then Czechoslovakia.

Our NMO was established, following the example of other European countries, to help people with bleeding disorders. In those days the life of a patient with a bleeding disorder was difficult in Slovakia because of the absence of coagulation factor concentrates. The only option for treating haemophilia was anti-haemophilic

cryoprecipitate and, as far as we know, it was inefficient in preventing permanent bleeds and permanent joint damage. So, the first goal of our newly established society was to improve the level of treatment in Slovakia. This literally meant to bring the coagulation factor concentrates into our country. Czechoslovakia was, in those days, a federation of the Czech Republic and Slovakia with each country having the ability to manage its own issues. Both the Slovakian National Haemophilia Centre and the Slovak NMO engaged in discussions with public authorities on the matter of access to treatment. With kind assistance from our friends from abroad, we finally managed to access coagulation factor concentrates for the treatment of haemophilia and in 1992 the first patient with haemophilia was administered with coagulation factor concentrate. In 1993, Czechoslovakia was peacefully separated into two independent countries: the Czech Republic and Slovakia (also known as the Slovak Republic) and the Slovak NMO continued its work in the newly established country.

Two years after the establishment of our society, in 1992, we started to provide summer rehabilitation camps for children and summer rehabilitation stay for adults with bleeding disorders. It is undisputable that meeting together is essential for patients with haemophilia. Our disease is rare and in 1990 the access to information for the common patient was limited. So, we saw it as our duty to bring the information to the patients. Another important issue for patients with haemophilia was, and still is, rehabilitation. We focused on this part of our work very intensively and we brought high quality rehabilitation performed by skilled and experienced physiotherapists to our camps and stays. Our first rehabilitation summer camp for children and adults took place in Turčianske Teplice, a very small and calm spa town in central Slovakia, in the summer of 1992. This venue was not a coincidence and there are two main reasons behind the choice of location. The first reason was that the town is host to a spa specialised in mobility

impairment and the second was that the venue is located in the middle of Slovakia and is easily accessible from every part of the country without too much travelling time, which is very important for people with impaired mobility. The camps were very successful and many people attended those stays.



*Participants during the summer camp (photo courtesy of the Slovakian NMO)*

We started an intense cooperation with the spa of Turčianske Teplice and we quickly became very close partners in helping people with bleeding disorders. New friendships in the society were formed and a new community started to grow and breathe. While providing rehabilitation, we saw how the function of joints was getting better from just two weeks of summer camp. The patients were told how to exercise at home in order to strengthen their muscles to prevent frequent joint bleeds and to live a better life.

Years after our first stay, due to increasing attendance, we separated the camp into the rehabilitation summer camp for children and rehabilitation summer camp for adults. They were still organised simultaneously and in the same venue because the proximity of patients of various ages was important to us. However, summer camp activities began to vary. As the number of units per capita in our country was slowly but regularly increasing, new issues emerged, such as the issue of prophylaxis. We started to teach our patients about the need for prophylaxis and its benefits. As a result the range of self-treatment widely increased and the summer camps were the perfect place to teach patients to self-administer coagulation factor concentrates on their own. Patients became more and more independent with their treatment, resulting in a better



*Participants during the summer camp (photo courtesy of the Slovakian NMO)*

quality of life thanks to their improved health status. In fact, better health meant that they could travel, spend more time with their families instead of being chained to a bed and lying in severe pain from joint bleeds.

In 2001 we started providing rehabilitation and educational summer camps for parents with newly diagnosed children with bleeding disorders of up to six years of age. These camps are aimed at parents who want to learn as much as they can about haemophilia and other bleeding disorders as well as genetics, planned-parenthood and

bleeding management, bleeding prevention and many other issues new parents of children with bleeding disorders struggle with. During the camps we answer questions they do not have enough time to discuss with their haematologist but we also teach them how to be absolutely independent with regard to their children's treatment by showing them how to properly administer coagulation factor concentrates. This camp is held simultaneously with the other summer camps for children because it is really important for parents who are absolutely new in the haemophilia world to see that older children with bleeding disorders can have a normal life. This is something that is very reassuring to them. Furthermore, these new parents have the opportunity to speak to the members of our staff who are mostly patients or close relatives of patients and together with them we can break myths and stereotypes about haemophilia and help them build self-reliant families.

2016 marks the 25<sup>th</sup> anniversary of our summer rehabilitation camps. There are still many things to improve but looking back we see the selfless work and efforts of many patients, relatives of patients and volunteers to make the life of people with bleeding disorders better. The Slovak NMO is also a member of the EHC and the World Federation of Hemophilia and we would like to thank all of those who helped us in becoming an established NMO from the beginnings until now.

## Ukrainian delegation in Lithuanian Summer Camp for children with hemophilia

*By Victor Kronykh and Sergiy Shemet from Всеукраїнське товариство Гемофілії, the Ukrainian Haemophilia Association*

*From 20-26 June 2016, the Lietuvos Hemofilijos Asocija, the Lithuanian National Haemophilia Organisation (NMO) of the European Haemophilia Consortium (EHC), organised a summer camp for Lithuanian children with haemophilia and also invited participants from Ukraine. Representatives from the Ukrainian NMO report on the experience.*



The Camp was held in the Open Air Museum of Lithuania in Rumšiškės on the picturesque coast of Kaunas Lagoon.

The children were engaged in various activities and competitions every day: they studied the healing properties of medicinal herbs, competed in baking traditional gingerbreads, participated in the celebration of the ancient holy day of Ioanne and

created a cartoon movie. During the camp, children spent the whole day outside in the open air and took part in physical activities, something that is not very common for boys with haemophilia in Ukraine. Most importantly these children learned how to live with haemophilia.

Ukraine and Lithuania have great historical relations and therefore it was very interesting for young Ukrainians to visit Lithuania, learn its traditions and make many new friends. Moreover,



taking part in this summer camp gave our volunteers a unique experience on how to organise similar summer camps in Ukraine.

We very much appreciate the invitation from our friends from Lithuania, as well as the support of the EHC for providing some funding for this trip.



*The pictures in the two pages above show the Lithuanian summer camp participants taking part in various activities (photos courtesy of the Ukrainian NMO)*

## Azeri NMO organises event on Multiculturalism and haemophilia

*By Hemofiliyalı Xəstələrin Respublika Assosiasiyası, the EHC Azeri NMO*

*Hemofiliyalı Xəstələrin Respublika Assosiasiyası, the Azeri National Member Organisation (NMO) of the European Haemophilia Consortium (EHC) held an event in June dedicated to multiculturalism titled 'Save the world and the health of children.' Here is the report of this event.*

Azerbaijan declared 2016 to be the 'Year of multiculturalism.' This decision was made by our President Mr Ilham Aliyev to reflect the traditions of tolerance in Azerbaijan and the country's contribution to multiculturalism and inter-civilisation values.

The event was attended by representatives of the Ombudsman Mrs Yegana Jafarova and Mr Mugalib Makhmudov as well as physicians treating children with haemophilia, Professor Mir Eldar Babayev and Dr Elmira Gadimova, leaders of non-governmental organisations.

The event was held as part of a concert with the participation of children with haemophilia and their siblings. Thirty-five children performed national dances, songs and poems from different countries, such as Azerbaijan, Turkey, Russia, Georgia, France, Germany, Japan, India, Ukraine and the United Kingdom

The purpose of this event was to show that children can lead a healthy way of life when there are factor concentrates and adequate treatment of haemophilia.



*Children performing during the event (photos courtesy of the Azeri NMO)*

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Под эгидой Ассоциации Больных Гемофилией Азербайджана 3 июня 2016 году было проведено мероприятие посвященное мультикультурализму под названием "Сохраним мир и здоровье детей."

В Азербайджане 2016 год объявлен "Годом Мультикультурализма."

Это решение принято президентом страны Ильхамом Алиевым, с учетом традиций толерантности в Азербайджане, вклада страны в межкультурные и межцивилизационные ценности.

На мероприятии участвовали представители Омбудсмен Егана Джафарова и Мугалиб Махмудов, врачи, которые занимаются лечением детей с гемофилией профессор Мир Елдар Бабаев и доцент Елмира Гадимова, лидеры неправительственных организаций.

Мероприятие проходило в рамках концерта с участием детей с гемофилией, их братьев и сестер.

35 детей исполняли национальные танцы, песни и стихи разных стран, таких как Азербайджан, Турция, Россия, Грузия, Франция, Германия, Япония, Индия, Украина, Англия

Цель этого мероприятия продемонстрировать здоровый образ жизни детей, когда есть фактор концентраты, медицинская забота о гемофилии.



*Children performing during the event (photos courtesy of the Azeri NMO)*

## Feature Articles

### Researcher spotlight: Dr Roseline d'Oiron

*Dr Roseline d'Oiron\* interviewed by Laura Savini\*\**

*For this issue of researcher spotlight we talk to Dr Roseline d'Oiron a clinician investigator and Associate Director at the Bicêtre Hospital Reference Centre for Haemophilia and Rare Congenital Bleeding Disorders at University Hospitals Paris-Sud, AP-HP, Bicêtre Hospital, Le Kremlin–Bicêtre, France. Some of our readers may know Dr d'Oiron from our last Annual Conference held in 2015 in Belgrade, Serbia, where she presented on 'Genetic and bleeding risk in carriers of haemophilia: diagnosis and care.'*

*In this interview we learn more about Dr d'Oiron's research interests, in particular with regard to carriers in haemophilia, and why she thinks it is time to break paradigms and start to acknowledge haemophilia as a disorder equally affecting men and women.*

#### 1) What are you currently working on?

At the moment, a big chunk of my time is dedicated to the organisation of the next conference of the European Association for Haemophilia and Allied Disorders (EAHAD) in collaboration with the executive committee. The event will take place in Paris in early 2017 (see pg 59).

Another project dear to my heart and on which I spend quite a bit of time, is the French registry on bleeding disorders (FranceCoag). This registry records real world data on patients affected by rare and congenital bleeding disorders including side effects such as anti-factor VIII or IX inhibitors and as such it has become a very important research tool.

Finally another topic of interest is the way in which we structure and organise our haemophilia centre and how we provide patients with a multidisciplinary approach for their treatment.



*Dr Roseline D'Oiron during the 2015 EHC Annual Conference*

#### 2) What does your average day involve?

A typical day of work will involve different activities including medical consultations with patients and the drafting of clinical protocols to ensure we can safely follow patients during labour, childbirth and also surgery.

I also spend a great deal of time interacting with clinicians in other disciplines or with other health care practitioners such as nurses and physiotherapists. I believe that a multidisciplinary approach for the treatment of haemophilia and other bleeding disorders is key as their condition is multifaceted and impacts patients in different aspects of their general health. These meetings do not just cover the treatment of patients and but also look at clinical studies. Additionally there is an ongoing dialogue between different services treating people with bleeding disorders such as

the maternity ward, the service for infectious diseases and the orthopaedics department and discussions are ongoing on how to better organise our interactions and ultimately better serve the patients.

An important part of my day also consists of providing a lot of advice directly to patients, in particular by telephone or emails. We receive many calls with questions from patients, parents and caregivers but also from non-specialist hospitals and/or from other smaller haemophilia centres on how to properly care for people with bleeding disorders in more complicated cases such as, for example, when inhibitors are present. In this respect our coordinating nurse plays a key role and is vital to this service because there is much information that she can already dispense as she has much experience and expertise in this area.

On a personal level, I also like to dedicate some time each and every day to catching up on reading novel scientific publications and bibliography, which I like to share with our team for their information and to discuss whether it can be relevant to our work.

In my centre we also carry out clinical trials. We are often asked to take part in clinical trials by pharmaceutical companies for novel products but we also initiate our own studies. For instance, a particular theme that I cherish is carriers and I often find myself asking questions on how to better treat carriers and women with bleeding disorders and one way to answer these questions is by conducting scientific studies.

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*For carriers in particular there are two main issues that colleagues and I are constantly trying to answer. The first one is how to reach out to known and potential carriers early enough so that we can accurately test, diagnose and give them all the necessary information they'll need to make informed decisions regarding family planning, prenatal diagnosis, child bearing and childbirth. The second point is that it has been suggested that for every three people with haemophilia there should be at least one woman with mild haemophilia and yet we do not see these women in neither our registries nor in our clinics. My questions is how to better identify these women.*

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For carriers in particular there are two main issues that colleagues and I are constantly trying to answer. The first one is how to reach out to known and potential carriers early enough so that we can accurately test, diagnose and give them all the necessary information they'll need to make informed decisions regarding family planning, prenatal diagnosis, child bearing and childbirth. Unfortunately every so often women arrive at our centre when they are already well into their pregnancy or have already given birth and they then have to digest a lot of information such as a diagnosis of being a carrier or of having themselves lower levels of coagulation factor VIII or IX and that their child will have haemophilia. This leads to very difficult situations where these women face many questions regarding their pregnancy, childbirth and the health of their child.

From my personal experience but also from what I hear from colleagues in France or abroad I can say that still today some carriers are deprived of the adequate information and knowledge on their condition to take informed decisions about their reproductive health and family planning.

This is due to various factors including a lack of information from non-specialist healthcare professionals or from their families.

This results from various very personal situations. It may be that the family knows or suspects that a woman is a carrier but decides, for whatever reason, not to share this information or at least not to explain what it concretely means to her so that she goes ahead with a pregnancy without fully realising what the consequences can be. Another situation is the lack of action taken by the clinician despite the disclosure of a carrier status by a pregnant woman. The simple fact that an anticipated multidisciplinary plan for delivery could effectively secure birth of a child with haemophilia should be shared more often and more widely.

So my question is: what else can be done by us, specialised healthcare professionals, to reach out to these women early enough so that we can carry out the right tests and give them a correct diagnosis, allow informed choices well ahead of their first pregnancy in order to ensure the safe birth of affected babies? This is something that truly keeps me up at night. Reaching out to them is not an easy task. In the past we have tried to reach them through family members that would come to our centre for consultations but that was not always successful. So now we have developed a leaflet for our patients that can be easily shared amongst the family members and that, we hope, will start a discussion within the family and have these women screened early enough so that we can give them all the necessary information about the choices available to them in terms of prenatal diagnosis, childbirth and treatment options for their children. My second research question on carriers that I am constantly puzzled by, and very interested in, is

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*Many women I meet are in favour of being labelled as mild haemophiliacs as they believe that this would make things easier for their medical follow-up.*

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the fact that we now know that approximately 30 per cent of them have factor levels similar to mild haemophilia. It has been suggested that for every three people with haemophilia there should be at least one woman with mild haemophilia and yet we do not see these women in our registries and in our clinics. As an example in the global survey from the World Federation of Hemophilia (WFH), women only represents three to four per cent of people with haemophilia. My question is how can be better identify and screen these women.

The problem for me is that there is no agreement between doctors, patients and patient organisation on how to label these women. Additionally, things are made even more complicated when carriers have normal levels of factor VIII or IX but experience bleeds as if they had mild haemophilia while others have reduced levels of factor VIII or IX (<40 per cent) but they do not present any abnormal bleeds. This is why I think that it is of utmost importance that physicians listen to their patients' narrative concerning bleeding episodes. In my opinion it is important not only tests for factor VIII or IX levels to look for a deficiency risk, but also to perform a bleeding score in order to have a more precise profile of the bleeding risk. Actually, this should also be done in male with mild haemophilia. In addition, tests for levels of factor VIII or IX levels should be both carried out prior to the pregnancy, as we know that pregnancies and other events such as, for example, pharyngitis, will raise normal levels of factor VIII and skew the test results.

Many carriers with low factor levels and bleeding experiences I meet are in favour of being labelled as mild haemophiliacs and I believe this would make things easier for their medical follow-up. Although, I think that many non-specialist healthcare professionals or families would be

confused if we tell them that a woman has mild haemophilia but is for example carrier of severe haemophilia. This would require a lot of education to ensure an appropriate understanding from families and professionals

### **3) Why is your work important? What do you hope the impact of your work will be?**

Besides what is mentioned above, it is my hope that through my work I will be able to improve the knowledge of carriers about their genetic diagnosis. I am hoping that known carriers will be better informed about their diagnosis and their bleeding profile so that we can improve not only their treatment and wellbeing but that of the whole family.

In parallel, I am hoping that this work will also draw the attention that men affected by haemophilia also contribute to the transmission of haemophilia by passing on the affected gene to their daughters. We need to emphasize that haemophilia is not solely transmitted by women and that affected males are also *carriers*.

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*From my personal experience I can say that still today in France many carriers are deprived of the adequate information and knowledge on their condition to take informed decisions about their reproductive health and family planning.*

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### **4) What other research question keeps you awake at night?**

Besides what I have already mentioned above, my hope is that we, as a community of patients, healthcare professionals and patient organisations, can work together to identify an appropriate care for those carriers that suffer from mild haemophilia with bleeding episodes that will appropriately reflect their situation and need for treatment and medical follow-up. I believe that unless there is an active dialogue between all parties, we will not be able to shift the current paradigm.

### **5) Tell us one thing that you learned about haemophilia and/or other bleeding disorders that really surprised you.**

There were two encounters at the beginning of my career that really marked me. The first was a consultation I had with a patient who had mild haemophilia but no bleeds, perfect joint scores, no co-infections or any other healthcare problems and yet this person was having difficulties in coming to terms with the fact that he had haemophilia and blamed the disease for a series of negative situations in his life, such as his employment situation and marital status. My second encounter was also during a medical consultation with a patient who was experiencing the total opposite of the first one. This individual had severe haemophilia, damaged joints, many co-morbidities and other medical problems and yet this person was meaningfully employed, happily married and a father. This dramatic difference really struck me and made me realise how much the environment and psychosocial situation can impact an individual in his or her perception of pathologies and how to deal with them. This also taught me an important lesson, which is that one can never make assumptions about the impact of a disease on an individual and especially as physicians we need to keep an open mind and listen to our patients and how they are living with their condition.

Another striking aspect of this disease and medical area is that time is very subjective and that the haemophilia centre becomes a part of the patient's life at different points in his or her life. For instance I once had a carrier bringing in her daughter for diagnosis, this girl must have been in her late teens and was diagnosed as a carrier. Then years passed and some fifteen years later, I saw this girl again, now a woman and pregnant, ready to become a mother. We just continued the conversation left besides during these years. Another example is that of a gentleman whose brother died due to a co-infection in our centre. Years later his niece gave birth to a child also in our centre. This gentleman was marked by how the same place could bring back terrible memories and yet give him new joyful experiences. In a way our work and place of work is linked to important moments in the lives of these individuals that concern life and death, events that can be sad and happy and that are interlinked.

#### **6) How did you become involved in this field and on this topic?**

As for many others, my specialisation was linked to exciting encounters and career opportunities. I started my professional experience in the onco-haematological department of another hospital where I was both working in the laboratory and treating patients affected by leukaemia and lymphoma. The hospital where I was working closed this department and I found another opportunity to work in my current hospital in the haemostasis laboratory.

What I love about my job is the duality of the clinical work and biology laboratory activity. I also like the fact that we need to help patients to transition from paediatrics into adult care and, finally, I appreciate the fact that as a healthcare professional specialised in a rare condition I need to excel in what I do. I love that I can be an information resource for both patients and other healthcare professionals. Again I think that this aspect is shared by many working in the area of rare diseases.

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*I am hoping that my work will also draw the attention to the fact that men affected by haemophilia contribute also to the transmission of haemophilia by transmitting the affected gene to their daughters. We need to emphasize that haemophilia is not solely transmitted by women and that affected males are also "carriers".*

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#### **7) What is the most frequently asked question about your work?**

A recurring question from my students is whether women can have haemophilia. I do not know precisely why but it is something that they find fascinating. Maybe it's because in our collective psyche we associate haemophilia with men and we assume that women cannot have haemophilia as they would not get through menses.

#### **8) What is the next big thing that is coming in your field of work?**

I think we are getting at a very exciting time in terms of novel treatment options and perhaps most importantly a novel approach towards the treatment of bleeding disorders, which is moving on from replacing the missing protein (coagulation factor) to improving the general haemostasis. Additionally, we are now having the first results for gene therapy with promises of cures of bleeding disorders.

### 9) If you had not been working on this topic, you would be working on...?

I wanted to become a cardiac surgeon but my husband thought that it would be a too time-consuming activity for me, little did he know that the field I ended up working in was equally time consuming. I also have a passion for playing the piano and would have loved to be a professional pianist.

### 10) What would be your advice or recommendation to someone with a bleeding disorder?

My advice to patients is 'Teach your doctor!' and 'Listen to your Doctor'! I think it's very important that patients share their narrative with their doctors on the world they live in. It is important for doctors to understand patients' reality and how the disease impacts their daily lives. However, patients should also give their doctors the opportunity to give their insight as they do have much expertise in their disease area. In short, ensure that your relation with your doctor leads to mutual exchanges.

*\* Dr Roseline d'Oiron is a clinician investigator and Associate Director at the Bicêtre Hospital Reference Centre for Haemophilia and Rare Congenital Bleeding Disorders at University Hospitals Paris-Sud, AP-HP, Bicêtre Hospital, Le Kremlin-Bicêtre, France*

*\*\* Laura Savini is the EHC Communications and Public Policy Officer*

## A new era of haemophilia treatment awaits

*By Glenn Pierce, MD, PhD\**

*Dr Glenn Pierce gives us a comprehensive overview of the novel technologies (some still in the pipeline, while others already marketed) for the treatment of haemophilia and how these same technologies offer hope not only for haemophilia patients but also for people affected by rarer bleeding disorders and inhibitors.*

The doctors told my mother when I was diagnosed with severe haemophilia: *"This is a good time to be born with haemophilia. We'll have a cure in five years."* Sixty years ago, that statement was ridiculous - the fact that factor VIII (FVIII) and von Willebrand factor were two separate proteins wasn't even known. But in 2016 a cure may actually happen within five to ten years. As new therapies with increasingly longer half-lives are appearing in clinical trials and the marketplace, the need for repeated injections multiple times a week is giving way to injections every one to two and even four weeks. Some are even asking: *"Do I need a cure if I can inject once or twice a month?"*

This is an unprecedented time for ground-breaking research in all areas of medicine! The world of bleeding disorders research has never had this much scientific attention. Today research is occurring in three main areas: extended half-life (EHL) factor products, bypassing agents, cell and gene therapy.

### Research area 1: EHL factor products

*What exactly is half-life?*

Half-life is the amount of time it takes for coagulation factor to decrease its circulating concentration by half or 50 per cent. It's calculated by taking a series of blood samples over a specified time span after infusing clotting factor and then measuring how much factor remains in

each sample. When graphed these measurements are called pharmacokinetic (PK) curves and they show how rapidly your body eliminates factor. Factor concentrates half-life may vary from product to product and from person to person, so it's important to know how long a particular brand of factor lasts in *your* body and this result may be significantly different than the average half-life of that brand. By knowing how quickly you eliminate factor from your blood, your haemophilia treatment centre (HTC) team can tailor a prophylactic dosing schedule specific to your needs.

For instance immediately after infusing 50 International Units per kilogram (IU/kg) of standard FVIII, the level of circulating FVIII in the body is at 100 per cent. If the product has a 12-hour half-life, then about 12 hours later, the FVIII level will be at 50 per cent (half has been eliminated). Then 24 hours after the original injection only 25 per cent is left. Two days after the initial injection, the FVIII level is at six point twenty-five per cent.



*Dr Glenn Pierce has contributed as a speaker and moderator at EHC events.*

*How does this work for a prolonged half-life product?*

If half-life is on average 50 per cent longer, like 18 hours, then 36 hours after the original injection, FVIII levels are reduced by two half-lives, so 25 per cent is left. Three days after the initial dose, FVIII is at six point twenty five per cent.

In other words when using a prolonged half-life product with an 18-hour half-life, you may be able to go an extra one to two days between

infusions, as compared to a standard product with a 12-hour half-life. One point is important: these are AVERAGES! They are calculated from individual patients who have longer or shorter half-lives. Each of us metabolises and eliminates the clotting factors at different rates. Generally what has been found is that if you have a shorter half-life with conventional clotting factors, your half-life will be shorter when using EHL products. Vice versa if you have a longer than average half-life with conventional clotting factors, your half-life will be even longer on EHL products. Thus each of us benefits from EHL products but the benefit is proportional to your individual half-life on conventional products.

**EHL FVIII**

Two prolonged EHL FVIII products have already been marketed in the United States (US) and one product has also been approved in Europe. One of the two products has a mean half-life of 19 hours, while the other one has a mean half-life of 14.3 hours. As noted above, conventional FVIII products have an average half-life of about 12 hours.

*Why are the two half-lives so different?*

Each product is manufactured using a distinct technology to prolong the half-life, which confers new properties to the FVIII resulting in the extension of FVIII half-life in different amounts.

Clotting factors, like all the other unique proteins in the blood, circulate for differing lengths of time: some proteins last for a few minutes or hours while others last for several weeks. Two proteins in particular, albumin and an immune antibody called immunoglobulin G (IgG) last for

more than 21 days. Albumin, also known as human serum albumin, is the most common protein found in blood plasma and makes up about 50 per cent of plasma proteins. On the other hand IgG, or immunoglobulin G, is a Y-shaped protein used by the immune system to fight infections by inactivating infectious agents like viruses or marking them for removal or destruction by other immune system cells.

*Why do some proteins last a long time and others not so long?*

The answer to this question helps us understand how the longer half-lives of proteins like IgG and albumin may be exploited to increase the half-life of clotting factors. Many proteins in the blood are absorbed and broken down by endothelial cells: the cells that line the blood vessels and IgG usually manages to escape this process. In fact, an area on the backend of the protein, called Fc, allows the protein to bypass the breakdown process and causes the endothelial cell to eject the protein back into circulation. Scientists were able to develop a recombinant form of FVIII fused to an Fc molecule. Through this process the endothelial cells eject the factor back into the bloodstream, extending its half-life. This resulted in an **FVIII product fused to Fc** (FVIII-Fc) with a 50 per cent longer half-life than standard FVIII products.

Another EHL FVIII uses a different technology to prolong its half-life called **PEGylation**. This is the process of attaching polyethylene glycol (PEG), a petroleum derivative that is found in a variety of products including cosmetics and food, to the FVIII molecule. The use of the **random addition of PEG to the FVIII** results in the protein being coated with PEG, protecting it from damage and destruction and resulting in a longer half-life of some 14.3 hours, i.e. 16 per cent longer than that of standard FVIII products.

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*It's the most exciting time in haemophilia because many technically cutting-edge research groups have been attracted to this disease area as it seems an easy target for gene and cell therapy. [...] Nonetheless hitting the target hasn't been an easy feat given the number of failures over the past 15 or more years. The incremental progress made by scientists brings our community closer to the goal of a permanent cure.*

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Two other prolonged half-life FVIII products use a different type of PEGylation called **site-specific PEGylation**. In contrast to the random PEGylation, site-specific PEGylation is highly controlled and results in the attachment of only one PEG molecule on each FVIII molecule. This has been accomplished by changing one amino acid on the FVIII molecule to allow it to function as a PEG binding site. A similar approach to the use of PEG is a technology called **glycoPEGylation**. In this process, a single PEG is attached to a sugar that is attached to a single site on the FVIII molecule. The precise control in the placement of a single PEG on each FVIII gives both of these molecules an 18- to 19-hour half-life, comparable to the FVIII-Fc technology described above. Both these prolonged half-life PEG FVIII products are still in clinical development, but their main clinical trials are completed.

A fifth approach to prolonging the half-life of FVIII involves making a slight change in the structure of the FVIII molecule. Normally FVIII is synthesised in the liver as a single long protein called a *single-chain*. When secreted from the cell, the single-chain FVIII molecule is broken into two parts,

or two connecting chains, which then travel in the bloodstream as a two-chain molecule. The two chains of FVIII can be bonded back together to form a more stable single-chain molecule. Data from clinical trials using this technique indicate that the **single-chain FVIII** has a half-life of 14.5 hours, similar to the FVIII prolonged with the random PEGylation technique described above and marginally better than the two chain FVIII products that have half-life of 12 hours.

Summary of EHL FVIII techniques and results		
Prolongation technique for FVIII	Average half-life	Half-life Increase compared to regular FVIII products
FVIII-Fc The FVIII protein is fused to Fc	≈ 19 hours	+ 50%
Random PEGylation The FVIII protein is coated with PEG	≈ 14.3 hours	+ 16%
Site-specific PEGylation The PEG is directly attached to the FVIII protein	≈ 18-19 hours	+ ≈ 50%
GlycoPEGylation Also a site specific PEGylation, except that in this case the PEG is attached to a sugar attached to the FVIII protein	≈ 18-19 hours	+ ≈ 50%
Single chain FVIII The two chains of the FVIII protein are bonded back together into a single chain	≈ 14.5 hours	+ ≈ 16%

*With one prolonged half-life FVIII product already on the market in Europe and more coming, how will you decide which one to use?*

Clinical trials results showed that the two marketed products in the US using FVIII-Fc and random PEGylation technique as well as the product using the single chain FVIII technique (still in development) were as effective as standard FVIII products in stopping bleeding episodes when used on demand. Additionally they can prevent, like all standard products, nearly all bleeding episodes when administered prophylactically in a variety of dosing schedules or dosing regimens. The new products were also shown to be safe. There were no unusual adverse events and no increased risk of inhibitor development. Prophylactic dosing regimens for standard FVIII products are typically three times a week or every other day to ensure that FVIII *trough levels*, i.e. the factor VIII level just before the next dose, are sufficient to prevent breakthrough bleeding. For prolonged half-life products like those using techniques such as Fc fusion, site-specific PEGylation and glycoPEGylation (two products using the two latter techniques are still in development) dosing once or twice per week is effective in preventing most breakthrough bleeding.

Because all EHL products were studied in different ways in their clinical trials, it's best to review the product inserts that come with each product (also available online after products are approved by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA)) and then talk to your HTC team about which is best for you.

A safety concern has been discussed since research into PEGylated FVIII started more than ten years ago: "*How is PEG removed from the body?*" The body does not metabolise or break down PEG into smaller units, as it does with natural compounds such as proteins and carbohydrates and small PEG are more easily excreted than large PEG. Additionally small PEGs are removed from the blood mainly by the kidneys and then excreted through the urine. On the contrary, larger PEGs do not easily pass through the kidneys and it's believed that most are excreted through the liver to the intestine and then eliminated in the faeces. PEGylated FVIII products use some of the largest PEG and due to the fact that it's not possible to eliminate every single molecule of PEG, because PEG is not broken down, some PEG remains in the body. Research has shown that the impact of PEG remaining in the body seems minimal but the long-term safety of PEGylated FVIII products has not been conclusively established. In fact, most other PEGylated drugs are used in other diseases for short periods of time and use smaller PEGs. Haemophilia is one of the first instances where PEG will be administered over many years and even decades. So it will be important to understand the safety risks versus benefits when considering a PEGylated factor and to discuss this with your health care provider.

### **EHL factor IX (FIX)**

Three technologies have been used to prolong the half-life of FIX.

The first one is the same ***Fc fusion technology*** that is used with FVIII as described above but in this case Fc is fused to FIX instead of FVIII. This technology significantly increases the half-life of FIX over standard FIX products from about 19 to 24 hours for standard FIX products to an average of 86 hours for FIX-Fc. Most importantly this product reduces the number of prophylactic infusions required to prevent bleeding. Standard half-life FIX products typically require twice-a-week dosing to maintain good coverage and prevent bleeding. By contrast the product using this EHL technique can be used weekly and in the clinical trials about half the patients had minimal breakthrough bleeding with every-two-week dosing. FIX-Fc has been licensed by the EMA.

The second prolongation technology for FIX uses ***albumin fusion technology***. This technique uses the same recycling pathway as described above for Fc but instead of using Fc, the FIX molecule is fused to albumin. Because, as described above, albumin circulates for at least 21 days, it can also be used to extend half-life when fused to other proteins. Good results have been reported from the clinical trials of the FIX-albumin fusion product and a very prolonged half-life of 101 hours has been observed in PK studies. The product using this extension technique was approved by the FDA for dosing every one to two weeks and was also approved by the EMA in April of this year.

The third prolongation technology is ***glycoPEGylation***, which is the same concept as the one used for FVIII as referred to above. In this case glycoPEGylation is used to attach PEG to one of two sugars on the FIX molecule. The clinical trial reports good results and a prolonged half-life of 92 hours. The glycoPEGylated FIX product also completed a successful phase III clinical trial in 2013 but has not yet been filed for marketing authorisation with the FDA or EMA.

All three of these EHL FIX products are effective and safe according to their clinical trials data. They each stopped bleeding episodes and prevented almost all breakthrough bleeding when used

prophylactically. No increased incidence of inhibitors was detected and no other unusual adverse events were seen in clinical trials. Dosing regimens are currently every seven to ten days for FIX-Fc fusion products with half the patients in the clinical trial achieving every-two-week-dosing. For FIX-albumin fusion products dosing is every one to two weeks. Finally, although the EHL FIX product using glycoPEGylation is not yet approved, its clinical trial tested weekly and longer dosing intervals with excellent results.

Summary of EHL FVIII techniques and results		
Prolongation technique for FVIII	Half-life	Suggested dosing for infusion
FIX fused to Fc (FIX-Fc)	≈ 86 hours	Every 7 to 10 days
FIX fused to Albumin (FIX-albumin)	≈ 101 hours	Every one to two weeks
FIX prolonged with GlycoPEGylation	≈ 92 hours	Every week or longer (still in development)

## Research area 2: Bypassing agents and biosimilars

Developing and managing inhibitors is the greatest unsolved problem in haemophilia today. Bypassing agents like recombinant factor VII a (rFVIIa) and other anti-inhibitor coagulant complex offer some control of bleeding in people with haemophilia and inhibitors (PWI) by skipping the need for FVIII or FIX in the clotting cascade. But these agents don't completely work when administered prophylactically and don't control bleeding as well as standard FVIII and FIX in people without inhibitors. Three widely differing scientific avenues are being researched to address the urgent need for better therapies for PWI.

### *Extending the half-life*

One technology involves prolonging the half-life of FVIIa, which has a very short half-life of about 2.5 hours and may require several infusions every few hours to bring a bleed under control. One product under development is extending the life of rFVIIa with albumin fusion. In early clinical trials this technique has demonstrated a half-life of 8.5 hours or three times longer than standard rFVIIa. One of the goals in developing an EHL FVIIa is to initiate and maintain the formation of a stable clot similar to clots achieved with infusions of standard factor concentrates. The hope is that by maintaining FVIIa in circulation for a longer time, with fewer infusions, a more stable clot will form as compared to standard FVIIa. No data are available yet on FVIIa-albumin's effectiveness. This is the same technology as FIX-albumin and takes advantage of the same recycling pathway used by Fc fusion clotting factors.

These next two novel approaches being researched by several companies don't involve the infusion of any clotting factors or bypassing agents.

### ***Bispecific antibodies***

You may know that FVIII works in the clotting cascade by bringing FIX and factor X (FX) together and activating them by in turn activating other clotting factors, which eventually will result in the formation of fibrin fibres. These are stringy proteins necessary for a strong clot. In the absence of FVIII or FIX, very little fibrin is formed and this results in weak clots that easily break down, causing prolonged bleeding, i.e. haemophilia.

A new antibody (see EHC newsletter April 2014, pg 35) is been developed to replace FVIII. Antibodies are, as mentioned above (see pg 48) Y-shaped proteins produced by the immune system. They typically have two arms that bind or stick to one target such as infectious agents (e.g. viruses) to eliminate them from the body. Through the process of recombinant DNA technology and genetic engineering scientists have been able to develop a bispecific antibody that binds to two different molecules. In this case one arm of the genetically engineered bispecific antibody binds to FIX and the other arm binds to FX. So that the antibody latches onto FIX and FX in the bloodstream and brings them together. Essentially the antibody is doing the job of FVIII.

In early clinical testing this bispecific antibody functions like FVIII and was effective in preventing bleeding in FVIII-deficient patients with and without inhibitors. That's right! This antibody isn't just for PWI but may be used by all patients with haemophilia A. Additionally it doesn't require venepuncture (an injection in the veins) as it's administered as a weekly subcutaneous injection. In these trials patients were protected from most bleeding episodes with the bispecific antibody product alone without the need for prophylactic FVIII treatment. Unsurprisingly this product has generated much interest in the haemophilia community and larger scale clinical trials using subcutaneous infusions once every one to two weeks are under way now.

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*Some are even asking: "Do I need a cure if I can inject once or twice a month?"*

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### ***Stopping naturally occurring inhibitors***

Finally there is another approach that doesn't involve the infusion of clotting factors and targets the part of the clotting cascade that shuts down the clotting process.

*How do we stop bleeding by stopping part of the clotting process?*

In addition to clotting factors like FVIII and FIX that participate in forming a blood clot, our bodies also have naturally occurring inhibitors that keep the clotting cascade in check by shutting it down. This is necessary, for instance, to prevent unwanted clotting that could possibly result in a stroke or heart attack. People with haemophilia have enough trouble making clots without their own coagulation inhibitors trying to shut down the process.

*Could these naturally occurring inhibitors be neutralised to allow the clotting process to proceed with little or no replacement clotting factor?*

This is the question that scientists are trying to answer with research focusing on two powerful naturally occurring inhibitors: one is tissue factor pathway inhibitor (TFPI) and the other is anti-

thrombin 3 (AT3). Two pharmaceutical companies have developed antibodies that can bind to and eliminate TFPI in the bloodstream. These are currently being tested in early human clinical trials to see if they can improve clot formation in patients with haemophilia and PWI by reducing the negative effect of TFPI on clot formation. No data on effectiveness are available yet.

Another pharmaceutical company has made a completely different type of molecule to inhibit AT3: it's called a RNA inhibitor. RNA is the message that DNA (genes) uses to make proteins in the cell. The RNA inhibitor binds to and eliminates the AT3 RNA, preventing the liver from making AT3 protein. Clinical trial data on humans suggest that the RNA inhibitor is effective in preventing bleeding when patients are given a monthly subcutaneous dose sufficient to block the production of most of the AT3 protein and without the use of any clotting factor. This anti-AT3 molecule will be tested in larger studies in haemophilia A, haemophilia B and all PWI.

The early clinical data for both the bispecific antibody and the RNA inhibitor are very encouraging when used in both inhibitor and non-inhibitor patients. Larger scale clinical trials are under way or will start soon to confirm and extend these data. If confirmed, both drugs may offer a meaningful advance for PWI and may be used by non-inhibitor patients instead of FVIII or FIX (ALN-AT3). Both drugs can be administered subcutaneously and will have prolonged interval dosing.

### **Research area 3: Cell and gene therapy**

Our community dreamed of a cure for haemophilia long before my haematologist's conversation with my mother in 1956. Since human gene therapy clinical trials began in earnest in 1990, haemophilia has been touted as an ideal disorder to research and cure. But it's now 2016 and we are still waiting. Are we much further along?

The goal of gene therapy is to somehow put the correct blood-clotting code (DNA) for making FVIII or FIX into our cells so they can then produce factor on their own. If made in sufficient quantities, this procedure would cure haemophilia.

The problem is how to get that clotting factor genetic code into our cells? In gene therapy the DNA with the correct code is transported into our cells by viruses. Viruses were chosen to transport the good DNA because they are very good at infecting cells. In fact they have evolved over hundreds of millions of years to become expert at injecting their genetic material into cells. A particular type of virus called **adeno-associated virus or AAV** has been the workhorse of gene therapy because when it infects humans, it causes no known disease and typically produces only a mild immune response. These AAV vectors (i.e. gene transporters) have been genetically engineered for gene therapy and have had their viral genes removed and replaced with FVIII or FIX DNA. The virus is then grown to very high quantities and injected into patients. Much of the virus goes to the liver, the normal site of FVIII and FIX production where it enters the liver cells and delivers the instructions for making FVIII or FIX.

Gene therapy, which sounds simple in theory, has many challenges: *“What's the best vector or transporter to use without causing an immune response that would destroy it? What vectors could we use that we're not already immune to? What vectors are capable of carrying a large gene such as the FVIII gene? What vectors can place the gene into a cell's DNA where we want it?”* The answers to these and many other questions are technically challenging and that's why it has taken researchers so long to get to this point of some early successes.

Over the past five or six years a small number of severe haemophilia B patients in a successful clinical trial at University College London (UCL) and the Royal Free Hospital London have been cured with gene therapy using a viral vector developed at St Jude Children's Research Hospital in Memphis, Tennessee. Their FIX activity is one to six per cent and they have few to no bleeding episodes.

Currently multiple haemophilia B clinical trials are being conducted. They are variations on a theme, testing improvements in all stages of the process from construction of the vector to the type of FIX gene to improvements in manufacturing. Results reported to date are cautiously encouraging with a few more patients making a small amount of normal FIX. One pharmaceutical company has licensed the St. Jude's/UCL technology and has enrolled five people with haemophilia B in a gene therapy clinical trial that started in 2015 with two of the five patients producing four point five and five point five per cent levels of FIX, based on a press release recently published.

In other haemophilia B gene therapy studies researchers have identified a super-active form of FIX, called **FIX Padua** that was first identified in 2009 in a man in Italy who was experiencing excessive clotting. This FIX variant is being evaluated for gene therapy by several groups because it might solve one of the current problems with gene therapy, i.e. low *expression* rates or in other words low factor levels produced as a result of gene therapy. The FIX Padua variant might solve this problem because it has about seven times the activity of normal FIX. So an expression of six per cent using a normal FIX gene would be equivalent to an expression of 42 per cent using FIX Padua. This would truly result in a cure for haemophilia B, even if not much FIX protein is made. Recently three pharmaceutical companies have taken this FIX variant into clinical trials. In 2015, one of the three companies reported some variable but, in some cases, positive data of FIX levels of ranging from zero to 26 per cent. A second company recently reported data in four patients using FIX Padua with expression levels in the 30 per cent range. These results are very encouraging and point the way for larger scale clinical studies.

#### *What about gene therapy for FVIII?*

FVIII is much more difficult to work with than FIX because of its large size. The viral vector almost every research trial is using is adeno-associated virus (AAV) and viruses have evolved to carry their own genetic material and not much else. In order to be used for gene therapy most of the viral DNA has to be removed and our DNA *payload* inserted. Some viral vectors can carry larger genetic payloads than others. AAV, unfortunately, can carry only a relatively small payload and the FVIII gene overstuffs this virus making production and manufacturing difficult. Still one company has an AAV-FVIII product in clinical studies and other gene therapy companies are actively pursuing this vector too. The AAV-FVIII currently being studied recently reported data that showed six patients receiving their high dose of AAV-FVIII with FVIII levels of four to 60 per cent in five to 20 weeks after receiving the injection. This preliminary result suggests more positive results for people with haemophilia A who will not be far behind the positive results seen in multiple clinical trials for people with haemophilia B.

Gene therapy for haemophilia may benefit from using a different vector other than AAV, for example one that can carry a larger payload and is more easily developed into a therapeutic product. Research is ongoing on at least one additional viral vector system, **lentiviruses**, which have been successfully used for gene therapy on bone marrow stem cells. Diseases such as sickle cell disease and some immunodeficiency diseases have been cured by using gene therapy to introduce corrected genes into bone marrow cells removed from the patient. The cells are then

grown to large quantities outside the body and reinjected into the patient curing or partially curing the disease.

Speaking of **stem cells**, these are the cells in the body that have the ability to produce any type of cell, including those cells that make up our tissues and organs. If cells from a haemophilic patient's liver could be removed via biopsy, cultured and turned into stem cells in the laboratory then the gene for FVIII or FIX could be placed into the stem cells and the cells grown in the lab to large quantities. These stem cells could then be changed into liver cells and reinjected into the same patient. The new liver cells would make and secrete FVIII or FIX into the blood and cure haemophilia. Is this science fiction? Maybe not. This kind of research worked in mice in two different laboratories in Korea and the Netherlands (see also EHC Newsletter May 2016 – pg 39).

It's the most exciting time in haemophilia because many technically cutting-edge research groups have been attracted to this disease area as it seems an easy target for gene and cell therapy. Haemophilia is also an attractive disorder for researchers to work with because the proteins involved, i.e. FVIII and FIX, do not have to be produced within strict limits, like say insulin in which too much insulin could kill you. In fact almost any level of coagulation factor will have a therapeutic effect leaving more freedom to researchers. Nonetheless hitting the target hasn't been an easy feat given the number of failures over the past 15 or more years. The incremental progress made by scientists brings our community closer to the goal of a permanent cure.

*\* Dr Glenn Pierce was responsible for the development and approval of some of the products mentioned in this article (i.e. the FVIII-Fc and FIX-Fc) when he was Senior Vice-President of Hematology, Cell and Gene Therapy and Chief Medical Officer for the Hemophilia Program at Biogen. Before that Glenn was Vice-President of US Research at Bayer HealthCare, responsible for the preclinical testing of PEGylated FVIII products. Glenn retired from Biogen in 2014 and is a consultant to BioMarin, Genentech/Roche and an advisor to Alnylam. He lives in California and travels frequently for haemophilia causes, especially the World Federation of Hemophilia's (WFH) Expanded Humanitarian Aid program. He is on the board of directors of WFH and serves on the Medical and Scientific Advisory Council (MASAC) of the National Haemophilia Foundation (NHF) based in the US. Glenn had haemophilia until a liver transplant in 2008.*

*The EHC would like to express its appreciation to Dr Glenn Pierce for drafting this review article on new developments in haemophilia replacement therapy. The opinions expressed in this article are those of Dr Pierce and do not necessarily reflect the views or opinions of EHC.*

## RNA interference technology: from discolouring petunia petals to treating haemophilia

*By Radoslaw Kaczmarek, Member EHC Steering Committee*

*Dr Radoslaw Kaczmarek gives us an overview of how RNA interference technology is being researched as a potential treatment for haemophilia.*

In the past two years we have been enjoying a constant flow of updates on new haemophilia treatment products (see pg 47). Most of these concerned extended half-life (EHL) clotting factor concentrates, but some also covered technologies targeting blood coagulation in entirely different ways. One such technology, which is now half-way through phase I clinical study, is the silencing of antithrombin III using siRNA, which stands for small interfering RiboNucleic Acid (also known as RNA).

*What is RNA?*

RNA is an essential element of the protein synthesis machinery. Before any protein is synthesised based on information (DNA sequence) contained in the gene that encodes it, that gene must first be transcribed into messenger RNA (mRNA). mRNA then serves as a direct template for protein synthesis. This is how clotting factors and other proteins in the body are produced. mRNA level most of the time correlates with the level of protein that it encodes. Compared to DNA, mRNA is unstable and short-lived. In addition, since unusual or foreign RNA (e.g. of viral origin) may be detrimental to the cell, many organisms developed ways to control and destroy it. One such mechanism is RNA interference. The phenomenon was discovered by accident in 1990, when plant biologists Carolyn Napoli, Christine Lemieux and Richard Jorgensen introduced two copies of the gene encoding enzyme responsible for purple colour in petunia, expecting the flower to turn more purple, but it turned white instead. They saw the same effect after introducing a small RNA fragment transcribed from the gene. Later, it turned out that introducing small RNA of similar structure to mRNA normally produced in the cell will squash that mRNA and, consequently, its respective protein (a phenomenon called 'silencing'). The petunia turned white because the purple colour enzyme was knocked down as a result of silencing its mRNA. Currently pharmaceutical companies are developing a drug that uses the same mechanism to correct coagulation by knocking down antithrombin III (ATIII).



*Dr Radoslaw Kaczmarek is a member of the EHC Steering Committee*

*What is ATIII and why knock it down to correct a bleeding disorder?*

Most of us would have a hard time finding anything favourable about inhibitors, currently the most serious complication of haemophilia treatment, but in fact effective haemostasis relies not only on clotting factors but also on inhibitors, and ATIII is one example of this.

While the inhibitors that we dislike and want no part of emerge as a result of an immune response, inhibitors like ATIII in healthy individuals keep blood from clotting excessively - by the way, this is a far more frequent cause of morbidity than

excessive bleeding. These inhibitors are produced throughout life along clotting factors and are unrelated to the immune system. When inhibitors like ATIII are lacking or do not work properly, the risk of thrombosis is raised, a problem lying at the other side of the spectrum from haemophilia. It was found that in haemophiliacs with concomitant defects in coagulation inhibitors, these defects ameliorate the bleeding phenotype by compensating for clotting factor deficiency. This observation inspired the development of a novel therapy that uses siRNA to knock down ATIII mRNA and thus also the ATIII protein. Since this mechanism of action bypasses factors VIII and IX, it offers another glimmer of hope for patients with inhibitors. But that is not all! ATIII inhibits coagulation primarily by inactivating thrombin, also known as factor IIa, a clotting factor downstream from the majority of clotting factors that are deficient in haemophilia and rare bleeding disorders, except factor XIII and fibrinogen. This means that this new treatment may potentially correct a majority of rare bleeding disorders, including factor V, VII and X deficiencies.

So far, the drug has been successfully tested in three healthy volunteers and 12 haemophilia patients with no thrombotic adverse events reported. More importantly, the drug is administered subcutaneously and is capable of correcting coagulation to an equivalent of >25 per cent factor VIII, which remains stable over three months. Although this approach is, in principle, not a gene therapy, it certainly brings us closer to a cure than most of them. Hopefully, it stays on the right track throughout the rest of the study.



# Calendar of Events

## EHC Events

- Oct 7: EHC Annual General Assembly – Open to NMOs only  
*Stavanger, Norway*
- Oct 7-9: [EHC 29<sup>th</sup> Annual Conference](#) – Open to all  
*Stavanger, Norway*
- Nov 18-20: EHC Workshop on New Technologies in Haemophilia Care – Open to selected NMOs only  
*Berlin, Germany*
- Nov 28: EHC Round Table on Patient-reported outcome measures – Open to NMOs only and selected participants  
*Brussels, Belgium*
- Dec 1-4: 1<sup>st</sup> Inhibitor Summit – Open to NMOs only  
*Barretstown, Ireland*

To find out more about EHC events visit <http://www.ehc.eu/calendar-of-events/events/>

## Other events:

### 2016

- Oct 20-22: 3<sup>rd</sup> Congress on Controversies in Thrombosis and Hemostasis (CiTH) & 8th Russian Conference on Clinical Hemostasiology and Hemorheology  
*Moscow, Russia* – More information at <http://congressmed.com/cith/>
- Nov 8-9: EPF Conference on Patient & Family Empowerment for Better Patient Safety  
*Brussels, Belgium* – More information at <http://bit.ly/2clURBt>

### 2017

- Feb 1-3: 10<sup>th</sup> Annual Conference of the European Association for Haemophilia and Allied Disorders (EAHAD)  
*Paris, France* – More information at <http://eahad2017.com/>
- Mar 3-5: 7<sup>th</sup> International Symposium on Women's Health Issues in Thrombosis and Haemostasis  
*Barcelona, Spain* - More information at <http://www.whith.org/>
- May 16-17: 24<sup>th</sup> International Workshop on Surveillance and Screening of Blood-borne Pathogens  
*Zagreb, Croatia* – More information at <http://bit.ly/2cYXnvg>
- Jul 8-13: XXVI<sup>th</sup> Congress of the ISTH  
*Berlin, Germany* – More information at <http://www.isth2017.org/>

# EHC Annual Conference 2016 Programme

## Friday 7 October

- 08.30-12.30 hrs: EHC Annual General Assembly (open to EHC NMOs only)
- 13.30-14.30 hrs: Conference session on: 'Organisation of Haemophilia Care in Norway'
- 14.30-16.00 hrs: Pfizer symposium: 'Partnering to improve outcomes in clinical trials, clinical care and total health'
- 16.30-18.00 hrs: Youth debate 'There will be blood: Young patients vs doctors debate - the future of haemophilia care'
- 18.00-19.00 hrs: Conference session on: 'Updates on dental care and von Willebrand treatment'

## Saturday 8 October

- 8.30-10.00 hrs: CSL Behring Symposium: 'Advancing the provision of haemophilia care in Europe - Reviewing the patient need'
- 10.30-12.00 hrs: Conference session on: 'New Developments in haemophilia care'
- 12.00-13.30 hrs: Novo Nordisk Symposium: 'Taking care of your joints: Challenges and opportunities of an active lifestyle'
- 14.30-16.00 hrs: Conference session on: 'Inhibitors'
- 16.30-18.00 hrs: Baxalta Symposium 'The pathway to a new alliance for prediction, prevention, eradication and treatment of inhibitors'
- 18.00-18.30 hrs: Conference session on: 'WFH Update'

## Sunday 9 October

- 08.30-10.00 hrs: Clinical debates
- 10.30-12.00 hrs: HCV Symposium
- 12.00-13.30 hrs: Conference session on: 'Patient-reported outcome data'

For the full programme, please visit [www.ehcconference.org/](http://www.ehcconference.org/)

# Announcements

## Web-RADR

The European project [Web-RADR](#): Recognising Adverse Drug Reactions is looking for feedback from patients and users of medicinal products!

### About Web-RADR

Web-RADR is developing a mobile app for patients and healthcare professionals to report suspected adverse drug reactions to national EU regulators, and investigating the potential for publicly available social media data for identifying drug safety issues. Reports received via the mobile app will be compared to those received via established reporting schemes for completeness, quality and value for detection of safety issues.

Launched in September 2014, this three-year project seeks to utilise the powers of social media and new technologies for pharmacovigilance purposes. It arose in response to the ninth call for Innovative Medicines Initiative (IMI) projects 'WEBAE – Leveraging Emerging Technology for Pharmacovigilance', and is based on the belief that modern pharmacovigilance practices should adapt to these new ways of communicating.

Led by a consortium of world-leading experts from industry, regulatory agencies, and academia, this project will deliver an EU-wide mobile phone app that enables users to report Adverse Drug Reactions (ADRs) directly to their National Competent Authority (NCA). There is potential to use the app as a platform for patients and clinicians to access accurate, timely, and up-to-date information on pharmacovigilance issues. The project will also develop text mining techniques for publicly available data on social media sites, complementing existing methods of signal detection.

### About the survey

The survey is about an app for mobile phones and tablets to report side-effects and receive safety information of medicines, which can be, for instance, a warning about newly detected side-effects.

The survey is targeting patients and consumers from Croatia, France, Germany, the Netherlands, Portugal, Spain and the United Kingdom and has a result the survey has been translated into the corresponding national languages.

Results of the survey will be used to:

- Improve the app that has recently been developed within the Web-RADR project.
- Increase the general knowledge about opinions and preferences with respect to (1) reporting side-effects and receiving safety information about medicines through an app, and (2) the reporting of side-effects in general.

Patients and consumers of medicines are asked to complete the survey, which is anonymous and will take approximately 15-20 minutes.

Click one of the links below to enter the survey in your preferred language:

**General link:** <https://www.unipark.de/uc/WEB-RADR/PT/>

**German:** <https://www.unipark.de/uc/PT/DE/>

English: <https://www.unipark.de/uc/PT/EN/>

Spanish: <https://www.unipark.de/uc/PT/ES/>

French: <https://www.unipark.de/uc/PT/FR/>

Croatian: <https://www.unipark.de/uc/PT/HR/>

Dutch: <https://www.unipark.de/uc/PT/NL/>

Portuguese: <https://www.unipark.de/uc/PT/PT/>

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## A message from SAVE ONE LIFE

The fight against haemophilia can be a mission. Living with haemophilia is difficult enough with medication. But without medication haemophilia must be a nightmare, as is the case in most developing countries. That is why I am now contact person of Save One Life in Europe. The motivation to do something for these children was born from a through awareness of how fragile life can be. But everything has not gone smoothly.

The concept of Save One Life is pretty familiar. People in richer countries pay a monthly fee for the care of a child with haemophilia in developing countries. The family uses the money often for transport to the hospital and pain management, but as well for daily necessities. It is possible to communicate with each other, but often the children come from very poor families and buying a stamp is already exacting. If haemophilia occurs in a family, there are many stories. This also applies to us.

As a young girl I knew I was a carrier. I grew up in a family with haemophilia B. A total of six people were affected. We played with bandages and syringes. Then I knew already I wanted to go to poor countries. Later, after my studies International Communication I started working for Doctors without Borders and travelled to the toughest places in the world. I realized that there is much suffering on all fronts.

When my husband was transferred from the Netherlands to Luxembourg to work for the European Commission, we had a difficult start. We had two boys with haemophilia one after the other. In the hospital we often had to speak in French or German. There are only about thirty patients and there is no treatment centre in Luxembourg. Our oldest son has lost two-thirds of his blood due to a tongue bleeding. He was all white and survived with a close call. We really struggled and were very isolated in the beginning. I was dead tired at home with two small children. Luckily they both received a port-a-cath and we were more independent. In addition to his demanding job my husband usually administered the injections. Meanwhile, I suffered myself from several bleeds. Then I often went with the boys to a spa with thermal water in Mondorf-les-Bains. A temporary transfer to Brussels brought some air.

Back in Luxembourg our boys, now eleven and nine, are doing very well at the European School. At first I was over-worried and had to be treated psychologically. But now we have more contact with other haemophiliacs in Luxembourg. It is a small country so the patients all know each other and come together for dinner twice a year. Also we have been on the Luxembourg television.

I have not only seen but also experienced how fragile life can be. Now I can be there in particular for haemophilia patients in developing countries who have to endure so much pain from internal

bleeding, often become handicapped and sometimes do not reach adulthood. What do they all go through? I'm busy every day to make Save One Life more popular in Europe, because it is originally an American organization. We sponsor ourselves a child with haemophilia in India and still want to sponsor a child in Africa. Two years ago I went to the World Haemophilia Conference in Melbourne Australia. From many countries patients limped inside. I almost cried because of so much recognition.

Living with haemophilia makes you vulnerable, but also alert and eager. It seems like you are walking on a tightrope while others walk on the ground. You too can further utilize this balancing and calculating behaviour and show your commitment to those who really need it. Join us and sponsor a child with haemophilia in the developing countries. Save one life.

*Marelle Hart is the European representative of Save One Life ([saveonelife.europe@gmail.com](mailto:saveonelife.europe@gmail.com))*