Bloodline

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THE H WORD

17 April was World Hemophilia Day. Across the globe our community took this day to share stories of resilience during the COVID-19 pandemic. This year's theme was "Adapting to change: sustaining care in a new world". President of the World Federation of Hemophilia, Cesar Garrido commented that "the COVID-19 pandemic has made life challenging for people with a bleeding disorder—but we can't stop striving for Treatment for All. World Hemophilia Day is a platform for showing the world that our community is resilient and we will overcome this new challenge as we have overcome other challenges in the past."

To mark this day, lighting up landmarks around the world in red has gained momentum. Perhaps you noticed a landmark had been illuminated on 17 April? Rotorua, Hamilton, Christchurch, Wellington and Palmerston North all took the opportunity to light up a landmark and show solidarity on World Hemophilia Day.

Although we can always improve care and treatment for people living with a bleeding disorder in New Zealand, I think we can all be thankful that our response to the pandemic means accessing treatment remains mostly unchanged, access to appointments is still possible, and events can still go ahead. We are one of the few places where this is possible.

I hope you enjoy catching up on all things HFNZ in this edition of Bloodline.

Deon York
HFNZ President

From the CEO

BY SUE ELLIS

As we continue to live under the umbrella of Covid-19, the last four months have seen a number of changes as staff have moved onto other opportunities and new staff starting. At the end of last year, it was sad to say goodbye to Ross who took up another role with the muscular dystrophy organisation and to Amber as she moved to Australia to be with whānau. However, it is not a final goodbye to Ross as he continues to support the walking group in Christchurch. Thank you Ross.

Welcome to Rosie Maguire as the new Outreach Worker for the Southern region and to Laura-Lee Perawiti as the Outreach Worker for the Midland region. Both Rosie and Laura-Lee have quickly taken on their roles and have been out and about getting in touch and meeting with members. With further recruiting for the Northern Outreach Worker role, it is hoped this vacancy with be filled by the time this Bloodline goes to print. A huge thank you to Lynne Campbell from Central Region who has been our 'national' ORW during the recruitment process. I also want to thank the HTC staff who have taken the new Outreach Workers under their wings and are helping to guide them on all matters related to bleeding disorders.

The planning for the Youth camp in July is now well underway after needing to postpone the April date while new staff were recruited and appointed. With the resources now in place, we have the camp organised for July 17th – 20th with the leadership day on the 16th July. The theme is "*The Seven Summits*" in line with the Bombardier Blood movie that will be shown at the camp. I know this event is one that our youth have been waiting for for some time so it is great that it is now going ahead. In light of the ongoing global pandemic, we will continue to keep a watchful eye on the safety concerns to ensure we have a successful event.

In January, I attended the Global Haemophilia Advocacy Leadership Summit, sadly not in person due to the global pandemic, but two early morning zooms at 2am NZ time! The theme was "*Finding the North Star, Securing our Future*". There were some interesting presentations including the impact of Covid-19 on health policy, looking at the correlation between good policy and good treatment over the decades. From the 1970s on plasma derived medicinal products through to the 2020s on gene therapy and the legislative regulations and policies that were built around the improving and innovative treatments. There were also discussions on the importance of stakeholder engagement and advocacy leaders, and making a case through a united voice. Our President Deon, spoke as a panelist on "*New Leaders: The Future of Advocacy*".

Over the last four months I have continued to maintain our important relationships with industry, including meeting and discussions with Takeda, Roche, Sanofi, and CSL Behring, all of whom have supported us through grants for events and projects. Our website development is one project that is well and truly on track so look out for the new refreshed version in the next few months.

I want to thank all those very generous people who have continued to support us through their donations and bequests to the Foundation. This financial support has helped us to continue to provide the support and care to members during a time of economic uncertainty. A big shout out also to the Kiwifirst teams who have worked hard to keep the HFNZ in the hearts and minds of people as businesses dealt with managing their financial situation with the impact of Covid-19. With vaccines now on the horizon, there will be more certainty in our world.

In the meantime, ka maioha ahau ki a koutou katoa mo to tautoko me to manawanui – I appreciate you all for your time, support and patience.

Sue Ellis

Chief Executive

HFNZ staff at staff meeting in March

Welcome to our new Outreach Workers

BY PHIL CONSTABLE

On 15 March the HFNZ staff team was pleased to be joined by two new Outreach Workers. Laura-Lee Perawiti started as the Midland Outreach Worker, while Rosie Maguire started as the Southern Outreach Worker. Both Rosie and Laura-Lee will be reaching out to members in their areas over the coming weeks.

Here's a bit about them...

Laura-Lee descends from the tribes of Waikato, Raukawa, Rereahu and Maniapoto and currently resides in Kirikiriroa / Hamilton.

She is a registered indigenous Māori and bicultural social work practitioner, and has a background in tertiary and primary education, disability including mental health, child protection, and whānau advocacy. She has worked and held various roles within the government, non-government, and Iwi sectors.

Laura-Lee also runs a social services business that provides indigenous Māori and bicultural supervision to frontline government and non-government practitioners and students, including education and training in traditional Māori healing, and transitional support services.

Outside of these roles she is a mother to three young men, and newly a grandmother. She is an iwi board member, and an effective hapu, marae, and community member.

You can connect with Laura-Lee by calling/messaging her on 021 762 121 or by emailing her at laura-lee@haemophilia.org.nz.

Rosie is a registered primary and drama teacher, who began her career in the classroom. After leaving teaching she worked in project management, before starting a career in media. Working her way up to a being a producer for children's television, Rosie has had the pleasure of working on many different creative projects and has worked with communities from all around the country.

She is looking forward to jumping into a new line of work through HFNZ, and connecting with the haemophilia community of Te Waipounamu.

You can connect with Rosie by calling/messaging her on 021 656 804 or by emailing her at rosie@haemophilia.org.nz

We welcome Laura-Lee and Rosie, and look forward to the fantastic skills and experience they bring to the HFNZ whānau.

HFNZ Youth Camp 2021

Here comes Youth Camp

BY PHIL CONSTABLE

After a bit of a wait, and a couple of false starts, it's time for HFNZ Youth Camp.

The venue is booked, and the programme is coming together, now all we need is you!

Growing up is exciting, challenging, and often very confusing. When a bleeding disorder is added to the mix the challenges of young adulthood only increase. The HFNZ Youth Camp, for 10-18 year-olds, uses a combination of education, fun, and peer and mentor support, to help young people move to the next stage of managing their condition. The focus is on being

well-informed and better able to make decisions about their bleeding disorder treatment, education, work, life-style and relationships.

Youth Camp is an important part of the HFNZ journey. Beginning with Family Camp, when children are newly diagnosed, we provide educational events to support our members through every stage of life. Once children have 'graduated' from Family Camp they're ready to start learning self-care skills that will help them manage in the world as they move towards adulthood. That's where Youth Camp comes in. By involving young leaders from within the Foundation, who have been through Youth Camp themselves, we provide a supportive peer-based environment, where children feel seen and understood. Add in the knowledge and experience of our wonderful clinical teams, and our Outreach Workers, and you've got a recipe for some fantastic learning.

The 2021 Youth Camp theme is Seven Summits, reflecting the feats of Haemophiliac Chris Bombardier scaling the highest peaks on all seven continents. We will be watching Chris' movie, Bombardier Blood one evening at camp. The camp will focus on skills and resources to help HFNZ youth to be prepared for whatever life may bring. It will include health and dietary advice, physical activities, the opportunity for personal reflection, and lots of FUN!

Where: Blue Skies Centre, Kaiapoi. www.blueskies.org.nz

When: Saturday 17 July - Tuesday 20 July, 2021

Fees: The Camp fee is $160, or $250 for two children and is non-refundable. This includes travel, all meals, accommodation, and activities. You will be invoiced following completion of registration.

We understand this can be a lot all at once, and we don't want money to be a barrier to attendance. So, if you would like to set up a payment plan through online banking, or pay at a later date, please contact Leanne at admin@haemophilia.org.nz.

Registration is online at: https://2021youthcamp.lilregie.com/

If you have a child aged 10-18, please help us by applying as soon as you possibly can and completing all details. If you are registering more than one child, please complete for one child then use the Save and Add another Person button.

Registration closes on Friday 28 May!

We're really looking forward to this fantastic event. See you in Kaiapoi!

World Haemophilia Day 2021

BY PHIL CONSTABLE

Multiple venues in Wellington, Christchurch, Rotorua, and Hamilton lit up red in support of World Haemophilia Day on Saturday, April 17, to increase public awareness of haemophilia and other inherited bleeding disorders.

This year the NZ venues included Wellington's Michael Fowler Centre, Christchurch Airport's control tower and Airport Arch sculpture, Hamilton's Victoria Street Bridge, the Palmerston Nth Clock Tower, and several spaces in Rotorua's city centre. Last year over 70 such landmarks decided to light it up red worldwide, including Moscow's Ostankino Tower, Niagara Falls in Canada, and Trafalgar Square in London.

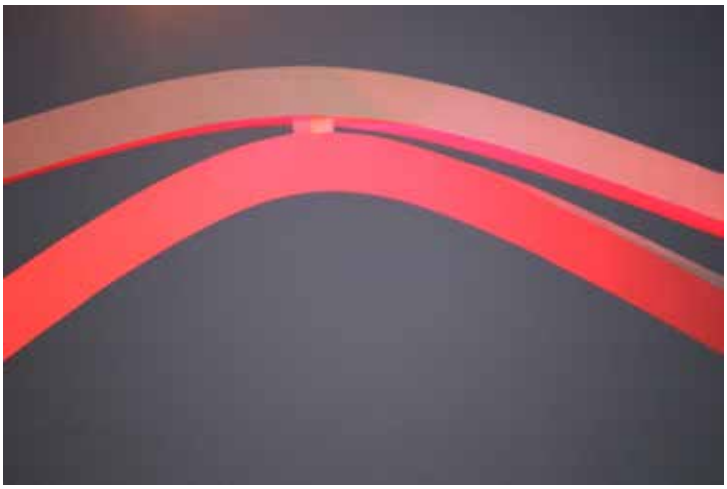
World Hemophilia Day is about bringing the global bleeding disorders community together. With the COVID-19 pandemic having a major impact on people with a bleeding disorder, that objective has never been more important. The world has changed greatly over the last year, but one thing hasn't: we are still in this together.

For the HFNZ, World Haemophilia Day is also an opportunity to recognise all the support and care people with bleeding disorders get from those around them.

Those living with inherited bleeding disorders like haemophilia, access a significant amount of their care, support, and advocacy through family and whānau, which come in many forms, as well as medical teams, friends, and colleagues. These communities share the ability to come together and help improve people's lives.

HFNZ Chief Executive, Sue Ellis, said: "A lack of public awareness of bleeding disorders means that families and friends must often take on a great deal of responsibility for their friends and loved ones, and this very often goes unnoticed. World Haemophilia Day is for people with a bleeding disorder to raise awareness of their condition, and to simultaneously give a very special thank you to their biggest supporters."

Christchurch Airport Terminal



Christchurch Airport Arch

HFNZ President, Deon York, said: "World Haemophilia Day is an opportunity to celebrate the inspirational individuals, committed healthcare professionals, and families and whānau living with the impacts of a bleeding disorder."

"If you are wondering why your local icon has gone red, it is to honour all those living with an inherited bleeding disorder in New Zealand, and their families and whānau, and to acknowledge the 75% of the world who do not receive adequate treatment and care" says York.

"In New Zealand we know of approximately 900 individuals who live with haemophilia A or B, and over 200 with von Willebrand's or another rare bleeding disorder, but we also know there are others, and as awareness grows so do the numbers of people who reach out to us for assistance".

It's really special to see public places around New Zealand, and the world, lighting up in support of our members and their families and supporters. While inherited bleeding disorders are rare, it's important to know that our members are seen and valued.

Michael Fowler Centre Wellington

Southern Walks 2021

BY KYLE CUNNINGHAM

IT'S TIME TO POLISH UP YOUR WALKING SHOES FOR 2021!

I hope everyone has had a great holiday period and has ample goals ahead for 2021. A new year brings us more opportunities to get out with our friends and whānau, enjoy some fresh air and get some exercise in.

Below is the (tentative) Haemo-Hike Schedule for 2021. Thanks to all who make the effort to get amongst it. We have a strong crew of regulars and our (in)famous Haemo Nurse/Physio combo pair ensure we are well-factored and moving efficiently.

This year we would love to add some more attendees to these walks so please, if you haven't been along – reach out with your queries or your feedback. If you have been along, thanks for making it a special time so far and please encourage others within the community to come along if you get the chance. You people are the best advertisement to anyone thinking about joining.

As always this operation relies on feedback, and remember, these walks are run by this community, for this community. If you have an idea, please share it – we would love to hear from you. We can get more into the nitty gritty later on but for now here is what the schedule looks like:

~~**28 Feb - Coastal path Lyttelton (Picnic/BBQ)**~~
Done. Loved it!

~~**28 Mar - Bowenvale > Sign of the Kiwi Café**~~
Done too. Also spectacular!

2 May - Return to the Mighty R A P A K I

30 May - Taylors Mistake > Godley Head

27 Jun - South Boundry Track Circuit

28 Jul - Cashmere > St Martins - Old Stone House River Walk

26 Sep - Gebbies Pass > Sign of the Packhorse (Picnic)

31 Oct - Bowenvale (Alternate start) > Sign of the Kiwi Cafe

28 Nov - Bridle Path - Gondola (Picnic)

Please get in touch if you have questions, queries, comments or ideas. This is a team effort!

To register your interest contact Kyle at mrcunninghawk@gmail.com or Ross at patersonfamily@actrix.co.nz.

An audit to explore the use of ultrasound imaging in Auckland

BY CAT POLLARD, ADVANCED CLINICIAN PHYSIOTHERAPIST, AUCKLAND REGIONAL HAEMOPHILIA SERVICE

As some of you may have experienced, the specialised haemophilia physiotherapists have been using ultrasound imaging as part of their examinations. Alongside physical measures such as joint range of motion and strength, the ultrasound has allowed us to look deeper inside joints to identify early signs of damage, as well as helping to confirm and monitor bleeding episodes.

Ultrasound imaging for haemophilia has been used since the 1980's but recent advances in technology have made scanners cheaper and more accessible, which, alongside the development of new assessment protocols, have made it possible for ultrasound to be undertaken by non-expert examiners.

The haemophilia physiotherapists started training to perform ultrasound in 2017 and now all four physiotherapists (in Auckland, Hamilton, Wellington and Christchurch) have access to their own ultrasound scanners.

To determine how useful the addition of ultrasound has been within our practice, an audit to explore its use within the Auckland Region over a 16 month period was performed. During this timeframe, despite several lockdowns from COVID-19 and disruptions to services, 67 first contact ultrasound assessments were performed, with 29 additional follow-up assessments.

The ultrasound was used for four purposes:

1. As part of the yearly joint health screening assessment using the Haemophilia Early Arthropathy Detection with Ultrasound protocol (or HEAD-US for short) (number = 38)
2. For suspicion of a bleeding episode (number = 24)
3. To assess damage of a single joint (number = 3)
4. To monitor myositis ossificans (bone formation in a muscle, which can occur after trauma) (number = 2).

HEAD-US JOINT SCREENING

Image: HEAD-US assessment protocol being performed on a patient

The HEAD-US explores the elbows, knees and ankles (the joints most commonly prone to bleeding episodes). This meant within the 38 people assessed a total of 228 joints were examined. The purpose of the assessment is to detect and grade any changes to the synovium (which is the layer surrounding the joint which helps produce fluid to keep the joint lubricated); the cartilage (the protective coating covering the bone ends); and the bones. When a bleed occurs, the blood that leaked into the joint is removed by the synovium, but the process of this irritates and inflames it, causing it to grow. This enlarged synovium becomes easier to pinch when the joint is moving, triggering another bleed. Bleeding events also cause damage to the cartilage, which slowly wears it down, exposing the bone underneath. Each bleed can lead to a viscous cycle of more frequent bleeds and more damage occurring, therefore identifying any changes which may precipitate this is important to stop this cycle from continuing.

Table 1: Discrepancies between clinical and ultrasound findings

	Damage identified	Occurrence
Ultrasound findings positive but clinical assessment negative	Synovitis	4
	Swelling	2
	Cartilage	3
	Bony changes	3
Clinical assessment positive but ultrasound findings negative	Swelling	2
	Range of motion restriction	3

Results of the HEAD-US revealed that only seven people assessed had normal ultrasound findings, 14 people had few abnormal joint changes and 16 moderate to severe damage was noted. In most cases, findings from the HEAD-US strongly correlated with the physical examination findings, so if joint damage was suspected with physical examination, this was confirmed with the ultrasound. However, in 17 of the 228 joints assessed, differences between physical examination and ultrasound occurred. In 12 of these cases, ultrasound imaging identified problems that had not been found during the physical examination; while five cases involved clinical assessment identifying problems which were not recognised with ultrasound (see Table 1).

The addition of the HEAD-US ultrasound to the standard physical examination measures had a number of implications:

In eight cases the assessment findings indicated that the prophylaxis regime of clotting factor replacement therapy

may be suboptimal and recommendations for an increase to dosage were made.

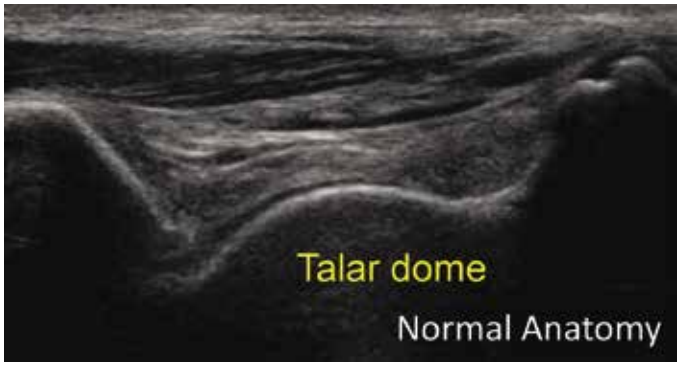
Bleeding events were detected in five cases in which the patient had not realised they were experiencing a bleed. This identified the need for better recognition and management of their bleeding episodes.

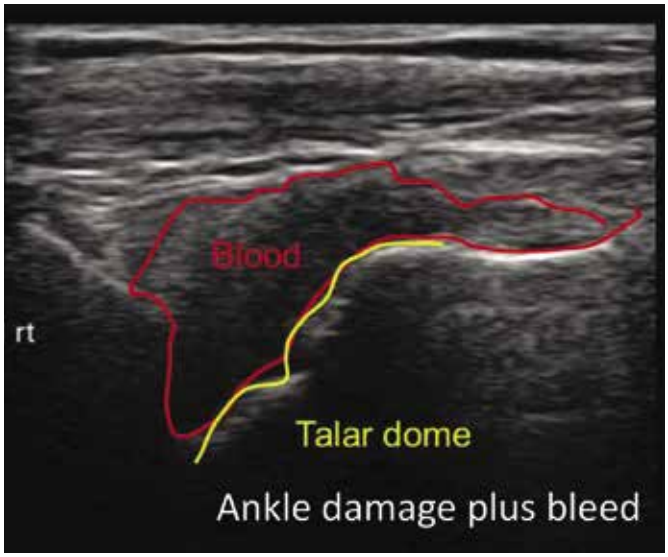
In one case the ultrasound revealed swelling within a joint felt to be due to chronic synovitis (rather than a bleed) this avoided the need for additional clotting factor therapy, a cost saving of between $3360-5040, based on 2-3 doses of clotting factor replacement therapy.

SUSPICION OF A BLEEDING EPISODE

Ultrasound imaging was performed for suspicion of a bleeding event in 24 cases, 19 involved assessments of joints and 5 cases involved a muscle.

In most cases the ultrasound was able to confirm physical examination findings, however in 3 cases discrepancies occurred whereby physical examination and patients' reported symptoms indicated a bleed but the ultrasound disconfirmed this. This avoided the need for additional clotting factor (resulting in cost savings between $10,000-15,090).



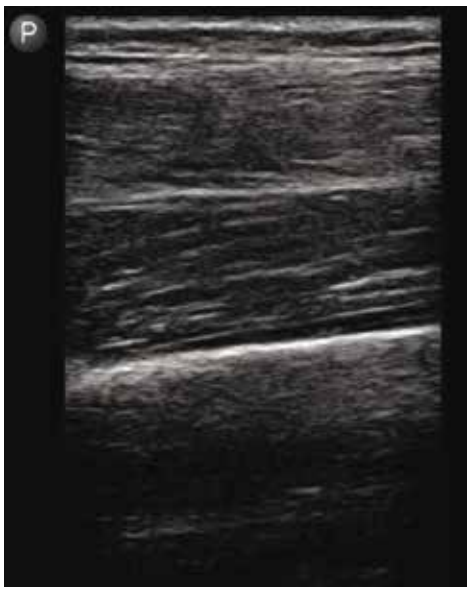


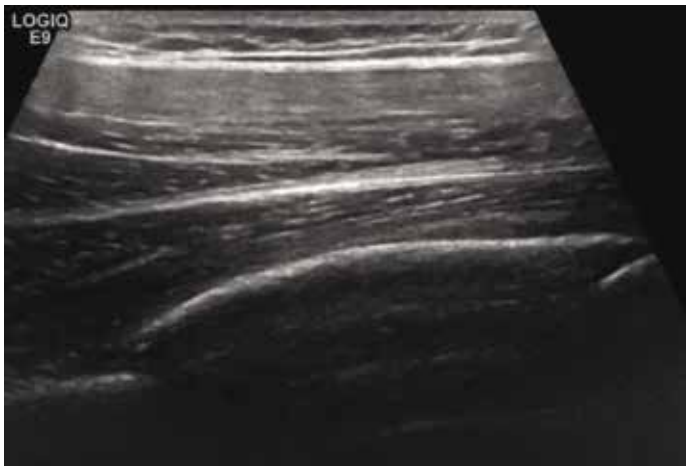
ASSESSING DAMAGE OF A SINGLE JOINT

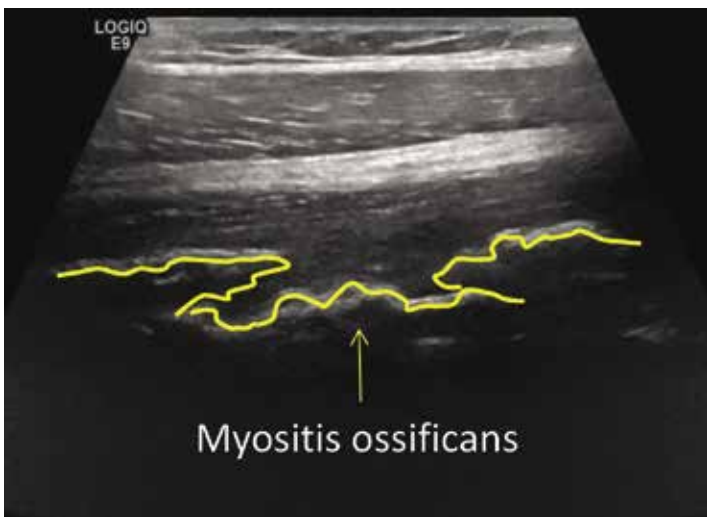
In three cases ultrasound was able to demonstrate degenerative changes of the ankle. Visual demonstration of anatomy helped to reassure individuals that the discomfort they were experiencing was not a result of bleed events. Understanding the difference between bleed related and arthritic pain can help to reduce the use of unnecessary, additional clotting factor treatment (as factor only helps to stop bleeding but does not effect degenerative changes). Again this will lead to further cost savings and guide ensure more appropriate management strategies, like targeted pain relief, orthotics or exercise.

MONITORING MYOSITIS OSSIFICANS

In two cases the ultrasound was used to monitor myositis ossificans, a condition in which bone tissues forms within a muscle following an injury. Monitoring was performed to ensure that re-bleeding did not occur and that the site was reducing in size over time. Quick and accessible imaging within the clinic allowed monitoring without repeated referral to radiology for specialised imaging. Additionally, as the initial symptoms of pain and restricted movement improved overtime, it was easy to forget that the area was still vulnerable. The ultrasound served as a visual reminder that on-going caution was required.







SUMMARY

Ultrasound has used for many years in haemophilia care, but until recently its use was limited to radiology departments which required long waiting times and only allowed imaging of problematic joints. With changes to practice and technology we are now able to add ultrasound to our standard physiotherapy assessments with substantial benefits to quality of care, improved outcomes and significant cost savings to the Health Service.

Are you living with Haemophilia A?

P3 Research in Wellington is looking for volunteers to help study a potential new treatment for people with Congenital Haemophilia.

To take part in this study you will need to:
Be male, aged 18 - 75 years
Have a diagnosis of Congenital Haemophilia A
Be in good health or have other medical conditions that are well controlled

You can not:
Have any other known coagulation or haematologic disorders
Be taking medication to suppress the immune system

The study involves:
2 clinic visits, and a follow up phone call
All study participants will receive the investigational drug (no placebo)

You will be reimbursed for attending study visits and for reasonable travel expenses

For more information and to see if you may be eligible, phone: **0800 737 883** to speak with one of our team, or apply online by visiting: **www.p3research.co.nz** and follow the links to the 'current studies' page.

P3 Research
trialling tomorrow's medicines today

Revised WFH guidelines for the management of Haemophilia

The third edition of the WFH Guidelines for the Management of Hemophilia has just been published in the journal, *Haemophilia*!

You can access the journal publication here: https://onlinelibrary.wiley.com/doi/10.1111/hae.14046, and read the introduction below.

This new edition of the World Federation of Hemophilia (WFH) guidelines for the management of haemophilia comes at an exciting time in the evolution of the diagnosis and treatment of this condition. Since the publication of the second edition in 2012, tremendous advances have been made in several aspects of the management of haemophilia. These include genetic assessment as well as therapy with many innovative therapeutic products including extended half-life factor VIII (FVIII) and factor IX (FIX) products, a bispecific antibody, and haemostasis rebalancing drugs now in clinical development.

All of these allow for more effective haemostasis than was possible in the past.

Laboratory monitoring of therapies is better defined and prophylaxis is accepted as the only way to change the natural history of bleeding. There are highly effective therapies for patients with inhibitors. Outcome assessment with validated clinimetric instruments is widely advocated and practiced.

All these advances are reflected in this third edition of the WFH guidelines, with new chapters devoted to several of these topics along with a new chapter on principles of care that aims to provide a framework for development of a comprehensive healthcare system for haemophilia including advocacy and empowerment for people with haemophilia (PWH). The recommendations in this edition were all developed through a formal evidence-informed and consensus-based methodology involving multidisciplinary healthcare professionals (HCPs) and well-informed PWH. While directed primarily at HCPs, these guidelines should also be very useful for PWH as well as advocacy organizations.

Source: https://elearning.wfh.org/resource/treatment-guidelines/

INTRODUCTION

BY ALOK SRIVASTAVA. DEPARTMENT OF HAEMATOLOGY, CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA. ALAIN WEILL. WORLD FEDERATION OF HEMOPHILIA, MONTREAL, QC, CANADA. GLENN F. PIERCE. WORLD FEDERATION OF HEMOPHILIA, MONTREAL, QC, CANADA

With more than one million print and online distributions in six languages and more than 1000 citations in peer-reviewed articles since its publication in 2012, the World Federation of Hemophilia (WFH) clinical practice resource, *Guidelines for the Management of Hemophilia*, 2nd edition , has served the community of hemophilia care providers and people with hemophilia extensively. Endorsed by the International Society on Thrombosis and Haemostasis (ISTH), the WFH guidelines were also the first hemophilia management guidelines to be accepted by the National Guideline Clearinghouse (NGC), formerly run by the Agency for Healthcare Research and Quality (AHRQ) of the United States Department of Health and Human Services (https://www.ahrq.gov/gam/index.html).

Over the past five years, unprecedented progress has been made not only in the development of newer therapeutics for hemophilia, but major paradigm shifts have also occurred in many of the principles governing the planning and philosophy of hemophilia treatment. Given the progress in genetic analysis technologies, in addition to much wider access, their applications in hemophilia have moved from the research arena to an increasingly greater role in the management of patients and their families. The advent of newer clotting factor concentrates (CFCs) with extended half-life has not only led to decreased burden of care for patients; more importantly, extended half-life CFCs have made it possible to maintain significantly higher factor trough levels on regular replacement therapy than has been possible with standard half-life CFCs. The bar of hemostatic safety was raised even higher with the introduction of non- CFC hemostatic agents such as the novel bispecific monoclonal antibody. This agent achieves hemostasis equivalent to approximately 15% FVIII levels, with subcutaneous administration and substantially less frequent dosing compared to CFCs. People with hemophilia treated with these newer therapies are now able to participate in many more activities than ever before without fear of bleeding. In addition, structured outcome assessment has been a relatively unevolved aspect of the management of hemophilia. With greater emphasis over the past few years on its significance in routine management of hemophilia, several clinimetric instruments are now being used for the standardized assessment and documentation of both hemostatic and musculoskeletal outcomes.

To acknowledge these advances and establish them more firmly in clinical practice, several modifications have been made in the third edition of these guidelines. New chapters have been added to provide the required detail to the following topics: genetic assessment; prophylaxis with hemostatic agents to prevent bleeding; management of inhibitors; and assessment of outcomes. An additional chapter defines the principles of management of hemophilia to provide aspirational benchmarks during the evolution of these services, within the local contexts of countries around the world.

Certain semantic changes introduced in this edition should be mentioned. The term “episodic” rather than “on demand” has been used to describe any hemostasis therapy after bleeding, as this term better reflects the concept of this practice. In keeping with the definition provided by the Scientific

Standardization Committee of the ISTH, the term "exposure day" has been replaced with "exposure" to encompass all CFC replacement doses administered within 24 hours.

To ensure that bias was avoided as much as possible, a rigorous consensus- based methodology was adopted for formulating the final recommendations in these guidelines. An independent methods and process expert, unrelated to the field, was appointed alongside the content lead. All recommendations were informed by a comprehensive and systematic review of the relevant scientific literature and developed through an anonymous modified Delphi process resulting in evidence- informed consensus-based recommendations. Importantly, in addition to the experts in hemophilia care and related clinical disciplines, the Delphi panels included well-informed patients who also had the opportunity to review the manuscripts and the literature, and vote on the recommendations. All these steps are described in detail in the Methodology chapter.

It is also important to note that the final chapter drafts were reviewed internally both by the full panel and within the WFH, as well as by external subject experts prior to submission for publication. All these reviewers have been acknowledged at the end of the guidelines along with many others whose contributions have been invaluable to their development. A final round of independent peer review was also conducted by the journal before publication. It is also important to note that these guidelines have been endorsed by the Asian-Pacific Society on Thrombosis and Hemostasis, European Haemophilia Consortium, and National Hemophilia Foundation (USA).

As a result of all these modifications, the guidelines have become more comprehensive than the previous edition. However, to preserve their easy readability, the text remains structured using short sentences in bullet points. Detailed mechanistic explanations or descriptions of the original data underlying recommendations have been avoided. However, all relevant references have been cited and are listed at the end of each chapter.

It is hoped that the clinical care community, for whom these guidelines are primarily intended, will find them even more useful than the previous editions. These guidelines may also serve as a resource to support education, advocacy, and decision- making related to hemophilia treatment and the delivery of care. In addition, they should help identify gaps in evidence upon which the recommendations have been formulated to help direct appropriate clinical research in these areas. As in the past, the electronic version of these guidelines is available on the WFH website (http://www.wfh.org). These guidelines will be updated, added to, or modified as significant new data or evidence justifying change become available. This will keep the guideline content current and cognizant of the advances that are expected in the coming years, particularly in the area of gene therapy for hemophilia, which will need to be included in more detail once the ongoing clinical trials are over and products are registered.

Source: https://onlinelibrary.wiley.com/doi/10.1111/hae.14046

Regions and Groups

HFNZ's Regional and Group committees enable all our members to participate in the running of the Foundation, and to connect with and support one another. Due to the Covid situation, events have been limited this year. Here's what's been happening in your area.

CENTRAL REPORT

BY ANA CLULEE

A variety of events have been happening in the Central region, even with COVID.

BJ Ramsay the Haemophilia nurse and Helen Dixon the physiotherapist joined the masters exercise group Christmas party on 18/12/20 at the Supply Room restaurant.

The Christmas event in Palmerston North was a huge success, with over 40 in attendance. Thanks to Ashley for organizing this event.

The fishing trip was well attended by 17 people. The vessel sailed from the Mana cruising club, which was central and easier to get to for some members for a gentler trip. The afternoon session worked well for everyone.

The celebrations were organised for World Haemophilia Day on Saturday 17 April. This event was held at the Murrayfield Museum cafe in Levin. The venue was excellent and provided fun activities for members. There was also a presentation on twinning with our Pacific Partners Fiji on the day.

NORTHERN REPORT

BY HEMI WARETINI

Kia ora e te whānau. I hope you all have had a good summer, and managed to enjoy some time in the sun with your loved ones.

Northern had a fantastic Christmas party at the zoo. It was great to get together in person and meet new people after a year of social distancing. Everyone had a great time, and enjoyed seeing fellow HFNZ members for the first time in a while.

We were very sad to see former Northern Outreach Worker Amber leaving. However, we were glad that we were able to farewell her in person at the Christmas party, and have the opportunity for members to share stories/appreciations of the positive impacts she has had.

Keep your eye out for upcoming events in the Northern region. We will send out invites as these are planned.

We're always looking for additional committee members so contact info@haemophilia.org.nz if you're interested in chatting to current committee members about how you can help.

MIDLAND REPORT

BY CASSANDRA CHRISTENSEN

Our Midland committee was really excited to finally be able to hold our family day out recently after having a couple of postponements due to Covid.

We spent some time in Rotorua at the 3D Trick Art gallery, which proved to be a lot of fun for all ages. While our numbers were smaller than we have previously had, it was a great time for all of those who attended, and a fantastic chance to get to know Laura-Lee our new outreach worker over a picnic lunch down at the lakefront.

Midland are looking to organise some more events moving forward and have a committee meeting on 2 May for anyone who has any ideas or wishes to attend! Please get in touch at c.d.christensen12@gmail.com, as we would love to have you come along.

SOUTHERN REPORT

BY JAMES POFF

Well, I guess as I'm writing this report that we are all slowly seeing some light at the end of the very long Covid tunnel. It has been a long journey for all of us, with some more challenges ahead I'm sure.

Speaking of challenges, the belated Southern AGM was going to being held via the Zoom on-line platform. However, due to some challenging technical issues the first two planned meetings have not gone well at all. However, all is not lost as the saying goes, "third time is a charm" – watch this space ...

The National Council finally met face to face last month in Wellington and the exciting news is that the next Council meeting is scheduled to be held in Christchurch – scheduled for Saturday 12 June, mark this date in your diary as there are plans for local members to be involved.

The Southern Walks have continued, with two walks having been knocked off so far this year, first walk was around part of the inner Lyttleton Harbour, and the second on the Port Hills. Both were well attended and we are all (mostly) looking forward to the upcoming planned walks.

Another piece of very exciting news for the Southern region is the appointment of Rosie Maguire as the new Southern Region Outreach Worker. On behalf of the Southern Branch: welcome aboard Rosie!

YOUTH

BY COURTNEY STEVENS

We kicked off our first meeting of the year back in February with the intention of refocusing our attention on what we can do as a committee this year following a bit of a stagnant 2020.

Our main areas of interest remain twinning with Nepal, and how we can make this work remotely in the post-COVID world, and a focus on regional events. We are due to have our next committee meeting soon, to discuss options for a HFNZ Youth Weekend event, which we are intending to run concurrently with the Nepalese Haemophilia Society's Youth Committee later this year.

We understand that WFH has been working on some remote twinning guidelines and are hoping to use these to assist us with our twinning proposal which is due in May this year.

Again, keep your eye on the calendar for some upcoming regional events and reach out if you need anything, or are keen to get involved.

Get in touch with your Outreach Worker, or find HFNZ Youth on Facebook to find out more.

Study Identifies Cytokine Target for Treatment-Resistant Hemophilia A

BY JONATHAN ALICEA

Elevated B cell activating factor levels in children and adults were associated with the development of FVIII inhibitors, which may lead to FVIII infusion failures.

Findings from a new study shed light on the mechanisms behind patient unresponsiveness to coagulation protein therapy for hemophilia A.

More specifically, investigators note a key target that may lead to treatment failure in up to 30% of patients.

Currently, hemophilia is the most common inherited bleeding disorder, which affects 1 in 10,000 men across the globe. Since patients lack coagulation factor VIII (FVIII), therapies are typically aimed at infusions to replace the missing protein.

Some patients, however, become treatment resistant due to the development of neutralizing antibodies, or FVIII inhibitors.

Nonetheless, an investigation into the immune response mechanism, led by Bhavya Doshi, MD, and colleagues at the Children's Hospital of Philadelphia (CHOP), examined the regulatory role of cytokine B cell activating factor (BAFF) towards FVIII inhibitors.

THE CONTEXT

Previous research has shown that BAFF has some role in certain autoimmune diseases, as well as in antibody-mediated transplant rejections.

"Recent studies in allograft transplant recipients demonstrate that high BAFF levels prior to transplant are associated with antibody-mediated rejection and elevated levels following α-CD20 therapy may also contribute to the failure to induce humoral tolerance to the graft," the investigators wrote.

In addition to BAFF, a proliferation-inducing ligand (APRIL) expression is notably increased under proinflammatory responses.

Despite these observations, however, the investigators note that the mechanisms behind FVIII inhibitor development have been very much unclear.

THE FINDINGS

The investigators used plasma samples from 69 pediatric patients undergoing recombinant FVIII therapy, in addition to samples from mouse models, to determine whether BAFF may help generate and sustain FVIII antibodies.

Of the pediatric patients, 24 had FVIII inhibitors.

From their analysis, they found BAFF levels to be higher in patients with persistent FVIII inhibitors compared to those without inhibitors (1.30 vs. 0.99 ng/mL, respectively, P = 0.021).

"Moreover, BAFF levels decreased from baseline in hemophilia A inhibitor patients who underwent ITI [immune tolerance induction] and achieved FVIII tolerance from 1.43 ± 0.63 to 0.81 ± 0.32 ng/mL (P = 0.025)," the investigators observed. "In comparison, those who failed ITI had steady levels at 1.33 to 1.23 ng/mL (P = 0.246.).

A similar pattern and trend in BAFF levels was also noted for an adult population (n = 46), although noninhibitor patients saw a generally higher level of BAFF.

Furthermore, a receiver-operating characteristic (ROC) analysis of the pooled pediatric and adult data showed that BAFF levels greater than 1.03 ng/mL had 68.3% sensitivity, 63.8% specificity, and likelihood ratio of 1.89 for the presence of FVIII inhibitors.

The mouse models revealed that using prophylactic anti-BAFF therapy prior to FVIII treatment successfully prevented inhibitors. As for the mice with already-developed inhibitors, treatment with anti-BAFF and rituximab had an effect of reducing FVIII inhibitor titers.

"Our data suggest that BAFF may regulate the generation and maintenance of FVIII inhibitors, as well as anti-FVIII B cells," said co-investigator Valder R. Arruda, MD, PhD, director of CHOP's NIH-funded Center for the Investigation of Factor VIII Immunogenicity, in a statement.

"Given that an FDA-approved anti-BAFF antibody is currently used to suppress the immune response in autoimmune diseases, future research should explore the use of this treatment in combination with rituximab to achieve better outcomes for hemophilia A patients resistant to FVIII protein replacement therapy," he indicated.

The study, "B cell–activating factor modulates the factor VIII immune response in hemophilia A," was published online in *The Journal of Clinical Investigation*.

Source: https://www.hcplive.com/view/study-identifies-cytokine-target-treatment-resistant-hemophilia-a

Takeda Donating Hemophilia Treatments for 5 Years to WFH Aid Program

BY AISHA I ABDULLAH PHD

The World Federation of Hemophilia (WFH) announced that Takeda has joined its WFH Humanitarian Aid Program, agreeing to large, annual donations of treatments for people with inherited bleeding disorders like hemophilia in developing countries.

Takeda, with this commitment, builds on 30 years of supporting WFH programs, becoming a "contributor" level sponsor in humanitarian aid.

Specifically, the company agreed to provide the group with 15 million international units (IU) of factor VIII (FVIII), and 5 million IUs of bypassing agents every year for the next five years.

"This five-year product donation aims to help the WFH in improving access to treatment, including prophylaxis to protect joint health," Julie Kim, president of the Plasma Derived Therapies Business Unit at Takeda, said in a press release.

People with hemophilia A, the disease's most common subtype, lack the FVIII clotting protein, and are typical treated either with replacement therapies that supply the factor, or bypassing agents that "bypass" its need. Both replacement therapies and bypassing agents may be given on-demand to treat bleeds, or prophylactically to prevent them.

"At Takeda we recognize the need to advance the standard of care for those living with a rare bleeding disorder, as well as the importance of tackling disparities in access to treatment worldwide," Kim added.

The WFH Humanitarian Aid Program was established in 1996 to improve access to care in developing countries for people with hemophilia and other inherited bleeding disorders. The group partners with patient organizations in a given country to ensure reliable and consistent access to treatment.

Aid given through the program supports treatment in emergency situations, for acute bleeds, surgeries, and as prophylaxis. To date, WFH reports that this program has distributed over 800 million IUs of products to more than 100 countries.

Since the 1990s, Takeda support for WFH efforts include its World Bleeding Disorder Registry (WBDR), an online platform open to hemophilia treatment centers worldwide to collect standardized patient data, and the Global Alliance for Progress (GAP) Program, aiming for better diagnosis and treatment of people with hemophilia and other bleeding disorders.

"Takeda has collaborated with the WFH for over 30 years, playing an important role in several of our programs," said Alain Baumann, CEO of the WFH.

"We are thankful that Takeda has now extended their support to the WFH Humanitarian Aid Program. This will allow the WFH to do even more to support bleeding disorders communities in need around the world," Baumann added.

Source: https://hemophilianewstoday.com/2021/04/02/takeda-donating-hemophilia-treatments-5-years-wfh-humanitarian-aid-program/

Manual Therapy Improves Joint and Quality of Life Outcomes in Hemophilic Arthropathy

BY JONATHAN GOODMAN, MPHIL

Physiotherapy and exercise combined are effective, without causing pain and bleeding, for increasing functionality, joint health, and quality of life (QoL) among patients with hemophilic arthropathy (HA) of the elbow, according to research published in *Haemophilia*.

The elbow joint is a common site of recurrent hemarthrosis, leading to HA in some patients, which can lead to chronic pain, decreased limb function, and reduced QoL. Orthopedic treatment can, furthermore, lead to an increased risk of bleeding and infection. While a number of exercise recommendations exist, their varying effectiveness, and whether at-home exercises are superior or non-inferior to physiotherapy, is unestablished.

Manual therapy, a type of physiotherapy that aims to increase biomechanical flexibility and joint function, involves the application of controlled force to joints and soft tissue. While this therapy is becoming more frequent in the HA setting, little data exist on its use on the elbow joint.

For this study, researchers evaluated, in comparison to a home exercise program, the effectiveness of a manual therapy and exercise program on pain, range of motion, muscle strength, joint health, functionality, and QoL among patients with HA of the elbow.

Overall, of the 20 patients assessed for eligibility, 9 were randomly assigned to the manual therapy group and 8 were assigned to the home exercise group. Baseline characteristics between the groups were similar, with an average age of 24 years; 88.3% of patients had hemophilia A while 11.7% had hemophilia B, and 94.2% of patients had severe disease.

In the manual therapy group, bleeding frequency and activity pain decreased, while elbow range of motion and flexor strength increased; these patients also had statistically significant improvements in joint health, functionality, and QoL.

While patients in the home exercise group also had improvements in activity pain, QoL, and some ranges of motion, patients in the manual therapy group had significantly superior results overall in range of motion – including elbow flexion, supination, and pronation – as well as joint health and functionality.

"Manual therapy ... was effective and safe in reducing frequency of haemarthrosis and activity pain and, improving all [ranges of motion] of the elbow, flexor muscle strength, joint health of the elbow, upper limb functionality and quality of life in patients with HA in elbow joint," the authors wrote. "However, home exercises showed improvements in limited parameters such as flexion and extension [ranges of motion] of the elbow, activity pain level and quality of life."

Reference: Tat AM, Can F, Tat NM, Sasmaz HI, Antmen AB. The effects of manual therapy and exercises on pain, muscle strength, joint health, functionality and quality of life in haemophilic arthropathy of the elbow joint: a randomized controlled pilot study. *Haemophilia*. Published online February 24, 2021. doi:10.1111/hae.14281

Source: https://www.hematologyadvisor.com/home/topics/bleeding-disorders/manual-therapy-effective-treatment-hemophilic-arthropathy/

Adult Weekend 2020

THE YEAR AHEAD

17–20 July, 2021

- Youth Camp
  Blue Skies, Kaiapoi

Late 2021

- Women's Weekend
  Date and venue to be determined

Early 2022

- National Family Camp
  Date and venue to be determined

Visit www.haemophilia.org.nz for more information on bleeding disorders, HFNZ News, and past issues of Bloodline

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