



Hemophilia
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HEMOPHILIA DAILY

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Improving assessment of QoL

Assessment of health-related quality of life (HRQoL) is vital for evaluating the well-being of patients with hemophilia, their individual experiences of the disorder, multi-dimensional perceptions, and physical and psychological functioning, Alessandro Gringeri (Italy) said at yesterday's *Quality of Life in Hemophilia* plenary.

"The perception of well-being and health are equally important and, therefore, we should take into account quality of life and not just objective science," he asserted. "The overall well being as subjectively perceived by the individual, affected or not by a disease, must not be ignored or considered secondary to other parameters – it should be equal."

Over the past three decades, a number of instruments have been developed internationally to assess HRQoL in children and adults. The United Nations Development Programme's Human Development Index is based on criteria including health, longevity, literacy, school enrolment and standards of living.

More recently, disease-specific instruments have been developed for children and adults with hemophilia to better capture and quantify all the aspects of their well-being in different developmental phases of life. "In order to provide the expensive treatment for hemophilia, it is important

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Yıldırım Çelik

More than 2500 delegates enjoyed yesterday's Cultural Event with a visit to Topkapi Palace

In the Halls

In your mind, what is the greatest obstacle to achieving treatment for all?

We need to empower national member organizations so that they can lobby their governments. We have to coordinate our efforts, reach out, shout for help, make it loud and clear that we need a safe blood supply and adequate availability of factor concentrates – not necessarily for free, but at least subsidized by the government.

-Philippines

There's obviously a huge disparity between the developed and developing world, especially in terms of how quickly innovations are introduced and improvements in standards of care. Also, there are big gaps in the availability of some important kinds of treatment, such as mental health support.

-Canada

Poverty. There are big differences from country to country, but in the end it boils down to money. Even if you convince your government that haemophilia is important and they need to provide supplies for patients, it still might not be possible.

-Ecuador

At least in Europe, the main obstacle is still the availability of prophylaxis for everyone. Some patients are still being treated with factor concentrates but the situation seems better than in most other parts of the world. Even in the US, some concentrates still aren't readily available or affordable – FXIII for instance.

-Germany

There's a bigger role for manufacturers to play, but I want to say clearly that I think they are trying already to help. In some countries supplies are only available from one or two companies, so that can be a real problem with shortages and cost.

-South Africa

Steady progress in dental care continues

Leading experts in hemophilia dental care described some of their clinical case studies and research experiences yesterday, demonstrating how far the field has advanced since the mid-20th century.

“When we started, there were very difficult years,” said Wellington Cavalcanti (Brazil), who has worked with hemophilia patients for 38 years. “No one knew about oral surgery with hemophilia – people with hemophilia were afraid of the dentist and dentists were more afraid of hemophiliacs.”

At the time, the only resource in Brazil was gelfoam sponge for use following extraction. In Argentina, human dry placenta was the only available option, but its use during dental extraction resulted in substantial bleeding.

In 1975, Cavalcanti performed the first removal of a mandibular hemophilic

pseudotumour on a nine-year-old patient with moderate hemophilia. The patient remained in hospital for 85 days due to the difficulty of maintaining the mandibula. A second case of mandibular pseudotumour presented in 1977 in a 13-year-old with moderate hemophilia. The patient had a dental extraction with positive results, but returned six months later with a large pseudotumour on the right side of his jaw. The pseudo-tumour was removed but complications kept him in hospital for 188 days.

The introduction of the fibrin sponge, fibrin sealant, and antifibrinolytic agents heralded a new era in dental treatment for people with bleeding disorders, allowing outpatient oral surgery. A case of hemophilic pseudotumour in 2005 was treated efficaciously and the patient discharged in only eight days, Cavalcanti reported.

Andrew Brewer (Scotland) described a case in 1997, involving a 66-year-old man with moderate FIX deficiency, who required a lower dental clearance. Factor coverage was provided before the procedure and teeth were extracted under local anesthesia. There was considerable bleeding but fibrin sealant was applied to the socket before sutures were put in. Hemostasis was achieved and the patient admitted overnight. However, eight days later the patient returned complaining of chest pain. Brewer reported that prolonged bleeding in the elderly patient resulted in reduced hemoglobin, which, in turn, reduced the blood's ability to carry oxygen, and was responsible for the onset of angina-like chest pain. Treatment with blood transfusion and repeated FIX infusions was needed to achieve hemostasis. 🌐

Improving assessment of QoL

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to prove that it is substantially improving quality of life for patients,” he said.

HRQoL instruments help evaluate the benefits of new and existing treatments from the perspective of the patient's values and expectations. Gringeri emphasized the importance of reliable, standardized and validated instruments in order to monitor the progress or deterioration of patient well-being. HRQoL should be considered an essential part of medical management. It provides the “qualitative dimension of functioning” and encompasses the individual experience of illness both physically and psychologically to disease-related and treatment-related symptoms.

It is also essential to design HRQoL instruments for different age groups, since concepts of well-being differ among small children, adolescents, young adults, and elderly people, he explained. The European Haemophilia Quality of Life Questionnaire Index allows for the comparison of different age groups. 🌐



Yildirim Çelik

Wellington Cavalcanti takes questions from delegates in the Dental Meet the Experts Panel

Living with hemophilia: a challenge families face together

Living with hemophilia can be a lonely journey, accompanied by feelings of isolation, anger, denial and frustration. It's a burden that affects not only the individual with the bleeding disorder but their whole family as well. Panelists in yesterday's session, *Sharing a Hard Life: How Hemophilia Affects the Family* recounted some of the challenges they bear in dealing with the disorder, as well as strategies for managing them.

Robert Lamberth (Australia), who lives with the "troika of complaints" – hemophilia, HIV and hepatitis C – noted that the plight of the rest of the family is often overlooked. Parents worry about bleeding episodes, mobility issues, and ramifications on the affected child's schooling and career. Siblings sometimes feel they are missing out on their parents' attention or resent that the needs of the child with hemophilia always seem to come first.

He emphasized the importance of psychosocial support for the whole family, especially during childhood and adolescence. "Dedicated bleeding disorders social workers and counsellors should be part of every centre, and we should be striving to achieve this in every healthcare delivery system."

Mohammed Aris Hashim (Malaysia) has two adult sons with severe hemophilia. He described the economic and social burdens experienced by families in developing countries. "Bleeding incidents are traumatic since it calls for the head of the family to make a very tough decision. It's a choice of either putting food on the table, buying bus tickets to the hospital, buying factor concentrates if the family can afford it, or buying cryoprecipitate, fresh frozen plasma, or blood." A month's income often equals one single infusion, he noted.

Haydee Benoit de Garcíá (Dominican Republic) gave a poignant account of her efforts to help her son overcome the adversities of hemophilia. "The first years were a struggle because every time he had a bleed we suffered...When it was time for him to begin school, my husband wanted homeschooling, but I insisted he go to school and play with children his age. I did not want to put my son in a bubble. Adolescence came with constant conflict over which activities he could engage in. Sometimes he hid his bleeds until he could not sustain the pain."

Social worker Elizabeth Fung (US) shared coping strategies for patients, parents, and treatment centres and emphasized the importance of resilience in the face of adversity: "What is right with you is more powerful than anything that is wrong with you." 🌍

Can we count you in?

Show your support of the WFH and its work in three easy steps:

1. Stop by the WFH Resource Centre in the Exhibit Hall to make a donation in support of Treatment for All.
2. Add your name and wish to our Treatment for All donor wall.
3. Pick up a sticker and wear it to show your support.

All donations will be used to support WFH programs and activities to improve care for people with bleeding disorders worldwide.



Delegates take advantage of an opportunity to view one of more than 300 posters currently on Display in the Exhibit Hall; new posters will be displayed today and tomorrow

Yildirim Çelik


Steady progress in gene therapy and bioengineering

Since the advent of recombinant technology and the increased understanding of the molecular background of hemophilia in the 1980s, there has been great hope that advances in molecular biology would lead to improvements in the pathogenesis, diagnosis, and treatment of hemophilia. While impacts on pathogenesis and diagnosis have been profound, advances in actual treatment have been somewhat slower to materialize. However, recent trends in gene therapy, novel proteins, and cell-based interventions hold real promise, according to presenters at the *Progress in the Molecular Biology of Inherited Bleeding Disorders* session.

The production of bioengineered facsimiles of plasma-derived clotting factors promises a range of treatment products that are safe from contamination, inexpensive, and potentially limitless in supply. This could allow for expanded prophylaxis and more product availability, Steven Pipe (UK) said. Recombinant DNA technology has produced good clinical results using bioengineered FVIII, FIX, and FVIIa. Although therapeutic costs remain high, there are several strategies in development that will increase the efficiency of bioproduction, potency, stability, immunogenicity, and clotting factor half-life.

Kathy High (US) stressed that gene therapy could prove extremely useful in the treatment of hemophilia because it could deliver a consistent level of coagulation factors that can be maintained over a long period of time, effectively preventing bleeds.

There are two possible approaches, she said. The first inserts the transgene directly into a stem cell via an integrating vector, such as adeno-associated virus (AAV), and the integration occurs across the whole genome. This can be dangerous because of the possibility of poorly targeted insertion, resulting in mutagenesis. The second uses an AAV-mediated gene that is transferred directly into skeletal muscle or hepatocytes.

Injecting AAV-mediated FIX into muscle tissue has resulted in high expression of FIX but low circulating levels in both animal and human trials, High said. Current studies on hemophilic dogs have shown long-term high level expression (over 10%) and improved circulation using intravascular delivery. Trials injecting into the liver led to the discovery of a human-specific immune response to AAV-transduced hepatocytes. An upcoming clinical trial has been amended to include a short course of immunosuppressant drugs to suppress this response. 

Sessions to watch for

C1.2 Donna DiMichele will be delivering the Arosenius Lecture, *Aspects of Surgical Procedures in Early Infancy*, at 11:00 in Marmora.

C1.4 Delegates will have the chance to hear presentations on an impressive array of topics in the Medical Free Paper Session. The session starts at 11:00 in Dolmabahce A.

Presenters are Raul Perez Bianco, Andreas Tiede, Peter Turecek, Peter MacLean, Andrea Gerhardt, Giancarlo Castaman, Kirstine Ovilsen, Peter Johansen, and Elena Santigostina.


C2.2 Although we now have a better understanding of von Willebrand disease, there is still disagreement about optimum diagnosis and treatment approaches. The issues relevant to Type 1, 2N, and 3 will be reviewed in the Anadolu Auditorium today at 3:00.

Presenters are Paula Bolton-Maggs, David Lillicrap, Jenny Goudemand, and Erik Berntrop.

C2.6 New developments and advances in laboratory tools are aiding diagnosis and treatment of bleeding disorders. Hear a comprehensive review of approaches for the measurement of coagulation at 3:00 in Halic.

Presenters are Jorgen Ingerslev, Benny Sorensen, Giancarlo Castaman, John Lloyd, and David Varon.

Publishing Workshop Don't miss a great opportunity to learn more about the editorial and publishing process with the editors of *Haemophilia*, the official journal of the WFH, and other communications experts.

The workshop takes place from 5:30 to 7:00 in Dolmabahce A. 

Program Updates

Reminder

There is still time to get tickets for tomorrow's Farewell Dinner, which promises to be a splendid evening of dining and entertainment. Tickets are available for USD 75.00 at the registration desk while supplies last.

There will be an MSK Committee meeting in Dolmabahce A from 12:45 to 2:15.