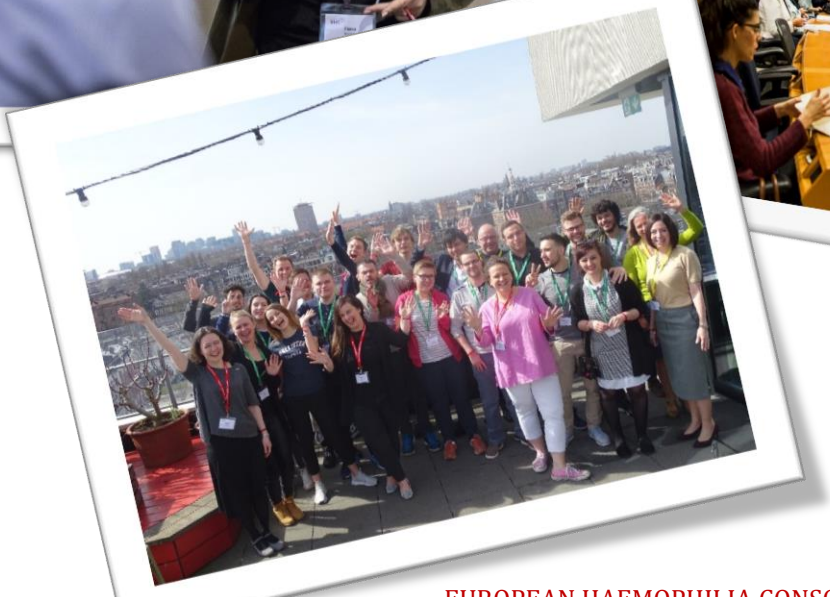
May – August 2018

EHC NOW!

Compilation Newsletter



EUROPEAN HAEMOPHILIA CONSORTIUM

EHC NOW! Newsletter Compilation May – August 2018

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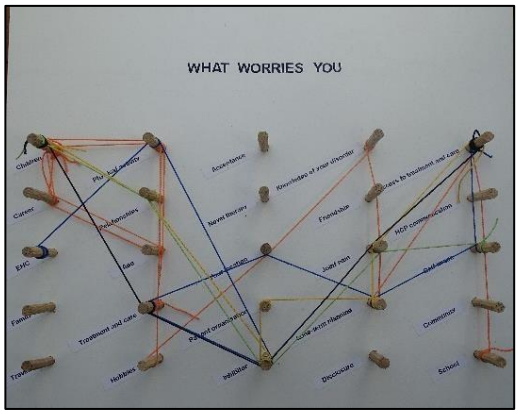
EHC NOW!

Comprehensive Care in Haemophilia: Intimacy and relationships

Interview with Greig Blamey, Senior Vice-Chair of the World Federation of Hemophilia (WFH) Musculoskeletal Committee; Interview taken by Alison Dougall, dentist and member of the EHC Medical and Scientific Advisory Group.

Fighting for access to quality haemophilia treatment and care, frequent infusions and the worry of an inhibitor: though these issues are faced by all in the community, when filtered through experience everyone has their own story with rare bleeding disorders. What challenges you? What do you want to see changed, what makes you happy? At the recent World Federation of Hemophilia (WFH) Congress the European Haemophilia Consortium (EHC) explored these questions for insight into what is important on an individual level. Tracing their answers with a piece of yarn, patients, health care providers and caregivers left a "footprint" of what matters to them in their experience with rare bleeding disorders. While taking part, many participants noticed one answer we had failed to include as an option - intimacy and sexual health. Often avoided as a topic, having a bleeding disorder impacts intimacy and leaves many questions on how to integrate them in personal relationships.



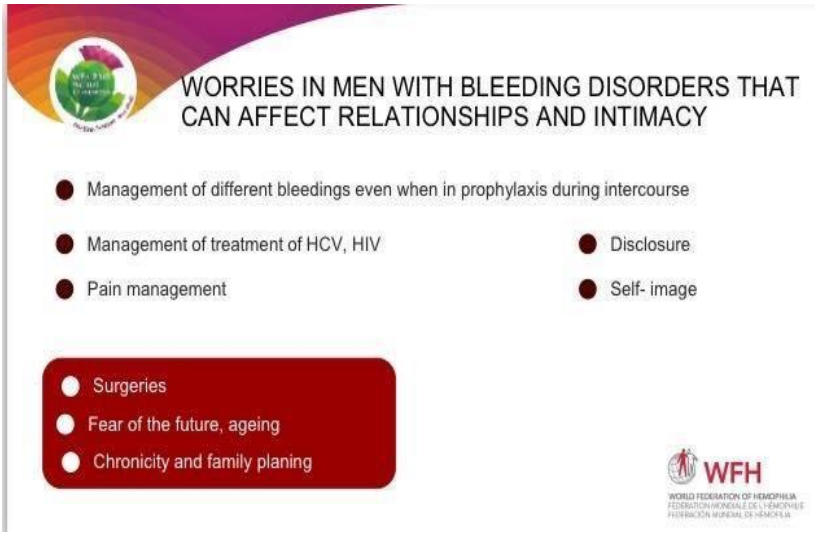
At the WFH Congress, Alison Dougall, dentist and member of the EHC Medical and Scientific Advisory Board, caught up with Greig Blamey, Senior Vice-Chair of the WFH Musculoskeletal Committee, after his presentation on intimacy and rare bleeding disorders. His message? Patient lives have more than one side, involving psychosocial concerns, dental concerns, musculoskeletal concerns, and so on. Just as important is the intimacy concern and it is time to broaden the conversation.

AD: *First, congratulations on your recent role as Vice-Chair of the WFH Musculoskeletal Committee. What are your visions for the Committee?*

GB: What I really want to see is the Musculoskeletal Committee forming stronger bridges and links with all of the other interprofessional committees that exist. We are seeing a real movement towards personalisation and individualisation of care for all people with haemophilia and other rare bleeding disorders and there is a lot more we could be doing if we connect our efforts. We can all learn from each other and find out what it is we can do to help each other's work.

AD: *Yes, the care has to be completely comprehensive…*

GB: It is interesting because patients have a full life that involves psychosocial concerns, dental concerns, musculoskeletal concerns. The conversation needs to be broadened. Just one example I heard today during a presentation of how elbow range of motion and upper arm mobility and

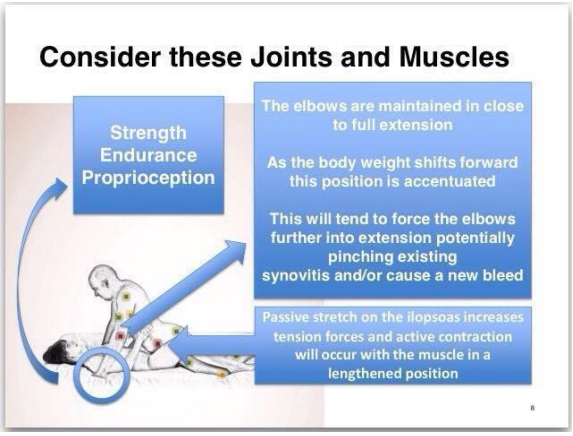


function impacts the ability to maintain proper oral health. It is just a perfect example of how two disciplines can be paired together.

AD: *You did a presentation earlier on intimacy and relationships when having a rare bleeding disorder. Will you talk a little more about that?*

GB: Intimacy and the sexual health of people with haemophilia has been an interest of mine for a long time. It first appeared in the programme of the WFH Congress in 2006, so only 12 years ago did we really start talking about this openly. A lot of people have questions: the patients and the health care providers. This is something patients don't feel necessarily comfortable talking about and often we as treaters, feel that since they don't bring it up, they don't want to discuss it.

There is a range of issues to discuss: everything from the psychosocial barriers to communicating with partners, to the physicality of sex and just issues that come as a child develops into an adult, the way that their sexual development occurs.



AD: *What is the best way in terms of going forward with educating the community?*

GB: Maybe the best way is to make sure that your patients know that this is something we want to hear from them if they are comfortable to bring it up. They should choose who from the treatment team they are comfortable with - it may be that they are more comfortable with their physio, it may be their nurse, their haematologist or their dentist. Bring it up and if that person doesn't have the answers, they will help you connect with the right person. What matters is that these issues are mentioned because

knowing this information is important – what positions are more suitable for people with rare bleeding disorders, how to minimize your chance of a bleed during sex. There are many available resources.

Click here to catch the interview in video format (starting at 4.55).

EHC NOW!

New EHC staff member: Fiona Brennan

Interview with Fiona Brenna, EHC Community Programme Officer; Interview by Raia Mihaylova, EHC Communications Officer.

Fiona Brennan first came on board with the EHC in December 2017 while replacing Kristine Jansone, EHC Inhibitor Programme Officer, during her maternity leave. Enthusiastic, creative and well established in the community, she has been a great addition to the team and has now taken on a new EHC position. Though many of you already know her well, we would like to introduce you to Fiona through this next interview, in which she shares her impressions of organising many EHC activities and also offers some news about an exciting project that has recently been established.

RM: *How did you think it would be coming to the EHC?*

FB: Obviously I was very excited. But coming from an NMO, particularly in Ireland, to a European organisation, I wasn't sure how interactive it might be with members and the community. I kind of expected it to be a bit more removed but that wasn't the case at all. I have gotten to speak to loads of the members and it is exactly the same community that I have been part of, just on a broader scale, so it is really nice.

RM: *What is one EHC event that you really enjoyed working on up until now?*

FB: I worked on the Inhibitor Summit in Barretstown in 2017. That was my first EHC event. I loved it. It was so great to see so many people coming from so many different countries. I really enjoyed that and it's great to have the kids there as well because there is high energy and it is fun. Then I did the EHC Youth Leadership Workshop, which was great. It is really nice to work in a small group and you get to know each other quite well. There are 16 participants there so it is a really intimate group, which is really lovely. I then moved on to the EHC Leadership Conference and that was a bit bigger, you get to meet the patient organisation leaders, which was a different experience again but equally fun. They have all been great.

RM: *What is your background in?*

FB: I did my undergraduate degree in Psychology. I did my Master's in Applied Psychology and as a punishment, I am doing my PhD in Psychotraumatology.

RM: *What is your new position now at the EHC?*

FB: Again, I am focusing on the youth activities. I will be looking after the Youth Leadership Workshop but also we will be launching a new, very exciting project called the Youth Fellowships, which some in the community may have heard of. I will be coordinating that.

RM: *I will stop you there and more information on this will be coming out soon!*

2018 EHC Youth Leadership Workshop

EHC NOW!

EHC Round Table on Women and Bleeding Disorders: A call to action

By Raia Mihaylova, EHC Communications Officer

On June 19th, the European Haemophilia Consortium (EHC) held a Round Table on Women and Bleeding Disorders in the European Parliament, bringing the important topic into discussion with Members of the European Parliament (MEP), patients, health care providers and representatives of the pharmaceutical companies. Chaired by MEP Jana Žitňanská (European Conservatives and Reformists Group, Slovakia), the event was also supported by MEPs Nessa Childers, Norica Nikolai, Dr Miroslav Mikolášik and Dr Cristian Bușoi, the last four of which are part of the MEP Group on Rare Bleeding Disorders that works together with the EHC to address challenges faced by the community on a European level (meet the members and hear what their goals for the group are here).

"76 % of men with von Willebrand Disease (VWD) are diagnosed by the age of 10, while 50 % of women with VWD are not diagnosed until after the age of 12, which is a big difference. Therefore, it is crucial to raise awareness in order to educate both the public and the medical society."

MEP Dr Miroslav Mikolášik
EPP, Slovakia

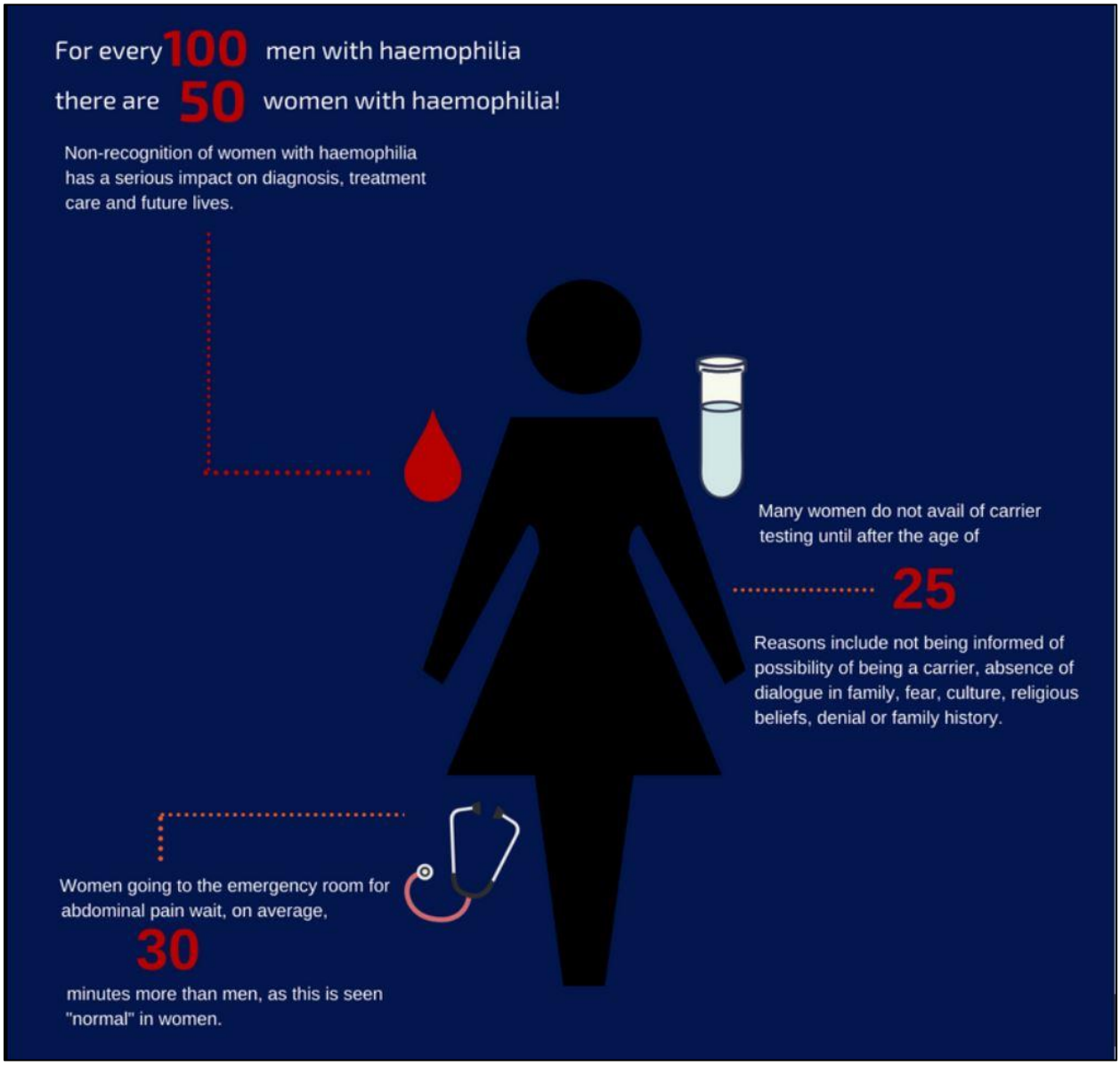
"I am glad that today the topic of women with rare bleeding disorders is finally brought to the agenda of the European Parliament. I am sure the interesting presentations will give us – policymakers – better clarity on how to concretely address the challenges of these patients."

MEP Cristian Bușoi
EPP, Romania

As data evidence is imperative for pushing for improvements and change, the event was a powerful testimony to the barriers women with bleeding disorders face and how these issues have long been overlooked. Though concrete data and research is still lacking, medical experts presented statistics around what is currently known. Beyond the diagnosis and treatment challenges, Professor Roseline d'Oiron, EHC Medical and Scientific Advisory Group member, pointed out that this patient group has to battle through discrimination on a regular basis:

"Just imagine that a woman arriving in an emergency room with abdominal pain, related to her bleeding disorder, will have to wait on average 30 minutes longer compared to men because it is 'normal' to have abdominal pain if you are a woman. And then there is a decreased quality of life

that is directly related to the heavy menstrual bleeding. And this is coming every month, it is not like at the same level, when you have 20 % of factor VIII, for example, in a man, he will not have this challenge each month. It is really important to emphasize this point."



During the Round Table, the EHC unveiled results from its survey on women and bleeding disorders, answered by clinicians, haemophilia treatment centres and over 700 individuals from throughout Europe. Presented by Declan Noone, EHC PARTNERS programme consultant, reports outlined that women with platelet disorders and other factor deficiencies are largely misdiagnosed and face a lack of effective treatment options.

Telling the story behind the numbers, patients also talked about their personal experience with having a bleeding disorder.

Evelyn Grimberg, member of the Dutch Haemophilia Society and the EHC Women and Bleeding Disorders Committee, shared some of the treatment challenges she faced during childhood due to being diagnosed with Glanzmann Thrombasthenia:

"Starting with the hormones wasn't that easy, there was a lot happening in my body because the hormones changed it. I started to realise that I was different from my friends, that it has that much of an impact that I couldn't go to school every day."

Ana Pastor, also member of the EHC Women and Bleeding Disorders Committee, displayed through her story the many challenges women face – both as a patient with a bleeding disorder and a mother to a person with haemophilia:

"I have a bleeding disorder but at the time of finding out my son had haemophilia that completely overtook my life. I was not a person any more, I was just his caregiver – no one could take better care of him than me. At that time, I had profuse nose bleedings but I wasn't taking care of myself because I was concentrated on taking care of my boy. There was a time that I was bleeding every day for 2-3 hours and that is when my mother intervened. Almost shouting and crying she told me "Ana, if you want to take care of your son, you have to take care of yourself first. And somehow, those words echoed in my head and they made a change."

Furthermore, Professor Roseline d'Oiron covered some of the less known barriers, such as women not being regularly offered and knowing the benefits of carrying out genetic testing. Even when aware of the chance of being a carrier, women don't know that there is a risk of intracranial hemorrhage while giving birth and that genetic testing can lead to establishing protocols that secure both the maternal and fetal health during delivery.

The energy and emotion that was part of the Round Table provoked many key take-aways and a call for action to address these issues. Dr Paul Giangrande, chair of the EHC Medical Advisory Group, shared what stood out to him in an interview taken by Naja Skouw Rasmussen, member of the EHC Steering Committee and Women and Bleeding Disorders Committee.

PG: *For me, the key message was that there are many unmet needs of women with bleeding disorders. I think the most important thing is to involve and spread the message beyond*

haematologists. We need to work with gynecologists, for example, to point out that women who have heavy menstrual bleeding may not just have fibroids or other physical causes, but we need to focus on these women and consider doing blood tests.

I think it's not just the novel therapies we need to look at, I think some of the existing treatments at the moment are clearly not being applied properly to women with bleeding disorders. To start out with, women with factor VIII deficiency who are carriers of haemophilia, why should they not be treated with DDAVP, for example, which I think is widely under-utilized, or in fact factor VIII treatment. We heard from a lady today that she receives fresh frozen plasma, which is, in my view, unforgivable at this time. Also, Professor d'Oiron made a very important point that sometimes women have problems with health insurance because from a health insurance point of view, companies will say "well, why is a woman getting recombinant factor VIII, for instance, which is only meant for men with haemophilia?" But I think there are a number of treatments that are simply not promoted for carriers of haemophilia and women with VWD. DDAVP, desmopressin, I think is useful in many cases but it is not widely promoted. Tranexamic acid is also a very useful agent which can control heavy menstrual bleeding in women with bleeding disorders and again, is not used as widely as it should be.

As addressing the above-mentioned issues is a collective responsibility, the EHC is proud to announce that we will be piloting a historic Europe-wide conference for women and bleeding disorders in spring of 2019. We encourage a broad and wide participation from all members of the European bleeding disorders community to discuss steps in moving forward. Details will follow soon!

EHC NOW!

2018 World Federation of Hemophilia (WFH) Congress

Interview with Dr Beatrice Nolan, paediatric haematologist and member of the EHC Medical and Scientific Advisory Group (MASAG); Interview taken by Dr Alison Dougall, dentist and member of the EHC MASAG.

The 2018 World Federation of Hemophilia (WFH) Congress took place from May 20th - 24th in Glasgow, Scotland, and reached its highest attendance yet, with over 5000 participants – patients, health care professionals, patient organisations and pharmaceutical industry representatives. With such a diverse group and expertise, the event has always been an opportunity to receive up-to-date haemophilia treatment information and discuss steps on how to move forward as a global community.

The European Haemophilia Consortium (EHC) was also in large presence and had an exhibition booth that showcased our work and latest initiatives. It was there we met up with Dr Beatrice Nolan, paediatric haematologist from Dublin, Ireland and member of the EHC Medical and Scientific Advisory Board, to hear about her impressions of the Congress. Find out what information surprised her in the following interview!

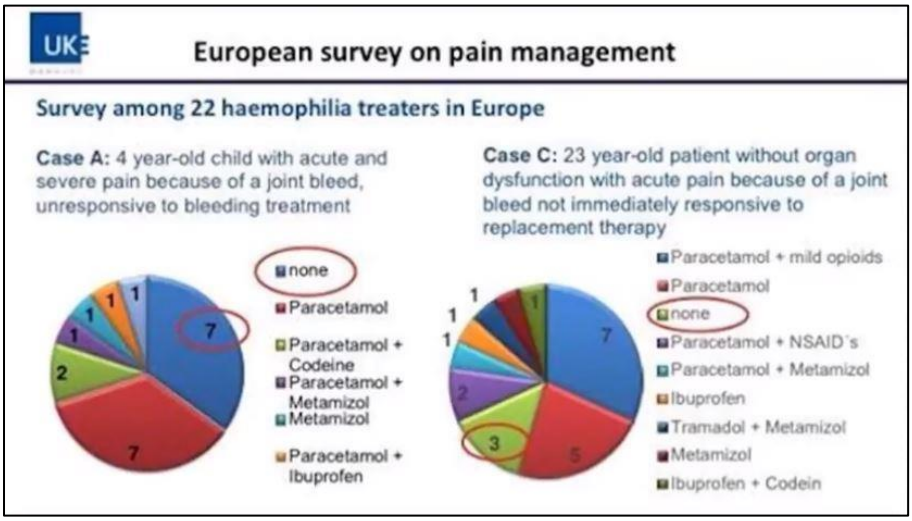
Dr Alison Dougall, (left) together with Dr Beatrice Nolan

AD: *What are your impressions of the Congress so far?*

BN: Well, it has been busy. I have bumped into so many people from Dublin. Loads of people from Dublin are here. It has been good so far.

AD: *Which of the sessions have really caught your eye or grabbed you?*

BN: I have been to the sessions on the new therapies – extended half-life factor and gene therapy – but there was a really interesting one this morning on pain perception. It is not just about pain, not just about how you process pain, but about how your brain reacts to chronic pain. It's about the psychology of pain and how your body adapts to pain, and how your brain can even change with pain. For me, as a paediatric haematologist, this was interesting because we don't tend to treat joint bleeds in children with pain relief. We were presented two scenarios – a four-year-old boy comes in with a joint bleed and he is in pain, there is a list of medications with which we can treat and one of the options was not to, and then a twenty-year-old man comes in with the same bleed, with the same list of options and most people wouldn't treat the child but they would treat the adult for the pain. Dr Katharina Holstein, who gave that presentation, was saying it is more important to treat the child because that's when the child learns to perceive pain in haemophilia. It's not just about pain, it's about the perception of the pain and the psychology, the stress, the depression that comes with pain. I guess not everybody talks about that. We always talk about children not needing pain relief because they have so many distractions. Of course we treat the child, but we are more inclined to give pain relief to an adult than to a child and that's how you set that child up to perceive pain for the rest of his life.



AD: *So do you think that's going to change your attitude going home?*

BN: I think so, yes. I think so because I had never really thought about it like that. You know, a child feels pain for a couple of days and he will be up and running around again. They have a fairly high threshold. I had never really thought that you are setting up their thought process for life. And then the other thing about "rest is best, hurt not harm," she said that that may actually be counter-productive because you are putting a certain mindset into the parents and into the child's mind. There is a sort of a hypervigilance about pain. I just thought that was quite fascinating.

AD: *So, I know Ireland is one of the countries that has switched to the longer acting factors. What is being said, what has been your experience?*

BN: I know we say it all the time, but it's not a 'one size fits all' process. I think a lot of the time people are talking about how wonderful extended half-life factors are for less frequent infusions. But not everybody wants less frequent infusions. What I have found is that people have different expectations from the factor and different requirements. We've put children who were on daily standard half-life factor on daily extended half-life factor because they are very active, they are

playing sports every day. But we've got people on everything from once-a-day infusions, to twice a week, to alternative days. It is to try and tailor that product to that person's lifestyle. People have different requirements.

AD: *And I think that is very important to share because I think we need to learn about the actual truth of switching over. I think the more information you can gather, the more interesting.*

BN: And we have changed everybody now. Well, I'd say, we have no previously untreated patients at the moment to put on factor. But everybody in Ireland over the age of two is on extended half-life or in the process of switching.

AD: *Congratulations.*

BN: It was a lot of work for the nurses. Because we are trying not to waste previous product and we are trying to coordinate hospital visits because the first dose is given in the hospital. And then there are follow-up visits. So it is a lot of work for the nurses.

I think the change in practice for nurses will provide so much to learn from, through sharing experiences.

AD: *Listen, it has been wonderful to chat to you. Thank you very much for your time, Beatrice!*

Click here to catch the interview in video format.

EHC NOW!

The European Principles of Inhibitor Management

By Paul Giangrande, EHC Medical Advisory Group Chair and lead author of the European Principles of Inhibitor Management

The European Haemophilia Consortium (EHC) and the European Association for Haemophilia and Allied Disorders (EAHAD) have collaborated on the development on a document which sets out the basic principles of care for the management of people with haemophilia and inhibitory antibodies. They were presented for the first time at the recent EHC World Haemophilia Day event in Brussels on April 19th and they will shortly appear in print in an academic journal[1]. These guidelines follow on from a number of previous initiatives, most notably the original European 'Principles of Care' document which was published a decade ago as well as the recommendations which have emerged from the various meetings hosted by the Council of Europe's European Directorate for the Quality of Medicines (EDQM), in which the EHC played a key role.

The process involved a thorough review and evaluation of published literature and clinical guidelines on the topic, as well as a series of face-to-face meetings in Brussels. In all, it took around 18 months to formulate the final text. A total of twenty-one people from thirteen countries contributed to the development of these guidelines. This international working group was also very much a multidisciplinary one and included people with inhibitors.

Recent surveys conducted by the EHC have highlighted that, despite recent major advances in the understanding and treatment of inhibitor development in patients with haemophilia, management of many of these patients remains suboptimal and highly heterogenous across Europe. It is hoped that publication of this document will set a benchmark to improve standards of care.

The ten principles are set out in headline form in the table below:

Table 1: Ten European Principles of Inhibitor Management
1. Awareness of the incidence of inhibitors and risk factors throughout life
2. Early recognition and accurate diagnosis
3. Optimal organization of care and communication between all stakeholders
4. Haemostatic treatment with bypassing agents in inhibitor patients
5. Inhibitor eradication by immune tolerance induction (ITI) therapy
6. Access to, and optimal preparation for, surgery and other invasive procedures
7. Provision of specialist nursing care

8. Provision of tailored physiotherapy care and monitoring
9. Access to psychosocial support
10. Involvement in research and innovation

The following is a brief summary of individual points. Please consult the published manuscript for full details.

1. Awareness of the incidence of inhibitors and risk factors across the life-span.
The incidence of inhibitor development is approximately 30% amongst patients with severe haemophilia. Genotype constitutes the principal risk factor, whilst environmental risk factors are less clearly understood. The first 50 exposure days (EDs) constitute the highest risk period for the development of inhibitors in severe haemophilia. Discussions on treatment options should take place with the parents of PUPs before starting treatment.

2. Early recognition and accurate diagnosis.
Early recognition and accurate diagnosis are essential for successful management. All previously untreated patients (PUPs) should be closely monitored and regularly screened for inhibitors. Screening should also be performed prior to surgery or other invasive procedures and whenever the clinical response to conventional treatment is deemed inadequate.

3. Organization of care and communication between all stakeholders.
The coordination and organization of multidisciplinary inhibitor management, and regular communication between the multidisciplinary care providers, are the key elements of effective management. Once diagnosed, every patient who has developed inhibitors should be followed up in one of the certified European Haemophilia Comprehensive Care Centres (EHCCC) or European Haemophilia Treatment Centres (EHTCs).

4. Haemostatic treatment with bypassing agents
There are currently only two licensed bypassing agents: both products have been demonstrated to be similarly effective in treating patients with inhibitors. It is advisable for haemophilia treatment centres to have both products readily available as some patients seem to respond to one agent better than the other.

5. Inhibitor eradication by immune tolerance induction (ITI) therapy.
Currently the only way to eradicate an inhibitor is through prolonged exposure to FVIII (or FIX) by frequent administration of these concentrates at high dosage. Breakthrough bleeds should be treated with bypassing agents, given on demand or prophylactically in selected patients. ITI is a demanding and resource-heavy treatment, and the patient (or parents) should receive detailed information before initiation of ITI. A plan should be in place for the management of those patients who fail to respond to ITI.

6. Access to, and optimal preparation for, surgery and other invasive procedures.

Patients with inhibitors are often denied surgery or any invasive procedures as these entail high cost and are also perceived to carry a significant risk of bleeding. However, there is now an extensive body of evidence proving that surgery may be carried out safely and effectively under cover of bypassing agents. This may also prove cost-saving in the long term. Regular dental reviews are strongly recommended along with effective methods of preventative home care.

7. Provision of specialist nursing care.
Provision of high quality specialist nursing care for haemophilia patients with inhibitors is of the utmost importance. A key nursing responsibility is the administration of replacement factor and bypassing agents through both peripheral venous access and central venous access device. The development of an inhibitor affects the whole family, especially when diagnosed in a young child. The nurse offers support throughout the inhibitor management process.

8. Provision of tailored physiotherapy care and monitoring.
Provision of physiotherapy is focused on maintaining optimal musculoskeletal function. Assessment and management of bleeds requires a careful balance of rest and activity; often with slower progress than with inhibitor-free patients. If optimal functional recovery after every bleed is not achieved, both in joint and muscle bleeds, the long-term consequences will be significant.

9. Access to psychosocial support.
Inhibitors are a major burden for the patient, as well as for the family and caregivers, and the immediate social network. Members of the multidisciplinary care team should be proactive and refer patients to a social worker and/or psychologist when any needs are identified. Local and national patient organisations are also a very good source of advice and support.

10. Involvement in research and innovation.
Improvements in clinical outcomes for inhibitor patients will increasingly depend on future research and innovation. It is highly desirable that patients with inhibitors are registered with treatment centres where innovations and contribution to research are accessible. National patient registers can help to identify eligible patients for relevant clinical trials.

This document has been accepted for publication in the *Orphanet Journal of Rare Diseases*. This journal has an established track record of publications in the field of haemophilia and as very similar 'impact factor' (an independent scoring system used to measure scientific merit of a journal) to *Haemophilia*. A major advantage of publication in this journal is that it offers unrestricted access to anyone via the internet, by contrast with most other journal which limit access only to subscribers or people with institutional access. EAHAD and EHC intend to develop more joint publications in other areas relating to haemophilia and other bleeding disorders.

You can access the published article here.

[1.] Giangrande, P.L.F., Hermans, C., O'Mahony, B., de Kleijn, P., Bedford, M., Batorova, A., Blatný, J. and Jansone, K., 2018. European principles of inhibitor management in patients with haemophilia. Orphanet Journal of Rare Diseases, 13(1), p.66.

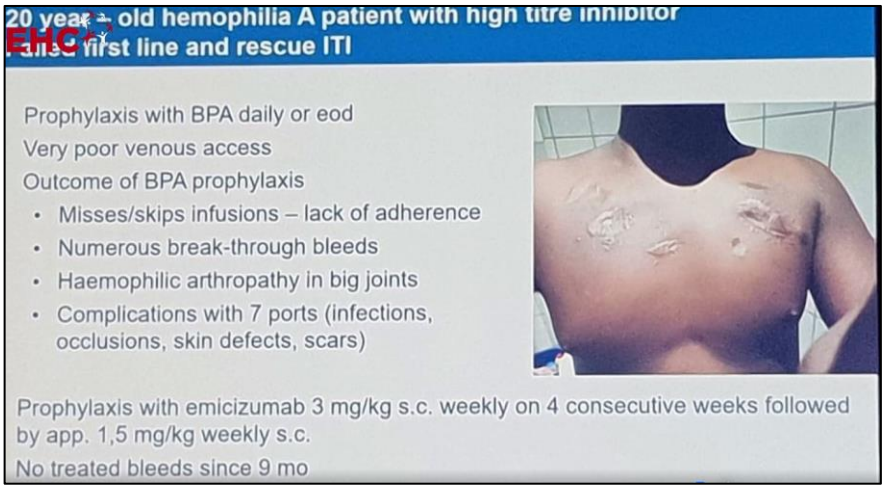
ISTH SSC 2018: Education, Innovation, Collaboration

Highlights from the 2018 ISTH SSC meeting from Dr Radoslaw Kaczmarek, EHC Steering Committee member, and Declan Noone, EHC PARTNERS Programme consultant.

There are a number of events throughout the year that are key platforms for medical updates and discussions around issues that come with treatment advances. The International Society on Thrombosis and Haemostasis (ISTH) Annual Scientific and Standardization Committee (SSC) meeting is one such event, with the 64th edition taking place from July 18-21st in Dublin, Ireland. This mouthful title covers the comprehensive way topics are presented, each from a medical, scientific and collaborative angle.

The EHC had a number of staff and Steering Committee members attending the event, allowing us to cover more presentations relevant to the bleeding disorders community. Below we outline three main areas that received widespread attention during the meeting.

One heavily discussed topic was von Willebrands Disease (VWD) and the challenges in diagnosing people with low von Willebrand Factor (VWF) levels. This includes reasons such as differences in bleeding assessment tools, where one could produce a score displaying symptoms of low VWF, while another rejects it using the same assessment domains. This brought into discussion issues such as what should be considered as heavy menstrual bleeding and what that might mean for a patients' life, with clinical data showing that 80 per cent of women with low VWF experience such a symptom.



Another prominent topic covered was the advantages that novel subcutaneous therapies are bringing, apart from the obvious improvements in treatment. Dr Carmen Escuriola-Ettingshausen, a peadiatrician and member of the EHC Medical and Scientific Advisory Group, gave an example, presenting a case of a young boy with poor venous access who had had to have seven different operations in order to get treatment in him. Not having to put people through that in the future displays the added benefit of subcutaneous

treatment, which many stakeholders, such as regulators and payers, often try to equate with convenience.

Finally, the meeting dedicated much attention to the usually under-reported concept of gene therapy for people with inhibitors. Due to the tolerogenic environment which the liver provides, gene therapy could actually tolerize patients with inhibitors to factor VIII. However, this also brings up the question of what happens in the opposite situation – if a patient who has had gene therapy develops an inhibitor because they needed treatment for the first time and in that event, should he be put on immune tolerance induction (ITI)? The answer is difficult and is one that won't be known until the community crosses that bridge, but it is important to already start the conversation around such issues.

Many of the presentations from ISTH SSC can be found online at academy.isth.org.

For more in-depth discussions between Dr Radek Kaczmarek and Declan Noone, please click here.

EHC NOW!

Not So Mild: von Willebrand Disease vs low von Willebrand Factor

Interview with Dr Michelle Lavin, coagulation haematologist; Interview taken by Declan Noone, EHC PARTNERS Programme consultant.

There are numerous studies that show that there is an eight-year overall delay in diagnosis with von Willebrand Disease (VWD) due to not recognising its symptoms. Diagnosis could become even more difficult when faced with having low von Willebrand Factor (VWF) levels, many times because of the bleeding assessment tool that was used.

Dr Michelle Lavin, coagulation haematologist from the Irish Centre for Vascular Biology, talks about the difference between having VWD and reduced levels of VWF. Learn about the newly published results on what it could mean to have low VWF levels of 30-50 per cent: like that 89 per cent of women with low VWF experience heavy periods.

DN: *Dr Lavin, I attended a wonderful talk you gave on clinical diagnosis of patients with low von Willebrand Factor. One of the things that you brought up was discussing the difference between reduced von Willebrand factor levels and a clinical diagnosis of von Willebrand Disease.*

A lot of patients get told "you have von Willebrand Disease" and then they get 'upgraded' almost to a low von Willebrand Factor. I am just wondering, how do we go about educating people about what happens, what the difference is, between having von Willebrand Disease and having low levels of von Willebrand Factor?

ML: That's a really great question because everything changed really in 2008. It was recognised more and more that if your plasma von Willebrand Factor level was less than 30 per cent of normal, you were more likely to have a cause in your von Willebrand Factor gene that is responsible for that. Factor levels of 50 per cent is the cut off where it becomes normal, less than 50 per cent is 'reduced.' But with people who have a level between 30 and 50, it was felt that there is more of a risk for bleeding rather than with true von Willebrand Disease. But of course if you have been told for years that you have type I von Willebrand's and now you have low von Willebrand Factor, that doesn't mean a lot to you as a patient. And also, it wasn't really clear, did it cause a lot of bleeding, how do we manage it, how did you differ from people with type I von Willebrand Disease? So we set up a study in Ireland and we are very thankful that there has been huge support from patients

and the community. We looked at the challenges that people who have low von Willebrand Factor face in terms of bleeding and what treatments they have had and how they responded to it. And from it, we got a lot of data. It showed that patients with low von Willebrand Factor can actually experience quite significant bleeding, more than we expected to see. I think what is really important is that if you take the general population and you just decided to take blood samples from people on the street, you would probably find about 1 in 100 people have low von Willebrand Factor levels. But we only see about 1 in 10,000 people registered with low von Willebrand Factors as a bleeding disorder. There are probably additional causes of bleeding, that we don't yet fully understand, that contribute, beyond just the low levels of people who have low von Willebrand levels. So they can experience quite significant bleeding and it differs from the type I patients because the levels aren't quite as low and can, in fact, even increase with age and may increase to a normal level when they are in their 50s and 60s. Again we are not entirely sure if that gets rid of the bleeding tendency because there can be other things that contribute to the bleeding.

DN: *One of the things you mentioned is the difference between the bleeding assessment tools.*

ML: Yes, the critical thing in the diagnosis of low von Willebrand Factor levels is if you bleed or not. Because as I said, you may have low levels but that may never be a problem for you. So we really have to try and decide and work with patients to determine if they have a tendency to bleed or not. Because we don't want to make people get a diagnosis and have another thing added to their medical condition unless it is actually relevant to them and to their future. Bleeding assessment tools are really useful because instead of just making a list of symptoms like bruising or heavy periods, we can actually objectively assess them using standardised questions, to which responses are given a graded number. It is between 1 and 4 for every domain and there are 13 different domains. Domains were common problems like nosebleeds, bruising, heavy periods, bleeding after dental extraction, oral cavity bleeding (bleeding after brushing your teeth), and bleeding after child birth. It was less common for people to experience things like bleeds into their joints or bleeds into their brain and spinal cord. They wouldn't really happen in patients with low von Willebrand Factor but they are included in the questionnaire.

There are two most commonly used questionnaires, and these questionnaires have been around for 13 years. They have really evolved over time to make them more streamlined so there are less questions for patients to answer and we can still get a composite result. The two most common questionnaires are rather unfortunately named for a presentation – the Condensed MCMDM-1 VWD score – which is quite a mouthful. And then the International Society on Thrombosis and Haemostasis (ISTH) BAT. Both are commonly used in the assessment of people with low von Willebrand Factor and von Willebrand Disease. But in fact we found that the condensed score doesn't work as well for menorrhagia (abnormal heavy bleeding at menstruation). When we looked into that, we found really significant differences. The same patient, the same information – some people were scoring 0 using the condensed score for that bleeding domain, and some were scoring 3 out of a maximum 4, so there is a big difference there. It actually came down to "did you go to your doctor and tell them you have heavy bleeding?" Because if you never reported it to your doctor, you get 0 using the condensed score, whereas if you had heavy periods since your very first period and had heavy periods for the last 12 months, you got a score of 3 with the ISTH BAT.

Or if you have clots or flooding or changing your pads more frequently than every two hours, or if you needed time off work or school, you can get scores using the ISTH BAT. Some of the questionnaires don't take into account the patient reported symptoms that they are living with and not recognising them as abnormal bleeding.

On the next page, read part II of the interview with Dr Lavin on why teenage girls who report heavy menstrual bleeding should be the target demographic group we need to focus on and how we can "try to change things rather than wait for people to bleed their way to a diagnosis."

Click here to catch the interview in video format.

EHC NOW!

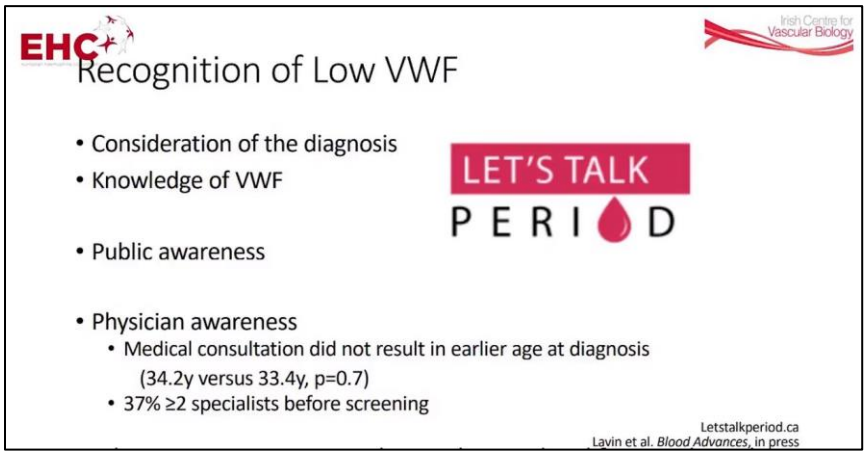
Let's Talk Period

Interview with Dr Michelle Lavin, coagulation haematologist; Interview taken by Declan Noone, EHC PARTNERS Programme consultant.

A large percentage of teenage girls who experience heavy menstrual bleeding, one of the most common symptoms of von Willebrand Disease (VWD), do not get referred for haemostatic testing or for von Willebrand Factor screening. What can we do to change this and how can we educate both the clinicians and community to recognise these symptoms? Find out in part II of our interview with Dr Michelle Lavin, coagulation haematologist.

DN: *So one of the things that you mentioned was that out of 89 per cent of women who self-reported heavy menstrual bleeding, only 60 per cent went to the clinician and got further information. The other statistic is that only 8 per cent of teenagers who go to clinicians with heavy menstrual bleeding get von Willebrand screening.*

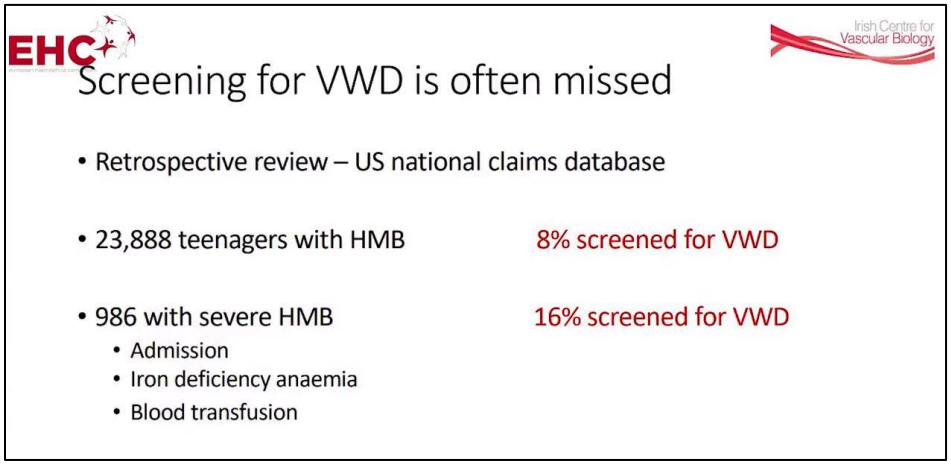
ML: The first statistic was from our own study, where we looked at 120 women with low von Willebrand Factor levels. We found that although 89 per cent of them reported heavy menstrual bleeding, only 60 per cent ever mentioned it to a doctor prior to finding out they had low von Willebrand Factor. We shape our acceptance of how heavy periods should be by what our mothers tell us, what they themselves have experienced, what our sisters have experienced or what our friends have experienced. But people are slow to discuss their symptoms and slow to recognise what is abnormal. The big take-home message is that if you are bleeding for longer than seven days, if you need to change your pads or tampons more frequently than every two hours, or if you are passing clots, that is not normal and you need to actually have that checked out. If a doctor tells you that is normal, don't accept that and try to get haemostatic testing. One in five women will have heavy menstrual bleeding at the time of periods and out of those women, one in five will have a bleeding disorder. So if you look at Ireland, we have about 1,000,000 women who are between the ages of 15 and 45 based on the census from 2016. That means there are 200,000 women in Ireland who have heavy menstrual bleeding, out of which up to 40,000 could actually have an underlying bleeding condition contributing to it. These are huge numbers. It is actually beyond haematology, it's a public health issue. We are working really proactively; we had students working on a student innovation challenge on how to reach out to the community and to the public about what's normal and what



is abnormal. We had some great ideas feeding back and we are hoping to take that forward into a public awareness campaign for both physicians to recognise what is abnormal and for people in the community to recognise when their periods are actually not normal.

DN: *That is a very important point. I know there is the male verses female clinician and who you get is influential to what you report. There is an importance in just saying it and in responding to the issue. In terms of education, what do you think is the best way to get that across to women, to explain "you need to talk about this?"*

ML: I think the demographic that are particularly vulnerable are teenage girls. You mentioned one of the studies that we referenced, which was a study of the American public data base, looking at the amount of teenagers that have reported heavy menstrual bleeding and then have been coded with a diagnosis of heavy menstrual bleeding. It is just under 24,000 girls who had heavy menstrual bleeding as teenagers and just under a 1000 of those had had a blood transfusion or had severe iron deficiency or required hospital admission. That has an amazing impact on your life, if you have gotten to the point where you needed to go to the hospital or have had a blood transfusion as a teenager for your periods, something needs to be done about that, that has gone too far already. But of those, only eight per cent of the overall 24,000 had a von Willebrand Factor screening and 16 percent of the girls who were admitted to the hospital or had had a transfusion, or had low iron, had von Willebrand factor screening. According to the 2001 American College of Obstetricians and Gynecologists guidelines, all those girls should have been checked. Because if you are a teenager with heavy menstrual bleeding, we need to be checking and making sure we are not missing an underlying bleeding disorder. I think for me, they are the real target demographic we need to focus on because then we can catch people and identify them as having a bleeding disorder before they get pregnant, before they have an operation, before they get a tooth out and try to change things rather than wait for people to bleed their way to a diagnosis. That's why we engage with the Royal College of Surgeons in Ireland. We run a summer research school and we had a recent student innovation challenge where we put that task out to students. These are third and fourth year medical students and they have a better grasp of social media than I do. We got some really great suggestions back about putting information leaflets, not just out in the community, but at the aisles where sanitary items are sold or in general practitioner (GP) practices. A really good one was that in other countries that have freshman's week in college, when people start off in college, to hand out sanitary pads or tampons and information about what's normal and what is abnormal. I personally think it would be great if some of the tampon and pad



companies had a sticker on their pack that if you are using a whole box of super plus tampons, you need to do something about it. You shouldn't be getting through that much in a month. I think by virtue, the women picking up the heaviest tampons, the biggest pads, they are the women we need to be saying to "have you thought about this?"

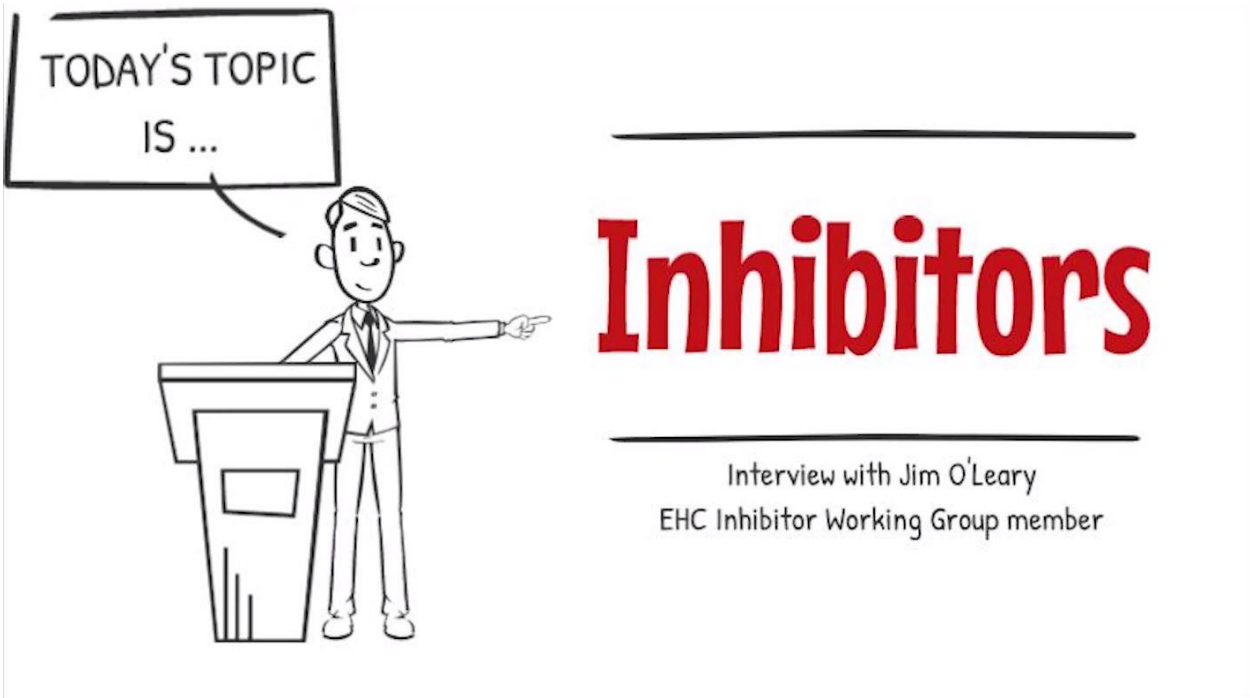
DN: *"Let's have a discussion"*

ML: Yes, exactly.

DN: *Wonderful, thank you. We could clearly talk about this all day, but we have very limited time. Thank you for sharing this information with us!*

Click here to catch the interview in video format.

EHC NOW!



Interview by Raia Mihaylova, EHC Communications Officer

As it is all too well known by the community, having an inhibitor to treatment product is the biggest challenge in haemophilia today. What is not well-known are the exact causes for why some patients develop one, while others don't. Beyond having the medical information, sharing of experience can help affected individuals approach their inhibitor in a more positive way. Jim O'Leary, member of the EHC Inhibitor Working Group, has had an inhibitor for the majority of his lifetime and shares what has helped him throughout the years.

RM: *How long have you had an inhibitor?*

JO: I have my inhibitor for 48 years, I was 14 when I developed it, in 1970. I had only had treatment for about one year prior to developing the inhibitor.

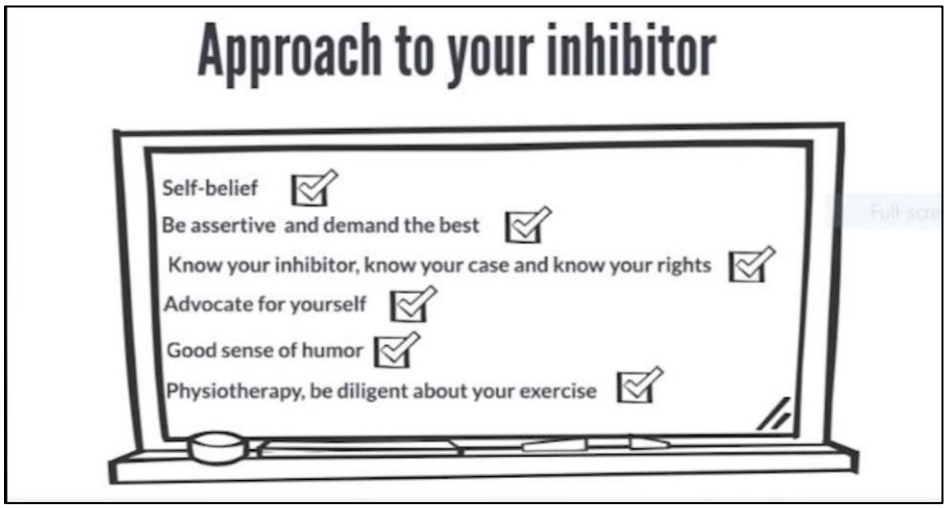
RM: *So you have gone through the teenage stage of life and adulthood with an inhibitor. Over the years, what has helped you to live positively with an inhibitor?*

Do you have some advice that you can give?

JO: I think the main thing is to develop self-belief, that you are not limited by your inhibitor any more than you are limited by your haemophilia. And you can achieve anything you want, if you set your mind to it and believe that you can do it, you will get there. That would be the first piece of advice.

Second one, I'd say, is to be assertive about the treatment you get and demand the best, because you are the most important patient as far as you are concerned. So it is important that, with doctors, with medical teams, and also with employers and schools, you demand the best and get the best.

RM: *Be knowledgeable…*



JO: Correct. Know your inhibitor, know your case and know your rights. It's important, because you have to advocate for yourself. If you don't, there are going to be too many people out there to advocate for you, so it's important to do it for yourself.

And the final piece of advice I'd say is – develop good sense of humor, because it gets you through the bad days.

RM: *This is in terms of mindset. Is there anything physical that you can think of that you did, that helped?*

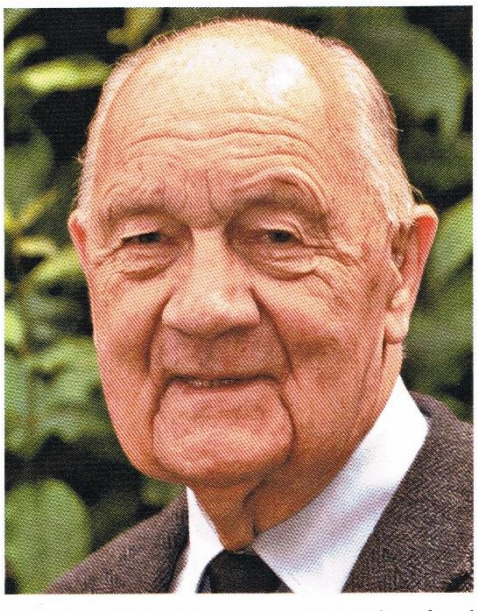
JO: I would say physiotherapy is the key, especially if you have an inhibitor, because the arthropathy is a big issue. We all develop bad joints over the years from repeated bleeds. So doing the physio, being diligent about doing your exercises, even though sometimes you don't feel like doing them, it is important in order to stay fit, because as you get older it becomes more of an issue.

RM: *How do you feel about the state of where inhibitor care and treatment is going right now? Because for a long time it was kind of in a stalled mode.*

JO: Well, I have used the same by-pass product since 1984. And nothing has changed, it has not improved, it is exactly the same. But this year, now, there is a new treatment being licensed, and there is a whole new range of novel therapies coming on the market, the whole landscape is changing. And hopefully inhibitors won't be an issue. And we are really looking forward to the gene therapy in 5-6 years' time, where we may be able to eliminate the disease altogether.

In Memoriam

Professor Dr Marc Verstraete



It is with sadness that we say goodbye to Prof Dr Marc Verstaete, professor at the KU Leuven (KUL) University, Belgium, who passed away on the 16th of August 2018.

Born in Brugge in 1925, he received his Doctor of Medicine degree in 1951 at the University of Leuven and specialised further in Basel, Oxford and New York. In 1957 he established a laboratory at KUL, where he did research on haemostasis, clotting and thrombolysis. Through his research, he made a fundamental contribution towards defining the difference between haemophilia A and B, as well as helping to define von Willebrand Disease. He also discovered drugs that dissolve vein clots and prevent cardio patients from having a stroke.

In 1958 he helped to create the Belgian Haemophilia Society.

Throughout his career and thereafter, Prof Dr Verstraete received recognitions that included becoming an Honorary Member of the Royal College of Edinburgh and London, the American College of Cardiology and the American College of Physicians. In 1981 he was nominated as lecturer for the Wright-Schulte Memorial and the Robert P Grant Medal (1993). He was also member and Chairperson of the Royal Academy for Medicine in Belgium.

The culmination of all his work can be seen in the establishment of the Centre for Molecular and Vascular Biology, with a medical personnel of more than 200 people, and the creation of the Department of Blood and Vascular Diseases at KU Leuven, both of which he led.

We express gratitude for Prof Dr Verstraete's immense contributions to the bleeding disorders community and send our sincere condolences to his family, friends and colleagues.

EHC NOW!

AFH Congress 2018: Innovating for a better future

Interview with Olivia Romero-Lux, member of the French Haemophilia Association (AFH) and EHC Steering Committee; Interview taken by Raia Mihaylova, EHC Communications Officer.

Innovations or revolution? That was the guiding question of the French Haemophilia Association's (AFH) 45th National Congress, which took place from June 2nd-3rd in Nancy, France. The 350 participants – patients and health care professionals – tackled this question in relation to novel haemophilia therapies coming to the market and how they will revolutionise health care. Extended half-life treatments, non-factor replacements and the anticipation of gene therapy are changing the daily lives of patients and the AFH is preparing their community through education, workshops and exchange of experience.

"Change" echoed throughout the whole event, as the Association welcomed a new President and CEO – Nicolas Giraud and Fabrice Pilorgé, respectively.

Olivia Romero-Lux, member of the AFH and EHC Steering Committee, attended the Congress and shares what stood out to her from the weekend.

RM: *There was a lot of information presented at the Congress, did anything surprise you? What is your take-home message?*

OL: It was not really a surprise but definitely the confirmation that the AFH needs to train patients in light of upcoming new products that do not have the same mechanism of action as the existing ones. The hope is high but we need to be prepared and to be able to understand the benefits and risks of each treatment solution.

RM: *You were one of the speakers at the event, can you briefly summarise some key points of your presentation?*

OL: I moderated a workshop on Europe and disparities in access to treatment. Amanda Bok, CEO of the EHC, and Philippe de Moerloose, former EAHAD President, attended and made high-level presentations on the European Principles of Care, comprehensive care and on the PARTNERS programme developed by the EHC for the 14 less-privileged European countries we serve, in terms of access to treatment. I think it was an eye-opener for the participants and I'd like to thank Amanda and Philippe for giving such interesting and in-depth presentations on how patient representatives and health care professionals can collaborate towards meeting the interests of our community.

RM: *Presentations aside, what is your top highlight from the weekend?*

OL: The French Society has undergone a huge revolution under Thomas Sannié's presidency but it was probably time to change our leadership to build on the momentum and write a new page in our history. Now, a new President has been elected - Nicolas Giraud - and we are very proud to have a person with von Willebrand Disease (VWD) to lead our Society. This is definitely a sign that things are changing and that our community takes into account all inherited rare bleeding disorders, not just haemophilia, even if haemophilia is in our DNA.

RM: *As you mentioned, there were a lot of emotions throughout the event – Thomas Sannié, President of the AFH for the last six years, is stepping down. You have worked closely with him on numerous occasions, what is your 'goodbye' message to him?*

OL: When I started as a volunteer in 2000, Thomas was probably the first person I met and it was love at first sight for me ☺ The man was a visionary, I could tell. I'm so honoured to have collaborated with Thomas and I've grown so much thanks to him. And funnily enough, I was elected to the Board of the French Society last Saturday and I'll be in charge of International Actions, where Thomas will still support our work by leading the Afath* program, our development plan to accompany French-speaking African countries. So, I'll get to keep working with him in the years to come…

RM: *There was a quote on Twitter in response to the Congress that the AFH will have to be innovative in the near future about their role as a patient organisation. How do you see its role, will it change in the next 5-10 years?*

OL: I think the AFH has to support our community in two ways. First, we need to educate and train our members in order for them to be in control of their care. New molecules, new treatments, new protocols are on their way and this is a complete game-changer. We also need to pave the way for those who are expecting therapeutic solutions for VWD, or other bleeding disorders where solutions are still too scarce. Second, we need to build our capacities in public health and data collection as budget constraints are going to be a major element in reimbursement and market authorisation. We need to be able to elaborate more fine-tuned advocacy tools to prove our case when the time comes to assess new medicines, especially where business models do not yet exist, like for gene therapy. Those are very exciting times for the community and the AFH definitely has to be innovative to make sure we stay focused on what is relevant for us.

The EHC congratulates Nicolas Giraud and Fabrice Pilorgé and wishes them success in their new roles as President and CEO, respectively, of the AFH.

Twitter Feed from the Congress
#CNAFH2018

Feature Articles

Researcher spotlight: Professor Johannes Oldenburg

Interview with Professor Johannes Oldenburg, Director of the Institute of Experimental Haematology and Transfusion Medicine and the Haemophilia Centre at the University Clinic, Bonn, Germany; Interview taken by Raia Mihaylova, EHC Communications Officer.

As haemophilia is a life-long condition for patients on the one side, it is matched on the other side by medical experts that have dedicated their life to understanding and improving its treatment and care. One such medical expert is Professor Johannes Oldenburg, Director of the Institute of Experimental Haematology and Transfusion Medicine and the Haemophilia Centre at the University Clinic in Bonn, Germany. Among his various roles, he is also part of the European Network on Inhibitor Research (ENTIRE), a multidisciplinary team formed to address the complex interplay between patients' genetic and environmental-related risk factors for developing an inhibitor, which we introduced to you in previous EHC NOW! material. We are now excited to also welcome Professor Oldenburg to the EHC Medical Advisory Group. In this interview, read about why he decided to join the group and his thoughts on novel haemophilia therapies.

RM: *We are excited to welcome you as a member of the EHC Medical Advisory Group. Why did you decide to join, what in your view is the aim of the group?*

Professor Oldenburg spoke at the EHC Round Table on 'Clinical Trials in Haemophilia A', which took place at the European Parliament

JO: First, I have to say that I felt very honoured that I was invited to join the EHC Medical Advisory Group. I think that this group is very important because the EHC has a lot of activities around haemophilia, so the group is very active in trying to go ahead with the developments in haemophilia and tries always to balance these developments for the patients and also the suspected benefits for the patient. I really like to be part of this active group. I myself have been in the haemophilia field for more than 30 years, we have a big centre here (in Bonn), we have quite a lot of experience. I am part of most of the new product studies and I think that my advice could be helpful because of my experience.

RM: *As we know, we are entering, so to say, the next stage of advancement in haemophilia treatment. The emergence of novel therapies is not only going to bring change to treatment regimes and patients' quality of life, but also to health care systems, haemophilia comprehensive care centres and so on. What are your thoughts on this changing treatment landscape?*

JO: The intensity of prophylaxis for patients, for example, is becoming better with the new therapies because they will level out the protection for bleeds and the quality of prophylactic treatment. With respect to the extended half-life products, it is now much easier to come into the range of higher trough levels of above three per cent in haemophilia A and especially in haemophilia B, because products have much longer half-life. With the non-substitutive therapies at the moment we have experience with Hemlibra for patients with haemophilia A and inhibitors. The protection level almost corresponds to the mild haemophilia phenotype. We now have to wait on what the study results will show for the non-inhibitor patients and how the other non-substitutive approaches, such as Fitusiran with the downward relation of antithrombin – or TFPI antibodies in general, on which several companies are working – will perform in a prophylactic setting. But overall, the level of protection will increase. The challenge, I think, is to provide these treatments without having a very significant cost increase, because for the health care system – I can make an example with Germany – the average cost for a haemophilic patient on prophylactic treatment is about 250,000 Euros per year and we have to build these new therapies into the cost model that already exists in the various countries.

RM: *As you mentioned, with novel therapies it is now very important to monitor for side effects and for how efficacious they are. How long does this monitoring phase last before it is safe to conclude their health outcomes?*

JO: I believe that these new therapies will require a lot of education for patients and for haemophilia care centres because their concept is completely different. On one hand, we provide prophylaxis that is subcutaneous and can be given once weekly or once monthly, so it is extremely convenient for the patient and it provides very good protection level. But we still may have emergency cases, such as in the case of an accident, for example. Then appropriate action will be needed, where we have to consider potential side effects. New drugs also have limitations. For Hemlibra, we have some limitations with inhibitor patients, we cannot use aPPC products as we have used them before. So we have to learn new ways of management and this will take a few years; it won't be in the next 1-2 years. We will need more time until we really know whether the management of the patient with the new products is as safe as the management with the products in the past.

RM: *You are the Director of the Institute of Experimental Haematology and Transfusion Medicine and the Haemophilia Centre at the University Clinic in Bonn. You have published hundreds of articles, are a member of various journal editorial boards and the list goes on. What are you currently working on?*

JO: Currently, my major work refers to the upcoming clinical studies with the non-substitutive therapies. We are also very much interested to participate in the Phase III gene therapy trials this year, that is the clinical study programme that is in the works. With the haemophilia centre, we are

also working on long-term outcome measures in haemophilia, like joint health, to try to define the measures that we have to implement to have a very good evaluation of the outcome of these different therapies that are coming. These are the two main focus areas when participating in the new studies that are coming. I think it is very important to gain experience yourself with these new products and to implement the outcome measures for joint health and be able to evaluate these therapies from a long-term perspective.

RM: *Is there anything that keeps you up in at night in relation to work?*

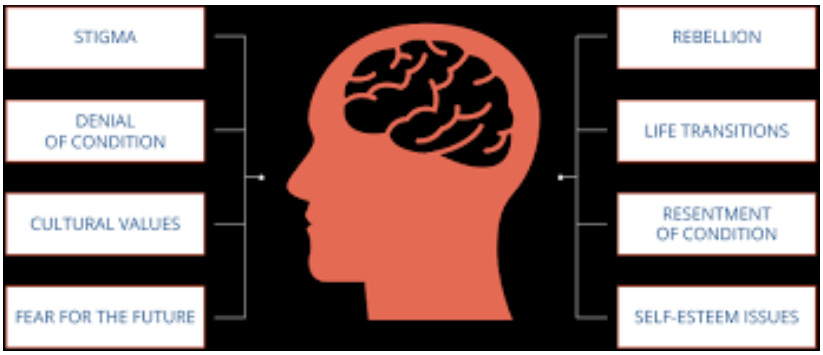
JO: No, I just feel extremely happy at the moment and confident because for the last 30 years, we had a huge milestone with regards to recombinant clotting factors and now we have the next steps. It is not just a single drug or concept, it is a burst of drugs and concepts coming. I find this to be a fascinating time for patients and the haemophilia centres.

RM: *The International Society on Thrombosis and Haemostasis (ISTH) Scientific and Standardization Committee (**SSC**) Conference is coming up in July in Dublin. What are you looking forward to hearing presented there?*

JO: I am very interested in the updates of the clinical trial programmes. There will be quite a number of updates. There are a lot of initiatives within the SSC subcommittees that are also very helpful. For example, one will meet on the topic of the laboratory assays that will be playing a very important role in the future because we have to decide how to best monitor the treatment of our patients with the various laboratory tests in the light of all these novel therapies coming.

Psychology in haemophilia: keeping one eye on the future, the other on what remains with us

Interview with Nicola Dunn, Individual & Family Therapist, Specialist in Haemophilia, Katherine Dormandy Haemophilia Centre and Thrombosis Unit, Royal Free Hospital; Interview taken by Raia Mihaylova, EHC Communications Officer.



Having haemophilia is a journey that can bring physical, mental, emotional and social challenges on top of the issues that come with everyday life. This makes psychosocial support all the more important for people with haemophilia, yet it is the least integrated area in comprehensive care. In an effort to shed more light on the topic, I sat down with Nicola Dunn, a psychotherapist in the field of haemophilia, to talk about the concerns the different age groups within the community have. While each experience is unique, there are many common traits that are present for everyone from diagnosis to adulthood.

RM: *You have worked as a psychotherapist in the field of haemophilia for longer than 18 years. What are some changes you have observed over that time – are people reaching out more, have the issues changed?*

Nicola Dunn

ND: In terms of people's openness towards support for their emotional well-being, yes, it has changed quite a bit. I think there are general cultural factors that are operating in Europe, which have encouraged that. Whether that is through the media or through people in the public eye who appear to have quite successful lives coming out and talking about the fact that they struggle with their emotional well-being, I think there is a greater comfort with it, particularly for men, which is fantastic.

The issues have also changed. When I was doing my placement, the pressing issues were around the tragedy of HIV infection and later, with hepatitis C. In that situation, it was people having a diagnosis of HIV, whether that was in a family with their son or whether it was an adult man. They were coming to terms with the condition, which they had received through their treatment product.

So it was the shock of that, it was dealing with not having a lot of information available, also for the local communities. There was a feeling of not being able to be 'out' about their diagnosis. It was something that they had to hide in order to protect their family or in the case of parents, to protect their child from what might happen at school and so on. It was a very difficult time for people in the haemophilia community. The treatments were new and not as sophisticated as they are now. People were losing friends who had haemophilia within their cohort. Some obviously weren't affected, which led to a kind of survival guilt as well.

There were a lot of things that were happening at that time period. We didn't have recombinant treatment products, they were only plasm-derived ones. We didn't have prophylaxis in the same kind of way as we do now. If I am to contrast that with the issues that people come to me with now, the main one is the development of inhibitors. Something that the haemophilia community has always had to deal with is that not everybody gets dealt the same hand of cards, in a way. Their haemophilia is unique, the treatments that work for one person don't always work for another person. You are part of a community but it doesn't mean that you are all having quite the same success with the treatments that are available. I think that is something that we need to bear in mind. Also HIV has obviously not gone away and it is something for us not to forget about, because otherwise it feels as if we are leaving those patients behind. We are always focusing on what is new and I think that we need to keep one eye on the future and on what is unfolding and we need to keep another eye on what remains with us.

RM: *As you said, the issues are very different whether they are based on the history of haemophilia or ones that come with different age groups. Can you share some of the most common psychosocial concerns that people with haemophilia have within each age group?*

ND: Because the patient cohort I work with is in London and London is hugely multicultural, our department is multicultural and our patient group is multicultural. We have a group of patients who have been born in the UK and then equally, we have another significant group of patients who have come to the UK at a certain point of time – often as an adult or

maybe as an older child – so they have had a different treatment history. We have people who have had the advantages and resources of excellent haemophilia care and we have others who have had to manage with what was available to them. Now they find themselves in the same patient group but with a very different impact on their body and on their psychological issues.

Childhood

ND: If we were to go through the different age groups, starting out with the first years of a young boy's life (0-5 years old), I would say the challenges are having the whole family coming to terms with the haemophilia and the young boy's development within the context of friends and school. It is about 'how active can I be?' and 'how can I discover myself?' because to a large extent, you find yourself through your environment. How much is allowed and what is not allowed? Traditionally, when we had the plasma- derived products and it was basically on-demand rather than on prophylaxis, the general thought and advice was 'no sport.' So no football; none of the team sports that are popular in the UK and Europe were allowed. Now it is different, we even recommend sports. Probably not boxing or rugby because of the number of injuries, and while we do encourage involvement, it does require a commitment to prophylaxis. So it has gone from a 'no' to a 'yes,' but…'

Teenage Years

ND: When we get into teenage years, I always say that at this point, we have a new patient. We need to consider this because the treatment responsibility is being transferred over to the teenager. Often, the challenges are around prophylaxis treatment. If they had good treatment in the past, the young boy may not remember having particularly significant bleeds. Sometimes, unfortunately, it may be necessary for the patient to have an inconvenient bleed in order for them to think "I really need to commit to my treatment product."

Then there are some slightly new things – treatment was previously less effective and there was damage to joints at an earlier age. What we have now is an increasing pressure on young men around body image. They look to their icons, either from the sport or music industry or wherever, and body image is a big part of that. Particularly for patients who may have come from elsewhere and have had less availability of treatment, or even UK- based patients that maybe didn't adhere to their prophylaxis, if there was any change in their limbs or something else, they are very conscious of that. I think we really need to consider that this sort of pressure of body image that women are well aware of has also transferred over to our young men.

Young Adulthood

ND: The issues that arise in the 20s and 30s are around building a career. Most young people these days have an interest in exploring the world and want to travel, and then they have to again consider their haemophilia when making a choice: availability of treatment product and treatment centres, could they work abroad and if so, where? So they are facing a wider world. Once again, at each transition the question is "and how does my haemophilia impact me now?" Then of course it's also about choosing a partner and answering questions about having or not having a family.

Another thing for young people is that, generally, it seems that anxiety is quite a big issue. Normally, when young men come to me, the words they would use are "I feel stressed." So we would try to unpack what that stress is – whether it is about identity, whether it is about a feeling that the haemophilia is stopping them from doing something that they want to do, whether it is unhappiness about body image, whatever it is. That would often be the entry point and it is good that they have a word for it because that enables them to ask for help and support.

Adulthood

ND: In the 40s to 50s there is a mid-life evaluation that happens to most people. People are thinking about how they want the second half of their life to be. Then we move on to ageing with haemophilia, which previous generations didn't necessarily do, as their life expectancy was reduced. We are looking at joint health and for patients that didn't have treatment products as young people, that is obviously more problematic. We are thinking about what point is the right point for someone to have a significant orthopaedic intervention, like a joint replacement. People normally choose it when they feel that the pain or the impact on their lifestyle is such that they are prepared to go forward with the process.

Understandably, there are concerns and it's a little bit like the treatment – you don't have any guarantee about how this intervention will turn out for you. We can talk about what happens in populations but we can't say how it will be exactly for the individual. One guarantee, however, is that one knee, for example, will be different to the other knee. We don't want people to be disappointed by the intervention but rather that they feel like they have chosen it with enough information. Part of my job is to accompany them through all these stages.

Overall, throughout all the age groups, patients sometimes come with a lack of trust, they just feel like they haven't been given the full information. Or they have had a lot of trauma as a child. This can be something like being locked in during the day while their parents are working because it was a concern that they would hurt themselves and the family wouldn't be able to pay for the treatment factor. All of these things impact who a person takes themselves to be and what it means to have value as a human being. For example I see patients who feel guilty because they have seen

their families struggle financially to pay for treatment product. There are a lot of things to be worked through.

RM: *Talking concretely about women who are carriers, they often feel a lot of guilt that they have passed on the gene to their child. What do you say to these mothers?*

ND: The first thing is that I get them to tell me about their experience with that, because it is often unique. Then I would really be in dialogue around two elements: one, we all know the scientific facts and the fact that it's not the parent who chooses to pass on the gene. We know that, but we need to stress it more. That's the scientific side of it. Then we look at the emotional side. I would say that the reason they feel guilty is because that's a natural process for a nurturer. Guilt gives responsibility and it is kind of built into us.

I would also look at it from the gender point of view. There was an interesting paper, which looked at male response to guilt and responsibility. Men are often more skilled than women at developing a narrative, which considers aspects like fate and destiny and actually puts responsibility outside of the parents.

Women need to have an opportunity to talk about it. It's about how we create a new narrative following the diagnosis and in going forward. It is looking at it from a perspective that your child's life comes with these opportunities and these challenges. They won't actually exist without having this particular genetic composition.

RM: *I have read on a few occasions that some patients have noticed that when they are in a good mood and high spirits, they experience less pain or joint bleeds. Do you have any observations on that – can state of mind affect bleeds?*

ND: There is a physicality to pain. But my experience is that mood is a magnifier. A low mood would magnify pain and a more buoyant mood would actually ease it. There are things we can do in actually harnessing mood and creating buoyancy. We may very well, therefore, not always but many times, get an accompanying effect in patients' experience with pain.

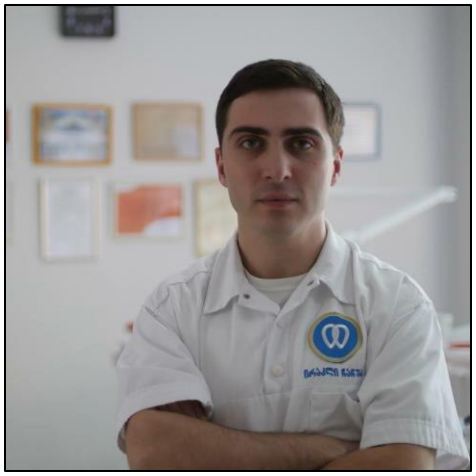
For suggestions of additional resources or contact information of psychologists in the field of haemophilia, you can get in touch with the EHC at office@ehc.eu

EHC NOW!

Profile: Dr Irakli Chachua

Interview with Dr Irakli Chachua, dentist in Tbilisi, Georgia; Interview taken by Raia Mihaylova, EHC Communications Officer.

Oral care is an important part of comprehensive care for people with haemophilia and other bleeding disorders, yet it is often disregarded out of fear or lack of concern. On the other hand, there are many dentists who are not fully prepared to treat patients with haemophilia. Dr Irakli Chachua, who himself has haemophilia himself, had such an experience during his childhood and decided that one day he will open a dental clinic that addresses this challenge. Now a reality and named after his favorite band (keep reading to find out more), Dr Chachua sat down with me to talk about his goals and what he is doing to help spread awareness of the advantages of having proper oral hygiene.



RM: *You are quite young and already have many years of professional experience. How did you first decide to become a dentist?*

IC: I grew up in a family in which my mother, uncle and grandmother all worked in fields close to medicine. I decided when I was a kid that I wanted to become a dentist. Also, when I was a little boy, I had an experience with needing to extract one of my wisdom teeth. I visited several dental offices but not a single dentist wanted to provide the appropriate dental treatment. They were afraid because I had haemophilia. From then on I got interested in providing appropriate treatment for patients with haemophilia and other bleeding disorders and that's how I became a dentist. I am an oral surgeon, implantologist and I am a periodontist.

The most common problem right now is that the dentists practicing in Georgia don't have information regarding what haemophilia is, what kind of complications it can create, the care required after surgery, etc. When I was a student, I had this idea to establish a dental clinic that focuses on treating patients with haemophilia and other bleeding disorders. Right now, we have been running for two years and we have many patients and good results.

RM: *What are the most common dental concerns for people with haemophilia?*

IC: The most common dental problem is proper oral hygiene. No matter if the patient has haemophilia or not, if they have gingivitis or other soft tissue inflammation, it is normal to have bleeding from the oral cavity. This bleeding becomes more serious if the patient has haemophilia. They stop to brush their teeth because they are afraid to have a bleeding episode; instead they infuse with factor concentrate thinking that if they get their treatment, the bleeding will stop. But

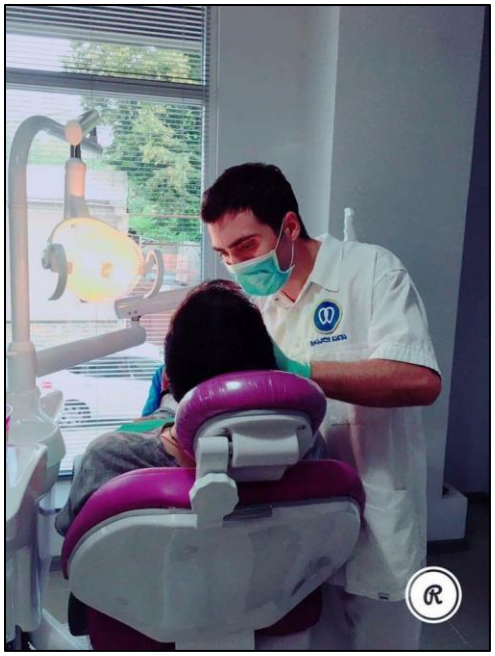
it's not like that, gum bleeding isn't because of their haemophilia, it is a result of not taking care of a dental problem. They don't visit their dentist regularly and, due to poor oral hygiene, they will get serious dental diseases in the future. We then would have to extract the tooth and it becomes a surgical procedure that the patient might be afraid of and then he might not do it on time. This is the common problem we are facing as dentists. We are trying to raise awareness about haemophilia: it is not a problem to brush their teeth, to visit their dentist, to have good oral hygiene, to clean their oral cavities and to remove the bacteria All this leads to *less* bleeding. The patient should visit their dentist regularly – every six months – just to have their oral cavity checked, to find out if there is a problem at an early stage so that we can have minimal invasion and to protect them from further inflammation. This check-up is painless and results are very good if they visit us every six months.

RM: *You mentioned that having haemophilia to a large extent led you to become a dentist. Has having haemophilia affected you in any other way, personally and professionally?*

IC: When you want to become a dentist or doctor, you have to read a lot of literature, a lot of books. Then you have to implement all this theoretical education into your practice. When I had a bleeding episode in my knees or in my arms, I couldn't walk and I wasn't very physically active. All I could do was read as many books as possible. So, haemophilia affected me in a positive way! Many other kids that are out playing football, for example, don't have enough time to read even though they would like to. I had the opposite situation, so it affected me in a positive way.

I don't consider myself special, I am a normal guy who has very lazy blood ☺ I call my blood 'lazy blood' because a normal person can have their blood clot in five minutes; I need 30 minutes. This is the only difference. If I didn't have haemophilia, I wouldn't have the opportunity to meet with other people from various countries, both professionals and colleagues.

For example, the World Federation of Hemophilia (WFH) gave me an opportunity to visit London for one month as a dentist. I visited the Royal Free Hospital and also the Royal London Dental Hospital. It was a great experience, I met with other colleagues, trained with them, learned from them and we are now implementing this knowledge in Georgia.



RM: *Can you talk a little more about your clinic?*

IC: It is called the 'Dental Clinic Zeppelin.' It has two dental units; we have all kind of modern equipment and dental procedures, including tooth filling, extraction, implantation as well as peadiatric dentistry, orthodontic, and all the dental treatments. Right now, the aim is to provide the proper dental treatment to patients with haemophilia and other bleeding disorders.

RM: *It is called Zeppelin?*

IC: It is named after the British rock band Led Zeppelin, of whom I am a huge fan of! I couldn't name it 'Led

Zeppelin' so I just dropped the Led. It became very popular in Georgia – everybody knows there is the 'Zeppelin Dental Clinic.'

RM: *It is very clever, I like it! What does your typical day look like?*

IC: I wake up at seven in the morning. I do a little sport. I come to my dentist office and I see patients. We have a schedule. From 9-12, we have the big implant procedures. Then we have the periodontist procedures, then tooth filling and so on. Also, I have students from two universities, I teach them special surgical procedures and periodontistry. They have very good information about haemophilia because I always try to talk to them about haemophilia and how to provide the proper treatment since you never know if someone with haemophilia will come to their office. We have to be prepared for all kinds of situations.

RM: *You did training in London, you have travelled quite a bit and now work in Georgia. Have you observed any difference in haemophilia patients and their approaches to going to the dentist?*

IC: Well, in London, for instance, the patients are going regularly to their dentist – every six months. They don't forget about these appointments. In Georgia, we don't have that kind of situation right now. Patients are afraid or don't have the time. But we are trying to explain to them that if they visit the dentist every six months, their dentist will perform painless procedures and the worse kind of visits will be prevented. This is preventive dentistry. Some of the patients listen, some refuse to and those who refuse have more complicated dental diseases. We are trying to figure out how to get them in the habit.

The one thing I always tell patients is not to use so much factor concentrate when they have gum bleeding. They have to refer to a dentist and the dentist will identify what the problem is and then provide appropriate treatment. So save your factor concentrate, don't 'overdose!' It is essential to visit the dentist because 99 per cent of the time, if there is a bleeding in the oral cavity, it is due to poor oral hygiene. A five-minute dental procedure will prevent further bleeding and save factor concentrates!

RM: *Is there anything that will surprise people about you?*

IC: I have a guitar hanging in my dental clinic. Patients that visit are always looking at the guitar; they don't understand why it is hanging here! I decided to hang my first guitar because when I was in London, a dentist – Dr Guy Roberston – who I really admire as a dentist, a friend and a person, has a guitar in his office. I liked it as an idea and did the same. Patients are always very stressed, sometimes just even from the smell of the clinic, from the environment, from the fact that everything is white, so we are try to create an environment where patients will be relaxed and not think about their pain. The guitar sometimes makes them feel like everything will be okay. If they behave very well, they are allowed to play it ☺.

EHC events coming up

September 07-09	**Tenders and Procurement Workshop** Amsterdam, Netherlands Open to NMOs only
October 5-7	**2018 EHC Conference** Brussels, Belgium Open to all To register, please visit https://conference.ehc.eu/
November 20	**Round Table on Switching from Standard Therapies: Where do Novel Therapies Fit In** Brussels, Belgium Open to select participants
November 23-25	**New Technologies in Haemophilia Workshop** Location to be confirmed Open to NMOs only
December 6-9	**European Inhibitor Summit** Barretstown, Ireland Open to NMOs only