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ABSTRACT SYMPOSIUM ON THE DIAGNOSIS OF VENOUS THROMBOSIS AND PULMONARY EMBOLISM

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AMY SHAPRIO’S VIEW ON HAEMOPHILIA CARE IN THE 21ST CENTURY

Amy Shapiro is a paediatric haematologist who received her medical degree at New York University School of Medicine, New York, USA. She completed her paediatric internship, residency and fellowship in paediatric haematology/oncology at the University of Colorado, Health Sciences Center. She became Associate Professor of Paediatrics at the Indiana University School of Medicine before her current position as the medical director of the Indiana Hemophilia and Thrombosis Center (IHTC) and adjunct professor of paediatrics at Michigan State University. The IHTC was founded in 1999 and is now one of the largest federally funded haemophilia treatment centres in the United States. IHTC operates clinics state-wide, and continues to be involved in numerous clinical trials, while offering patients cutting-edge therapies and access to research protocols.

Shapiro’s lecture will focus on haemophilia care in the 21st century. Haemophilia is caused by an absence or decreased amount of one of the clotting factors. Haemophilia care has undergone substantial improvements during the past 40–50 years. Clotting factor concentrates were not sufficiently refined to enable self-administered treatment at home until the 1970s. Unfortunately, these advances led to transmission of viral diseases including HIV and hepatitis, resulting in an increased burden of morbidity and mortality, especially during the 1980s. Throughout the past two decades, product development, including the advent of recombinant concentrates, has greatly improved the safety and availability of therapy and the focus of care is shifting towards prevention and management of disease sequelae. Long-term substitution therapy (prophylaxis) of the missing clotting factor is the recommended treatment in severe haemophilia, but several questions remain to be elucidated such as when to start and how to optimise these regimens, and when or whether to stop this expensive treatment. The major side-effect of treatment, development of inhibitors to the infused concentrate, is the main threat to the health of patients and consequently the subject of intense research. Development of new products with improved pharmacokinetics is the next step to improved therapy. This and other developments in the care for haemophilia patients will be discussed.


The ISTH has recently endorsed the second edition of the World Federation of Hemophilia’s Guidelines for the Management of Hemophilia. In its careful review, the ISTH noted the involvement of many experts from around the world, not only within the writing group but also in the elaborate review process. The society stated that these practical guidelines for the management of hemophilia clearly incorporate a wide range of views, and that the recommendations are consistent with current best practice.

Hemophilia is a rare disorder that can be complex to diagnose and to manage. These guidelines, compiled and reviewed by global experts and based on the best available evidence, contain clinical practice recommendations on the diagnosis and general management of hemophilia, including factor replacement therapy, musculoskeletal complications, inhibitors, and transfusion-transmitted infections. By compiling these guidelines, the World Federation of Hemophilia (WFH) aims to assist healthcare providers seeking to initiate, maintain or enhance hemophilia care programs, encourage practice harmonization around the world and, where recommendations lack adequate evidence, stimulate appropriate studies.

The second edition of the Guidelines for the Management of Hemophilia is available in the journal Haemophilia and on the WFH’s website at www.wfh.org.
TISSUE FACTOR AND BRAIN CANCER

In today’s lecture Dr Janusz Rak will focus on his favourite coagulation factor, tissue factor (TF), and its role in brain cancer, with glioblastoma multiforme (GBM) in particular. Dr Rak will discuss the question, as to whether tissue factor expression and coagulation activation are merely an unspecific epiphenomena associated with brain malignancies, or if they constitute parts of intrinsic and diverse genetic programmes driving the disease. His talk will include unpublished work on the links between profiles of coagulation factor expression (coagulome) and the emerging molecular subtypes of brain tumours, as well as some of his explorations of the non-coagulant effects of tissue factor in animal models of glioma. Finally, he will present new data on procoagulant and oncogenic extracellular vesicles (oncosomes) that may pily engage in professional discussions on these subjects, however, he will be equally pleased to talk about his ideas on unmet medical needs, scientific challenges, and most importantly, ways to stimulate talented young people to engage in scientific careers.

“Great questions, for which answers will probably be highly context-specific. We find that upregulation of TF is associated primarily with the classical subtype of GBM, which also expresses high levels of EGFR (a receptor with known oncogenic activity). This may not be the case for proneural GBM, in which TF may play a different (or no) role. I think that in the context of classical GBM TF likely contributes to the pathogenesis of tumours at several different levels, including as a signalling molecule, biological regulator, and as potential trigger of pro-coagulant events. The latter could act as a source of morbidity and a part of the vicious circle of clotting, invasion and growth. I think that many cell types express TF, but our experimental work points to tumor cells themselves, as the major source of this activity. Whether this is corroborated by independent studies remains to be seen.”

This will be the first time Dr Rak is visiting Amsterdam. At ISTH, he will be primarily found at talks about cancer, procoagulant microparticles, and new anticoagulants. He will happily engage in professional discussions on these subjects, however, he

for Kazuyoshi, progress starts with access to good haemophilia care

With limited access to doctors and information, Kazuyoshi’s parents formed a local patient association. Today, Kazuyoshi continues their work all over Japan.

At Novo Nordisk, we partner with patient associations, policy-makers and physicians to lead a coordinated response to inadequate haemophilia care. By involving more stakeholders, we facilitate concrete joint actions, including improved access to treatment, support and education resources for people with haemophilia and their families. We also work as a partner to improve access to care in the developing world, driving sustainable solutions that are changing possibilities for people with haemophilia wherever they live.

Find out how Novo Nordisk is changing possibilities in haemophilia at changingpossibilities.com
Tips & Funny facts about the Dutch

What's the Deal with Drop?
Dutchies truly love their liquorice or drop as it is known in the Netherlands. You can find it in nearly every shop from supermarket to candy shop. There is a flavour or type of drop for every taste from sweet to salty, hard to soft. Drop comes in many shapes and sizes from small green peas to large Muntdrop chewy coins.

The Netherlands boasts the highest per capita consumption of liquorice in the world, with each person eating more than 4 pounds (2000 grams) per year!

Although the Dutch (as well as Scandinavians and Germans) love black liquorice, many people do not enjoy the taste, especially the salty varieties.

Gezellig!
If Dutch is not your native tongue, you'll soon realize that gezellig is not only difficult to translate, it's also a challenge to pronounce. Give it a shot: “he-sell-ick”, starting and ending with the typically Dutch ‘g’ sound.

According to Wikipedia, this word is considered to be an example of untranslatability: “An example of untranslatability is seen in the Dutch language through the word gezelligheid, which does not have an English equivalent.” It derives from gezel, meaning companion or friend.

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EVOLUTION OF MUSIC: SURVIVAL OF THE FUNKIEST

Armand Leroi is a Professor of Evolutionary Developmental Biology at Imperial College London – as well as TV presenter and author. Most of his research is about metabolism in worms, but recently he had begun to study something quite different – music.

Music is a cultural artefact and important in our daily lives: we make music to express our deepest emotions. But where does music come from? How does it change? Leroi argues that it can be studied using evolutionary theory. With transmission from one individual to another music tunes sometimes change (“mutate”), mix (“recombine”) or are favoured over others (“selection”) and so the musical population evolves.

Leroi has studied the evolution of music in cultures throughout the world, but also in the lab. Together with computer scientists, he developed a system called “DarwinTunes”. In DarwinTunes a population of musical loops is generated which is subjected to selection by an audience which rates its musical quality. This forms the selective pressure: loops with a high rating mated with other highly rated loops and produced a new generation of loops. There’s no composer in the system: just the power of Darwin’s natural selection mechanism.

Delving into the DarwinTunes populations, Leroi and his collaborators discovered that the music does not evolve forever. After 500 generations it stopped improving. Why? The answer to this question touches on some of the deepest problems of evolutionary theory. It may even have lessons for how we think about the frequency of disease-causing genes in the human population. Haemostatic genetic polymorphisms meet survival of the funkiest? Perhaps! This inspiring Presidential Symposium lecture will show how the forces that shape our bodies and our cultures are really not that different at all.
EVOLUTION OF ALTRUISM: LESSONS FROM CHIMPS FOR HUMANS

“The possibility that empathy resides in parts of the brain so ancient that we share them with rats should give pause to anyone comparing politicians with those poor, underestimated creatures,” writes Frans de Waal in his article “Do you humans alone ‘feel your pain?’” in the Chronicle in 2001. Frans de Waal is a pioneer in studies on social interaction and altruism in animals. He says: “I’ve argued that many of what philosophers call moral sentiments can be seen in other species. In chimpanzees and other animals, you see examples of sympathy, empathy, reciprocity, a willingness to follow social rules. Dogs are a good example of a species that have and obey social rules; that’s why we like them so much, even though they’re large carnivores.”

Frans de Waal (1948) is a Dutch primatologist and ethnologist. He is the Charles Howard Candler professor of Primate Behaviour in the Emory University psychology department in Atlanta, Georgia, and director of the Living Links Center at the Yerkes National Primate Research Center and author of numerous books including Chimpanzee Politics and Our Inner Ape. His research centres on primate social behaviour, including conflict resolution, cooperation, inequity aversion, and food-sharing. He is a Member of the United States National Academy of Sciences and the Royal Netherlands Academy of Sciences.

He matches his theories with experimental research. In one of his famous experiments, published in the Proceedings of the National Academy of Sciences, he tested seven female chimpanzees to see if observations of the species’ generous behaviour in the field matched their decisions in a lab. Given a choice of two coloured tokens, one that guaranteed a banana treat for two and the other that gave a reward for the chooser only, the chimps tended to pick the social option. During his lecture at the Presidential Symposium at the ISTH Frans de Waal will provide an overview on his current views of social interaction and behaviour as observed in animals and how they could provide a lesson for human beings.

TO SPIT OR NOT TO SPIT: MEASUREMENT OF ANTICOAGULATION STATUS IN SALIVA

Human saliva is often described as being 99.5% water. But the other 0.5% could contain potential biomarkers for a diversity of diseases. Besides water, saliva contains many important substances like glycoproteins, various enzymes and even up to 8 million human cells and 500 million bacterial cells per ml. The complexity of the contents of saliva offers us the opportunity to monitor general wellness, and assess oral health and disease. In his lecture “Measurement of anticoagulant status in saliva”, Dr Waander van Heerde will address a newly developed method for the measurement of biomarkers in saliva. The determined biomarkers in the saliva reflect the INR status in patients treated with vitamin K antagonists (VKAs). This method, for which Van Heerde and colleagues filed a patent application, is based on a validated method of saliva sampling, determining the level of biomarkers in the saliva sample and correlating the amount of these biomarkers to the blood coagulation status. Dr Waander van Heerde performed his PhD research at the Department of Biochemistry at the University of Utrecht. Since 2000 he is a staff member at the Laboratory for Haematology of the RUNMC.

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ABSTRACT SYMPOSIUM ON THE DIAGNOSIS OF VENOUS THROMBOSIS AND PULMONARY EMBOLISM

Acute deep vein thrombosis (DVT) and pulmonary embolism (PE) represent two manifestations of a similar clinical pathological process, together often referred to as venous thromboembolism (VTE). Established concepts and the latest evidence on the diagnosis of VTE will be the focus of the lecture by Dr Menno Huisman on Thursday the 4th of July. Dr Huisman is a well known investigator in the field of diagnostic management of VTE.

The pillars of the diagnostic management of patients with suspected VTE are clinical decision making, D-dimer assays and imaging tests. Numerous studies support a standardised strategy consisting of these three diagnostic modalities to optimise safety and cost-effectiveness. The diagnosis of ipsilateral recurrent DVT by ultrasonography poses a problem, because persistent ultrasonography abnormalities after the initial thrombosis are present in a high percentage of patients. The feasibility of CT or MR techniques for this clinical challenge will be discussed by Dr Huisman.

The imaging test of choice for the diagnosis of PE nowadays is multi-row computed tomographic pulmonary angiography (CTPA). CTPA studies showed a high sensitivity and specificity and have demonstrated that it is safe to withhold anticoagulant treatment if CTPA has excluded acute PE. Besides these advantages, there are also disadvantages associated with widespread use of CTPA. With the development of the CTPA technique and the low threshold for using this technique at the Emergency Department smaller subsegmental emboli may become visualised. Further disadvantages of CTPA are the contraindications in patients with an allergy to iodinated contrast material and in patients with severely impaired renal function. Finally, the radiation dose of a single CTPA is considerable and is associated with an increased risk of cancer. This risk is especially of interest to the younger, female patient during reproductive age. The diagnostic approach for these specific cases will all be discussed in the lecture by Dr Huisman.

In the near future, most progress in this field can be expected in improved imaging possibilities with, for instance, MR applications for recurrent thrombosis. Safety and cost-effectiveness will be important pillars in this research. The State of the art lecture by Dr Huisman is interesting for every clinician confronted with patients with a clinical suspicion of VTE.

EVOLUTION OF CAUSAL INFERENCE: BUSTING PARADOXES

Many of us will remember their first ISTH congress. Most researchers will debut with a poster, few with a talk. Rarely, a debut ISTH performance involves a lecture at the Presidential Plenary Symposium, as is the case this year. Dr Miguel A. Hernán graduated from medical school in Madrid (1995) and is currently affiliated with the Harvard School of Public Health (MPH, 1996; MSc in Biostatistics and PhD in Epidemiology, 1999). Perhaps underappreciated for his most interesting cameo performance in the Youtube video “Baby Got Dag”, he has been involved in multiple scientific projects that have resulted in 100+ publications. His research is focused on methods that can detect causal inference, ultimately to guide policy and clinical decisions. In the area of cardiovascular diseases, he has studied pharmacological, nutritional, and lifestyle interventions to reduce incidence of cardiovascular disease.

Dr Hernán, what paradoxes will you be busting today?

"Many empirical results in the medical literature have been labelled as paradoxes. For example, we often hear about Simpson’s paradox, the obesity paradox, the birth weight paradox, the whatever paradox... During this talk I will argue that these apparent paradoxes may result from misguided interpretations of simple statistical analyses. Once we adopt a modern causal inference approach -many would say a common sense approach- the paradoxes vanish, and we find ourselves smiling at our own naiveté."

All those in need of busting their own whatever paradox, please make sure to attend the Presidential Plenary Symposium. You will leave with a smile.
Come to the Biogen Idec and Sobi booths to find out more about developments in haemophilia.

Booths: 204 & 255