Haemophilia.ie

Representing People in Ireland with Haemophilia, von Willebrands & Related Bleeding Disorders

Magazine of the Irish Haemophilia Society

Winter 2020

The Society at a Glance

74	46	1474	1023
I.H.S. Volunteers	Planned Giving Contributors	Facebook Followers	Twitter Followers

FROM THE EDITOR

Welcome to our Winter Magazine and I hope you are all keeping well, and like all the I.H.S. staff, are getting excited for Christmas!

Saying 2020 has been a strange year is an understatement; it has been extremely trying on us all for sure. A lot has changed during 2020 but it was another busy year for the I.H.S. with some big announcements and steps toward new and exciting treatments. In the spirit of end of year reflection, that is the theme of my article on Page 8.

Looking to the future, over on Page 3, you can see the provisional programme for our Virtual AGM & Conference 2021. There are more specifics on the AGM in Brian's CEO Report, along with a look at new treatments and Covid-19 & Vaccines, over on Page 4. Brian also continues to chart the evolution of Haemophilia Care in Europe, part three is on Page 14.

Elsewhere, there is news of educational grants awards for 2020, details of Patient Advocacy Service and we have some insight how haemophilia care has continued during the pandemic with Sheila Roche, Clinical Specialist Physiotherapist in St. James's Hospital.

On page 18 and 19, there are useful updates and news, and over on the back cover, you'll find hospital opening hours for the Christmas period.

I would like to thank everyone who contributed to our publications this year - be that writing articles, sending in ideas, photos or feedback - and of course, thank you all for reading the magazines, without you, there would be no magazine!

Wishing you all a very Happy Christmas and a healthy and prosperous New Year.

Barry

IN THIS ISSUE

The Irish Haemophilia Society is delighted to announce a Virtual AGM & Conference 2021. The conference will take place March 1 - 4.

The event is free to attend but you must register beforehand, and registration will be open in January 2021. More details will be sent to members in the new year.

PROVISIONAL PROGRAMME

Monday, March 1: 18:00 - 20:00

Treatment

18.00 – 18.45	**Review of Novel Therapies**
18.45 – 19.00	**Break**
19.00 – 19.45	**An Overview of Gene Therapy**
19.45 – 20.00	**Discussion Panel**

Tuesday, March 2: 18:00 - 20:00

Comprehensive Care

18.00 – 18.20	**Covid-19 and Vaccines**
18.20 – 18.40	**The Use of Technology**
18.45 – 19.00	**Break**
19.00 – 19.20	**Dental Care**
19.20 – 19.40	**Resilience and Mental Health**
19.40 – 20.00	**Targeted Physio at Home**

Wednesday March 3: 18:00 - 20:00

Changing face of treatment in Ireland/vWD

Parallel Sessions

18.00 – 18.45	**Update on vWD Treatment and Care**
18.45 – 19.00	**Break**
19.00 – 20.00	**Living with vWD**

Parallel Sessions

18.00 – 18.30	**Update on iPATH**
18.30 – 18.45	**Break**
18.45 – 19.45	**The Changing Face of Treatment in Ireland**
19.45 – 20.00	**Questions and Answers**

Thursday, March 4: 18:00 - 20:00

18.00 – 20.00	**Annual General Meeting 2021**

CEO REPORT

Clinical Trials and Novel Therapies

In early December, one of the webinars organised by the Society focused on clinical trials for children with haemophilia being undertaken by the team at Children's Health Ireland (CHI) in Crumlin. Over the past several years, the haemophilia community in Ireland have participated in several important clinical trials. These have included clinical trials on extended half-life Factor VIII (FVIII) and Factor IX (FIX) products in both adults and children, clinical trials on a FVIII mimetic, Emicizumab (Hemlibra) in adults and an anti-thrombin inhibitor, Fitusiran in children. We have also participated in our first clinical trial in gene therapy in adults and others are on the horizon. Ireland is particularly suited to participation in clinical trials as we have a well organised network of three comprehensive care centres and one treatment centre who collaborate closely, a national register and a culture of attending meetings which has afforded the Society and the Doctors opportunities to explain the products under clinical trial prior to starting the formal process of obtaining informed consent.

Participation in clinical trials also affords both the doctors and the people with haemophilia an opportunity to experience the newer products and assist us in evaluating the products when the time comes to assess them after they are licenced. Participation in this way can increase our speed of access to new therapeutic options as we have an opportunity to assess them following experience using the products. Ireland was the first country globally to switch all people with haemophilia A and B to extended half-life factor concentrates and one of the first to make Emicizumab an option for all those with severe FVIII deficiency. The confidence in making these decisions was assisted by real life clinical experience with these products prior to licencing via participation in clinical trials.

There are currently three new clinical trials which will be starting at CHI, Crumlin in 2021. These are for BIVV-001, a new extended half-life FVIII, MiM8, a FVIII mimetic and Marstacimab, an anti-TFPI which can be used to treat either FVIII or FIX deficiency.

BIVV-001 is an extended half-life FVIII based on the FC fusion EHL FVIII currently used in Ireland, Elocta. The half-life is further extended by adding in a portion of the von Willebrand molecule and an additional substance called anX-ten. The addition of the vWF molecule prevents VWF in the blood from limiting the increase in half life. In the earlier (Phase 1/2) clinical trial, BIVV-001 demonstrated a half-life which was 3 to 4 times as long as with standard FVIII. And at the higher dose used, a trough level of 17% was achieved one-week post infusion. This appears as if this therapy may allow for once a week prophylaxis with FVIII with very good levels of protection.

The FVIII mimetic MiM8 is a bi-specific antibody similar to Emicizumab (Hemlibra) in its mode of action. In preclinical studies, the company claim that it shows 15 times more potency than Hemlibra. This would be a subcutaneous injection similar to Hemlibra.

The anti-TFPI, Marstacimab, is also a subcutaneously injected product which inhibits anti-thrombin. This is one of the coagulation rebalancing agents. Interestingly, this is one of the products which can be used to treat people with FVIII or FIX deficiency, with or without inhibitors.

Following the Society organised webinar on these clinical trial products in December, further webinars will be organised in the first quarter of 2021 to provide more details on the individual products and the individual clinical trials for those who may be interested in learning more or in enrolling.

A webinar will also take place in January with the team from the National Coagulation Centre to provide an update on clinical trials being considered in adults. These will include some of the same products discussed above in addition to some observational stage clinical trials on Gene Therapy for both Haemophilia A and B.

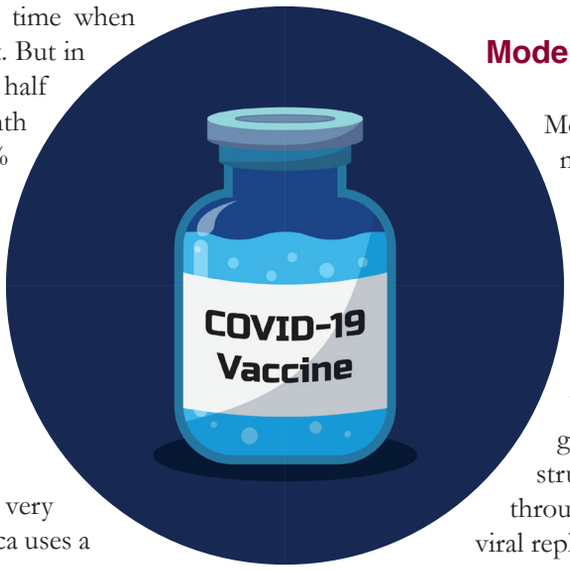
The first Gene Therapy clinical trial, which was for FIX deficiency, in which Irish people with haemophilia were enrolled have just reported their main data from the first 6 months of their final phase (Phase 3) of their clinical trial. Three people from Ireland were enrolled. This Gene Therapy - called AMT-061 - reported on the 54 people with Haemophilia B who were treated with the Gene Therapy vector, 6 months post treatment. The average FIX expression level achieved was 37%. 1 individual did not respond, and a second individual had a poor response as he received only a partial dose (probably due to a reaction at time of infusion). Of the 54 treated, 39 had no bleeding episodes in the 6 months. 15 individuals had a total of 21 bleeding episodes collectively. 9 of the 54 required steroids due to liver inflammation, which is a low proportion compared to other Gene Therapy trials. Interestingly, this is the first Gene Therapy trial where people were able to participate even if they had pre-existing antibodies to the AAV vector used as a delivery system. 23 of the 54 treated had pre-existing antibodies. These results are encouraging, and we now await the 12-month data on all 54 people.

Covid-19 and Vaccines

There has been a lot of good news about coronavirus vaccines in the week prior to writing this article. At least three of the experimental vaccines show very good efficacy, at least according to information released by the makers in press releases (although we await the publication of the full scientific

data in peer reviewed publications or journals).

Pharmaceutical company Astra Zeneca working in collaboration with researchers at Oxford University released results demonstrating that their candidate vaccine prevented Coronavirus infection 62% of the time when people got two doses a month apart. But in a subgroup of volunteers who got a half dose followed by a full dose a month later, the vaccine appeared to be 90% effective.



That averages out to 70% efficacy. The vaccines made by the Pharmaceutical company Pfizer Inc and biotechnology company Moderna appear to protect against symptomatic infection 95% of the time.

Pfizer's and Moderna's vaccines use very similar technology, while AstraZeneca uses a different approach.

Here's a look at the technology behind some of the candidates that are the furthest along in development - mostly in Phase 3 clinical trials, the last step before seeking the go-ahead from regulators around the world.

Pfizer and BioNTech vaccine

Pfizer and its German-based partner BioNTech use a new approach to making vaccines that uses messenger RNA or mRNA.

This design was chosen for a pandemic vaccine years ago because it's one that lends itself to quick turnaround. All that is needed is the genetic sequence of the virus causing the pandemic. Vaccine makers don't even need the virus itself - just the sequence.

In this case, BioNTech researchers used a little piece of genetic material coding for a piece of the spike protein - the structure that adorns the surface of the coronavirus, giving it that studded appearance.

Messenger RNA is a single strand of the genetic code that cells can "read" and use to make a protein. In the case of this vaccine, the mRNA instructs cells in the body to make the particular piece of the virus's spike protein. Then the immune system sees it, recognizes it as foreign and is prepared to attack when actual infection occurs.

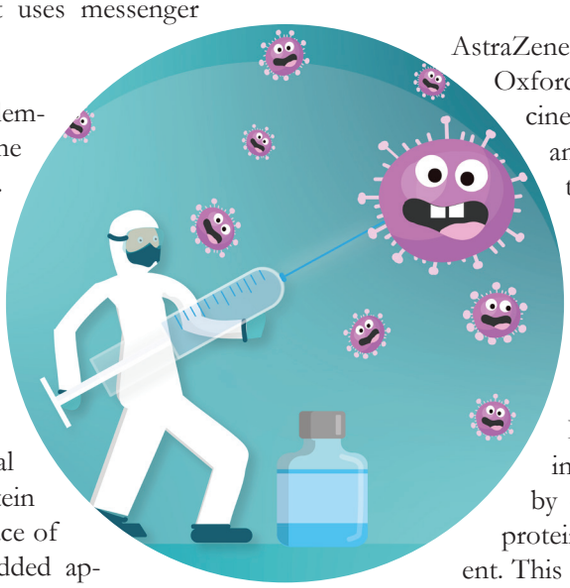
MRNA is very fragile so it's encased in lipid nanoparticles - a coating of a buttery substance that can melt at room temperature. That's why Pfizer's vaccine must be kept at ultracold temperatures of about minus 75 degrees C. That means special equipment is needed to transport and store this vaccine.

Moderna vaccine

Moderna's vaccine is also based on mRNA. Similar to the Pfizer/BioNTech vaccine, its codes for cells to make a piece of the spike protein. That was a careful choice - scientists had to pick a piece of the virus they thought would not mutate, or change much, as time passed. The virus uses the spike protein to grapple the cells it attacks, and the structure does appear to stay stable through generation after generation of viral replication.

Moderna has come up with a different formulation for the lipid nanoparticles to protect the mRNA in its vaccine. These formulations are corporate secrets, but Moderna thinks its approach is better and said its vaccine can be shipped at minus 20 degrees C and can be kept stable for 30 days at 2 degrees to 8 degrees C, the temperature of a standard home refrigerator.

AstraZeneca Vaccine



AstraZeneca's vaccine, made with a team at Oxford University, is called a vector vaccine. It uses a common cold virus called an adenovirus to carry the spike protein from the coronavirus into cells. (This should not be confused with the various adeno associated viral vectors - AAV - used in several Haemophilia Gene Therapy clinical trials).

It also aims to make people's bodies in essence produce their own vaccines by churning out little copies of spike protein, but the delivery method is different. This adenovirus infects chimpanzees but doesn't make people sick. It was modified so that it doesn't replicate itself - then genetically engineered to inject cells with the DNA encoding for the full coronavirus spike protein.

It's a cheaper way to make vaccines - but slower than using RNA. The company has pledged to make its vaccine available inexpensively to countries around the world. The vaccine can be kept stable for six months at standard refrigerator temperatures.

Society Communication

The Society have organised very interesting webinar meetings by Zoom in the last number of months. In addition to very useful updates from the NCC and CHI at Crumlin, we have been able to have clinical guest speakers from abroad speak on various topics. This included a webinar on Age-ing in Haemophilia from Prof. Mike Makris from Sheffield in the UK and Covid-19 and Haemophilia from Prof. Cedric Hermans from Belgium. Updates have also been provided on the roll out of Hemlibra (Emicizumab) as an option for people with severe FVIII deficiency.

At the time of writing this article approximately 43 children and 25 adults had switched to Hemlibra. CHI Crumlin have also been able to remove several port-a-caths from children without any requirement for additional FVIII. In late November, Dr. Beatrice Nolan from CHI presented a webinar where parents were able to ask questions and share some of their experience on Hemlibra and in December, Dr. Niamh O Connell and Dr. Alison Dougall presented on experience here with use of Hemlibra in surgery and dental surgery. Dr. Dougall will also shortly be initiating a research project on dental surgery with Hemlibra.

Society AGM and Conference 2021

While the news about vaccines is encouraging, it may not be until late in the first half of 2021 that many people may have access to a Covid-19 vaccine. With that reality in mind, we have decided that the AGM and Conference will be held virtually over four days from Monday, March 1st to Thursday, March 4th. The Conference will run over three days for two hours each day from March 1st to 3rd and the Society AGM will be held on March 4th. We have chosen the time slots from 6pm to 8pm to enable as many members as possible to attend. We will be putting together an exciting, innovative and informative programme featuring guest speakers from home and abroad. This will be more than just a series of zoom webinars we are planning to use a professional platform if possible, to give members more of a real conference experience. Pre-registration for the Conference will be required as is normally the case for the AGM / Conference although we will not be charging a registration fee. A broad outline is included in this issue of the newsletter and further details including an AGM pack will be mailed in January.

I want to finish this message by thanking the staff for their trojan work to date during the pandemic. The entire team have shown great flexibility and commitment and I hope that you have benefited for the many publications, e-Zines and webinars organised and the phone calls from staff to keep in touch which were made on a constant basis.

I wish you all a wonderful, peaceful and safe Christmas in a year where, perhaps, Christmas will have more meaning for many people than at any time in the past.

Brian O'Mahony

Thanks to everyone who applied for an educational grant from the I.H.S.

This year we received a lot of applications once again, which is brilliant!

The I.H.S. educational grants are hugely beneficial and go some way to helping cover the expense of education.

The sub-group of the board met (virtually) over the past few weeks to discuss and score all the applications so we are delighted to announce the recipients of the main grants are as follows:

Maureen & Jack Downey Educational Grants

First Prize	Conor Birkett	€4,000
Second Prize	Nicole Chun	€2,000
Third Prize	Nathan O'Hagan Doyle	€1,000

Margaret King Educational Grants

First Prize	David Moriarty	€2,000
Second Prize	Niamh Birkett	€1,000
Third Prize	Aoife Horan	€500

Father Paddy McGrath Educational Grant

Bleeding Disorder Category:

First Prize	Belen Fernandez Mora	€1,000

Family Member Category:

First Prize	Tadgh Moriarty	€500

I.H.S. Response to Pandemic 2020

2020 has been a year like no other in living memory. Our lives have changed dramatically since this time last year, which seems like a much simpler time. Things we saw as normal, like cinemas, pubs, gigs, festivals, sporting events, holidays etc. can seem like a distant memory at times.

In the face of adversity people have proved incredibly resilient and have adapted to the new situation all the challenges that entails – the same can be said for the I.H.S. As a society we have had to adapt, pivot and approach things differently too as the pandemic put pay how we provide support and services to members.

When reflecting on 2020, it is good to remember that the year began brightly for our community with the landmark announcement in early March that the first person with haemophilia had been treated with gene therapy in Ireland. A huge step forward in terms of treatment, what had once seemed like a pipedream was now becoming a reality.

In the days following this announcement the society held its AGM & Conference in the Slieve Russell Hotel in Cavan, not only was it a great weekend but it was a taste of things to come. With 30 minutes to registration opening, we were informed that 8 of our scheduled 11 speakers could not attend in person due to the escalating coronavirus situation and the requirement for health care workers to be very cautious. This presented us with a challenge to which we responded; re-organising the programme and with the assistance of technology, have three of the main speakers deliver their presentations over the weekend remotely. The quality of the sound was excellent. The presentations were clear, and questions were answered. In fact, it demonstrated the benefit of using technology to have speakers contribute remotely – something that was to become a more regular occurrence.

In the week that followed the AGM, the Covid-19 situation continued to deteriorate across Ireland culminating in the Taoiseach announcing the closure of schools, colleges and childcare facilities. The society had already made the decision for staff to work remotely for a time and began making this a reality – the staff have not been all together in the office since Thursday, March 12th.

As we, and all of you, got to grips with how our work and home lives were drastically altered, the society's initial work centred around postponing upcoming in person events, being in regular contact with the Comprehensive Care Centres and relaying information as we received it and contacting members by phone as home and hospital visits to members by staff had to be suspended.

Our normal home and hospital visits to members we're no longer possible and remain impractical for the most part. In an emergency or where there is a requirement for a face to face meeting, we will of course facilitate this where possible. Our individual outreach to members has been primarily through regular phone calls to members to see how you are all coping and to deal with any issues that arise where we can be of assistance. Our outreach co-ordinator, Robert Flanagan has made in excess of 1,400 phone calls to members since March, allowing us to keep in touch and also to identify issues proactively.

Our communication strategy has undergone a drastic change

with a far greater focus on digital. Our in-person meetings and events had to be cancelled or postponed and looking back now, we were remarkably fortunate to be able to hold our AGM and Annual Conference in March just before the pandemic struck. In place of the cancelled events we organised a number of virtual events – October Conference, von Willebrand Disorder, Mild Haemophilia & Haemophilia B – and have been complimented by a regular series of webinars using Zoom. There have been 36 organised up to December and they have proved popular, as have the recordings uploaded to YouTube. We worked to ensure that there were topics of interest generally as well as catering for topics of specific interest to adults or to parents of children with bleeding disorders.

Our publications strategy has evolved throughout the year too with an increasing emphasis on digital publications. Our e-Zine went from monthly to weekly and more recently fortnightly, as a means of circulating up to date news and information from the society and comprehensive care centres. It has proved a popular choice and we significantly increased the number of subscribers by a third, to almost 500, and thus allowing us more rapid, real time and regular communication.

The Winter Magazine is the tenth publication produced this year - all but one, produced remotely - with a mixture of digital and hard copy editions, the former made much more palatable with the 3D FlipBook feature on the website. We have posted more information on our social media platforms and regularly updated content on our website. For example, at the time of publication there have been 113 news updates on our website and by contrast, there were 45 in the entirety of 2019!

Our Twinning programme with our twinned organisation in Jordan - the Jordan Thalassemia and Haemophilia Society - also continued at a pace, all online of course. So far, we've focused on governance issues, publications and communications, events and membership and strategic planning. The webinars have been well attended by volunteers and board

members from Jordan. This method of communication will not entirely replace face to face meetings but for specific work programmes and topics, it has been surprisingly effective and allowed our twinning programme to continue despite the pandemic.

How we deliver our support and services will continue to evolve in future – in the long term it will most likely take the shape of a blend of old and new, both can complement each other considerably. We will of course continue with publications, both digital and hard copy but will continue to roll out more content online and explore new platforms and mediums for getting information to members.

We would obviously like to see a return to hosting at least some in-person events when it is safe to do so and in line with public health guidelines. This is something we will explore for 2021 but we will also continue with webinars, replacing some information events and supplementing information provided at other events. Similarly, we would like to see a return to home and hospital visits – when safe to do so.

The pandemic has been and continues to be a challenge, but we have used this challenge innovatively and constructively to reimagine, redirect and renew how the society works in providing support and services now, and into the future.

Barry Healy

Haemophilia Services During Covid-19

Covid-19 has drastically altered all our lives throughout 2020. We have all had to adapt and change how we think, act and approach things; something as simple as going to the shops is unrecognizable from this time last year.

However, one of the areas that has faced the greatest upheavel and disruption is surely the health care sector. We wanted to examine how haemophila services were impacted, reacted and evolved throughout 2020 by asking the people best placed to offer us an insight; health care workers at the heart of the service.

We hope to continue this as an ongoing series and first up we have Sheila Roche, Clinical Specialist Physiotherapist in St. James's Hospital.

The 6th of March 2020 – the day Covid-19 directly impacted me and my work life. Prior to this there had been talk of this new virus but nobody knew how it would really affect us. But that day I was in Birmingham at a Haemophilia physiotherapy meeting and received a phone call out of the blue from one of our consultants to say that the National Coagulation Centre (NCC) had made the decision to cancel all outpatient appointments from the following Monday and this included our physiotherapy appointments. This included cancellation of the weekly multidisciplinary Haemophilia clinics where we get to catch up with our severe Haemophilia patients along with the monthly orthopaedic clinic and the newly set up weekly exercise and lifestyle class.

Returning to work the following week it was very hard to know what to expect – we all felt we were going to be faced with a tsunami of Covid patients so there was a lot of anxiety amongst staff in those initial weeks and that still comes and goes as we see numbers in the community and hospital go up and down. But for me in those initial days of the Covid-19 pandemic my time was spent looking after any of our inpatients in the hospital, but inpatient numbers also started being reduced as elective procedures were gradually cancelled.

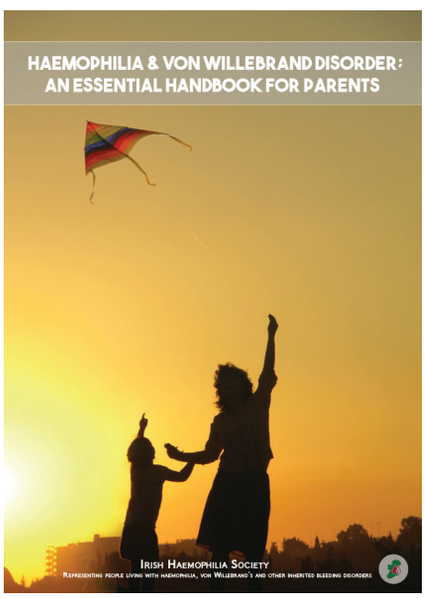
Here in St. James's Hospital there was a very quick response to how we dealt with our patients and their outpatient clinic appointments. We initially switched to a telephone consultation but by the end of March we were fortunate enough to be up and running with video consultation using the Blue Eye platform – an Irish based company. I am very lucky to work in two departments the NCC and the physiotherapy department who were very proactive in this move to Telehealth. As a physiotherapist whose background was in musculoskeletal physiotherapy and in particular manual therapy which I have a Masters in I was initially wary and stressed by a move to video calls. As in my eyes a huge part of a physiotherapists role is a hands on assessment. But it has become

a great way to check-in with patients and carry out an initial assessment or as a follow up to an initial face to face consultation. It has become a great adjunct and positive outcome of the pandemic.

Telehealth has allowed us to have calls with patients all around the country who are unable to attend due to current restrictions or those closer to us geographically who would understandably rather not attend the hospital. Nonetheless, I never thought I would be taking my temperature on a daily basis, recording it and wearing a surgical mask, gloves and goggles when seeing patients. Now it is the norm to put a mask on first thing in the morning and no one bats an eyelid and who knows we may never return to being mask free in the hospital setting.

Despite all these new challenges the initial lockdown gave me and Mark who I job share with the time and opportunity to plan our service for the future. We switched our exercise class to Zoom and received great feedback from the participants. We hope that this something that we can roll out in the New Year and if anything the pandemic has shown us that we can now include all our patients no matter where they are in the country with the advent of telehealth.

Sheila Roche



Parents Handbook

As a parent, when a child is diagnosed with a bleeding disorder, you may feel scared, worried and even guilty. It may be an especially hard time for those with no family history of the condition.

It is important to remember that with good treatment the child with a bleeding disorder has every chance of growing up as an active, fit person who can participate in family, school and later working life. Because bleeding disorders are rare conditions parents may feel isolated and alone and it is very helpful to be put in touch with others in a similar position - and we hope that this publication is a useful, reassuring and helpful resource.

If you would like a physical copy, please contact the office on 01 657 99 00. For a digital copy, see haemophilia.ie or scan the QR Code

Hyde Square Apartments

Hyde Square Apartments

A quick reminer that our apartments at Hyde Square are available to:

- People with haemophilia or related bleeding disorders from outside of Dublin, when attending St. James's Hospital or Our Lady's Children's Hospital, Crumlin for treatment, for a hospital appointment or for a review clinic.

- An immediate family member, a spouse, a partner and/or child of the person with haemophilia or related bleeding disorder from outside Dublin, when attending St. James's Hospital or Children's Health Ireland at Crumlin for treatment, for a hospital appointment or for a review clinic, or while a family member is an in-patient.

If you would like more info or to make a booking, please contact Julia in the office on 01 657 9900.

A nominal fee of €10.00 per booking, per night will be levied to offset the cost of cleaning and routine maintenance.

A newly established Patient Advocacy Service is offering support to people in Ireland who want to make a complaint about the care they have received in a public hospital.

The Patient Advocacy Service (PAS) provides free, independent and confidential information and support to people making a formal complaint about their care in a Health Service Executive (HSE) funded public acute hospital.

Provided by the National Advocacy Service for People with Disabilities (NAS), the Service was set up following a recommendation in the Health Information and Quality Authority's (HIQA) 2015 report into the Midland Regional Hospital Portlaoise and the Ombudsman's 2015 report 'Learning to get Better'.

People looking for support can contact the Patient Advocacy Service confidential helpline on 0818 293003 to speak to a trained advocate who will help them to get information on the HSE's complaints investigation process, called 'Your Service, Your Say'.

The professionally trained independent advocate will support and empower the person making the complaint, with the aim of highlighting their views and concerns.

The advocate will explain how to write a formal complaint and what to include in it. They will also help with preparation for meetings with the HSE about their complaint, and they will help the person explore their options following a response from the HSE to their complaint.

Service Manager for the Patient Advocacy Service, Claire Lehane, explains their role: "Until now, people in Ireland who experienced difficulties in the Irish health service often felt there was nowhere for them to turn.

"The newly established Patient Advocacy Service offers patients the guidance and information they need to make a complaint when they are unhappy with the care they receive. It is free, independent and run by our professionally trained patient advocates, who will use their compassion and knowledge to guide people through the HSE complaints process."

The Patient Advocacy Service was commissioned by the National Patient Safety Office in the Department of Health and is managed by the National Advocacy Service for People with Disabilities.

People looking for support can contact the Patient Advocacy Service helpline on 0818 293003. The helpline is open Monday to Friday from 10am until 4pm, including lunchtimes.

You can also email **info@patientadvocacyservice.ie**.

Find out more at: **patientadvocacyservice.ie**

Irish Haemophilia Society

TRAVELLING OR STUDYING ABROAD?

What you need to know...

If you are relocating or studying abroad there is a lot to consider before you travel. Each country has their own rules and regulations that you must follow to ensure you receive equivalent healthcare to what you receive here in Ireland.
Most countries cover emergency/urgent healthcare that is required while a person is visiting, in accordance with your health/travel insurance. However, this usually does not extend to regular haemophilia treatment and does not cover prophylaxis nor regular on demand therapy.

How do you plan your trip to ensure you will receive the equivalent healthcare?

1

Call the I.H.S.

Call us as soon as possible. We will help you with all of the stages and help with any queries.

2

Call Your Treatment Centre

They will advise you on how much factor you will need to bring. It is important to request a letter from your treatment centre which gives details of your treatment.

3

Find the nearest treatment centre

For Europe see - http://www.euhanet.org/centrelocator/
For the rest of the world see - https://www.wfh.org/en/resources-education/treatment-centre-directory

4

Apply for the correct VISA

To find out what VISA you need and how to apply see: https://www.dfa.ie/travel/visas/visas-for-irish-people-going-abroad/

5

Get adequate health insurance

A company that does provide insurance cover for pre-existing medical conditions including haemophilia is a company called Blue Insurance. They can be contacted by:
Ph. 0818 444 449 or at www.blueinsurance.ie .

6

Pack essential items

If you are carrying treatments and medications it is very important to ensure that you have a travel letter from your haemophilia treatment centre for customs. You should also carry your haemophilia card which was issued from your haemophilia treatment centre.
For travelling within Europe, you should have an EHIC card (European Health Insurance Card). This entitles you to necessary healthcare in the public system of any EU/EEA member state.

Irish Haemophilia Society
First Floor, Cathedral Court,
New Street, Dublin 8
Tel: +353 (0)1 657 99 00

@irishhaemophiliasociety
@HaemophiliaIRL

HAEMOPHILIA CARE IN EUROPE PART THREE: 2010S

We are now in an exciting time of unprecedented innovation in relation to haemophilia care in Europe and the probability is that we will see even more innovation in treatment in the next five years. This will bring opportunities but also challenges in relation to access. To help us predict the future, it is worthwhile to examine the past. Brian continues with part three in a series examining 'Past Progress and Future Promise', an expanded version of an article published in the Journal *Haemophilia* in August 2020.

2010's: Decade of Innovation & Constructive Engagement

Hepatitis C

The developments in haemophilia replacement therapy were matched, and exceeded by development of direct acting antivirals for treatment of hepatitis C. The development of sofosbuvir and subsequent DAAs led to a revolution in Hepatitis C treatment with SVR rates of up to 97%. This has led to the situation where Hepatitis C can now be effectively eradicated in the haemophilia population in Europe. This remains a vital objective as Hepatitis C was the main cause of mortality in people with haemophilia in Europe for many years.

Having active hepatitis C infection with an underlying inherited bleeding disorder is a combination which we must seek actively to break. It is salutary to reflect that, despite the very real clinical benefit of these new therapies, access was initially slow and limited in many countries due to the perceived high economic cost. The initial cost became a political issue in some countries and changed the debate around health economics. With the passage of time since the first DAA was licenced and competing DAA products on the market, cost per person has significantly reduced. This has been assisted by some innovative pricing models (Netflix model in Australia), and competitive tendering in countries such as Ireland. The economic cost, even at its zenith, was cost effective for people with haemophilia with Hepatitis C due to the very high cost of treatment for advanced liver disease in that population coupled with the current high cost of haemophilia treatment. The debate has increased the focus on health economics and the realisation that, when a new or more effective therapy is available, it does not mean we will automatically have access even in the wealthier economies.

Development of Novel Therapies

The development of Extended Half-Life (EHL) CFCs was the first major innovation in haemophilia treatment since recombinant CFCs were introduced in 1994. To date, we have seen the licencing of 5 EHL Factor VIII (FVIII) concentrates and 3 EHL Factor IX (FIX) concentrates in Europe.

These long-acting CFCs enable PwH to be treated less frequently or at the same frequency but to a higher trough level, thereby increasing protection from bleeding. For EHL Factor IX CFCs, both objectives are achievable. Frequency of infusion could decrease from twice weekly to once every 1-2 weeks, reaching Factor IX trough levels up to 27% [7]. For PwH on Factor VIII prophylaxis, treatment could now be infused twice instead of 3 times weekly. Alternatively, the same infusion frequency could be maintained, and trough levels started to move from 1% to between 3% and 5%. Clinical trials are progressing for improved EHL Factor VIII, such as BIVV-001 where coupling of Factor VIII to both the Fc fragment of immunoglobulin and the DD3 fragment of von Willebrand Factor (vWF) may lead to significant prolongation of half-life to ~33 hours [8].

Non-replacement therapies (NRTs) have also emerged, including emicizumab (Hemlibra), a bispecific antibody which mimics the action of FVIII. Licenced in 2019 by the European Medicines Agency (EMA), emicizumab may be used for prophylaxis in PwH with and without inhibitors [9], [10] providing a level of protection akin to FVIII trough levels of 10%-15%. In clinical trials, emicizumab significantly lowered annual bleed rate (ABR) and significantly increased the percentage of PwH with zero ABRs. Subcutaneous delivery significantly reduces treatment burden for those with poor venous access, needle phobia, or children. Bypassing agents for those with inhibitors and FVIII CFCs for those with Haemophilia A are still required for bleeding episodes. Innovative re-examination of the coagulation cascade has led to development of novel replacement therapies that, instead of replacing missing factor, reduce the effectiveness of natural anti-coagulants within the cascade. Fitusiran, an antithrombin inhibitor, and several anti-Tissue Pathway Factor Inhibitor (TFPI) antibodies are in clinical trials. These products can theoretically be used subcutaneously for either haemophilia A or B, with or without inhibitors, and may also have some utility in rarer bleeding disorders. None of these rebalancing agents are currently licenced, and development of 2 of the 4 anti-TFPI agents has been halted due to reports of unexpected thrombosis. Improved understanding of the complex coagulation cascade will be useful in addressing future issues. Gene therapy (GT) clinical trials are demonstrating exciting potential. The first patient dosed in the longest running FIX trial has now passed the 10-year mark with steady levels of factor expression [11]. Many clinical trials for FVIII and FIX GT are now underway with 8 phase 3 trials for FVIII and 6 phase 3 trials for FIX. Several have been prioritised by the FDA and the EMA [12]. The first FVIII GT is expected to be licenced later this year, and the first FIX GT to follow in late 2021. GT offers the prospect of changing severe haemophilia into mild haemophilia or even normal, offering the prospect of a phenotypic or functional cure.

Collection of outcomes data is vital to demonstrating the impact of new therapies and promoting continued investment in haemophilia. Haemophilia-focused outcome tools have also been developed by patient leaders (e.g., Patient Reported Outcome Burden and Experience [PROBE] survey tool) and produced unique disease-specific insights and evidence [13].

Constructive Engagement and Principles of Haemophilia Care

The engagement of clinicians and the Europeam Haemophilia Consortium (EHC) with European Directorate for the Quality of Medicines & HealthCare (EDQM) has been very constructive. Following the EDQM meeting in 2009 (14), further EDQM organised meetings were organised in 2013, 2016 and 2019. The recommendations emanating from those meetings and published in peer reviewed journals (15,16,17) demonstrate the real beginning of effective engagement led systematic planned milestones for development of haemophilia care in Europe. For the first time these recommendations have provided benchmarks against which the current level of haemophilia treatment and care in any country in Europe can be measured and compared. In terms of advocacy, the utility of the recommendations was strengthened by the acceptance of the recommendations by the Committee of Ministers on two occasions in resolution CM/Res (2015) 3 (18) and again in Resolution CM/Res (2017) 43 (19). In 2012,2015 and 2018 the EHC carried out further surveys of European countries to ascertain the extent of progress with implementing the principles of haemophilia care and the extent to which previous EDQM recommendations were being implemented (20, 21,22).

The EDQM process and the resulting resolutions from the Committee of Ministers have provided national haemophilia societies with powerful and effective tools to assist them in advocating for improved access to treatment and care. The clinicians and patient organisations can now jointly or separately approach their health Ministries or key decision makers and advocate for the levels of treatment and care set out in the EDQM recommendations or incremental progress at least toward achieving this bolstered by the fact that they are now stating, not just their national opinion, but quoting official recommendations from the Council of Europe. An example of the incremental progress in the recommendations is per capita use of FVIII. Prior to 2009, the minimum per capita use recommended was 1 IU per capita. In the 2009 EDQM recommendations, this was increased to 2 IU per capita, in 2013 to 3 IU per capita and in 2016 to 4 IU per capita. These increases were based on clinical evidence and opinion and changes to recommended treatment regimens including the belated recognition in 2013 that prophylaxis for adults with severe haemophilia should also be considered, leading to an increased per capita use in many countries. No minimum per capita use was recommended for FIX. This was belatedly dealt with by EDQM with a recommendation in 2015 for a minimum FIX use of 0.5 per capita. The per capita recommended minimum use for FVIII or FIX was not increased in the EDQM recommendations from 2019 as the availability of extended half- life FVIII and

FIX CFCs renders the concept meaningless unless we devise a system for comparing standard and EHL units for this purpose. This is not insurmountable. Given the similarity in half life extension between all the licenced FVIII EHL CFCs, a correction factor based on probable decreased usage when compared to standard FVIII could be employed. Experience in several countries has demonstrated an approximate 20% reduction in FVIII use when EHL is used so a reasonable correction factor would perhaps be 0.8. The situation for FIX is different. The 3 licenced EHL FIX CFCs all have significantly different half-life extensions and therefore in comparing them to standard FIX, 3 separate correction factors would be required. In the 2019 EDQM recommendations (17), recognition was given to the potential for EHL CFCs to allow for an increased trough level to protect joints. For the past 40 years, the objective of prophylaxis was to maintain a trough level of at least 1% to avoid spontaneous bleeding episodes. This has been beneficial and has resulted in much lower ABRs than seen with on- demand treatment. However, standard prophylaxis, while delaying joint damage, did not always prevent it. Annual Bleed rates of 3 to 5 remained commonplace. With EHLs, higher trough levels and greater protection from bleeding are now attainable. The EDQM recommendation for 2019 stated that minimum trough levels of at least 3% to 5% should be attained to protect joints. This is a significant step forward in thinking in Europe. Combined with the recommendation that prophylaxis should be available to all people with haemophilia, this gives the prospect of real clinical improvement.

Recommendations also look at the organisation of care in Europe. There are new recommendations on strengthening and harmonising existing national registries in Europe in order to facilitate pooling and comprehensive evaluation of data. This is a recognition that, with all the new innovative products coming to market, we need systematic and continued collection of post marketing surveillance data to properly assess the medium and long-term beneficial effects of these new therapies. EDQM have also recognised that patients with haemophilia, particularly those using non- replacement therapies and gene therapy should have their treatment and care supervised by comprehensive care centres such as the certified European Haemophilia Comprehensive Care Centres (EHCCC). This echoes an earlier joint recommendation issued by EAHAD and EHC and gives recognition to the informal system of certification of centres as EHCCC or European Haemophilia Treatment Centres (EHTC) which has been in place since 2015 with the active participation and oversight from a group including EUHANET, EAHAD and EHC. Other important EDQM recommendations have included a recommendation for use of prophylaxis in adults (2013), the establishment of a formal body for haemophilia in each country (2013), prioritised access to treatment for hepatitis C (2016), collection of outcome date (2016) and the encouragement of national or regional tender boards for haemophilia medications which should include both haemophilia clinicians and patient organisation representatives.

Some of these guidelines were influenced or informed by the European Principles of Haemophilia Care or the survey data of European countries collected by EHC. Formal bodies were recommended by the Principles of care and the establishment of such bodies was tracked by the EHC data collection. National Haemophilia Councils or committees (23) have been established in a significant number of European countries. At their best, they provide a forum where doctors, patient organisation leaders, and health care officials together with payers can discuss and agree the development of haemophilia policy on a national level. They promote collaboration and an agreed set of objectives between haemophilia treaters and the patient organisation which in turn can lead to a clear and agreed approach when dealing with governments and officials. Collection of outcome data is vital if we are to demonstrate the impact of new therapies and the continued investment in haemophilia and measures such as the widely used EQ-5D-5L in addition to specific outcome tools developed by patient leaders such as the Patient Reported Outcome Burden and Experience (PROBE) survey tool have started to produce interesting outcome data (13).

Economics and procurement

In an era of unprecedented innovation, economics will play a key role. The recommendation to have National or regional procurement of haemophilia medications is an acceptance of the fact that these relatively expensive, complex medicines are best purchased in a systematic national method. The products are not interchangeable. The decisions should always be informed by safety and efficacy and expertise which will not be readily available to many hospitals or insurance companies in small fragmented procurement systems. (24) EHC data has clearly demonstrated (25) the beneficial economic impact of national tender or procurement systems where the patients and doctors are involved. In this scenario, there is a statistically significant lower cost when compared to systems where both are not involved. With both involved, you get an improved scientific and clinical assessment of the product options, avoid the possibility of divisive opinions leading to sub optimal decisions and obtain economy of scale in purchasing larger quantities for an entire country possibly for more than one year. In Ireland, per capita use of FVIII has increased three-fold in the past 16 years and all FVIII used by 2019 was EHL FVIII. Similarly, all the FIX used was EHL FIX. This was achieved with a national budget which had not increased in the past 17 years due to an effective national approach to tenders which formally includes, clinicians, patient leaders and payers (26).

Data collected by EHC from 2009 to 2016 demonstrated a trend to increased access to CFCs in many western and central European countries. Progression of access to treatment could be seen differently in 3 sets of European countries (22). In the first group consisting primarily of several western European countries, access to treatment has increased significantly. In a second group, mainly consisting of central European countries and Russia, access to treatment has im-

proved linked primarily to an increase in home treatment, prophylaxis for adults and availability of immune tolerance therapy. In the third group, consisting of several mainly eastern European countries, economies have been growing without a parallel improvement in access to haemophilia treatment. These countries use of replacement therapy remained stubbornly below the European recommended per capita use. The EHC used criteria based on EDQM recommendations to classify 14 European countries as below the minimum standard of care. This meant that some or all of these 4 criteria were not met: Minimum FVIII use of 4 IU per capita, minimum FIX use of 0.5 IU per capita, all children with severe haemophilia having access to prophylaxis and national tender or procurement board including both doctors and patient organisation leaders. Using these criteria, EHC developed the PARTNERS (Procurement of Affordable Replacement Therapy Network of European Relevant Stakeholders) programme to encourage sustainable improvement in access to replacement therapies in these countries. EHC engaged with the Health Ministry, key Doctors and patient leaders in each country. The objective was to encourage Governments to increase their national supply of replacement therapy by purchasing on a multi- year national basis which would not require any significant increase in the national budget. Several of these countries had very inefficient purchasing systems with purchase of low volumes at relatively high cost, constraints due to inability or unwillingness to think or act beyond the scope of a one- year budget, unwillingness to think outside the box, corruption in some cases and systematic inertia in others. The programme has led to a significant improvement in access to treatment in several countries and a detailed analysis for each country of the barriers to improved access.

Brian O'Mahony

References:

7. Eaton L. Haemophilia patient had variant CJD agent in spleen. BMJ. 2009;338:b705.

8. Hagen P. Blood Transfusion in Europe: A White Paper (Vol 68). Strasbourg, France: Council of Europe Press; 1993. Accessed June 10, 2020.

9. Hermans C, Dolan G, Jennings I, et al. Managing haemophilia for life: 5th haemophilia global summit. Eur J Haematol. 2015;95:1-25.

10. O'Mahony B. WFH: Back to the future. Haemophilia. 2004;10(s4):1-8.

11. Colvin BT, Astermark J, Fischer K, et al. European principles of haemophilia care. Haemophilia. 2008;14(2):361-374.

12. O'Mahony B, Noone D, Giangrande P, et al. Haemophilia care in Europe: a survey of 19 countries. Haemophilia. 2011;23(4):e259 -e266.

13. Syed YY. Nonacog beta pegol: a review in haemophilia B. Drugs. 2017;77(18):2003-2012.

14. Seth Chhabra E, Liu T, Kulman J, et al. BIVV001, a new class of factor VIII replacement for hemophilia A that is independent of von Willebrand factor in primates and mice. Blood. 2020;135(17):1484-1496.

15. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab prophylaxis in hemophilia A with inhibitors. N Engl J Med. 2017;377(9):809-818.

16. Pipe SW, Shima M, Lehle M, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. Lancet Haematol. 2019;6(6):e295-e305.

17. Nathwani AC, Davidoff AM, Tuddenham EGD. Gene therapy for hemophilia. Hematol Oncol Clin North America. 2017;31(5):853-868.

18. Doshi BS, Arruda VR. Gene therapy for hemophilia: what does the future hold? Ther Adv Hematol. 2018;9(9):273-293.

19. O'Mahony B, Pastarnak A, Noone D, Skinner M. Patient reported outcome data on switch from standard to extended half life in Irish adults with haemophilia. Special Issue: Abstracts of the XXVII Congress of the International Society on Thrombosis and Haemostasis. 2019;3:1-228.

20. Berger K, Klein HG, Seitz R, Schramm W, Spieser JM. The Wildbad Kreuth initiative: European current practices and recommendations for optimal use of blood components. Biologicals. 2011;39(3):189-193.

21. Giangrande P, Peyvandi F, O'Mahony B, et al. Kreuth IV: European consensus proposals for treatment of haemophilia with coagulation factor concentrates. Haemophilia. 2017;23(3):370-375.

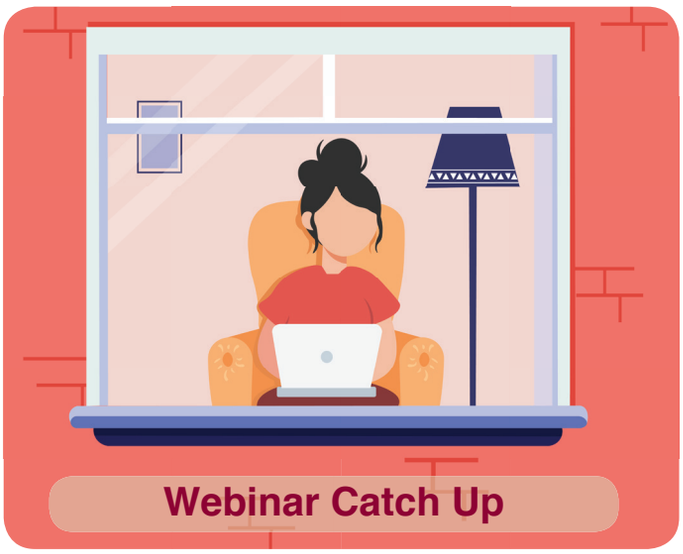
22. Giangrande P, Seitz R, Behr-Gross ME, et al. Kreuth III: European consensus proposals for treatment of haemophilia with coagulation factor concentrates. Haemophilia. 2014;20(3):322-325.

23. Resolution CM/Res(2015)3 on principles concerning haemophilia therapies. 2015. Accessed June 10, 2020.

24. Resolution CM/Res(2017)43 on principles concerning haemophilia therapies. 2017. Accessed June 10, 2020.

25. Peyvandi F, Berger K, Seitz R, et al. Kreuth V initiative: European consensus proposals for treatment of haemophilia using standard products, extended half-life coagulation factor concentrates and non-replacement therapies. Haematologica. 2020:242735.

26. (eISB), electronic I. S. B. (2004). National Haemophilia Council (Establishment) Order 2004. S.I. No. 451/2004. Accessed June 3, 2020.



If you missed any of our webinars over the past while, you can now catch up with them on our website and YouTube.

We are delighted with the webinars; insighful topics and great interaction with members. Some of the topics include:

- Update on New Children's Hospital with Eilish Hardiman, CEO
- Exercise and Physical Activity for Children with Paula Loughnane, Senior Physiotherapist at CHI Crumlin
- The Role of the Advanced Nurse Practitioner in Haemophilia

You can find the recordings on YouTube & haemophilia.ie, or scan the QR Code below.

SCAN ME

Join our e-Zine Readership

Our E-zine is the easiest, hassle free and most comprehensive way to keep up-to-date with all things I.H.S.

This electronic magazine is delivered straight to your inbox.

To sign up, simply email barry@haemophilia.ie or fill in your details at haemophilia.ie.

New vWD Info Booklet

The I.H.S. is delighted to announce a new, updated information booklet on von Willebrand Disorder (vWD) .

We hope it will provide readers with a better understanding of vWD and the treatments available and an opportunity to get answers to all those unasked questions. What is Von Willebrand Disorder (vWD)? How is vWD inherited? Types of von Willebrand Disorder? What are the symptoms? How is it diagnosed? How is it treated?

You can read / download the digital version on our website - see the QR Code above - and for hard copies, please contact us at info@haemophilia.ie

Brian O'Mahony Award

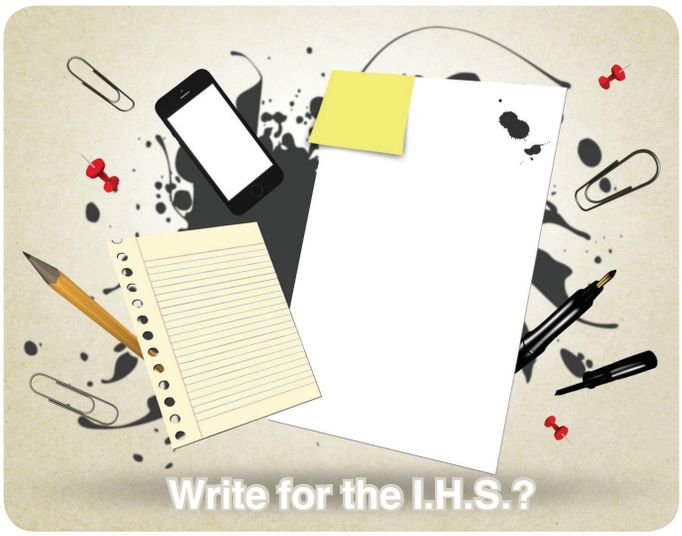
Nominations are now open for the 'Brian O'Mahony Award for outstanding contribution to haemophilia care in Ireland'.

Nominations can be proposed only by members of the Society. Members of the current board or staff cannot be nominated. If you would like to nominate an individual who, in your opinion, has made a real difference in haemophilia care in Ireland, please send your nomination to:

info@haemophilia.ie

The closing date for nominations is January 20, 2021.

Noticeboard



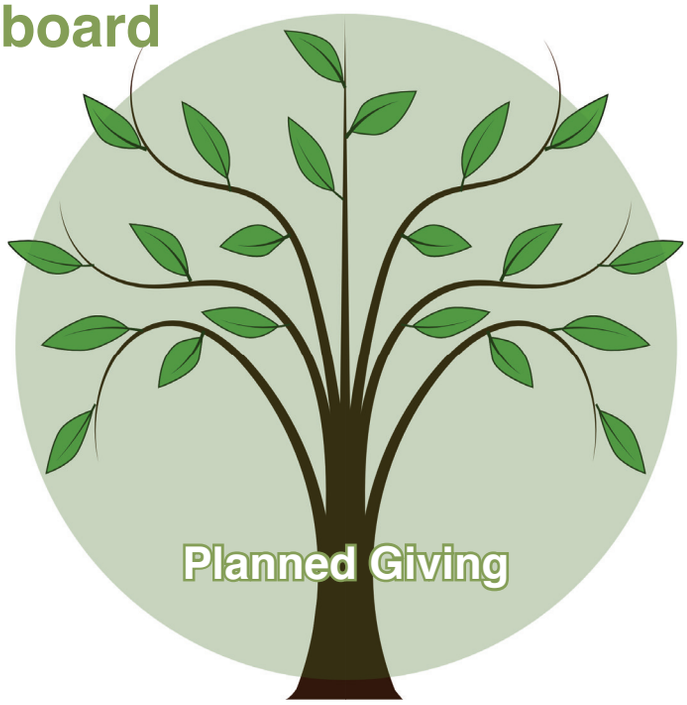
Do you enjoy writing?

Do you like sharing your experiences or feel that other people's perspectives have helped you in the past?

Maybe you had a particularly benefi cial or enjoyable time at one of our conferences or maybe you would like to share a story about you and your experience with a bleeding disorder.

If any of the above are true, we would absolutely love to hear from you!

If you would like to contribute and write an article for the I.H.S. just contact Barry in the office at 01 657 9900 or via barry@haemophilia.ie



If you would like to make a difference to others, please consider signing up to our Planned Giving. Contributions can be made monthly, even €10 a month can make a difference or maybe you would prefer to make an annual contribution. The choice is yours, how much and when is totally up to you, and you can cease your contributions whenever you want.

This ongoing support for the work of the I.H.S. goes a long way to help us provide and improve on the services and support we give our members.

To sign up, or for more information, please contact Nina on 01 657 9900 or email nina@haemophilia.ie.

Novel Treatments in Haemophilia & other Bleeding Disorders: A Periodic Review I 2020 – Issue 2

The therapeutic landscape in haemophilia continues to change rapidly and it can be difficult to keep up to date.

The Society has adapted a publication compiled by the European Haemophilia Consortium to produce a comprehensive update on 'Novel Treatments in Haemophilia & other Bleeding Disorders: A Periodic Review'. It is designed to be informative for both people with bleeding disorders and health care workers.

It is available to read / download from our website, or scan the QR Code.

For physical copies, please contact the office.

Provisional Hospital Opening Hours for the Christmas Period

National Coagulation Centre & H&H Assessment Unit – St. James's Hospital

Tuesday 22 December 2020 - as normal (8.30am - 5pm)
Wednesday 23 December 2020 - as normal (8.30am - 5pm)
Thursday 24 December 2020 - closed
Friday 25 December 2020 - closed
Saturday 26 December 2020 - closed
Sunday 27 December 2020 - closed
Monday 28 December 2020 - bank holiday service
Tuesday 29 December 2020 - closed
Wednesday 30 December 2020 - closed
Thursday 31 December 2020 - closed
Friday 01 January 2021 - bank holiday service

Normal services from Monday, January 4, 2021

The walk in assessment unit in H&H will operate as per out of hours and weekends with 24 hour cover.

Out of Hours Service Phone: (01) 410 3132 (after 5pm Monday to Friday, and at weekends or bank holidays).

Patients who need emergency assessment or advice should phone the H&H Ward prior to attending, or alternatively contact St. James's Hospital via the main switchboard on 01 410 3000 and ask for the haematology SHO on call.

Cork Coagulation Centre - Cork University Hospital

Tuesday 22 December 2020 - as normal (8am - 5pm)
Wednesday 23 December 2020 - as normal (8am - 4pm)
Thursday 24 December 2020 - closed
Friday 25 December 2020 - closed
Saturday 26 December 2020 - closed
Sunday 27 December 2020 - closed
Monday 28 December 2020 - closed
Tuesday 29 December 2020 - closed
Wednesday 30 December 2020 - closed
Thursday 31 December 2020 - closed
Friday 01 January 2021 - closed

Normal services from Monday, January 4, 2021

The Haematology Registrar is on call throughout the holiday period and can be contacted through the CUH switchboard at 021 454 6400.

Children's Health Ireland at Crumlin

Tuesday 22 December 2020 - as normal (8am - 5pm)
Wednesday 23 December 2020 - as normal (8am- 5pm)
Thursday 24 December 2020 - limited elective activity
Friday 25 December 2020 - closed
Saturday 26 December 2020 - emergencies only
Sunday 27 December 2020 - emergencies only
Monday 28 December 2020 - limited elective activity
Tuesday 29 December 2020 - limited elective activity
Wednesday 30 December 2020 - emergency only
Thursday 31 December 2020 - limited elective activity
Friday 01 January 2021 - closed

Normal services from Monday, January 4, 2021

FYI: The Haematology Oncology Service always remains open but the Haematology Oncology Day Unit & Service only operates Monday - Friday & closes for public holidays.

In the case of an emergency, please contact the hospital on 01 409 6100 and ask for the haematology registrar on call.

The Irish Haemophilia Society office will close for Christmas at 3pm on Wednesday, December 23 2020 & will re-open on Monday, January 4 2021 at 9am.

In the case of an emergency, please call 01 657 9900 where contact details for our emergency contact person will be found.

Wishing you all a very Merry Christmas & a peaceful New Year from the board & staff of the I.H.S.