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Haemophilia Society of Singapore 25 Years On



The Haemophilia Society of Singapore celebrated its 25th Anniversary in December 2010 with a dinner for 60 members and their families.

The society was founded on the basis of helping people with haemophilia cope with their hereditary deficiency of clotting factors, in their medical treatment and social support.

The Executive Committee is wholly voluntary, consisting of people with haemophilia, parents and friends. With no operating base viz. an office space, and a part-time accounts assistant as the only staff, there are minimal overhead costs. The bulk of the financial expenditure goes toward the subsidy of treatment at the treatment centres in SGH, NUH and KKCH.



Dr Tan Hooi Hwa

Haemophilia Society of Singapore 25 Years On - Cont'n from Pg 1



What have we got to show for it?

Definitely, our members are more confident in home therapy, introduced with the setting up of treatment centres at NUH, SGH and KKCH. The factor concentrates are now readily available.

There is better access to the caregivers, and thankfully, there are heads in the relevant departments who show empathy to our members.

With our membership in the World Federation of Haemophilia, since 1987 HSS has access to information and updates on haemophilia care. Participating in the World Congress of WFH also gives us contact with the experts in haemophilia management. The HSS also had assistance in the initial phase, from the WFH in impressing on the Ministry of Health of the importance of adequate clotting factor replacement.

Some of our members have gone on to be successful professionals, but still a very small number. With our token awards for good scholaristic results, HSS hopes to encourage more to scale the academic heights.

Also, it is encouraging to see more networking support among the members.

Our wishes for the Years Ahead

That the HSS is where we are today is due to the dedication and altruism of those who serve in the

committee. There is a need for renewal, from within the society.

If those with haemophilia do not step up to continue the work of the society, then outside forces, especially from the authorities, will see this inertia as a reason to question the existence of the society.

Already administrative rules are in place as a totalitarian approach to all societies, given an Institution of Public Character (IPC) status. No doubt its purpose is to increase transparency and accountability, but it also discourages voluntarism.

Always, there will be the problem of fund raising, especially for a society the size of HSS. On the one hand, if we have too much in reserves over our annual needs, institutional donors will not give. On the other hand, if we do not make an effort to get more funds, then MOH feels we are not making full use of the IPC status (The society is also expected to use our funds for public education of a condition that is present at birth and not one that is preventable e.g. heart or kidney disease). It would be the greatest wish that the government could raise the subsidy for factor replacement therapy, and fund local research into treating haemophilia. The latter would be a great feather in the cap for the country, if a cure is found.



Haemophilia Lunch Gathering Day

17 November 2010



Hi my name is Ng Kheng Chew, 11 years old. I am haemophilia A, severe. My mum organised a Haemophilia Lunch Gathering Day event at my place on 17 November, Hari Raya Haji. There were a total of 7 families altogether and the haemophilia kids are Kenji, Kai Jun, Kai Ern, Benjamin, Dominic, Kaustubh's brother and myself. There were a total of 21 guests in my house.

As I just had an injury on my left foot, my mum took



this opportunity to let Auntie Kah Bee do an infusion on my left hand and Kenji diluted the Factor 8. Auntie Kah Bee demonstrated the procedure in detail to the haemophilia mums who were not familiar with intravenous injection. Many parents even said that I have good veins. Indeed, I have!

My mum prepared different types of food for the lunch. They were very delicious! All the families enjoyed the food very much and all the kids were engaged with different games, like iPad, monopoly, lego, beyblade, IQ puzzle etc. We took a group picture as well. It was so much fun and I hope we can have such an event again in the future.



Although I am a haemophiliac and have been exempted from school PE, I feel that it is alright as I still do many activities that my parents allow me, like cycling, riding wave-board etc. In fact, I can ride wave-board very well and I notice that it improves my balancing and strengthen the muscles of my ankle and knee.

Mum told me that although I am haemophiliac, I am not alone and life has to go on. We should try our best to live a normal life and I wish haemophilia can be cured in future.



Haemophilia Arthropathy - Role of Radionuclide Synovectomy

Haemophilia workshop 28th December 2010

Talk given by Dr Koh Pei Lin

Consultant, Division of Paediatric Haematology Oncology.

University Children's medical Institution

National University of Singapore

Joint bleeds and subsequent joint damage (haemophilia arthropathy) cause major problems in people with Haemophilia.

The talk covered the following:

- A. Frequency and sites of joint bleeds.
- B. How joint bleeds cause joint damage.
- C. Treatment options for haemophilia arthropathy (damaged joint).

A. Bleeding sites in order of frequency:

1. Haemarthrosis (joint bleeds) 70% - 80%
2. Muscle/soft tissue 10%-20%
3. Other major bleeds 5%-10%
4. Central nervous system (CNS) bleeds <5%

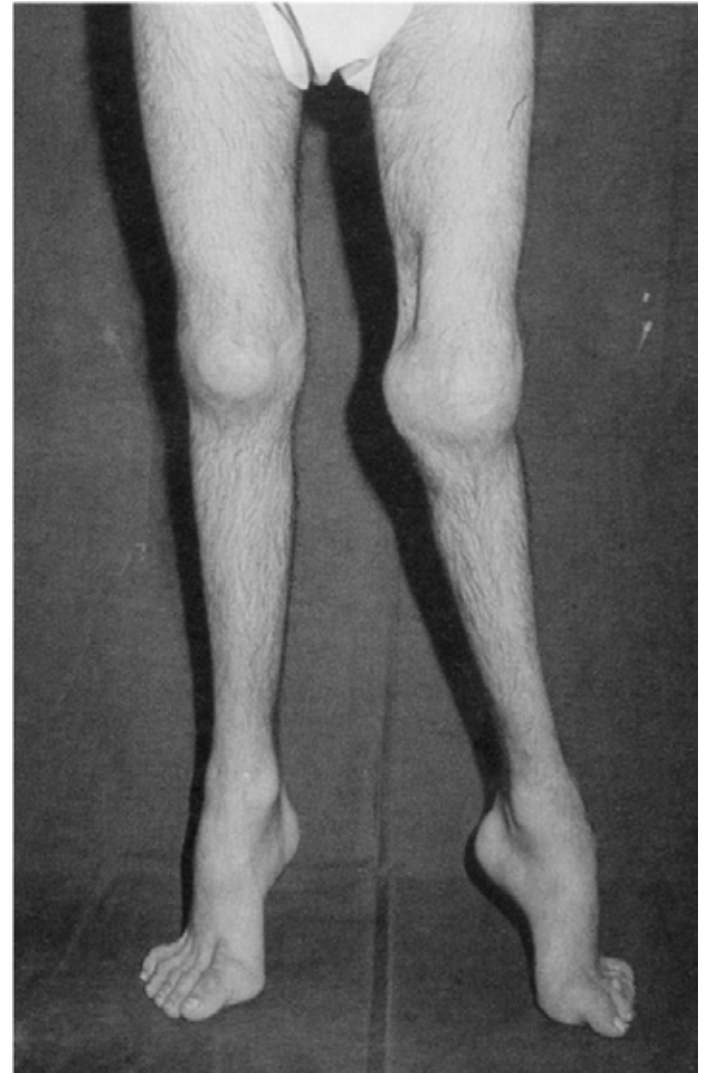
For joint bleeds, the frequency is as follows:

1. Knee 45%
2. Elbow 30%
3. Ankle 15%
4. Shoulder 3%
5. Wrist 3%
6. Hip 2%
7. Other 2%

Symptoms vary with severity of bleed viz. minor bleed (bubbling feeling and tingling), medium bleed (swelling and pain). The condition will heal. In the major bleed, the joint is boggy, swollen with muscle wasting, morning stiffness, chronic pain and movements limited.

B. Joint bleeds cause damage because:

1. Iron in blood leads to inflammation.



2. Synovium removes the blood breakdown products (Synovium - lining of the joint space).
3. With recurrent bleeds, the synovium becomes thickened and rich in blood vessels.
4. Thickened synovium bleeds more easily, leading to restriction of movement.

The leads to a chronic self perpetuating cycle of haemarthrosis, synovitis, and haemarthrosis causing deformity of the joint, contractures, pseudo tumour formation (soft tissue and bone) and fracture.

C. Management of haemophilia arthropathy involves:

1. Secondary prophylaxis. It is important to treat any joint bleeds early to prevent further damage by blood. If recurrent bleed occurs in a joint (target joint: more than 3 bleeds in a single joint within 6 consecutive months), secondary prophylaxis should be carried out to prevent bleeding, with infusion of clotting factors, on alternate days or 3 times a week.
2. Physiotherapy which helps to strengthen the muscles around the joints, improves proprioception, and range of movement by relieving joint stiffness.
3. Synovectomy i.e. removal of the synovium which is thickened and bleed easily. This can reduce the number of joint bleeds and further damage, but cannot reverse existing joint damage. This can be done by surgical or non-surgical means. In surgical synovectomy, it involves either open or arthroscopic techniques. It is more invasive, needs hospitalization, higher risk of bleeding, and more factor concentrates for the surgery to prevent bleeding. Chemical synovectomy e.g. with Rifampicin is cheap, requires multiple weekly injections, is

painful, and is not available in Singapore.

Radionuclide synovectomy, available in Singapore involves injection of a radioisotope into the affected joint e.g Yttrium, phosphate, rhenium, gold. It is an outpatient procedure, has low risk of bleeding and needs less factor concentrate to cover the procedure. The joint needs to be immobilized in a splint for 2-3 days, followed by physiotherapy. Up to 70% - 80% of patient do not bleed anymore in the affected joint. It improves the range of movement of the joint and is more effective in less severely damaged joints. However, it does not reverse existing bone or cartilage damage. The procedure is very safe, as thousands of cases have been done in both haemophilia and non-haemophilia conditions. There is no reported joint growth plate disturbance i.e it does not affect the bone growth in children, small risk of bleeding and joint infection.

There is a theoretical risk of cancer. In 2 cases, leukaemia was reported after procedure in haemophilia patients but it was unlikely to be the cause of the cancer. No other cancer was reported in thousands of patients.

4. Arthrodesis; fusion of the affected joint.
5. Joint replacement surgery.

Feedback

I would like to thank Dr Koh and the Haemophilia Society for organising the Haemophilia Workshop on 18 Dec 2010. The presentation given by Dr Koh very simple and informative yet provided a very in depth impression for my son, Yu Fei to see the consequences that he might face if he does not take good care of himself. He has been discussing and asking me lots of questions after the workshop on how to take care of himself when playing or running with his friends in childcare centre.

I like the presentation slides as it contains a lot of useful information which I can share with Yu Fei on and off as he grows up so that he will know very well of his condition. I would very much appreciate if the powerpoint slides can be emailed to all participants or all parents of the Haemophilia Society so that all

of us can benefit from it.

For the home therapy workshop, it is a good experience for Yu Fei and me also to learn how to inject the factor. With the demonstration by some of the boys who self infusion themselves, it gives the younger ones a preparation that they too need to self infusion themselves one day and they should be brave enough to do it.

Lastly, I got to make friends with some mummies at the workshop where we shared our feelings, experiences and we get to learn from one another. I even exchanged contact numbers with one of them so that we can keep in contact whenever possible. I would like to conclude that this is a very good and fruitful workshop.

Message from Gek Cheng

Experts Share Medical Breakthroughs, Challenges at Hemophilia 2010

Alison Street, MD

WFH VICE-PRESIDENT MEDICAL CONGRESS
MEDICAL SCIENTIFIC COMMITTEE CO-CHAIR

Renowned leaders in bleeding disorders research and care converged in Buenos Aires to discuss state of the art themes. Here are some highlights from this year's outstanding contributions.

AGEING POPULATIONS

The bleeding disorders community is now facing similar challenges to the general population, as improved treatments and longer life spans bring problems of ageing to the forefront of hemophilia care. Dr. Gerry Dolan (U.K.) spoke of new health issues people with hemophilia face as they age. Heart disease, cancer, kidney failure, and osteoporosis are all increasing, with 77% of seniors over 65 having two or more chronic conditions. There is very little experience managing multiple medical conditions in older people with hemophilia. Previous data on cardiovascular disease in people with hemophilia has been mixed, but it now seems that hemophilia is not protective against atherosclerosis. An ageing population with bleeding disorders will use substantially more clotting factor concentrates, as well as experience a gradual increase in inhibitors. More data need to be collected on the magnitude and optimum treatment of age-related disorders to assist advocacy for adequate services.

PROPHYLAXIS

Dr. Victor Blanchette (Canada) reviewed data on the well-documented benefits of primary prophylaxis, and the more limited data on secondary prophylaxis, particularly in adolescents and adults. The optimal regimen for initiating and escalating primary prophylaxis is still undetermined, and the role it plays in individuals with severe von Willebrand disease as well as other rare bleeding disorders must be investigated.

Cost-benefit analysis for treatments is a critical issue. Dr. Alok Srivastava (India) proposed the introduction of prophylaxis programs in developing countries even as soon as 1 to 2 international units of clotting factor concentrates per capita is available. He advised that all programs should include careful measurements of musculoskeletal outcomes.

JOINT IMAGING

Dr. Andrea Doria (Canada) spoke of magnetic resonance (MRI) and ultrasound imaging techniques which detect earlier changes in hemophilic joints than X-rays. Already, MRI delivers critical information on sub-clinical bleeds not available through conventional radiography or clinical examination. Standardized protocols for data acquisition and interpretation of images are required.

LIVE MUSCULOSKELETAL SURGERY

During a pre-congress session, two surgical procedures performed by Dr. Horacio

Caviglia (Argentina) were broadcast live from Hospital General de Agudos Juan A. Fernández. The first was a revision of a hip fracture in a 64-year-old man with severe hemophilia A. The second patient, a 16-year-old with severe hemophilia B and synovitis of his knee, had the genicular arteries embolized under imaging control. This required comparatively small amounts of factor replacement and is an exciting alternative to arthroscopic synovectomy.

WOMEN AND BLEEDING DISORDERS

Although rarely affected by hemophilia, women are equally likely as men to have other bleeding disorders. Dr. Andra James (U.S.A.) stressed the importance of combining the expertise of hematologists and obstetricians/gynecologists to ensure optimal management. She reviewed existing guidelines and standard practices in managing menorrhagia and other gynecological bleedings, pregnancy, and childbirth. These important issues, as well as prenatal diagnosis and the management of psychological impact and quality of life, were further explored in a pre-Congress session chaired by Dr. Rezan Kadir (U.K.) and Flora Peyvandi (Italy).

NEW TREATMENTS

People with hemophilia may soon require infusions only once a week or less, due to a cluster of novel therapies with the possibility of "impressive extension in half-lives,"

People with hemophilia may soon require infusions only once a week or less, due to a cluster of novel therapies with the possibility of “impressive extension in half-lives,”

Dr. Claude Negrier

Dr. Claude Negrier (France) reported. This should also bring improved quality of life and reduced treatment costs. Several strategies have been used to extend the half-life of treatment products, including site-specific pegylation of the factor VIII and IX molecules. The safety and efficacy of all novel products will need to be carefully assessed through well-designed international clinical trials. Determining immunogenicity is the major question that will arise. Dr. David Lillicrap (Canada) described animal models that could lead to better pre-clinical methods to predict inhibitor formation.

GENE THERAPY

Much-anticipated breakthroughs in gene transfer therapy are still taking shape, including a number of new, non-traditional approaches. Dr. Paul Monahan (U.S.A.) presented animal research supporting the potential of treating with clotting factor concentrates directly into target joints, while a new understanding of co-localized von Willebrand factor and factor VIII suggests feasibility in using platelet-directed expression of factor VIII as a gene therapy treatment for hemophilia A, according to Dr. Robert Montgomery (U.S.A.). Dr. Margaret Ozelo (Brazil) described *ex vivo* delivery of therapeutic transgenes using modified blood outgrowth endothelial cells.

INHIBITORS

Dr. Donna DiMichele (U.S.A.) presented preliminary final results from the recently terminated International Prospective Randomized Immune Tolerance Study, which showed some clinically significant differences between high- and low-dose regimens. Patients on low-dose took twice the time to record both a negative inhibitor titer and then to achieve tolerance. Dr. Charles Hay (U.K.), presenting safety data

from the same study, showed no difference in catheter infections, but significant increase in bleeding in the low-dose group, particularly before achieving a negative titer.

In her Arosenius lecture, Dr. Kathy High (U.S.A.) explained how gene therapy can both reduce the risk of inhibitor formation and treat its occurrence via induction of clotting factor-specific regulatory T-cells that lead to tolerance of the factor IX protein. Her colleague Dr. Valder Arruda (U.S.A.) described a gene therapy vector to effect continuous delivery of factor VIII protein, thus effectively preventing inhibitor formation.

Finally, Dr. Alessandro Gringeri (Italy) outlined the progress of the SIPPET (Survey of Inhibitors in Plasma- Product Exposed Toddlers) study, comparing the incidence of inhibitors in patients treated with plasma-derived and recombinant products.

PRODUCT SAFETY

Dr. James Ironside (U.K.) reported on a probable case of asymptomatic transmission of variant Creutzfeldt-Jakob disease (vCJD) in a 70-year-old with hemophilia. This patient received significant amounts of factor concentrates, the most likely source of prion transmission. If levels of infection were high in these products, he said we would expect to have seen many more hemophilia patients with symptomatic vCJD.

Parvovirus B-19 continues to frustrate manufacturers' efforts to eliminate it from both recombinant and plasma-derived products. Dr. Jeanne Ann Jordan (U.S.A.) explained that it is highly resistant to current inactivation methods, with products from pooled donations appearing to have the highest rates of infection. Nanoexchange and chromatographic techniques are in development to further reduce risk.

LABORATORY DIAGNOSIS AND MONITORING

At a pre-congress workshop, Dr. Andreas Hillarp (Sweden) discussed the selection, use, and limitations of prothrombin time and activated partial thromboplastin time assays for detection of bleeding disorders. Dr. Ampaiwan Chuansumrit (Thailand) demonstrated her centre's bedside kit for diagnosing hemophilia A and B, and Dr. Angus

McCraw (U.K.) described the detection of inhibitors in acquired hemophilia patients.

In another session, Dr. Steve Kitchen (U.K.) discussed performing both one- and two-stage assays in all diagnoses of mild hemophilia A, since the condition is not excluded by finding a normal factor VIII:C level by one-stage assay. Dr. Claude Negrier and Dr. Yesim Dargaud (France) discussed methods of classifying the severity of bleeding disorders. Factor levels from clotting-based or chromogenic assays have variable correlation with clinical phenotype. Global coagulation assays like the thrombin generation test can show better correlation with bleeding tendency, but are not used to classify severity or screen for bleeding risk.

Dr. Cathy Hayward (Canada) highlighted the need for standardized lab testing to diagnose platelet function disorders. Without standardization, platelet disorders are both under- and over-diagnosed, leading to inconsistent treatment.

INFECTIOUS COMPLICATIONS

HIV and hepatitis C (HCV) infections continue to be of great concern to people living with bleeding disorders. Dr. Margaret Ragni (U.S.A.) noted that HCV infection remains the leading cause of end-stage liver disease. In those with HIV co-infection, treatment with highly active anti-retroviral treatment also improves HCV symptoms. Dr. Kenneth Sherman (U.S.A.) detailed promising new drugs in the development for treatment of HCV and noted that pegylated interferon would continue as part of treatment in the foreseeable future, as single-drug therapy is less successful due to the high mutagenicity of HCV.

I would like to extend my sincere thanks to all the speakers and presenters who contributed to the success of this congress. Please give us your feedback as to program development for the WFH 2012 World Congress in Paris. ■

Additional coverage of the Hemophilia 2010 World Congress, including the State of the Art papers and the Book of Abstracts, can be found on the WFH website at www.wfh.org.

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2011/2012**

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International Event

Haemophilia Conference 2011

Haemophilia Foundation Australia

20 to 22 October

Novotel Sydney Olympic Park

Sydney

www.haemophilia.org.au

Forth Coming Events

- Dental Care Workshop at NUH**
on 19th March 2011,
2nd Saturday of March School Holidays.
Time - 9.00am to 11.00am.
Will include home therapy teaching.
- The Executive Committee wishes all our members
a Happy and Healthy Lunar New Year of the Rabbit.**

If you would like to give your support towards the welfare of people with haemophilia in whatever way, please drop us a line or send your donations to:

The Haemophilia Society of Singapore
Farrer Road P.O. Box 0273 Singapore 912810

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