ACTIVATED
Newsletter of Haemophilia Foundation
Australian Capital Territory

HAEMOPHILIA FOUNDATION
AUSTRALIAN CAPITAL TERRITORY

PATRON
Dr Richard Pembrey AM,
MB BS, MD, FRACP, FRCPA

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President's Report

As another disrupted year edges closer to its end, I imagine a collective sigh of relief will accompany it. It's been a tough year for many in Canberra with the extended lockdown, the concern around COVID-19 and the cancellation of social and sporting activities. This included cancellations to a number of HFACT events which were planned for the second half of 2021. Look forward to 2022, I'm hoping that things return back to normal, or close to it, and that many of the social events cancelled in 2021 proceed in 2022. Fingers crossed!!!

I attended the 20th Australian Conference on Haemophilia, VWD and Rare Bleeding Disorders, held on 8-9 October 2021. The event was 100% virtual and I admit I was curious to see just whether a virtual conference would work (succeed). Well in my view it was a great success and I passed my congratulations onto HFA for its hard work and good planning for pulling it off. I was also honoured to be invited to give a short talk at the conference, as part of a plenary, about my expectations and hopes for future treatments as a parent of children with a bleeding disorder. Overall, I was positive about where we have gotten to and what lies ahead and so my message was very much an optimistic one.

This positive message was reinforced by the discussions and presentations around the latest treatments which are on the horizon. These treatments, many of which are in different stages of trials, should, if they become available, cater for individuals with different types of bleeding disorders. Many within the community have marveled at the advancement from Hemlibra, however, not everyone with a bleeding disorder has been able to benefit from it or has chosen to move onto it.

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This is the last President's report for 2021 but it will not be my last report. I put my hand up once more for the President's role at HFACT's AGM and was pleased to receive the support to continue in the role. I would also like to thank the rest of the HFACT Committee who will support me and the bleeding disorders community in the ACT and surrounding regions over the coming year. Thank you to Rebecca Minty (Vice President), Jenny Lees (Treasurer), Shauna Adams (Secretary) and Len Minty (Committee member) for continuing on the Committee for another year. Also thank you to HFACT's Counsellor Kathryn Body who continues to do a great job in sometimes difficult circumstances.

Lastly, I would like to wish you all a merry festive period and enjoy whatever holidays you have planned. See you in 2022.

Claudio Damiani
President

Treasurer's Report

The Treasurers Report for the financial year ending 30 June 2021 was presented to the AGM on October 19, 2021. It is printed below for your information. A copy of the Annual Report, including the full financial statements is available on the HFACT website (hfact.org.au) for your information.

Thank you to all those who have renewed their membership for 2021-22.

Treasurer's Report 2021

The main source of income for HFACT is the ACT Health Directorate who provided $44,694 for the provision of counselling and related support services for the group. This, combined with the supplementary COVID-19 Grant and the carry-over grant amount from 2019/20, provided total grant funding of $49,582. Grant funding provided 80% of the income for HFACT during 2020/21.

The income from fundraising and contributions ($2,663) represented 4% of all income received.

There was no income from trading and operating activities this year.

HFACT once again benefited from the Australian Tax Office's Cash Flow Boost program. $10,000 was received during the year.

The total income of the HFACT during 2020/21 was $62,267.

As in previous years, the major expenses of the HFACT were associated with the provision of a counselling and support service to persons with haemophilia and other bleeding disorders. Direct costs (wages, superannuation, transport, leave reserve) totalled $49,594. The total hours of service provided by the counsellor (676 hours) is above the minimum agreed level of service set under the service contract with ACT Health Directorate.

A decrease (47%) was recorded in the sum expended during 2020/21 for direct member support services ($4,964). This reduction is due to the impact of COVID-19 and the inability to undertake the usual group activities with the community. A small grants program was run during the year and provided $2,000 to 4 recipients. Additional funds were spent on functions and direct support to our members.

The total expenditure of the HFACT during 2020/21 was $52,132 which is 1.5% less than the previous year.

Carry-over grant funding for 2020/21 is $11,660. This includes the remaining $3,700 of the COVID-19 supplement and $7,957 from the grant.

The financial outcome for HFACT for the year was a surplus of $10,135. As of 30 June 2021, the net assets of HFACT are $40,619 which is 33% more than the previous year.

Jenny Lees - Treasurer

October 2021

Jenny Lees

Treasurer

HFACT social event

Summer dinner get together

February 5 2022

The ACT bleeding disorders community will have the first get together for 2022 on Sat 5th February. It will be a relaxed, family-friendly evening. Save the date!

More details to come.

Personal Stories

Reprinted with permission from National Haemophilia, No 215, September 2021.

Finally cured of hep C - Gavin's story

Gavin Finkelstein is President of Haemophilia Foundation Australia (HFA) and Haemophilia Foundation Western Australia (HFWA). He has severe haemophilia A. He talked to HFA about living with hepatitis C, treatment and being cured. Our thanks to Gavin for sharing his personal story.

For Gavin, growing up with severe haemophilia had meant living with joint bleeds. His generation became adults before the arrival of prophylaxis treatment to prevent bleeds and Gavin had relied on plasma-derived clotting factor concentrates to manage his bleeding episodes whenever they occurred. The regular bleeds resulted in arthritis and other joint and muscle damage.

1*Gavin Finkelstein*

'As they say, pain was my constant companion, but not my friend.'

What he didn't realise at the time was that another unfriendly traveller had also hitched a ride on his treatment products – hepatitis C virus, which had infected blood products like clotting factor concentrates through blood donations. By 1993 Australia had introduced new safety measures to prevent transmission of hepatitis C in blood products, but in the years before then Gavin had already been exposed to hepatitis C through his treatments many times.

Some years earlier Gavin had been told he had non-A non-B hepatitis – the name for hepatitis C before there was a test - but little was known about it at that stage. When his diagnosis with hepatitis C was confirmed in 1993, it had a very different impact on him.

'At first I freaked out,' he said. 'After living through the HIV epidemic, I thought I was going to die. I was very worried about transmission and passing it on to others. I broke off my relationship and was fearful about going into other relationships. It had a very negative effect on my motivation and my career.'

EARLY TREATMENTS

Early hepatitis C treatment with interferon injections and ribavirin tablets was prolonged and arduous, with difficult side-effects.

'I had 72 weeks of treatment in 2001-2, which was horrific. I was working the whole time, but it turned my mind to mush. I was forgetful, I was grumpy, I had no energy. It affected my home life as well as my work. Then I relapsed 6 weeks after the treatment finished, which was pretty demoralising.'

With the ongoing impact of hepatitis C symptoms – fatigue, brain fog, lack of energy and motivation – and his increasing arthritis and joint problems with haemophilia, Gavin took early retirement from his job in the public service but continued his volunteer roles with HFWA and HFA.

In 2009 he tried the pegylated interferon and ribavirin treatment again, but his treatment was stopped after 6 weeks when tests showed it wasn't working.

TREATMENT AND CURE

In 2016 the new direct acting antiviral (DAA) treatments for hepatitis C became available in Australia. They were described as 'revolutionary' – and in Gavin's opinion, lived up to their promise.

'I had one of the new treatments, Harvoni, and it was a doddle. One tablet a day for 12 weeks and minimal side-effects. And I was cured – it was fantastic. It was the best thing I ever did. Now I feel fine and my liver test results are good too.

Personal Stories Contd.

Checking liver test results to make sure his liver had recovered was an important step. This testing took place as a standard requirement when Gavin joined a clinical trial for a new haemophilia treatment, but he encouraged others to ask about testing if they didn't know what their liver test results were after being cured.

'Don't wait' was the message he had for others considering treatment for hepatitis C.

'Don't even think about it. Go for it – get it done. These new treatments have such positive results and there is hardly any impact on your life to undergo the course of treatment. There are several different treatments, so your doctor will be able to find one that suits your individual health and lifestyle.

'If you are worried about having hep C treatment, ask your haemophilia team or your hepatitis clinic to put you in touch with someone who has had the new therapies so they can have a chat with you about what it's like. These days you don't need to think about the implications for your work or home life because it's so easy to take and there are hardly any side-effects. And when you are cured it puts you in good stead to deal with the rest of your life with haemophilia.

HFACT Grants

The HFACT 2021 Grants Program offered HFACT members the opportunity to apply for a grant of up to $500 to support people affected by a bleeding disorder and inspire them to achieve their goals or try new things. It was open to members of all ages (not just persons with bleeding disorders, it could also be carers, siblings, children etc). HFACT's aim in offering these grants is to assist in improving the quality of life for members. This year, four grants were provided. Three recipients report back:

Tate Maguire used a HFACT grant towards attending rep netball comps and training.

Hey this is Tate. I have really enjoyed representing my area in netball, I have become really good at it and learnt loads of skills. We got to go to a few Carnivals and played against other states, it was hard at times but enjoyable. Thanks for the grant it has allowed me to travel long distances and be able to stay in accommodation and not have to drive straight home after games. It has allowed me this experience that I might not have been able to have without support. We hope to get to Sydney this year and this money will support that too, thankyou

Tate Maguire

Mitchell Maguire received a HFACT Grant that was put towards a gym membership.

Hey this is Mitchell Maguire. My gym membership has allowed me to go most afternoons, I have enjoyed getting fitter. I go with my mates and we get to do a range of activities and work outs, it has allowed me to go without having to worry all the time about the cost of the gym. Thank you for giving me this grant it is keeping me fit.

Mitchell Maguire

I am really grateful that HFACT supported me to purchase soccer dummy walls. They have allowed me to change up my training for soccer and really practice my free kicks and penalties. I really enjoy using them as part of my training. I think its important to keep fit and healthy so that my body can recover quickly from any injuries and having the soccer dummy walls helps me achieve this goal. I look forward to the soccer season starting so I can put all my practice to good use and score goals. Thank you to HFACT for supporting me!

Alessandro Damiani

8 | 9 October 2021
20TH AUSTRALIAN CONFERENCE
ON HAEMOPHILIA, VWD & RARE BLEEDING DISORDERS
EMBRACING A CHANGING WORLD

HFA Conference

The 20th Australian Conference on Haemophilia, VWD and Rare Bleeding Disorders

Embracing a Changing World

Watch conference sessions on-demand

It might be a month since The 20th Australian Conference on Haemophilia, VWD and Rare Bleeding Disorders but you can still catch many of the amazing sessions and personal stories from this huge event.

If you registered for the conference then simply head to the conference portal, https://haemophilia.delegateconnect.co/, log in, and click on 'Program on Demand' to navigate through all of the different sessions. If you didn't get a chance to register, you can still buy a ticket and access this great content.

The sessions, virtual exhibition booths, ePosters and Remembrance service will all be available until April 2022.

Conference Session Reports

Haemophilia Foundation Australia conferences are always interesting and always provide something different – either information or experience based. The 2021 conference - 'Embracing a Changing World' was no exception.

I have been attending conferences, and writing up sessions for HFACT, for several decades but this one was a very different experience for me. This time I was not just a delegate, but I was chairing a conference session. Not only that, but the conference was also online – I would be interacting through my laptop and would not know if anyone was watching or not.

Fortunately, the conference organisation used by HFA was brilliant and I found that chairing the session was not as difficult or stressful as it could have been. The thought that everything I said, every little stumble, was being recorded and would be available online for 6 months was a little unnerving though.

Getting Older

The session I chaired was 'Getting Older'. Like it or not we are all getting older each day. What is different for the bleeding disorders community is that now people with haemophilia, and other bleeding disorders, are living into old age as a matter of course, not exception. This presents issues that have not had to be addressed on a population basis before. The Getting Older session explored some of these issues.

The session covered a range of viewpoints – the patient point of view from Zev, clinical issues from Dr Mike Makris, and a panel discussion with a nurse, physiotherapist, and psychosocial worker.

Zev, at 70, has experienced the full range of haemophilia treatments – from no treatment at all (rest & ice) through to the current long-acting treatments that are available. His aim is to be able continue working and contributing to society. His challenges are mobility and fitness. He sees it as very important to maintain as much mobility as possible, given the damage haemophilia has done to his joints over the years, and fitness plays a role in this.

Some common threads through the session were:

Mobility and fitness

Maintaining and retaining mobility and fitness, particularly balance, as we get older is important. It helps with independence and quality of life. Many people with bleeding disorders already have joints that are rated as older than them and it is important to keep mobile for good health. Working on balance will reduce the likelihood of falls.

The recommendation from the physio on the panel is to work with a community-based physiotherapist for ongoing support and exercises, relying on hospital / HTC resources for treatment of bleeding episodes. Community physios are generally more accessible.

Co-morbidities.

People with bleeding disorders who are getting older are also prone to the 'usual' diseases of old age, for example: arthritis; heart disease; and dementia. Sometimes bleeding disorders will influence treatment options so it is important that your Haemophilia Treatment Centre continues to be involved in your care.

Treatment when aging / in care.

What happens about prophylaxis / treatment when self-infusion is no longer an option, or I can't get to the HTC? Will prophylaxis still be an option? There is no simple answer to these questions right now. Treatment may be an issue when it comes to aged care / nursing homes as some do not provide intravenous therapies. Community nursing may provide a service in some areas.

General Practitioner.

Finding and using a good GP, one who is willing to learn about bleeding disorders and communicate with the HTC, is important when getting older. HTC specialists are very familiar with bleeding disorders but have less experience with the general conditions that impact as we are aging.

Haemophilia and aging is a new field and, as with all new areas, there will be an element of trial and error as the community moves into this area, discovers issues and defines solutions. The 'Getting Older Hub' on the HFA website is a good source of resources: Getting Older Info Hub - Haemophilia Foundation Australia

Jenny Lees

The Changing World of Bleeding Disorders

The first plenary session at the recent "20th Australian Conference on Haemophilia, VWD and Rare Bleeding Disorders" looked at the rapidly changing treatment options that are becoming available to treat bleeding disorders. New treatments that are available now or in clinical trials or under development. It was an exciting session for me as I realised how different the outlook is now for couples who have an inherited bleeding disorder in the family facing the decision whether to have children.

The session entitled "The Changing World of Bleeding Disorders" started with three short personal experiences of using extended half-life (EHL) clotting factor treatment and/or emicizumab (Hemlibra), a factor VIII mimetic.

- The first speaker has moderate haemophilia A, and other comorbidities including vision impairment and mild palsy. The change to emicizumab, administered subcutaneously, brought about welcome changes in his life. The treatment is only once a week, it is simpler and he can administer it himself. It can be collected from the chemist, and it has enabled him to accept his haemophilia status, empowering him with a sense of freedom and independence.
- The second speaker is a mother of two obligate carrier daughters. One daughter, aged 7, has severe haemophilia diagnosed at 4 months. The family's quality of life improved when EHL factor became available in 2020. Using EHL treatment, the young girl had very few hospital admissions. Since starting emicizumab recently, she has not had an admission, just two very minor bleeds. So life is completely different. Mum no longer worries about her daughter going to school or to play with friends.
- The third speaker has severe haemophilia A and had been on self-prophylaxis for 21 years, 3 times a week. He started on EHL factor product 3 years ago and went on to treatment once every six days. The main benefit has been the ongoing care of veins with reduced venous access. Another benefit is the reduced amount of product and giving sets when travelling. His bleeds have been well controlled with prophylaxis, both before and after the transition to EHL product. He has only had one bleed while on EHL product.

The following two presentations were from Professor Huyen Tran and Professor David Lillicrap respectively. In much of what follows, rather than risk getting it wrong, I have used quotes taken selectively from each presentation to provide a combined summary.

Both professors gave a brief description of the coagulation cascade, an overview of haemophilia treatment and innovation in treatment since the 1950's to now, and then the newer products that are now approved for use and being introduced. As most Australian haemophilia patients, A or B, are now using EHL products or emicizumab, the older treatments are not covered in detail here. For that, viewing the conference session "on demand" is recommended. Instructions on how to do that are provided elsewhere in this newsletter.

Newer treatments can be divided into the following categories:

1. Modified recombinant factor concentrates, such as EHL products.
2. Intrinsic tenase complex innovations such as emicizumab.
3. Rebalanced haemostasis products e.g. Fitusiran, Concizumab.
4. Gene or cell based therapy, currently in clinical trials.

Only the first of these involves clotting factor replacement. The remaining three are non-replacement therapies

Modified recombinant factor concentrates

There are several technologies that are used to extend the half-life of FVIII or FIX. The FVIII or FIX protein is fused to another protein that has a naturally longer half-life in circulation.

One method is pegylation which tags polyethylene glycol (PEG) to the clotting factor protein. This inhibits elimination by the body thereby allowing the factor to circulate for longer. Adynovate (EHL FVIII) is an example of a product that uses pegylation.

Two other techniques are fragment crystalline (Fc) of immunoglobulin (IgG) fusion or albumin binding to a factor protein which allows the recirculation of the factor and therefore extends the half-life of factor concentrate.

A study of Alprolix, a long acting FIX concentrate that uses the Fc of IgG fusion technique, usage has shown that the half-life of EHL FIX is almost 100 hours compared to the shorter half-life of FIX of approximately 18 – 24 hrs. Depending on the individual, patients on Alprolix can receive their treatment once every 7 to 14 days.

Similarly, a study of Eloctate, a FVIII Fc fusion product, shows half-life extended to almost 24 hrs when its typically around 8 – 12 hrs.

Emicizumab

Emicizumab is a FVIII mimetic bispecific antibody that binds to activated FIX through one arm and FX through the other arm. It mimics to some extent FVIII co-factor activity. Advantages are infrequent subcutaneous delivery, that it works with inhibitor patients and the reduction in annualised bleeding rates (ABR) are very significant.

Since November 2020, Hemlibra is available in Australia to severe or moderate haemophilia A patients without inhibitors, and in patients with inhibitors, through haemophilia treatment centres. It is available to patients who can self-administer at home with oversight from their HTC and distribution includes through community pharmacies

Rebalanced haemostasis products

Both presenters showed a representation of haemostasis as a see-saw with coagulant proteins on one side and natural anti-coagulants on the other. In normal physiological blood clotting, coagulation factors FVIII, FIX, FXI, FX, FVII, FII and fibrinogen are held in haemostatic balance by anti-coagulants anti-thrombin (AT), protein S (PS), protein C (PC) and tissue factor pathway inhibitor (TFPI).

In haemophilia A, FVIII is missing from the coagulant side of the balance and the balance 'tips' toward the anti-coagulation factors AT, PS, PC and TFPI causing a bleeding problem. In contrast in anti-thrombin deficiency, the balance 'tips' toward the coagulation factors, increasing the likelihood of thrombosis.

In therapies such as anti-thrombin siRNA , the strategy is a re-balancing of haemostasis in patients with bleeding problems. For example, where FVIII is deficient, equilibrium is restored by inhibiting anti-thrombin production. So the balance is reset with a bleeding problem being balanced by an interference with an anti-coagulant protein. This strategy is not limited to FVIII or FIX, it works for any of the coagulation factors.

Three types of re-balancing therapy are available:

- Inhibiting anti-thrombin by reducing its production with siRNA (Fitusiran).
- Inhibiting TFPI with anti-TFPI antibodies (Concizumab) via subcutaneous injection.
- Inhibiting activated Protein C with novel bioengineered anti-APC Serpin agent.

Gene Therapies

There are two types of gene transfer therapy:

In vivo (Latin for "within the living") gene therapy is where an individual with a bleeding disorder receives therapy via injection of a vector modified to deliver a therapeutic payload such as FVIII, which is then secreted into the blood circulation. It is this type of gene therapy that is currently undergoing multiple ongoing clinical trials.

Ex vivo (Latin for "outside the living") gene therapy is where cells are removed from the individual with a clotting factor deficiency. The cells harvested or isolated are autologous cells (cells that come from the same individual who then receives the subsequent transfusion) which are either stem cells or long-lived progenitor cells. The harvested cells are then modified outside of the body to deliver a normal clotting factor gene. The modified cells are then expanded in number and then redelivered to the individual via transfusion. Hopefully the modified cells will then produce the factors that are missing in the individual.

Gene therapy for haemophilia is still at the clinical trial stage and there are at least 16 trials currently underway. The largest of these is the phase 3 GENEr8.1 AAV5 FVIII gene therapy trial. As at March 2021, it involved 132 individuals with severe haemophilia A who received an AAV5 vector which delivers human FVIII. The individuals had been followed up for 52 weeks. At the mid-point of the study their factors VIII levels had a mean of approximately 50 – 60% and a median level of around about 40%. At the end of one year the mean FVIII level was 42% and the median was 23%, with significant variability in the individual results – about 8% of individuals did not get FVIII expression detected in their plasma while some individuals had quite high factor levels over 200% - 300%. In the trial the median ABR dropped from 2.8 (before treatment) to 0 with a mean ABR of 4.8 ± 6.5 dropped to 0.8 ± 3.0. The annualised infusion rate unsurprisingly dropped from a median of 128.6 to 0 and mean of 135.9 ± 52 to 2.0 ±6.4 due to the transgenic protein that was being produced.

Summary by Dr Lillicrap:

- "The past two decades have seen an immense impact of innovative science on the treatment of inherited bleeding disorders. Not only for the haemophilia A and B but the potential for other disorders such as vWD and other rarer clotting factor deficiencies.
- We still need to use conventional replacement therapies optimally, and we also need to employ adjunctive treatments in some bleeding disorders. The innovation highlighted in this presentation does not mean that we will be throwing away the current conventional replacement therapies.
- Non-replacement therapies are now entering the clinic and have the potential to provide innovative treatment options for a wide range of bleeding disorders. This is certainly the case for haemophilia, vWD, FVII and FXI deficiencies and so on.
- In addition, gene therapy has also shown increasing promise in clinical trials and we may witness the first licenced product in the next 1-2 years.
- All these new therapies will require careful, extended follow up to evaluate the potential of adverse effects not evident in short term clinical studies."

Ron Lees

Haemophilia Treatment Centre Update

Where has the year gone? Christmas is soon upon us, and I feel as though we were just celebrating last Christmas! These past few months at the Haemophilia Treatment Centre have become busier due to COVID restrictions being lifted, dentists reopening, and surgery going full steam ahead. Fortunately, I haven't been busier due to bleeds – just preventing bleeds!

By the time you receive this newsletter, the haemophilia clinic will have happened and hopefully, everyone will be ready to start the new year in a very health state.

The feedback from the patients who are on Hemlibra has been very positive. There have been very few reports of breakthrough bleeding, even when the person has done something that would have previously required extra factor. We have been very proactive in changing everyone over to Hemlibra; I'm looking forward to the day when we can change the Haemophilia B people over to a subcutaneous injection to treat their factor deficiency!!

Just a reminder; if you are having any type of surgery or dental procedures, please let me know well in advance, so that everything you need can be organised and the appropriate people notified. I will be working over the Christmas and New Year period but will not be here on any of the public holidays. If you require attention on the days that I am not here, you will, unfortunately, need to attend ED.

Have a safe and merry Christmas and I look forward to catching up in the New Year.

Jayne Treagust

Advance Practice Nurse - Haemophilia Treatment Centre

Wishing the ACT and surrounds bleeding disorders community a happy festive season and a happy, healthy and safe 2022

We hope to see you in 2022!

From the HFACT Committee

Dates for the diary

HFACT get together	5 February 2022
HTC Bleeding Disorders Clinic	27 May 2022 (TBC)

Haemophilia Contact Details

Canberra Hospital

Main telephone: 5124 0000
Website: https://health.act.gov.au/hospitals-and-health-centres/canberra-hospital

Haemophilia Treatment Centre:

Mon to Fri 9am - 5pm **On duty nurse:** 0481 013 323
Via email: haemophilia@act.gov.au **More details at:** www.hfact.org.au/treatment

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Our Mission

"To improve the wellbeing of the haemophilia community through mutual support, networking, advocacy and striving for optimal health care."

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