Abstracts

Professional Development Session

PDS-01
The International Classification of Functioning as a framework for development of a core set of musculoskeletal measures in hemophilia

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The 'Evaluation of the non-bleeding joint', advised by the World Federation of Hemophilia during the early 1980s, originates from the period when focus was on pathology and impairments. Impairments like range of motion and pain reflect the function of organ systems, but not necessarily a person's perception and capacity to live a normal life. The development of the bio-psychosocial model required a new theoretical framework: the International Classification of Functioning (ICF). The ICF made it possible to describe the disability process independently of the underlying disease or disorder, which can be of utmost importance for allied health professionals, e.g. physical therapists. In hemophilia care and research we became familiar with the basic scheme of the ICF, consisting of body, individual and societal level. We became as well familiar with their contextual factors, i.e. personal and environmental factors, as essential parts of this scheme (especially in hemophilia). Besides classifying measurement tools, this system provides a better understanding of musculoskeletal problems in hemophilia. However, this does not automatically lead to an accepted 'core set' of measurement tools, for very different reasons: We deal with all ages: children, adolescents and adults; Access to clotting factor affects MSK outcome (world-wide diversity); Many subgroups do exist, based on comorbidities, like HIV, HCV Various professionals consider problems from different angles; Hemophilia Treatment Centres (HTCs) worldwide include different professionals; Focus was historically on medical issues and impairments (body level); Activities are underreported in both care and research and can be split up into Performance based and Self-reported; Measurements on participation are intermingled with Quality of Life. Recently researchers in hemophilia care agreed on the value of the ICF, and are trying to develop a 'core set' of instruments for outcome assessment. Regarding the differences in patients, in professionals and in HTCs this might not be the ultimate goal at this moment, but agreement on a 'minimal data set' might serve the two intended goals: optimal minimal outcome and research and can be split up into Performance based and Self-reported; Measurements on participation are intermingled with Quality of Life. Recently researchers in hemophilia care agreed on the value of the ICF, and are trying to develop a 'core set' of instruments for outcome assessment. Regarding the differences in patients, in professionals and in HTCs this might not be the ultimate goal at this moment, but agreement on a 'minimal data set' might serve the two intended goals: optimal minimal outcome and study; being able to compare studies.

Joint health based on physical examination

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Background: The World Federation of Hemophilia (WFH) evaluation system was designed in the early 1980s to evaluate joint arthropathy and has been cited in numerous studies. In the 1990s, modifications were made by hemophilia centres in Denver, U.S. and Stockholm, Sweden to address detection of earlier joint changes. The WFH scale had also not been tested for its psychometric properties. In 2002, the Hemophilia Joint Health Score (HJHS) was developed by the International Prophylaxis Study Group (IPSG) Physiotherapy Expert Working Group to detect early joint changes in children aged 4-18 years. It scores impairment (joint structure and function in the World Health Organization International Classification) of the six key index joints (elbows, knees, ankles). Version 1 displayed excellent reliability (ICC inter-rater 0.83; test-retest 0.89) and construct validity (moderate correlation with physician total joint score). Strengths and Gaps: The current version HJHS 2.1 has a comprehensive instruction manual and video, and it has been formally translated into 5 languages (French, German, Mandarin, Spanish, and Portuguese) and is accessible through the IPSG website (www.ipsg.ca). In a systematic review of outcome measures, Stephensen et al reported that the HJHS demonstrated acceptable construct validity, internal consistency and repeatability, but lacked the ability to discriminate changes in physical function. Reliability studies using HJHS v. 2.1 in China and Brazil yielded excellent results. Studies in England, Lithuania and Pakistan demonstrated high correlation with age and WFH score, ability to identify change in joint health and differentiate disease severity. Fischer and DeKleijn reported moderate to strong validity and strong inter-observer reliability (ICC 0.84) in a Dutch/Swedish cohort 14-30 years old.. Gaps noted include the need to define clinically important change (i.e. score/range), studies in older adults and normals. Concern about the length of time required to complete a full HJHS examination- limiting its usefulness in the clinical setting- has been raised. Addressing the gaps: Currently, a multi-centre study is being initiated in 200 adults with hemophilia and 120 normal adults through the age spectrum. Conclusion: The HJHS has been endorsed for use in children with hemophilia. Further studies will assist in addressing existing gaps in physical examination outcome measures.

Joint assessment based on imaging studies

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This presentation will provide an overview of the current status and next steps of imaging methods currently used in the assessment of hemophilic arthropathy, with special emphasis on ultrasound (US) and magnetic resonance imaging (MRI). MRI is considered the reference standard imaging method for
diagnosis of structural abnormalities in hemophilic joints. In order to compare joint findings in the same patient over time or in different patients cross-sectionally we should quantify joint damage. The International Prophylaxis Study Group (IPSG) MRI scale (0-17 points) and adjusted US (0-14 points) scale are semi-quantitative methods that use an additive approach to score abnormalities in the soft tissues (fluid, synovium and hemosiderin) and osteochondral tissues (erosions, subchondral cysts and cartilage loss). Because US is unable to visualize the central portion of joints some osteochondral items of the IPSG MRI scale cannot be scored with the US scale. The IPSG MRI scale was designed to assess early arthropathic changes by adding information not achievable with x-rays. Therefore, it is subjected to a "ceiling" effect in which once the joint receives a maximum score (=17) no further changes can be accounted even if there has been progression of arthropathy between two MRI scans. There are areas that require further MRI investigation in hemophilia which include association between presence of bone erosions and future development of arthropathy, and effect of different protocols (different echo-times) on overestimation of hemosiderin deposition on gradient-echo images. On the other hand, recent technology advances have enabled reduction of scanning time (parallel imaging), imaging of the entire body at once (whole body MRI), volumetric assessment of cartilage, functional assessment of cartilage (T2 mapping), quantification of minimal amounts of hemosiderin (ultra-short TE) which hold potential for revolutionizing the way we look at images of joints. Concerning US challenges with this technique remain which are associated with the compartmentalized view of the joint by US ("pieces of a puzzle") and operator dependence. Investigation of alternatives to overcome these limitations are needed such as the development of mechanical arms coupled to probes, three-dimensional US and fusion US-MRI, among others. Other topics that also require further investigation are assessing the effect of probe angulation on the patient’s skin, standardizing a single universal scale, developing scoring systems that incorporate both US and physical examination scores, refining point-of-care US protocols aiming at minimizing information loss, and assessing the value of US in longitudinal studies. Bearing in mind that the “major challenge for the hemophilia treater is to treat the patient without seeing what is being treated”, imaging can be an appealing diagnostic tool. Nevertheless, one should consider using different imaging techniques to answer different clinical questions.

**Measures of activity and participation in the hemophilia population**

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In any chronic disease, the functional outcomes (level of activity and participation) are the most valued by an individual and the family. The ICF (International classification of function) defines activity as “the execution of a task or action by an individual”, while participation as “the involvement of the individual in life situations”, within a sociocultural and physical environment. Fulfilling a social role (participation) will require the performance of multiple individual tasks in different combinations and different social roles can have an overlap of such activities. Measurement of participation can be complex due to its multidimensional constructs and there is no clear consensus on the best method to distinguish between activities and participation. Although the HAL and PedHAL have been developed as hemophilia-specific tools considering the involvement of the knee, ankle and shoulder as target joints; these are predominantly measures of activity rather than participation. FISH is an objective assessment of functional independence in PWH, but has a ceiling effect in those with minimal joint dysfunction. Self-report methods for assessment of physical activity include records or logs (e.g. Bouchard diary), which require the individual to record every activity done over a predetermined period of observation or physical activity questionnaires such as the International Physical Activity Questionnaire (IPAQ) which records activities under the various domains of domestic and gardening, work, transport and leisure activities done in a period of time. A quantitative score for the energy expenditure with these questionnaires can be obtained by computing the MET (Metabolic Equivalent) in minutes by weighting each type of activity by its energy requirement. Newer technological advances enables the objective assessment of physical activity using motion sensors, e.g., with an accelerometer. The advantage of using generic tools in hemophilia to assess participation such as the IPA (Impact on Participation and Autonomy Questionnaire) and the Participation Scale is that cohorts of different health conditions can be assessed and compared. Participation is the result of a dynamic process involving complex interactions among biological, psychological, social and environmental factors; hence these questionnaires require validation across cultures and languages.

**A core set of outcome measurement tools in patients with hemophilia**  
A systematic review of the measurement properties

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**Background:** In patients with haemophilia the evaluation of outcomes in all three domains of the ICF model (1. body structures and function, 2. activities and 3. participation) is critical to determine appropriate management for individual patients in clinical care and to compare the effects of treatment strategies. A large number of tools are available. In order to improve quality of clinical management and clinical research, we aim to reach consensus on a selection of instruments. These measurement tools need to be valid, reliable and responsive to change. Therefore, a systematic evaluation of the measurement properties of potential candidate tools is needed. **Aims:** We are
in the process of performing a systematic review with the aim to assess the measurement properties of potential candidate outcome measurement instruments used in adult and pediatric patients with hemophilia. A secondary aim is to identify gaps in the current knowledge on measurement properties in order to direct further research. **Methods:** Using a survey among comprehensive haemophilia treatment centres a set of outcome measurement tools was identified which are included in the systematic review. A systematic literature search to identify all available studies on these tools has been performed in Medline and Embase. The methodological quality of the studies is critically appraised using the QUADAS2 and COSMIN checklists. Measurement properties include reliability (internal consistency, reliability, measurement error), validity (content validity, construct validity, criterion validity) and responsiveness. The quality of the outcome measurement tools will be appraised by the rating proposed by the Cochrane Back Review Group. At the conference meeting the methodology and progress of this systematic review will be discussed.

**S01—Treatment Guidelines: Where do we focus our research?**

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Efficacy and safety of medical interventions, either pharmacological or not, have to be shown before their adoption. When several interventions of comparable efficacy and safety are available, cost-effectiveness has to be measured and used to guide health care decisions. The generation of evidence about efficacy, safety and cost-effectiveness requires careful planning of experimental studies. The first step is clarifying the underlying research question, ideally in PICOT terms: population (P), intervention (I) and expected result (outcome, O) are the three key components; whenever possible, comparator (C) and specific time frame (T) for outcome assessment are also included. The question is initially used for a careful review of the literature, to find out what is already known. The second step is selecting outcomes that are important to patients (patient centered outcomes, PCO), and defining the change in the outcome that makes a valuable difference (clinically important difference, CID). Since the final assessment of an intervention requires the global appraisal of the entire body of evidence about it, it is important to include those outcomes assessed in the studies retrieved in the literature search. The study question, the outcomes, and the criteria for success have to be described in a study protocol, where also the size of the population needed to show an effect and the analysis that will be performed are reported. The study protocol has to be ethically approved and submitted to a registry (e.g. clinicaltrial.gov) before the study start. Each question lends to a specific study design: questions about prognosis (the natural history of a disease) or etiology (side effects of treatments) usually require well designed observational studies; questions about efficacy of a treatment usually require a blinded randomized study (RCT); randomization minimizes confounding (concluding that the intervention works or does not work when in fact something else is responsible for the observed results) and blinding minimizes bias (conscious or unconscious mechanisms that favor the treatment under study). RCTs on the value of physiotherapy in the treatment of hemophilia included in a recently completed Cochrane Review will be used to discuss study designs with real examples.

**Are we all on the same page when choosing our outcome measures? Strategies to improve collaboration in research**

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Currently the regular infusion of clotting factor concentrates (prophylaxis) is recommended to prevent recurrent joint/muscle bleeding in individuals with severe hemophilia in order to avoid the development of clinically severe musculoskeletal disease. For maximum benefit primary prophylaxis must be started early in life in boys with severe hemophilia, generally before the age of 3 years or after the first spontaneous joint bleed. Challenges to the implementation of primary prophylaxis include the need for reliable venous access and the extremely high cost of long-term prophylaxis programs. As a result objective outcome measures are increasingly required to justify funding of prophylaxis programs. Selection of appropriate outcome measures requires knowledge of the many outcome measures that are in circulation, a number of which lack evidence of good measurement properties derived from well designed and conducted reliability and validity studies. To address these issues a meeting of experts in the field, including hematologists, orthopedic surgeons and physical therapists was held in Toronto, Canada in October 2014. The World Health Organization (WHO) International Classification of Function and Disability (ICF) model was used as a frame work to discuss the potential for developing a “core” set of outcome measures for use in persons with hemophilia treated with prophylaxis; a systematic review of selected outcome measures is in progress.

The results of this systematic review will identify areas that require further work including translation and culture adaptation of selected outcome measures for use globally.

**References:**


**Have we made any progress in radiographic outcome measures for hemophilic arthropathy?**

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The tremendous advancement of technology in the last decades has been reflected in the development of novel diagnostic tools for assessment of hemophilic arthropathy. Over the years imaging has become an appealing tool for evaluating complications of hemophilic arthropathy, for confirming joint bleeds and for assessing joint degeneration. There have also been marked efforts in developing avenues to facilitate access to imaging.
in the assessment of hemophilic joints by using point-of-care ultrasound and in the investigation of how ultrasound and physical examination can complement each other. Further, with the recent characterization and quantification of biologic markers of physiologic processes such as cartilage degradation, inflammation and bone turnover there has been a natural interest in improving our understanding on the biology of joints, genetic determinants of bleed and biomarkers of joint disease in hemophilia. Recently the concept of “marrying” information from biomarkers and imaging through “radiogenomics”, which relates to how imaging findings correlate with gene expression, has become a focus of research investigation. This novel concept aims to provide better understanding to disease process: by evaluating the pattern of joint degeneration one can look back at the clusters of patients who had a similar outcome and understand the mechanism of disease based on affected tissues. Clusters are created by merging genes and proteins that determine degeneration of tissue with corresponding clinical-imaging characteristics both at the structural (conventional imaging) and physiologic (functional imaging) levels. This better understanding of mechanisms of joint bleed, damage and repair can lead to drug discovery and to management based on stratification of patients into individualized therapies, the so called “personalized medicine”. In this presentation we will: Provide an overview of the progress of imaging technology towards diagnosis and follow-up of hemophilic joints, from plain radiography to ultrasound and magnetic resonance imaging (MRI), and finally to the novel era of “radiogenomics”; Summarize the evolution of imaging protocols and scoring systems for plain radiography, MRI and ultrasound over the years; Discuss the advantages, challenges and gaps in knowledge on “point-of-care” ultrasound; Explore possibilities in the research investigation of “radiogenomics” in hemophilic arthropathy.

Do patient registries increase the quality of research of musculoskeletal issues related to hemophilia?

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(Abstract unavailable)

Everything you always wanted to know about getting your paper published (but were afraid to ask)

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After centuries of stability, the publication of manuscripts in scientific journals has changed massively over the last 10-20 years. All journal submissions are now electronic and most of the world medical literature is readily available from a personal computer. Electronic communication has allowed faster review of manuscripts, decisions and publication. The number of journals has increased and authors should be very careful about which journals are genuine and which money making ventures are for commercial companies. The key points in getting a study published in any journal are good study design and execution and novelty. Authors need to choose a journal based on the Impact Factor and readership reach. The highest impact factor journals are unlikely to be read by members of the Haemophilia treatment team. Established researchers worry a lot about impact factor despite the fact that it can be manipulated and is a reflection of the journal rather than their paper. The journal Haemophilia publishes work from all over the world in the field of inherited and some acquired bleeding disorders. Papers from all the subspecialties including musculoskeletal, dental, laboratory, genetics and psychology are considered. Prospective authors should have a look at several issues of a journal to see the type of papers and style in which they are published before submitting their paper. For authors with no publication experience it is good to collaborate with a more senior established author at least initially. Common problems with manuscripts submitted to Haemophilia that reduce their chances of publication are very small cohorts of patients, describing something well known, reporting on a cohort which is largely of local interest, and papers written in poor English. Papers are not rejected just for the poor English and if the message is good, revision is likely to be invited. During the presentation advice will be given on how to maximise the chances of a manuscript being accepted for publication by a scientific journal.

S02–Hemophilic Arthropathy

Pathogenesis of hemophilic arthropathy: Lessons learned in the last 10 years

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Joint arthropathy secondary to recurrent bleeds is the most disabling and most expensive complication in persons with haemophilia (PWH). The very fact that with early commencement of prophylactic factor treatment with has dramatically decreased these complications in PWH suggests an important role for the presence of blood in the joint for the development of the arthropathy. In addition to the clinically obvious, recurrent subclinical bleeds can also contribute to joint damage in PWH. Also, once joint arthropathy has set in, prophylactic treatment may not always reverse further joint deterioration. The situation in PWH who develop inhibitors is worse with the unpredictable nature of the bleeds and due to the fact that prophylaxis with bypassing agents is extremely expensive. Although the exact pathogenesis of haemophilia arthropathy has not been elucidated, several in vitro, animal and human experiments have demonstrated blood-induced changes in all the ‘components’ of large synovial joints including i) the synovium itself, ii) the cartilage, and iii) the subchondral bone. The two major changes in the synovium are hypertrophy and hypervascularity, the key stimulant for which is iron released into the synovial fluid, which is both pro-inflammatory and proangiogenic. The consequence of neovascularisation in the synovium is predisposition to more bleeding since these new vessels are friable. This leads to a vicious circle of bleedàiron in the jointàsynovial hypertrophya hypervascularisationàfurther bleeds. The specific changes noted above provide rationale for synovectomy as a method to treat haemophilia arthropathy since removing the abnormal synovium breaks the vicious circle. Due to the deleterious effects of large amount of iron in the joint, there may be a reason to aspirate a joint which sustained a major bleed to reduce the total load of intra-articular blood and thus, the iron.
In PWH, cartilage changes occur even after the first haemarthrosis with changes more noticeable in younger age and with weight-bearing in experimental animals. Low bone mineral density or in severe cases, osteoporosis, has long been recognized in radiographs of PWH with affected joints. Additional bony changes that may occur include bony cysts and subchondral bone marrow oedema; however, the mechanism behind these changes is unknown. PWH with mutations in the haemochromatosis gene HFE mutations can have worse joint athropathy. Since haemophilic joint athropathy demonstrates changes of both degenerative and inflammatory joint conditions, where increased levels of thrombin activatable fibrinolysis inhibitor (TAFI) have been noted, antifibrinolytic agents may be a logical option in conjunction with factor concentrates, to reduce joint damage from the bleeding. Angiogenic mediators like VEGF have been demonstrated to increase in the serum of people with synovial damage and may serve as biomarkers for active synovitis, although the predictive potential of these markers need validation in large, controlled studies.

Are there any new strategies to provide local protection to articular cartilage against the deleterious effects of hemorrhages?

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The most common morbidity that results from hemophilia is bleeding-induced hemophilic arthropathy (HA), which once established may not be interrupted completely even by prophylactic clotting factor replacement. Several treatments have been proposed including blood aspiration, different molecular weight hyaluronic acid infiltration, platelet rich plasma infiltration, therapies based on interleukin (IL)-6 receptor antagonists, IL-4 plus IL-10, combined with factor VIII (FVIII) replacement, and intra-articular injection of Mesenchimal Stem Cells expressing coagulation factor. These methods seem to decrease synovial hyperplasia, hemosiderin deposition and macrophage infiltration, preventing blood-induced cartilage damage. The aim of the presentation is to describe the mechanism by which blood induce cartilage damage and to critically analyse the results of several studies on the prevention and treatment of the bleeding-induced HA.

Can the onset of hemophilic arthropathy be predicted by the use of serologic biomarkers?

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Progressive joint destruction resulting from intra-articular bleeding severely impacts quality of life in haemophilia. Diagnostic strategies are needed to detect early changes within the joint and to evaluate joint damage progression regularly. Imaging modalities, although very useful to detect late changes, have several limitations. An alternative approach could be the use of biochemical markers of joint tissue damage, small molecules or breakdown products that are released into the synovial fluid during joint tissue turnover. They are detectable in easy accessible body fluids like serum or urine. In haemophilia, it is demonstrated that a good cross-sectional correlation exists between radiographic joint damage and four biochemical markers of cartilage and bone turnover: urinary C-terminal telopeptide of type II collagen (uCTX-II), serum Cartilage Oligomeric Matrix Protein (sCOMP), serum C1,2C (sC1,2C), and serum CS846 (sCS846) [1]. A combined score of these biomarkers correlated best with the degree of arthropathy. The same four markers were tested for their sensitivity to change shortly after a joint bleed in hemophilia patients and in a canine model of blood-induced joint damage [2]. An increase in the levels of uCTX-II and sCS846 was demonstrated 5 days after joint bleeding in haemophilia patients, whereas in dogs, uCTX-II and sCOMP showed a clear change compared to baseline. This study demonstrates the impact of a single joint bleed on joint tissue turnover, and emphasize the sensitivity of biomarkers to the changes upon a bleed. Biomarkers related to active synovitis are also investigated. In this respect, it is demonstrated that plasma levels of vascular endothelial growth factor (VEGF), matrix metalloprotease (MMP)-9 [3] and osteopontin are increased in patients with synovitis compared to controls [4]. These studies indicate that biomarkers are a promising tool in detecting the destructive properties of joint damage. Prospective studies are needed to investigate the predictive value of biomarkers for the progression of joint damage and possibly treatment-efficacy.

References

Predicting hemarthroses and progression of arthropathy in hemophilia patients: Preliminary results on the prognostic value of MRI synovial changes

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Introduction: The current trend in advanced hemophilia care is to use sensitive imaging modalities, such as MRI, to detect minor intra-articular changes. The clinical consequences of these minor intra-articular changes remain unclear. To evaluate the clinical relevance of early changes detected by MRI this study assessed the predictive value of MRI synovial changes on future hemarthroses and progression of arthropathy.

Methods: Bilateral knees and ankles of 26 haemophilia patients, aged 12–29 years, were scanned using 3T MRI in 2008-2009. Progression of arthropathy on X-rays (from within 2 years of MRI to 5 years later) were scored by one observer, blinded for MRI findings, according to the Pettersson score. The prognostic value
of MRI synovial changes on the frequency of hemarthroses in the next five years was assessed using a negative binomial model (adjusted for disease severity, treatment strategy, taking clustering of multiple joints in a single patient into account). Results: In total, 52 knees and 52 ankles of 26 hemophilia patients were scanned, at a median age of 21 years. One joint was excluded because of incomplete bleeding history and one patient was lost to follow-up after the first evaluation. In February 2015, follow-up X-rays five years after MRI examination were available for 58% of joints. Comparing joints with and without MRI synovial changes, absence of hemarthroses after 5 years was observed in 38% versus 63% of joints respectively (p<0.05). Joints with synovial changes showed more hemarthroses in 5 years (adjusted rate ratio 3.1, p<0.05). In addition, MRI synovial changes were associated with 5 years progression of arthropathy on X-rays (5/16 vs 0/44 joints, p=0.01). Conclusion: Synovial changes on MRI were associated with a higher rate of hemarthroses and progression of arthropathy on X-rays after 5 years. Follow-up MRI assessment will be performed to assess the predictive value of initial synovial changes on more subtle arthropathy. Conflicts of interest: The present study was financially supported by an unrestricted research grant from Baxter BV, The Netherlands.

### S03 – Miscellaneous Issues – Part I

#### The iliopsoas Muscle – Biomechanics and the impact of dysfunction on lumbar stability and the lower limb

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The iliopsoas is a particularly challenging muscle to assess and treat in the context of haemophilia care, as its location makes it impossible to palpate or to visualise without advanced diagnostic imaging. Traditionally, conceptualized as a hip flexor and rehabilitated post injury, the full breadth of the muscle complex's functions and capabilities are not routinely considered. This anatomical and biomechanical review will highlight complementary functions of the iliopsoas complex, and connect those concepts to practical and clinical approaches for musculoskeletal professionals.

#### Acute compartment syndrome in the patient with hemophilia: Is an emergent release the best option?

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Compartment syndrome is fortunately an uncommon bleeding manifestation. It occurs when there is a critical increase in pressure within a confined osseo-fascial compartment. The subsequent decline in perfusion pressure can lead to irreversible tissue damage and cell death. The treatment is prompt surgical fasciotomy. In patients with haemophilia even trivial trauma result in an acute compartment syndrome. The clinical challenges posed are more complex and there is a risk of catastrophic bleeding. The first step in the management of ACS in PWH is to try to normalise the clotting derangement with clotting factor substitution. This can tamponade the bleeding and lower intra-compartmental pressures. The reports in the literature suggest that the majority of ACS cases in PWH will settle with clotting factor replacement and non-surgical management. If symptoms of ACS persist despite normalisation of the coagulation defect it is reasonable to measure the compartment pressure and consider surgical fasciotomy. In PWH and inhibitors there is however significant functional and surgical morbidity associated with a fasciotomy. The decision to operate becomes much harder to justify and certainly specialist haematological input and exhaustion of non-surgical methods are mandatory. There is little published literature on the subject and those undergoing surgery had significant morbidity including prolonged bleeding and a high amputation risk. Further prospective observational studies and the use of large databases with functional as well as haematological outcomes are necessary before surgical treatment guidelines can be ascertained.

Key references:  

### S04 – Where have we been and where are we going?

#### Haemophilia: What I wish for the future

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Current and future developments in haemophilia treatment and care hold out the prospect of major change and improvement in the quality of life for people with haemophilia. The availability of longer acting factor concentrates and their integration into clinical practice will allow a greater degree of personalised care based on individual pharmacokinetics, bleeding history and activity level. Gene therapy clinical trials have been encouraging. It is important that these developments do not result in an increased access to treatment and care solely in the wealthier countries and economies. I want to see the following developments: clinicians and people with haemophilia agreeing on their
individual treatment plan in a real collaborative partnership. Longer acting and the current recombinant and plasma derived factor concentrates are available as treatment options and where the economic cost of factors is structured to facilitate access to treatment for those in less economically resourced countries; With the new generation of direct acting antivirals, the eradication of Hepatitis C in haemophilia; The development of inclusive protocols for ageing with haemophilia and the acceptance of the efficacy and cost effectiveness of lifelong prophylaxis; Improved therapeutic products and choice for von Willebrand's and rare bleeding disorders; Ongoing collection of outcome data clearly demonstrating the positive impact of treatment and care; Certification and external audit of treatment centres and real patient centred care models being developed and implemented; A future where orthopaedic surgery in haemophilia is no longer routine and where physiotherapy can focus on health and fitness and not on recovery and damage limitation.

From prophylaxis to gene therapy: How close are we to a cure for hemophilia?

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Gene therapy has curative potential as illustrated by our pivotal study in haemophilia B (HB), an X-linked bleeding disorder in which a single administration of a novel adeno-associated viral (AAV) vector resulted in stable therapeutic expression of factor IX (FIX) for >4 years. This has enabled discontinuation of FIX prophylaxis and change in bleeding phenotype from severe to mild in some patients. These and other promising data provide a solid platform for developing AAV-mediated gene transfer approaches for a large number of disorders ranging from congenital deficiencies of clotting factors such as haemophilia A, to other genetic hepatodeficiency diseases, including inborn errors of metabolism. Progress made in this area will be discussed as will the remaining challenges.

What are the 21st century challenges in the musculoskeletal care of patients with hemophilia? Developed country perspective

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Remarkable progress in the musculoskeletal care of individuals with hemophilia has been achieved in the 20th century, continuing in the first decade of the 21st century. The life expectancy of individuals with hemophilia nears that of the normal population despite the tragedy of clotting factor pathogen contamination in the 1980s. Replacement clotting factor protein concentrates for the treatment and prevention of musculoskeletal bleeding were developed and tested in the clinical setting, establishing efficacy in preventing gross bleeding episodes. Uniform standard of care approaches to prevent the development of joint disease for individuals with severe hemophilia (e.g. prophylactic factor replacement in childhood) have been validated. The extent of this progress raises new challenges for 21st century care. Is severe hemophilia (as defined by circulating factor activity <1%) really one clinical entity, or is there a spectrum of patients who vary in their risk for the development of musculoskeletal disease? Is there a large population for whom adherence to prophylactic factor concentrate replacement will achieve normal joint health, but also an at-risk subpopulation for whom adjunctive therapies may be justified e.g. the anti-inflammatory disease-modifying drugs that have become an essential component of rheumatoid arthritis care? For those with severe hemophilia, can we justify prophylaxis for children and not adults? Based upon our understanding of the pathophysiology that develops when the joint is exposed to blood, can we justify practicing prophylaxis for individuals without inhibitors but withholding prophylaxis from those who have inhibitors? As we research new drugs and new treatment approaches, are 20th century study endpoints (e.g. the “annualized bleeding rate”) adequate to distinguish comparative efficacy of new products for the care of hemophilic muscles and joints? What biomarkers or imaging endpoints may help us distinguish efficacy and safety endpoints in an era when hemophilia researchers ask each other the question “What is a joint bleed?” (a question our colleagues in the 1970s did not debate)? And at the most practical level, while “normal life expectancy” is an unassailable goal, how must our health systems adjust to provide the specialized nursing care needs of the hemophilia population of advancing age? This hemophilia population, in addition to musculoskeletal concerns, shares 21st century general population healthcare burdens, including obesity, cardiac disease, and osteopenia.

What are the 21st century challenges in the musculoskeletal care of patients with hemophilia? Developing country perspective

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Can physical therapy interventions help in the (assessment and treatment) of hemophilic patient with no or limited lack of clotting factor concentrates in the 21st. century in developing what are the Opportunities and threats for such hypothesis. strength point that, physiotherapy, physical activity and sport are basic elements to improve quality of life and the physical fitness, increase muscular strength and endurance, cardiorespiratory endurance, and motor ability and to reduce the risk of musculoskeletal lesions and to prevent haemophilic complications. In general, professionals in haemophilia care believe that regular exercise and rehabilitation with physiotherapy is fundamental, particularly in such countries where replacement therapy is not readily available. Opportunity, it is essential that those with hemophilia are taught the importance of physical fitness at an early age. Sports activities should be encouraged to promote muscle strengthening and self-esteem. The choice of sports should reflect an individual’s preference, ability, and physical condition. Physical therapy services under the guidance of an experienced therapist is an integral component of comprehensive hemophilic care and plays an important role both in the prevention and treatment of musculoskeletal complication even with limited recourses.

Identifying and recruiting new hemophilia providers: Challenges and strategies

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Factor replacement therapy will probably not entirely eliminate the complication of hemophilic arthropathy. The cohort of
patients currently over 40 years of age is characterized by often severe disease. It is well recognized that a dedicated team should be involved in the treatment of patients with Hemophilia (PWH), especially those with inhibitors. Orthopedic surgeons need to be involved to offer state of the art care, since much need to be improved in orthopedic care for PWH. Current levels of data are largely inadequate to define best practices for many of the clinical scenarios facing these patients and their physicians. Concentrating expertise is a well-established method of improvement in care for such rare pathologies. There is thus a need for integrating the expertise of orthopedic surgery into the multidisciplinary management of PWH at all levels including non-surgical care, surgical care, education and research. We have been asked to explain the evolution of our team building approach in Montreal. In summary the challenges include: Through a coherent team approach, the adoption of best practices by concentration of expertise; improving the available expertise in physiotherapy and its impact on practices in adult hospitals where most patients undergo surgery; improving surgical expertise to the highest level. Prospective and comprehensive database collection to allow publication of meaningful data may be a significant factor for recruitment; any member of the team can present, publish and participate in education as well. Physiotherapy is a focus of our current efforts. Liberating physiotherapy staff for CME, and recruitment of additional staff are among the challenges a group like ours faces if we are to raise our standard of care. Further team developments will seek partnerships with individuals with whom improvements in the quality of care can be sought.

**S05 – Hemarthrosis/Synovitis – Part I**

**Are personalized prophylaxis regimens a better way to minimize articular damage in patients with hemophilia?**

*M. Lavin*

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Arthropathy is a major cause of morbidity in persons with haemophilia (PWH). Outcome measures in trials involving PWH focus on clinically evident joint bleeding. Recent research involving children and young adults with Haemophilia has identified radiological evidence of joint damage in bleed naïve joints. These changes have been attributed to subclinical joint bleeding (SJB). There is a dearth of research on SJB in adults with haemophilia. The long-term sequelae of damage induced by SJB remains unclear and the prevalence of SJB in PWH is unknown. In other arthropathies subclinical joint damage has been shown to be associated with poorer long-term joint outcomes. If this is extrapolated to PWH, the question remains as to how best provide prophylaxis in order to minimize progression of arthropathy. Traditional prophylaxis regimens for PWH focus on weight based dosing of factor concentrate. Given the considerable variation in factor VIII (FVIII) half life in people with severe Haemophilia A, a pharmacokinetic tailored programme offers an attractive alternative. Targeting of a trough FVIII level would reduce the time spent with FVIII <0.01 IU/mL, a known risk factor for clinically evident joint bleeds. It is unknown if same trough factor VIII/IX level would prevent both clinically evident and subclinical joint bleeds. A national trial involving personalization of prophylaxis regimens for people with severe Factor VIII deficiency is underway in Ireland. The efficacy of PK tailoring of prophylaxis regimens is evaluated using a target FVIII trough of 0.015 IU/mL. The impact of PK dosing on joint outcomes will be assessed, focusing on participants’ elbows, ankles and knees. Specialist physiotherapist review, Haemophilia Joint Health Score, X rays and Pettersson score, MRI and IPSSG score are performed at three points during the trial – trial entry, at crossover to PK tailored dosing and trial end. We hope that through this interventional trial we will gain better understanding of the impact, if any, of PK tailoring dosing in haemophilia on joint bleeds, both clinical and subclinical.

**Point of Care Imaging: A necessary tool in the modern hemophilia care model?**

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Hemophilic arthropathy is a disabling comorbidity characterized by synovial hypertrophy, cartilage destruction, and bony abnormalities and it cannot be prevented by clotting factor replacement. The arthropathy presents with joint deformities, range of motion (ROM) deficits and pain. Pain is often assumed to be caused by bleeding and treated with clotting factor concentrates. The recognition that modern hemophilia care requires improved diagnostic accuracy resulted in the introduction of point-of-care musculoskeletal ultrasound (MSKUS). MSKUS is a fast and sensitive imaging modality able to diagnose and differentiate between bleeding, effusions, synovitis and soft tissue abnormalities, and is already used in disciplines such as rheumatology and sports medicine. The results of 4 single center studies (n=10-65 joints) exploring MSKUS as diagnostic tool in hemophilia are summarized below. (Aznar JA, et al. Haemophilia 2013; Kidder W, et al. Haemophilia 2015). 1) Clinical assessment and/or patient-perceived cause of joint pains was inaccurate in up to 2/3rd of painful episodes. 2) Warmth/swelling and ROM deficits were non-specific and could not distinguish bleeding from non-bleeding events. 3) While pain caused by acute haemarthrosis usually resolved after 1 or 2 days of clotting factor infusions, haemarthrosis resolution could take weeks. 4) Portable MSKUS for home-based imaging was instituted successfully to follow resolution of hemarthroses. 5) For acute pain, MSKUS-guided treatment decisions encompassing factor replacement, physical therapy, anti-inflammatories, pain management and intra-articular steroid injections provided symptom relief in the majority of patients whose pain was uncontrolled with empiric treatment. 6) In chronic pain, inflammatory changes such as synovitis/ tendinitis/bursitis/fat pad inflammation prevailed (67%), together with other anomalies such as tendon tears/sprains (11%) or tendinosis/enthesopathy/ligament abnormalities (31%). However, 25% percent of those joints also had bloody effusions despite clotting factor prophylaxis. These findings indicate that our understanding of hemophilic joint disease is rudimentary and that pain is not caused by bleeding alone. Empirc management results in over- or under-treatment of bleeding and/or musculoskeletal conditions for which alternative treatments are preferable. MSKUS
is an important new tool in modern hemophilia care, enabling targeted therapy based on direct observation and new avenues for continued research.

Technical challenges associated with the use of ultrasound for the early detection of hemophilic synovitis

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Similar to other chronic joint disorders, high-resolution ultrasound is an excellent diagnostic modality to reveal joint effusion, synovial proliferation and subtle chondral and bone abnormalities occurring in the elbows, knees and ankles of haemophilic patients. It has proved to be sensitive to demonstrate joint effusions in suspected acute joint bleeds providing a tool to distinguish between intraarticular and extraarticular haemorrhage as well as to differentiate joint pain related to articular derangement from new bleeds. In these settings, the ability of ultrasound to objectivate findings may increase the confidence of the clinician in deciding the best treatment strategy. Ultrasound detects synovitis as a focal or diffuse thickening of the synovial membrane investing the joint recesses. Compared to other chronic joint disorders, the vascular response observed in haemosideritic synovial tissue is not as prominent as in the active phases of rheumatoid arthritis and looks more similar to the one occurring in degenerative osteoarthritis. Synovial tissue proliferation invariably corresponds to hemosiderin-enriched tissue as assessed on gradient-echo MR imaging sequences and may be a key feature, possibly representing a biomarker of true disease activity related to insufficient therapy regimens or noncompliant patients. Although some authors claimed on the ability of ultrasound to identify haemosiderin deposits, there is evidence that no echotextural difference exists between haemosiderin-enriched and haemosiderin-free synovial tissue based on one-to-one comparison of ultrasound and MR images. Some echotextural criteria and dynamic scanning with joint motion and probe compression can help to distinguish proliferating synovium from fresh haemorrhage, blood clots and fibrin deposition. Outside the context of an acute intraarticular bleed, a reliable distinction between synovium and serum effusion can also be readily accomplished with ultrasound. It is conceivable that ultrasound has potential to better clarify timing of formation and clearance rate of synovium after intraarticular bleeding episodes.

Specificity and clinical value of MRI for the day-to-day evaluation of hemophilic synovitis

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In the past, X-ray has been helpful to compare treatment outcome but MRI has been shown to more accurately assess a haemophilic joint and therefore it has been increasingly used during the last decades. MRI visualizes early abnormalities such as effusion, synovial hypertrophy, hemosiderin deposition and small focal cartilage defects without joint space narrowing. Data available so far already show the potential impact of MRI on hemophilia care. In a randomized clinical trial (1) MRI imaging of index joints was used as the outcome measure to prove the superiority of primary prophylaxis compared to on demand treatment for preserving normal joints in young children. In another prospective pediatric trial (2) MRI was able to detect soft tissue changes in index joints of children on prophylaxis who had no clinically evident hemarthroses supporting its potential for assessing subclinical joint bleed in hemophilia. In a recent cross-sectional study of adolescent and young adult patients (3) MRI was highly sensitive to assess the effect of age at prophylaxis initiation. Notwithstanding these evidences, several factors still limit the clinical applicability of MRI. Apart from the practical issues including cost, accessibility, time requirement and need for sedation in young children, the major limit is due to the lack of data on the evolution and long-term clinical relevance of MRI findings, in fact, there is uncertainty regarding whether early MRI-detected soft tissue and osteochondral changes can reliably predict arthropathy progression later in life. Furthermore, a number of tentative MRI scales have been developed to assess hemophilic arthropathy in clinical practice and research trials. Finally, the use of the same, recently developed, scale (4) should result in a more consistent assessment of hemophilic joints over time and between patient groups and should facilitate tailoring and optimization of prophylaxis.

Performance-based scores: A better way to monitor long-term changes in musculoskeletal function in hemophilia?

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Accurate assessment of the musculoskeletal function is necessary when assessing the effectiveness of any intervention programme, determining the course of illness and judging the results of any research designed to optimize functioning of an individual. Self-reported outcome measures of function can be influenced by psychosocial factors while performance based measures are observer assessments of an individual performing a task, done in a controlled environment. A systematic review by Stephensen et al. identified 41 studies and analyzed 14 clinician evaluated performance based measures used in children with hemophilia. These include standing balance, gait analysis (temporal spatial, kinematic and kinetic gait patterns), 6-minute walk test, maximal muscle strength, joint range of motion, maximal aerobic capacity, physical activity using a accelerometer, Movement Assessment Battery in Children, WFH Orthopedic Score, Colorado Physical Examination, Petrini Joint Score and Hemophilia Joint Health Score (HJHS). Good repeatability
and discriminative properties were seen with the walking and muscle strength measurements; however correlation with other measures of musculoskeletal impairment is required. The HJHHS showed acceptable construct validity, internal consistency and test-retest repeatability; however its ability to assess responsiveness is still to be determined. Genderan et al. measured functional abilities in consecutive patients visiting the Van Creveldkliniek with severe hemophilia A or B using four other performance-based tests (button test, 50 meter walking test, Timed-Up-and-Go test, and Figure-8 walking test) and compared these with the self-reported questionnaires in predicting disability as assessed by the Impact on Participation and Autonomy questionnaire. Disability was associated only with the self-reported scales indicating that patients perception about their abilities to perform reflect the way they respond to the functional limitations questionnaire unlike the performance tests which are objectively assessed by the clinician and is a true reflection of the musculoskeletal function with no overlay of the individual’s psychological component.

Recurrent joint bleeds from the early years of life resulting in progressive joint damage has long been the clinical hallmark of severe hemophilia A and B. Determining the optimal regime for prophylaxis to prevent joint bleeds and their consequences will require us to define and monitor clinical targets which are crucial for long term cost effectiveness and cost utility in a chronic disease such as hemophilia.

**Pharmacologic and non-pharmacologic strategies to minimize pain during the acute bleeding episode**

**K. Mulder**  
Winnipeg, Canada

The 2012 publication WFH Guidelines for the Management of Hemophilia was developed by a multidisciplinary international working group. These guidelines were based on the best evidence available at the time; treatment guidelines and practice statements were referenced and the levels of evidence were graded by an external reviewer according to the Oxford Center Evidence-Based Medicine system. A literature review is in progress to determine if there are any applicable updates to the information on management of pain during acute bleeding.

**Osteoporosis and hemophilia: Is this a real clinical problem?**

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Accumulating body of evidence has emerged during the last decade supporting an association between haemophilia (A and B) and low bone mineral density (BMD), both in adults and children. Heterogeneity between studies exists, regarding the criteria used for the definition of low bone mass and the population studied (the majority were patients with severe haemophilia). Most studies have yielded a prevalence of 50-80%, although its true prevalence by applying the criteria provided by the International Society for Clinical Densitometry, seems to be lower (27%). The process of bone loss is evident even from childhood. A recent meta-analysis further established that patients with haemophilia (PWH) have lower BMD both in lumbar spine and hip than their apparently healthy controls.

The pathogenesis of low bone mass in PWH is multi-factorial. Low physical activity and vitamin D deficiency seem to be independent predictors of low BMD. Viral infections, arthropathy and the severity of haemophilia are contributory factors. Secondary causes of osteoporosis (hyperthyroidism, hypogonadism, etc) may be also present. Despite the evidence regarding BMD, current data on fracture risk in PWH are scarce, reporting a prevalence of 16-18% and a relative risk of 21.4-24. However, whether haemophilia is an independent risk factor for fracture is unknown. In any case, haemophilic arthropathy and, perhaps sarcopenia, increase the risk of falls. Fracture Risk Assessment Tool (FRAX) may be used in PWH ≥ 40 years and BMD assessment (using dual-energy-X-ray absorptiometry-DXA) in those ≥ 50 years and those of any age who have sustained a low trauma fracture. Regarding the management of low bone mass, acquisition and maintenance of the highest possible peak bone mass should be the main concern from childhood. For this purpose, encouragement of a regular exercise program (resistance/weight-bearing and low-impact aerobic exercise) and fall-prevention strategies, is suggested. Optimal vitamin D supplementation (aiming at the level of 30 ng/ml), with 1,000 mg/day of calcium intake is recommended. In cases at high fracture risk, bisphosphonates or other medications approved for male osteoporosis (teroparatide, denosumab) can be considered. In general, a multidisciplinary approach conducted by hematologist, endocrinologist, orthopedic surgeon and physiotherapist is prudent.

**Immobilization and the correct pace of rehabilitation—Impacts on Pediatric patients with inhibitors**

**M. Bladen**  
Haemophilia Centre, Great Ormond St Hospital For Children NHS Foundation Trust, London, UK

Inhibitors to factor replacement are a serious complication of haemophilia care. Management of acute bleeds involves resting or immobilising the affected joint or muscle, but little is known about the theory or the specific physiotherapy management for patients with inhibitors. Immobilisation following bleeds is part of the clinical care of patients with haemophilia and is documented in the literature from 1964 to date. This presentation will review the literature on immobilisation and rehabilitation in haemophilia and inhibitors. Rest / immobilisation has been advocated for at least three days in patients without haemophilia, with the theory being to minimise factors that may affect the healing process and fragile fibrin bond required for healing (Houglum 1992, Hunter 1994). For patients with inhibitors healing is not normal and the risk of re-bleeding greater (Salinas 2014 and Hoffman 2010, Monroe 2012) and as such immobilisation and rehabilitation may be prolonged and require a slower pace. But with immobilisation comes a raft of other implications for the musculoskeletal system. Skeletal muscle loss occurs after 5 days of immobilisation in patients without haemophilia (Wall 2014). Muscle atrophy following bleeds in haemophilia has been...
Blood isn’t painful—Haemophilia, the individual and the pain “neurosignature”  

P McLaughlin  
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The issue of pain in patients with haemophilia (PWH) is a well recognised and often quoted major clinical issue in modern management. It is suggested that upwards of 50% of patients complain of pain in their joints associated with arthropathy. However, this figure takes no account of those patients who report pain independent of any obvious biological/anatomical evidence of damage, or indeed, the experience of an acute pain episode related to their bleeding diathesis. For many years, clinicians and patients alike have utilised the concept of ‘if in doubt, treat’, whereby any reported musculoskeletal pain was attributed to a suspicion of an acute bleed. This approach assumes as true, a biological nociceptive cellular injury (i.e. a bleed) as a baseline. This has 2 main problems –

1. The assumption that any pain in a PWH is associated with a bleed
2. Perpetuates the notion that factor concentrate can be used to alleviate pain. It is of course obvious that pain is a good indicator of an acute bleed if it presents alongside the symptoms of calor, dolor, rubor and tumor. But what if it doesn’t? Do we fully appreciate the reasoning process applied by patients or ourselves in approaching management of pain? Modern pain science dictates that pain should always be appreciated in a biological, psychological and social/environmental context, and that it should be considered an ‘experience’ unique to the individual involved. This is applicable to both the acute pain and chronic pain (>6weeks) setting. Humans do not have a dedicated pain receptor and as such pain, as an entity, should be considered as a brain output. Cerebral pain modulation is multifactorial and includes an individual’s beliefs, knowledge, social context, family, logic, previous history and culture to name but a few. This activated network of brain activity results in what is now termed a ‘pain neurosignature’ – a unique pain response. Haemophilia is a bleeding disorder with a complex genetic familial heritage, and the personal effect it has on an individual for full societal participation. Are we as haemophilia caregivers considering the biopsychosocial aspects of our patients when attempting to manage pain? This presentation will aim to review where our understanding of pain is presently in Haemophilia and highlight where we should be focusing development.

References
Materials and methods In this study the clinical experience of 34 synovium-angiolisis (embolization) of the knee in 31 patients with hemophilia who had synovitis of the joint in the period from September 2007 to January 2013. In three patients there was shown to repeat the procedure before the year to control sinovitis. All patients were performed one Rx and nuclear magnetic Resonanacis and were classified by clinical and imaging findings in one type of synovitis according to the classification developed by Fernández Palazzi. Grade I - no knee was not included in the grade II 21 knees (61.76%), grade III in 13 knees (38.24%) and IV no. The average patient age 20.45 years (7-39 years). 30 patients suffering from hemophilia A and hemophilia B. Two 1 (2) hemophilia A patients had inhibitors to Factor VII. Results After embolization performed average submitting a new hemorrhatis in the treated joint was 120 days (92-250 days). It assessed the number of bleeding embolization to 3months average was 0 (p <0.001), 6-month average was 0.2 (0 -1.67) with p <0.012 and 12 months the average was 0.33 (0 to 1.67) with p 0.024. Conclusion We consider the Sinovioangiolisis knee is an effective procedure since the 90.32% of patients had effective control of bleeding

When considering radiosynovectomy, which isotope should be used? A critical analysis of the evidence

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**Aim:** Radiosynovectomy (RS) is accepted as a simple and efficient therapy in patients with hemophilic synovitis. There are several radionuclides that can be used for RS and their availability is varied from one country to the other. In the current study the literature focusing on the RS in hemophilic patients are reviewed in order to investigate the most appropriate isotopes that should be used. Methods: A med-line search was conducted in the relevant English literature published in 2000-2014. Those articles focusing on the hemophilic patients and describing the details of the technique, isotopes, injected activity and clinical outcome are included. Finally 4 papers representing different clinical experiences from different geographical parts (USA, Brazil, Spain and Turkey) with varied isotope availability are selected. These articles are reviewed and rated following the Oxford Centre for Evidence-based Medicine – Levels of Evidence. **Results:** A brief table presenting the selected articles is presented 4 articles.

<table>
<thead>
<tr>
<th>Reference, year</th>
<th>Country</th>
<th>Study design</th>
<th>Isotope</th>
<th>No of patients (joints)</th>
<th>Injected joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silva M, 2001</td>
<td>USA</td>
<td>Observational</td>
<td>P-32</td>
<td>97 (130)</td>
<td>Knee, elbow, ankle, shoulder</td>
</tr>
<tr>
<td>Thomas S, 2011</td>
<td>Brazil</td>
<td>Prospective</td>
<td>Y-90</td>
<td>190 (245)</td>
<td>Knee, elbow, ankle, shoulder</td>
</tr>
<tr>
<td>Rodrige-Mer-chan C, 2011</td>
<td>Spain</td>
<td>Observational</td>
<td>Y-90, Re-186</td>
<td>78 (104)</td>
<td>Knee, elbow, ankle, shoulder</td>
</tr>
<tr>
<td>Kavalkh K, 2008</td>
<td>Turkey</td>
<td>Observational</td>
<td>Re-186</td>
<td>49 (63)</td>
<td>Elbow, ankle, shoulder</td>
</tr>
</tbody>
</table>

**Conclusion:** It is noted that the relevant literature is mostly originating from clinical case series which leads us to poor grades of evidence. Therefore objectively designed prospective trials are required to improve the evidence for the use of RS in hemophilia care. However, despite the differences in the methodology or the isotopes, clinical results presented in these clinical series are quite comparable.

Is radiosynovectomy a safe option for the treatment of hemophilic synovitis?

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(Abstract unavailable)

Surgical synovectomies: A thing of the past?

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The possibilities to assist persons with haemophilia in dealing with their affected joints, has dramatically changed over the last half century. Prior to Judith Pool’s discovery that cryoprecipitate contains the majority of the bloods factor VIII the orthopaedists role entailed dealing with contracted joints and providing fitted orthoses. Physical therapy and manual attempts to straighten out contracted knee joints were the gold standard of management. Early reports in the medical journals of surgery upon patients with haemophilia came from Storti (Italy), Ahlberg (Sweden), Pietrogrande (Italy), Hofmann (Germany), Gilbert (USA), Duthie (UK), and Luck (USA). Intra operative and post-operative factors were infused. Emphasis was made not to rely on electrocautery and that blood vessels should be tied off. This made the surgical procedure both protracted, and expensive. Alternative methods were sort after and one option was the use of the carbon dioxide laser Horoszowski, Heim (Israel). Our haematological colleagues progressed in removing Factor VIII and IX from blood and eventually to the manufacture of factor concentrates. Smith (UK) and Hofmann (Germany) proposed that some of the problems of knee synovitis were related to joint mal alignment and by long bone osteotomies knee pathology could be reduced. Weidel (USA), Eikhoff (Germany) and Erken (South Africa) were the fore runners of the use of the arthroscopy in persons with haemophilia. Surgical synovectomies could be carried out less traumatically and equally effectively. Although the cost was less than for open synovectomies the procedure was still expensive. Ahlberg (Sweden), Fernandez Palazzi (Venezuela), and Rivard (Canada) introduced both chemical and radioactive methods to eradicate synovial tissue. These methods are effective and cheap and have been the mainstay of management for the last 30 years. Merchán et al (Spain) the “scribe of haemophilia” have recorded this historical path in their various books. To answer the question; Is surgical synovectomy a thing of the past? Open surgical synovectomy per say is a historical procedure. Destructive synovium can be obliterated by approaches less traumatic and less expensive. Sohail (Pakistan) and Heijnen (Netherlands) have reminded us that the treatment of haemophilia abides to no global standard. Synovial proliferation has to be controlled one way or another and that could include an open synovectomy when none of the other procedures are available.

References of the 4 reviewed articles.

S08 – Chronic Arthropathy

The questions that we all get, and for which we have no answer: The efficacy of glucosamine, hyaluronic acid and platelet-rich plasma (PCP) for the treatment of hemophilic arthropathy

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(Abstract unavailable)

Value added role of physiotherapy: The impact of a new model of care

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In 2011, for the first time, a part-time designated physiotherapist joined the Haemophilia Care Team at the Wellington Haemophilia Treatment Centre with responsibilities for assessment and rehabilitation of acute and chronic musculoskeletal presentations, surgical pre-habilitation and rehabilitation, promoting exercise and weight control. Patients were seen in the community as well as in the hospital to enable ease of access and to try and prevent none attendance. KPI were set to assess all patients within 24 hours of reporting a bleed. One of the reasons for this was to help prevent treatment of arthritic pain with factor replacement products. An annual HJHS was to be carried out on all adult patients and a twice yearly HJHS on children. Patient DNA rates should be kept below 10%. The New Zealand National Bleeding Disorder database was interrogated to determine the costs of coagulation factor VIII concentrate usage for people with bleeding disorders treated by the centre for 2010 (prior to the appointment of a specialist haemophilia physiotherapist) and for 2013 (after two years of a haemophilia physiotherapy service). People with inhibitors, haemophilia B, symptomatic female carriers and people who moved into or out of the region between 2010 and 2013 were excluded from the analysis. No adjustments were made for changes in weight during this period. Between 2010 and 2013, total factor VIII product usage fell by 342,712 IU representing a 6.8% reduction. Patient satisfaction surveys response was that 100% of the patients who completed the survey (70% response rate) were satisfied or very satisfied with the physiotherapy service and that they agreed or strongly agreed that a designated physiotherapist service had improved the quality of their care.

Is multiple-site elective surgery a safe and cost-effective strategy in patients with hemophilia?

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Due to recurrent hemarthroses, persons with hemophilia (PWH) born before the 1970s have often developed hemophilic arthropathy in more than one joint and have to deal with pain, limited mobility, disability and adverse consequences on their quality of life (QoL). In such patients, orthopaedic surgery (joint replacement surgery or arthrodesis) of more than one joint of the lower limb might be indicated. In the general population, multiple-site elective surgery has been associated with an increased risk of perioperative and postoperative complications. In selected patients, improved perioperative management has recently reduced the number of adverse events, so this procedure have been re-evaluated and published studies have not reported any increased risk of complications. In PWH, multiple-site elective surgery could be indicated in order to reduce the time of recovery and return to professional activities as quickly as possible. Moreover, multiple-site elective surgery has the advantage of limiting the consumption of coagulation factors, resulting in a significant reduction of costs. In this setting, a tailored rehabilitation program is needed with special emphasis on the usefulness of hydrotherapy. Staged procedures should be considered when multiple-joint clinical improvement is possible after a single surgery. In conclusion, our recommendation is to perform multiple-site elective surgery in selected patients and in experienced multidisciplinary centres.

References

New strategies to decrease the risk of postarthroplasty infection: The role of prosthetic coatings

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Introduction: Despite improvements in perioperative medical care and aseptic surgical technique, infection rates after total joint arthroplasty in patients with hemophilic arthropathy remain as high as 16% [Silva et al, JBJS 2005]. In fact, infection remains the most common cause of failure after total joint arthroplasty in this high-risk population. Many advances in recent years have been achieved in an effort to modify the host environment and/or the implanted material to reduce the incidence of infection. Anti-infective surface coatings include silver ions, nitric oxide, iodine, antibiotics and antimicrobial peptides to inhibit bacterial viability at the implant surface and biofilm formation. Methods: Using a previously established non-invasive in vivo murine model that allows longitudinal study of post-operative implant infection, we assess multiple different antimicrobial and antibiotic coatings aimed at decreasing bacterial burden and biofilm formation. Coatings were sequentially applied to orthopedic-grade titanium implants and tested against S. aureus, S. epidermidis, and P. Acnes.
To fuse or to replace: A common question for ankle arthropathy

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The question of ankle replacement in Haemophilia needs to be considered in the context of haemophilic ankle arthropathy as a whole. The joint is frequently involved from an early age, where management revolves around control of joint bleeds, and symptomatic management including conservative surgery. End-stage symptomatic arthropathy often occurs at a relatively early age, affecting the individual’s ability in relation to work and leisure activities. Surgical decision making is currently dependent on surgeons’ evaluation of the relative merits of ankle replacement and arthrodesis. The evidence in support of ankle replacement in Haemophilia is confined to a few small case series (CEBM Level 4), and the most recent of these studies will be reviewed (1–3). Strauss et al (1) reported 11 ankle replacements in 10 patients aged 37–59 years with a follow up 1.2–5.4 years (mean 3 years). Nine patients were Hep C positive and 5 HIV positive. Two ankles developed deep infection requiring removal of the joint replacement. Satisfactory pain relief is reported in the remainder. Barg et al (2) reported 10 ankle replacements in 8 patients aged 26–57 years with a follow up 2.7–7.6 years (mean 5.6 years). Satisfactory pain relief is reported in all patients. Asencio et al (3) reported 32 ankle replacements in 21 patients aged 24–67 years with a follow up of 2.2–9.4 years (mean 4.4 years). Two were revised to arthrodesis because of persistent pain or loosening. Remaining patients had satisfactory pain relief. It is pertinent to review a large multicentre study comparing the outcomes of ankle replacement and ankle arthrodesis in the management of ankle arthropathy (4) (CEBM Level 3). Whilst in the early years the outcome of ankle replacement and arthrodesis are comparable, it is evident that complications continue to arise following ankle replacement where there is a steadily increasing need for revision surgery in the medium to long term. There is “level 4” evidence to show that ankle replacement can be of value in the short term, but there is level 3 evidence to indicate that this option should be used with caution in the likely expectation of the need for revision surgery in the longer term. Whilst there have been significant advances in ankle replacement surgery, given the current situation, arthrodesis will probably remain the treatment of choice for the majority of patients with haemophilic arthropathy affecting the ankle joint, but criteria need to be determined to identify individuals with a good chance of gaining long term benefit from joint replacement.

Reference List


Post-operative pain management strategies for musculoskeletal surgery: From pills to blocks

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There is no high quality evidence for best practice in pain management of haemophilia patient’s peri-operatively1. Large-scale surveys suggest haemophilia patients suffer with significant pain chronically and acutely2 but despite calls for research in this field randomized control trials are lacking3. Best practice statements highlight the safe use of non-steroidal anti-inflammatory drugs and cyclo-oxygenase inhibitors, as well as a World Health Organisation style pain ladder4. In recent years acute pain research, in general, has focused on comparative studies on local anaesthetic types, concentrations, and single shot versus catheter regional anaesthetic techniques5–9. These heterogeneous studies have tended towards operation-based research, for instance what’s the best technique for a total knee arthroplasty (TKA)? There is though, a rare but significant risk to regional anaesthetic techniques that are present in the general population but heightened in haemophilia sufferer10. Adjuvant analgesics have been studied, looking at the benefits of the peri-operative use of gabapentinoids, NMDA-antagonists, lidocaine and alpha agonists, with favourable outcomes such as reduced post-operative opioid requirements and improved patient satisfaction. All these have helped us in our peri-operative pain management but they have yet to show significant improvements on the incidence of chronic post-operative pain11 and do tend to increase both the financial and morbidity burden. Have we missed the point then? The majority of patients have good functional and pain outcomes following surgery, but a few patients, 6–15%1, go on to suffer significant persistent pain, disability and have associated high healthcare costs post-operatively12. A meta-analysis published this year in The British Journal of Anaesthesia13 has analysed the factors that predict persistent pain following TKA. Twenty-eight studies were included in this meta-analysis, and uni-dimensional and multi-dimensional outcomes were looked at from 3 months post-operatively to 7 years. The authors highlighted a moderate risk of bias based on lack of justifications of samples sizes and inadequate information on drop outs, but concluded that

at doses known to establish long-term bacterial infections. A novel, “smart” polymer using a poly(ethylene glycol) - propylene sulfide polymer (PEG-PPS) coating was then designed to combine passive antibiotic release to the local microenvironment with an active release mechanism in which reactive oxygen species created by the presence of infection encourage additional local release of antibiotic. This was compared to existing coatings.

Results: Antibiotic-based polymer coatings significantly reduced bacterial burden on the implant and in the surrounding tissue. Coatings with tigacyclione showed better bone penetration than those with vancomycin, with lower bacterial burden on the pin at all-time points. PEG-PPS coatings with active release showed more efficacies in eradicating infection than passive release coatings and nanosilber-based coatings in this model. Conclusion: Antibiotic linked implant coatings such as the one tested in this study provide a very promising approach to preventing periprosthetic infection. Further studies in larger animals and eventually human subjects are needed. Patients with hemophilic arthropathy remain a high-risk population with much to gain from the development of anti-infective technologies.

Abstracts
Interleukin-1beta drives blood-induced cartilage damage, not tumor necrosis factor-alpha: a new target for therapy?

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Objective: To unravel the role of interleukin (IL)-1b and tumor necrosis factor (TNF)-a in blood-induced cartilage damage, we investigated whether blocking IL-1b or TNF-a can prevent cartilage from blood-induced damage in vitro. Methods: Healthy human cartilage explants were cultured for 4 days in presence/absence of 50% whole blood. An IL-1b monoclonal antibody (IL-1bmAb), IL-1 receptor antagonist (IL-1RA), or TNF-amAb was added during blood exposure. Furthermore, IL-1bmAb or IL-1RA was administered directly or after a delay of several hours up to 2 days. Proteoglycan turnover was determined after a recovery period of 12 days. In 4-day whole blood cultures the effects of IL-1bmAb, IL-1RA, and TNF-amAb on the levels of IL-1b, IL-6, and TNF-a were determined. Results: Exposure of cartilage to blood severely impacted proteoglycan turnover. Addition of IL-1bmAb or IL-1RA resulted in a clear dose-dependent improvement in proteoglycan turnover up to normalization in the higher concentrations (see figure A for proteoglycan synthesis). In contrast, addition of a TNF-amAb, although demonstrated to inhibit the direct effects of TNF-a on cartilage, exhibited no effect on blood-induced cartilage damage (see table). The protective effect of IL-1bmAb or IL-1RA was most pronounced when administered within 8 hours after the bleed (see figure B for proteoglycan synthesis). Blocking IL-1b reduced IL-6 (~97% and -99%; both p<0.028 compared to blood only) and IL-1b levels (~99%; p=0.028), but did not affect the levels of TNF-a (+5% and +0% compared to blood only; both p=0.753) in whole blood cultures. Moreover, the TNF-amAb did not affect IL-6 or IL-1b levels (~3%; p=0.753; and ~5%; p=0.345 respectively). Conclusions: This study demonstrates that IL-1b is a crucial factor in the development of blood-induced cartilage damage in vitro, whereas TNF-a is indicated not to be elementary. This key role of IL-1b results at least partly from regulating the production of other pro-inflammatory cytokines, including IL-1b itself and IL-6. As therapeutic agents opposing the activity of IL-1b are readily available, further research is warranted to investigate its in vivo capacity in prevention and treatment of joint damage upon joint bleeding.

### Table: TNF-amAb cannot prevent blood-induced cartilage damage

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<th>PG synthesis (nmol/h*g)</th>
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Proteoglycan turnover in the absence (control) or presence of blood with or without TNFαs-mAb (10 mg/mL), expressed as median (IQR) (n=5 independent cartilage and blood donors).

P-values are compared to control conditions.
Background: Gait analysis may be useful in hemophilia care as it evaluates patients during a weight-bearing and dynamic situation. Additionally, it integrates the impact of multiple-joint arthropathy or muscle bleeds in contrast to separate joint assessment. Gait analysis is laborious and therefore expensive, however a novel, easily applicable, portable device named GaitSmart™ seems promising in different fields. Its applicability in hemophilia has not yet been assessed. Objective: To establish whether GaitSmart™ detects gait abnormalities in hemophilia patients. Methods: Hemophilia patient’s ≥12 years without recent joint or muscle bleeds, able to walk without assistive devices were included after informed consent. GaitSmart™ assessment consists of six sensors applied on the lateral sides of calves, thighs and pelvis and a stroll up-and-down a corridor (20m). Specific software that selects the most representative stride is used for gait analysis. Gait parameters included pelvis, hip, thigh, knee and calf range of motion; medial-lateral movement; stance flexion; joint symmetry and stride duration. The Hemophilia Joint Health Score (HJHS) was concomitantly performed by a trained physical therapist. Results: We included 106 patients, 29 of whom (27%) had arthropathy (table 1). Patients with clinical signs of knee or hip arthropathy (median HJHS 9, IQR 3-11) had corresponding gait deviations. Gait parameters in ankle arthropathy patients were within normal limits. Of 26 patients with an HJHS of lower limbs=0, 4 demonstrated deviating gait parameters. This was mainly caused by medial-lateral movement aberrations, slow stride duration or hip/thigh problems, parameters not well reflected by the HJHS (figure 1). Conclusion: This exploratory study suggests that GaitSmart™ assessment provides complementary information to the HJHS and is able to identify hemophilia patients with joint-specific arthropathy of hip and knee. However, the current sensor set-up does not seem to detect ankle arthropathy very well. Relevance and applicability to hemophilia care: Gait analysis provides objective information on patient’s functional musculoskeletal status and may be used to substantiate physiotherapy exercises, monitor bleed recovery or arthropathy progression. Gaitsmart enables rapid and efficient extensive gait analysis which can be performed during regular outpatient visits.

Rehabilitation after joint replacement surgery in haemophilic arthropathy: a retrospective analysis of twelve years’ experience on 181 admissions

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Aim of the study: to evaluate the effect of rehabilitation of the largest Italian experience after total joint replacement and others major surgical procedures in patients with haemophilia (pwh) on rescuing motor performance, autonomy in ADL and Quality of Life (QoL). Methods: the level of disability has been evaluated through the Barthel Index (BI). Pain level was determined with an eleven points Visual Analogue Scale (VAS), range 0 to 10, and Quality of Life (QoL) through EURO-QoL-5D. Evaluation included clotting factor’s consumption during rehabilitation and analgesic drugs use. Joint passive ROM (PRM) was measured through a hand inclinometer at the beginning and at the end of rehabilitation (by GIMA spa, Gessate, Italy) and it was considered the outcome measure for impairment. During the treatment period the intensity and the type of rehabilitation have been monitored through a daily clinical report. Results: between June 2003 and December 2013, 172 patients with haemophilia, for a total number of 181 hospital admissions, have been observed in the study time. Clinical features of patients are depicted in Table 1. Patients underwent to 2.7±2.1 hours/day of rehabilitation during an average length of stay (LOS) of 24.5±9.2 days. Over all patients presented an average improvement in disability (BI 68.9±39.3 vs 83.2±43.0 points, +34%, p<0.05), in PROM for TKR (from 40.4±24.0 to 77.0±33.6° in flexion and from 10.0±9.8 to 4.9±9.5° of extension deficit; +72%, p<0.05) and for THR (from 55.0±22.6 to 84.8±18.6° in flexion and from 5.0±8.5 to 0.9±5.4° of extension deficit; +33%, p<0.05) and for THR (from 55.0±22.6 to 84.8±18.6° in flexion and from 5.0±8.5 to 0.9±5.4° of extension deficit; +33%, p<0.05), in quadriceps strength (+1.4 according to MRC), pain (-2.5 points in VAS, p<0.05) and QoL (54.9±17.1 vs 75.2±16.3, +20 points, p<0.05) (Tab.1). Clotting factor consumption is summarized in Tab.2. Relevance and applicability to hemophilia care: our study describes one of the largest experiences in rehabilitation after major surgical procedures in pwh and furnishes a reference database for clinicians involved in rehabilitation process of pwh. Clinicians can find references about perceived quality of life of pwh after major surgery. Originality of the work: the results of rehabilitation are presented according to ICF framework and propose a standard functional evaluation dataset for future works and other clinicians.

Usefulness of musculoskeletal ultrasonography for early diagnosis of haemophilic synovitis—the results from the comprehensive health check for haemophilic patients

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The objective of the work: Musculoskeletal ultrasonography (MSUS), especially power Doppler ultrasonography (PDUS),
has become an essential diagnostic tool in clinical practice of rheumatic diseases, because it is sensitive modality for testing soft tissues including synovium, compared to X-ray. Also in the field of haemophilia, several fruitful reports have been published in recent years. We have introduced the comprehensive health check for haemophilic patients including MSUS to evaluate haemophilic arthropathy for the first time in Japan. The objective of this work is to verify the usefulness of MSUS for early diagnosis of haemophilic synovitis. The methods used: From 2012 to 2014, 88 joints (28 elbows, 30 knees and 30 ankles) in 15 haemophilic patients (13 haemophilia A patients and 2 haemophilia B patients) were evaluated by using gray scale ultrasonography (GSUS) and PDUS at the comprehensive health check for haemophilic patients. The severity of the haemophilic synovitis were evaluated semi-quantitatively by the scoring system proposed by Szkudlarek. In the scoring system, the findings of MSUS were graded from zero to three. The results of the intervention: Synovial hypertrophy and positive signal in PDUS were observed in 21 joints and 10 joints, respectively. In 21 synovial hypertrophic joints, 7 had no obvious clinical symptoms. Out of the 7 joints, 4 joints had positive signal in PDUS. The relevance and applicability to hemophilia care: The most remarkable finding of this work is the positive MSUS result in the asymptomatic joints. This emphasizes the importance of utilizing MSUS for the early diagnosis of haemophilic synovitis to prevent the progression of haemophilic arthropathy. The originality of the work: To the best of our knowledge, this work is the largest report of MSUS for the early diagnosis of haemophilic synovitis at comprehensive health check for haemophilic patients.

Developing an Understanding of the Impact of Exercise and Activity on Haemophilia

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Available guidance regarding exercise has emphasised the benefits of participation however specific guidance is lacking. Certain recommendations found in the literature require verification. Moreover, some recommendations appear to be based on the likelihood of catastrophic injury whereas other activities listed as acceptable may result in long term joint damage. A haemophilia literature review of the area produced little evidence of research into the real impact of specific sports or activities on haemophilia populations. A previously published Delphi Study investigating the potential of non-haematological factors to influence arthropathy development produced a group of factors relating to exercise and activity demonstrating how important this area is perceived to be. However, how they impact in a haemophilia population is unclear. An exploratory questionnaire has been developed based on these suggested factors. It examines historical exercise patterns, injury patterns and potential for unreported minor injuries. It gives an insight into the prescription of rehabilitation plans and the degree of concordance with the plans. Initial results will be presented and discussed in the context of available literature. Historical exercise results indicate that football (70%) is most likely to be played when joints are at their most developmentally vulnerable. Over 18 years, walking was the most common activity (80%). Rugby was the most commonly forbidden sport. 80% reported injuries in their most played sport. All reported sustaining minor injuries but not reporting them to the treatment centres; some self-treated with factor replacement and some assumed that injuries would just get better. Mean compliance with suggested rehabilitation programmes was 56.5%. The authors propose that activity recommendations should take place considering the effects of exercise in relation to catastrophic injury, potential to influence joint disease and potential to influence muscle bleeding versus the positive impact of exercise participation. This data can be derived from analysis of impact of sports on joint and muscle, and injury-to-exposure figures.

Deficit of functional ankle muscle strength is not found in young haemophilic patients with confirmed structural impairment

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Background: Children and adolescents with haemophilia (C&AwH) experiencing recurrent ankle bleeds are at risk to develop a target joint with subsequent functional deficit such as loss of muscle strength. However, conflicting conclusions can be found in the literature as regard to the extent of strength deficit in C&AwH probably because joint status was not confirmed by gold standard tool. Objective: To evaluate isokinetic ankle plantar flexors (PF) and dorsi flexors (DF) muscle strength of C&AwH and using the IPSG-MRI scale to define the extent of structural damage at both tibio-talar (TTJ) and sub-talar joints (STJ) level (consensus score provided by two blinded radiologists). Material and methods: Peak torque (PT) of DF and PF of 24 C&AwH (13.6±4.3 years, 21 HA, 3 HB, 19 severe, 5 moderate) were compared at 30 and 120°/sec with normative data established in 44 control healthy subjects (14.7±4.5 years) using multiple linear regression models including explanatory variables such as age and anthropometric characteristics. In a subgroup of 10 C&AwH, it was also possible to compare directly the affected (positive MRI-score) to the unaffected side. Results: Forty-six ankles were assessed for both MRI and isokinetic strength. Twenty-one ankles showed a positive TTJ and/or STJ MRI-score (MRI-score 4.8±4.1 and 2.5±3.1 respectively). Surprisingly, no difference was observed in PT for PF and DF at both speeds between normative values and both affected (N=21) and unaffected (N=25) ankles. This held true with the stricter positive MRI criterion of presence of positive osteochondral subcore (N=12). Furthermore, within the subgroup of C&AwH with an unaffected and affected ankle, no PT difference was neither observed between both sides although a significant difference in call circumference was measured (33.5 Vs 32.9 cm respectively, P=0.038). Conclusions: No ankle muscle strength deficit was found in C&AwH with evidence of structural damage.
These results suggest the presence of a possible delay between joint structural impairments and repercussion on muscle function. These results have also to be considered with caution as an absence of significant difference between C&AwH and normative data could be induced by a possible high inter-individual variation in muscle function in both normal and haemophilia population.

FP02–Free Papers II–Surgical

Primary total knee arthroplasty in haemophilia: a long-term experience with modern implants

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Introduction: Knee is the typical target of haemophilic arthropathy, representing the most frequent and disabling orthopaedic affection in these patients. Several treatments for all stages of arthropathy have been proposed with acceptable results. However, late stages of arthropathy need an unique solution, the Total Knee Arthroplasty (TKA). This is an established and validated procedure with smaller rates of complications with respect to the past. However it is a challenging surgery. Moreover, patients are often very young and during the decades the necessity of implants with a lower tendency to wear and better performance has arisen. Several series have been recently reported with very good outcomes but a significant rate of failures mainly related to aseptic and septic loosening, particularly in coinfected subjects. The aim of this study is to report the mid- to long-term evaluation of outcomes of TKAs with a modern implant with specific characteristics different from the standard used in other series. Methods: Forty-eight haemophilic patients underwent a TKA and followed by a multidisciplinary team dedicated to Haemophilia between 2001 and 2013. Sixty TKAs were performed. Eleven patients underwent a staged bilateral procedure with a 12-months interval; one patient underwent a simultaneous bilateral replacement. Thirty patients had Haemophilia A (7 with inhibitors), ten a Haemophilia type B (no one with inhibitors): in all cases a severe deficiency of factor was present. The mean age was 31.2 years (range: 23-58), and the mean Pettersson score was 10.1 (range: 9-13). A single modern implant was used (Genesis II®, Smith & Nephew, USA), characterized by a cemented Oxidized Zirconium femoral component and a titanium fixed bearing tibial component with cemented baseplate and pressfit keel. The mean preoperative functional ability evaluated by the Haemophilia Joint Health Score was 10.6 (range: 9-20). Results: At a mean follow-up of 8.3 years (range: 2.2-14.1 years), we recorded a single mechanical failure of the femoral component of an implant in a patient with inhibitors after a series of haemarthrosis: a revision 38 months after the index procedure was performed with no more complications. No cases of infection were recorded. All patients improved in their function and were satisfied. The mean postoperative functional score was 1.8 (range: 1-4). Conclusions: A close cooperation of a multidisciplinary team and the use of implants with modern biomaterials, excellent outcomes and few complications may be achieved in the management of the haemophilic arthropathy of the knee.

Critical study and medium term results of 40 ankle prostheses in 27 patients with hemophilia

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Recurrence of bleeding in the same joint leads to changes in inflammatory with synovial proliferation, degenerative arthropathy gradually forming the ankle is the target joint in childhood resulting from successive repetitions deformations foot / ankle, having repercussion in the long run on the poli articular chain of lower limb. The treatment was previously admitted ankle arthrodesis leading to good results. Pain, bleeding but zero mobility. Since 2002 we opted for that TAR conserve mobility, restores the bearing, rotation and protects other above and underlying joints. TAR poses particular problems: to prevent perioperative bleeding during rehabilitation, the time capsule and synovium are recovering OurExperience: 40 TAR 27 patients (13 bilateral) age 24-67 years 2 prostheses were used: AES and HINTEGRA Only 1 orthopedic surgical center and 2 senior surgeons specialist of this surgery the CRTH Montpellier totally managed prescribing factors. All patients were evaluated before and remote surgery functionally clinically and radiologically. The AOFAS and AFCP were scores evaluation used: Results: from 2July 2002 to September 2009 27 patients so 40 with TAR; 7 HIV positive patients Preoperative score 30 post-operatives score 81 Complications: 2 revisions by arthropdesis tibiotalar Intermediate Outcomes 81/100. We develop the advantages and difficulties of this surgery.

Total ankle replacement in hemophilic patients: a single centre experience

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From early childhood, the joints are the most common site of bleeding in haemophilics. Hemarthroses tend to recur at the same site causing structural damage that gradually involves synovium, cartilage and bone leading to chronic arthropathy. The availability of safe and effective clotting factor concentrates enables orthopaedic surgeons to perform elective surgery. Nevertheless, few studies have examined orthopaedic complications and outcomes in hemophilic patients treated for end-stage ankle arthropathy with total ankle replacement (TAR). To determine the clinical presentation, intraoperative and postoperative complications and evaluate the mid-term outcome in such patients treated with TAR. 29 patients with hemophilia with median age of 35 years (range = 24-54) were treated for end-stage ankle OA with 33 TAR performed by the same surgeon. The median duration of follow-up was 3 years (range = 0.5-8). Intraoperative and perioperative complications were recorded. Component stability was assessed with weight-bearing radiographs. Clinical evaluation included range of motion (ROM) tests using a goniometer. Clinical outcomes were analysed by a visual analogue scale, the American Orthopaedic Foot and Ankle Society hindfoot score and the Post Operative Italian Score (POIS) a patient
self-assessment questionnaire. Three patients sustained an intraoperative lateral malleolar fracture. In 10 patients delayed wound healing was observed and 2 early infections occurred and treated with open debridement. One secondary major surgery was performed for aseptic loosening. Median pain level decreased from 8 (range = 7-10) preoperatively to 1 (range = 0-4) postoperatively. Significant functional improvement including ROM was observed. All categories of POIS score showed significant improvement. Mid-term results of TAR in patients with hemophilia are encouraging. The total rate of intraoperative and postoperative complications was 10%. However, longer term outcomes are necessary to fully understand the clinical benefit of TAR in patients with hemophilia.

**Patellofemoral joint changes in hemophilic Arthropathy**

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**Aim:** To evaluate the anatomical changes in the patellofemoral joints of hemophilic patients radiologically and compare them to normal population. **Materials and Methods:** In this retrospective study 32 knees of 23 hemophilic patients (mean age: 30.84±12.48) were included; 42 knees of 42 patients (mean age: 31.38±10.72) who had undergone a magnetic resonance imaging for reasons other than patellofemoral symptoms were regarded as healthy controls. Dimensions of patella (mediolateral length and anteroposterior width) and distal femur (length of transepicondylar axis (TEA), lateral femoral condyle (LFC), length between the deepest point of patellar fossa and roof of intercondylar notch (notch depth, ND)), and sulcus angles were measured on axial magnetic resonance imaging or computed tomography sections. Results were adjusted according to the magnification ratios. Statistical analyses were performed utilizing SPSS v18. Independent samples t-test was utilized for comparisons between hemophilic patients and healthy controls. **Results:** Mean length and width of patella were 43.42±7.01 mm and 19.55±6.72 mm, respectively in the hemophilic group; and 48.39±6.67 mm and 26.19±1.80 mm, respectively in the control group. Length and width of patella were found to be significantly shorter in the hemophilic group (p values 0.001 and <0.0001, respectively). Mean length of TEA, LFC, and ND were 80.71±10.96 mm, 56.11±11.01 mm, and 26.72±8.49 mm respectively in the hemophilic group (89.58±4.75 mm, 67.31±2.79 mm, and 36.44±2.37 mm, respectively in the control group). Length of TEA, LFC, ND were significantly shorter in the hemophilic group (p values <0.0001). The mean sulcus angle was 128.12±15.82° in the hemophilic group, and 139.57±3.78° in the control group (p<0.0001). In the hemophilic group LFC was minuter, patellar fossa more deepened. Patellar tilt was present in 15 hemophilic knees (46.9%); six of which were medial and nine were lateral tilt. **Conclusion:** Morphological changes develop in the patellofemoral joints of knees with hemophilic arthropathy. Smaller size of LFC, deepening of patellar fossa and narrowing of length between patellar fossa and notch (ND) shows that bone stock is diminished in knees with hemophilic arthropathy. These should be regarded as important anatomic considerations especially when planning total knee arthroplasty.

**Bilateral total knee arthroplasty in patients with hemophilia: A safe and cost-effective procedure**

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**Introduction and Objectives:** Hemophilic arthropathy of the knee is usually a bilateral affliction. The patients usually refer for treatment in ages younger than osteoarthritic patients and do not have major comorbidities, being fit for bilateral simultaneous total knee arthroplasty. TKA is an expensive surgery especially in hemophilia patients. This study, we assess the safety and cost-effectiveness of simultaneous bilateral surgery in this patient population. **Materials and Methods:** A prospective case-control study was performed from April 2010 and April 2013 in which 8 patients (16 knees) underwent bilateral simultaneous and 19 patients (19 knees) underwent unilateral TKA with the same technical details. The range of knee motion and flexion contracture, KSS knee score, SF36 score of quality of life and WOMAC score was recorded for all patients. The duration of hospital stay and coagulation factor consumption was recorded. The need and the amount of transfusion were also recorded. All patients were followed for at least 6 months. **Results:** At the conclusion of the study, the KSS and WOMAC knee scores and SF36 score were not significantly different between the two groups. The mean consumption of coagulation factors was similar in two groups (150 vials in bilateral and 145 vials in unilateral group). Mean ROM and flexion contracture did not differ significantly in patients with bilateral procedure. The mean length of hospital stay was 15 days for bilateral patients and 12 days for unilateral patients, the difference being non-significant. None of our patients needed transfusion in any group. One patient in bilateral group developed superficial cellulitis in on knee, which resolved with wound care and antibiotic treatment. **Conclusion:** Bilateral simultaneous TKA seems a safe and cost-effective procedure in selected patients with hemophilic arthropathy. Our data did not show significant difference in outcome of the two groups. Considering the fact that unilateral patients will have to undergo another surgery for the contralateral knee, the factor consumption and length of hospital stay would be doubled compared to bilateral patients, significantly increasing the burden of the procedure. We recommend bilateral simultaneous TKA in selected hemophilia patients without the fear of increasing complication rate.

**MP-101**

**Cementless total hip arthroplasty in haemophilia: A step forward**

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**Introduction:** Hips do not represent typical targets of Haemophilia, but a hip altered by an arthropathy is disabling similarly to knees, ankles, and elbows in haemophilic patients. A Total
Hip Arthroplasty is often needed in case of severe arthropathy. Several series have been reported during the last decades with common features: small series, mid to long follow-up, cemented components, old generation implants with Ceramic-on-PolyEthylene bearings. Methods: Twenty-three haemophilic patients were treated by a cementless THA and followed by a multidisciplinary team dedicated to Haemophilia. Nineteen subjects had a Haemophilia type A, 4 type B. The mean age was 40.6 years (range: 28-60), and the mean Pettierson score was 11.3 (range: 10-13). Two modern models of THAs were used. The mean preoperative functional ability evaluated by the Haemophilia Joint Health Score was 12.5 (range: 10-22). Results: No failures and no complications were recorded at a mean follow-up of 8.1 years (range: 2.1-13.7 years). All the patients improved in their function and were satisfied. The mean postoperative functional score was 1.5 (range: 1-5).

Conclusions: By the close cooperation between haematologists, orthopaedics, and rehabilitative physicians, and by the use of modern generation implants and couplings, excellent outcomes and few complications may be achieved in the management of the hip haemophilic arthropathy.

MP-102
Joint lavage followed by viscosupplementation and triamcinolone in patients with severe hemophilic arthropathy – objective functional results

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Objective: To assess whether viscosupplementation in patients with severe hemophilic arthropathy associated with triamcinolone after washing with saline improves force and balance. Methods: Fourteen patients with knees hemophilic arthritis with and without involvement of other joints underwent joint lavage and subsequent injection of Hylan G-F20 and triamcinolone in all affected joints. The patients were evaluated with Neurocom® force and balance platforms for the following tasks: Step up and over (STP); sit to stand test (STS); one leg stance (UNI) and weight bearing squat (WBS) preoperatively, and at one and three, six and twelve months postoperatively. Results: Sixteen knees, 15 ankles, 8 elbows and one shoulder were treated. Six patients had musculoskeletal bleeding [ankle (1), leg muscles (2) and knee (4)] at 3 months affecting evaluations and results: STP showed improved lift up index for both right and left lower limbs in all moments (except 3 months postoperative) of evaluation (p=0.03 and p=0.02, respectively). STS results showed that the weight transfer mean (WT), the rising index mean and the average distance of the center of gravity to the central axis also improved significantly at 1, 6 and 12 months (p<0.001, p=0.002 and p=0.001, respectively). One leg stance showed improved speed with eyes opened or closed in most time points and specially at one year but were only significant for left and right and with eyes closed and left with eyes opened (p=0.02; p<0.001 and p=0.001, respectively). WBS improved in all degrees of flexion (0, p=0.001; 30°, p=0.001; 60°, p<0.001 and 90°, p<0.001).

Relevance and applicability to hemophilia care: This is an objective finding of the improved strength and balance of patients with multiple hemarthropathies subjected to joint lavage and infiltration with triamcinolone and Hylan G-F20. The originality of the work: This is the first description of the advantage of joint lavage finalized with Hylan G-F20 and triamcinolone infiltration in hemophiliacs registered by force and balance platform testing. Conclusion: Joint lavage followed by injection of corticosteroids and Hylan G-F20 improves balance and force even in severe hemophilic arthropathy.

Table 1. Multiple comparison results of the sit to stand test (STS) at baseline, 1, 3 and 12 months postoperatively.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison</th>
<th>Mean Difference</th>
<th>Standard Error</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline - 1 Month</td>
<td>0.31</td>
<td>0.12</td>
<td>0.07</td>
<td>6.32</td>
<td>0.94</td>
</tr>
<tr>
<td>Baseline - 3 Months</td>
<td>0.05</td>
<td>0.13</td>
<td>0.06</td>
<td>2.30</td>
<td>0.02</td>
</tr>
<tr>
<td>Baseline - 6 Months</td>
<td>0.01</td>
<td>0.11</td>
<td>0.05</td>
<td>1.09</td>
<td>0.31</td>
</tr>
<tr>
<td>Baseline - Year</td>
<td>0.04</td>
<td>0.13</td>
<td>0.04</td>
<td>3.09</td>
<td>0.00</td>
</tr>
<tr>
<td>VIT Transfer</td>
<td>1 Month - 3 Months</td>
<td>-0.05</td>
<td>0.13</td>
<td>0.04</td>
<td>3.09</td>
</tr>
<tr>
<td>1 Month - 6 Months</td>
<td>-0.04</td>
<td>0.14</td>
<td>0.02</td>
<td>2.91</td>
<td>0.04</td>
</tr>
<tr>
<td>1 Month - Year</td>
<td>-0.03</td>
<td>0.13</td>
<td>0.02</td>
<td>2.80</td>
<td>0.05</td>
</tr>
<tr>
<td>3 Months - Year</td>
<td>-0.01</td>
<td>0.13</td>
<td>0.01</td>
<td>2.69</td>
<td>0.04</td>
</tr>
<tr>
<td>6 Months - Year</td>
<td>0.00</td>
<td>0.15</td>
<td>0.00</td>
<td>2.45</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 2. Weight bearing squat (WBS) results according to moments of evaluation

| Variable | Moment | Mean | SD | N | IC (95%)
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>65.4</td>
<td>21.8</td>
<td>14</td>
<td>55.0</td>
<td>77.6</td>
</tr>
<tr>
<td>1 Month</td>
<td>54.2</td>
<td>6.7</td>
<td>13</td>
<td>47.6</td>
<td>54.9</td>
</tr>
<tr>
<td>3 Months</td>
<td>50.6</td>
<td>18.7</td>
<td>10</td>
<td>35.0</td>
<td>62.2</td>
</tr>
<tr>
<td>6 Months</td>
<td>52.1</td>
<td>5.4</td>
<td>12</td>
<td>49.9</td>
<td>55.1</td>
</tr>
<tr>
<td>1 Year</td>
<td>51.2</td>
<td>6.5</td>
<td>10</td>
<td>47.2</td>
<td>55.2</td>
</tr>
</tbody>
</table>

DEG 0

| Baseline | 70.2 | 27.0 | 14 | 56.1 | 74.3 |
| 1 Month | 52.6 | 16.4 | 13 | 43.7 | 61.5 |
| 3 Months | 52.8 | 19.5 | 10 | 40.6 | 65.6 |
| 6 Months | 46.2 | 11.3 | 12 | 41.8 | 54.5 |
| 1 Year | 45.0 | 7.4 | 10 | 43.4 | 52.6 |
| 3 Months | 75.5 | 23.8 | 10 | 61.5 | 80.6 |
| 1 Month | 47.7 | 11.9 | 12 | 40.5 | 52.9 |
| 3 Months | 57.6 | 25.2 | 8 | 40.2 | 75.1 |
| 6 Months | 51.7 | 9.4 | 9 | 45.6 | 67.8 |
| 1 Year | 47.9 | 11.8 | 8 | 35.7 | 56.1 |
| 6 Months | 81.8 | 20.4 | 4 | 61.8 | 100.0 |
| 1 Month | 50.6 | 13.6 | 7 | 40.5 | 60.6 |
| 3 Months | 41.4 | 11.0 | 5 | 31.7 | 61.1 |
| 6 Months | 52.2 | 11.1 | 8 | 44.6 | 59.9 |
| 1 Year | 49.6 | 11.3 | 7 | 41.2 | 57.9 |

DEG results: *Results limited to people who were able to perform the test in all these inclusion.
**MP-103**

First prospective results of joint distraction in severe haemophilic ankle arthropathy

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**Objectives:** Nowadays, the ankle joint is the most affected joint in youngsters with haemophilia. Joint distraction, an effective treatment in ankle osteoarthritis, has the advantage of preservation of the original joint without compromising subsequent conservative surgeries like arthrodesis, if still needed. In three cases evaluated in retrospect, good clinical and structural efficacy in haemophilic ankle arthropathy was demonstrated. The aim of the current study is to gather prospective data on clinical effectiveness and tissue structure changes in haemophilia. **Methods:** Haemophilia patients (n=10; ≥18 and <45 years) were eligible in case of severe complaints of arthropathy in the tibiotalar joint causing functional limitations, despite analgesics and conservative treatment. Ankle joint distraction using an Ilizarov external fixator was performed during 10 weeks. Clinical effectiveness was evaluated using standard questionnaires and physical examination. Functional tests, X-ray and MRI examination were performed at baseline and 1-year follow-up. **Results:** A 12 months follow-up is available in 3 patients. Age at time of surgery ranged from 22 to 33 years. During distraction, none of the patients experienced bleeding. Pin tract infection, commonly seen with external frame use, occurred in 2 patients, and was treated effectively with oral antibiotics. Pain (visual analogue scale) decreased from 65 (47-76) mm at inclusion to 6 (7-84) mm at 6 months and 12 (1-43) mm at 12 months follow-up. Functional limitations, measured by the Haemophilia Activities List and the Ankle Osteoarthritis Scale, improved in two patients in 6 months, and in all three patients at 12 months. Functional tests improved considerably in all patients at 1-year follow up (e.g. 6-minutes walking test increased from 560 (434-560) to 660 (574-688) meters). MRI revealed a decrease in volume of subchondral cysts and bone edema in all patients, and slight improvement of the joint space width in one patient (see figure). **Conclusion:** This first prospective study investigating the efficacy of joint distraction in haemophilic ankle arthropathy, showed clear clinical and structural improvement in all patients at 1 year follow-up. Although preliminary, these data indicate that joint distraction may be a promising treatment postponing more rigorous surgery like ankle arthrodesis in those patients not benefiting from conservative therapy.

**MP-104**

Total joint replacement in haemophilia A complicated by factor VIII inhibitor: A single centre experience

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**Objective:** Total joint replacement in patient with haemophilia complicated by high titre inhibitor is rarely undertaken. Our aim is to present the early results of joint replacement in this group of patients. **Methods:** From 2010 to 2014 five total joint replacements (4 knees and 1 hip) in 4 hemophilia A patients with high titer inhibitor were performed. Average age was 38.2 y (38–41y). Mean inhibitor titer was 251 BU/ml (3,9-563). In the “knee group” average preoperative Knee Society Score (KSS) (0-200), was 61; average Knee Score (0-100) - 24.75; average Function Score (0-100) – 36.25 and average Visual Analogue Score (VAS) (0-100mm) was 65mm. In patient with arthrophic hip the preoperative Harris Hip Score (HHS) (0-100) was 50.1, VAS – 50mm. In 3 knee procedures we used standard PFC Sigma implants (Johnson&Johnson), in one knee – PFC Sigma implant with prolonged stems and femoral augments was applied. In a patient with hip arthropathy the short-stem Proxima (Johnson&Johnson) implant was used. Perioperative hemostasis was achieved by administration of recombinant activated FVII (rFVIIa, NovoSeven) followed by activated prothrombin complex concentrates (APCC) (FEIBA, Baxter) during rehabilitation. **Results:** Average blood loss was 1429 ml (625-2510). The average number of red blood cell units transfused per procedure was 4 (2-7). Average hospital stay was 27.8 days (17-47). There were 2 cases of prolonged wound bleeding. There was one major complication – an ischemic stroke with hemiplegia that occurred on 11th postoperative day. At mean 1.8 years following knee surgery the average KSS was 136.25 (200), average Knee Score – 86.25 (0-100) and average Function Score – 50 (0-100). The latter result was strongly influenced by the hemiplegia (Function Score 5). Average VAS was 12.5 mm (10-20mm). In the patient with hip prosthesis 2.8 years following surgery the HHS increased to 96.9 (0-100) and VAS was 0mm. **Conclusions:** Total joint replacement is the method of choice in the treatment of end-stage arthropathy. Major surgery in patients with hemophilia complicated by high titer inhibitors are risky in terms of severe bleeding complications, nevertheless by-passing agents effectively prevented major bleeding in our patients. One should keep in mind however; that apart from bleeding, ischemic complications related to by-passing agents may occur.

**MP-105**

Total hip arthroplasty in patients with haemophilia

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1Department of Orthopaedic Surgery and Traumatology, Dr. Juan A. Fernández General Hospital; 2Haemophilia Foundation, Buenos Aires, Argentina

**Introduction:** Haemophilic arthropathy is a major problem that affects patients with haemophilia (PWH). Arthropathy of the hip is moderate in frequency in haemophilic patients so there is very few information about it in this particularly population. **Aim:** The purpose of this study was to review the results of total hip arthroplasty performed for haemophilic arthropathy at one single centre in the last 45 years. **Methods:** Thirty seven patients with forty one total hip replacements were performed in the Haemophilia Foundation in Buenos Aires, Argentina between 1969 and 2014. Thirty three men patients were haemophilia type A, three type B and one female carrier of the disease type B. The mean age was 42.3 years old (11-78). Were divided in 2 groups: 1969-1981 cemented arthroplasty (15 hips); 1993-2005 cemented or hybrid arthroplasty (26 hips, 18 non cemented...
Validation of the HAL questionnaire (Haemophilia Activities List) about perception of functionality in adults of a Program in Cali in 2014

A. Orajuela Upegui1, J. Humberto Ramírez2, J.M. Restrepo Avenia3, An. Fandino-Losada4

Objective: Validate HAL (Haemophilia Activities List) questionnaire measuring perceived functional ability in adults of a Program in Cali in 2014. Methods: A translation-retro translation process and cultural adaptation, writing and clarifying the questions. Then, a questionnaire of 42 items was applied to 73 patients with abnormal coagulation. Exploratory factor analysis (EFA) was performed to determine the validity of scale constructs and Cronbach alpha for the internal consistency of each one. The EFA was performed by analysis of principal factors and oblique rotation (promax) with loads greater than 0.5, and a “gray area” with loads between 0.37 and 0.49 by factor. Results: The measure of sampling adequacy (KMO) was 0.86. After testing the questionnaire with patients, 10 items did not fit culturally and they were withdrawn. From the remaining 32 items, three factors (domains) were finally extracted by EFA, which are: 1. Locomotion and leisure time, 2. Trunk, hip and lower limb, 3. Upper limb, dressing and home tasks. The Cronbach alpha for each domain was 0.95; 0.93; 0.86, respectively, showing good internal consistency. This study suggests a factorial structure which differs from the original one, with seven domains, but the current structure renders better psychometric properties for the Colombian population. Relevance: To have a self-rated instrument for functionality assessment is necessary for intervention plans according to needs and interests of each patient. Originality: The HAL is proposed by the World Federation of Hemophilia as an evaluation tool, no psychometric data of this scale for Spanish speaking population are known. This work was approved by both the ethics committee of the University of Valle, Colombia (as a Master thesis of Epidemiology) and the ethics committee of the Medical Center Imbanaco, Colombia.

Ankle arthropathy in hemophilia: At what age does it begin?

K. Mulder

Winnipeg, Manitoba

The CHPS study was a multi-center study that collected detailed data on a large cohort of boys beginning at age 1. Joint health was assessed using the Hemophilia Joint Health Score (HJHS). Study data, [Date of Visit, Months since baseline assessment, Age at visit, Presence/absence of active bleeding, Joint scores for left and right ankles, elbows and knees], was obtained on 56 subjects in order to perform secondary data analysis. Study period ranged from 6 to 17 years. For 69% of subjects, data is available for 10 years or more. Joint scores for each ankle will be plotted against age.
at assessment to investigate how many subjects showed clinical signs of ankle joint involvement (joint scores >1) during the study period, average age at which elevated joint scores appeared, and whether joint scores returned to baseline or remained elevated. Preliminary inspection of the data indicates that in several subjects there appear to be two spikes in joint scores; the joints seem to recover after the first spike, but scores remain high following the later spike. In these cases, further analysis will be done to see if their prophylaxis frequency was escalated and if this had any effect on the joint scores at subsequent visits. This study is important because to date there have been no longitudinal studies where joint health is measured in such detail. Much of the literature regarding the ankle joint in hemophilia describes arthropathy once it is established and suggests strategies to lessen its impact on function. It is known that radiological scores are not reversible; it is unknown whether clinical scores are reversible. The information gathered from this study could have significant implications for management during critical periods of growth and development. It may be possible that, with attention to subtle clinical findings and carefully timed interventions, development of ankle arthropathy may be delayed or even prevented.

**MP-109**

**Current joint health status of patients with haemophilia in London in 2014: A multi-centre retrospective review**

P. McLaughlin, M. Bladon, V. Patel, V. Roffi, N. Hubert, C. Richards, T. Bhandari, S. Classey

1 Haemophilia Centre and Thrombosis Unit, Royal Free London NHS Foundation Trust; 2 Haemophilia Centre, Great Ormond St Hospital; 3 Haemophilia Centre, The Royal London Hospital, Whitechapel; 4 Haemophilia Centre, Hammersmith Hospital; 5 Haemophilia Centre, St George’s Hospital; 6 Haemophilia Reference Centre, St Thomas’ Hospital NHS Foundation Trust, London, UK

**Background:** As part of specialist commissioning for Haemophilia care, NHS England have recommended that at least 50% of patients have a joint score and assessment carried out in 2014. Although it is well recognised that regular joint assessment for those on primary prophylaxis can highlight subtle changes in joint health, it remains unclear if it is useful to do on individuals with well-established joint damage. In 2013 physiotherapists working in Haemophilia care in the UK attended a workshop on the Haemophilia Joint Health Score (HJHS), thereby establishing a common competency framework for its use. **Objectives:** To identify the number of joint scores completed in the haemophilia patient population in London and determine the current state of joint health in this population in 2014. **Methods:** Six Haemophilia centres (adult and paediatric) in the London area were identified and agreed to participate. Data collection was a retrospective review of assessments between 1st April 2013 and 31st March 2014. Completed HJHS assessments with patient demographics were collated. No patient identifiable data was included with the assessments. **Results** The HJHS of 579 (494 severe, 85 moderate) patients (A and B) were collated, (age range 4 to 92). Almost 80% of registered patients with severe and moderate haemophilia had a joint score completed. Of this cohort, 26% (N=151) had a HJHS of zero. Almost 50% had a joint score recorded between zero and 6 (n=271). The average joint scores for those on primary prophylaxis was 3.2, increasing to 22 for those on secondary prophylaxis. The most affected joint in this cohort was the ankle, followed by the elbow and the knee. The elbow and ankle was found to be most affected in the moderate cohort. **Conclusions and relevance to care:** The joint health for a significant portion of this cohort would appear to be good. The wide variation in scores and age of patients highlights the need for the HJHS to be used alongside other clinical measures and assessments. This dataset may be useful in trying to benchmark the joint health of other cohorts of patients in the UK and further afield.

**MP-110**

**Physical activity in adults with severe hemophilia: What happens after a year of individualized prophylaxis?**

**S. Squire, S. Jackson, P. Camp**

1 BC Bleeding Disorder Program (adult division); 2 Centre for Heart Lung Innovation, Dept of Physical Therapy, U.B.C, Vancouver, Canada

**Objective:** Adults with severe hemophilia are reported to be less physically active than adults without hemophilia resulting in a sedentary lifestyle, which negatively impacts joint health. There is a paucity of studies evaluating objective measurements of physical activity in adults with hemophilia. Individualized prophylaxis may increase physical activity by reducing the number of yearly bleeds. This research investigated if a long-term individualized prophylaxis regime would increase physical activity in adult patients with hemophilia. **Methods:** Consenting adults with severe hemophilia A already on prophylaxis were recruited and started a new highly individualized prophylaxis regimen. Baseline activity was assessed using an accelerometer-based sensor system (Sensewear Pro Armband™) worn 24 hours/day for 7 days and repeated 12 months after initiation of individualized prophylaxis. Physical activity data was collected including total energy expenditure (kJ), active energy expenditure (kJ), minute-by-minute energy expenditure (METs), and number of steps. The patients were informally asked about the experience of wearing the accelerometer. **Results:** 8 patients participated with a median age of 23 years (range 21-33). After one year of individualized prophylaxis; (3 PWH daily, 5 PWH 3x/week); total energy expenditure increased 14096 kJ to 15099 kJ active energy expenditure (METS) increased 23%, time spent in physical activity increased from a range of 0:38:4:28 minutes to 0:55-4:45 minutes. Number of steps increased 24% from a daily average of 6336.18 to 8343.94. The majority of the patients wore the Sensewear an average of 20 hours/day over the 7-day period. Patients reflected positively on the experience of wearing the accelerometer and the role of providing self-motivation for increasing physical activity; many patients continue to measure their activities through technologies such as personal activity monitors and mobile applications. **Relevance and Applicability to hemophilia care:** Benefits of an individualized prophylactic regime over a one-year period included an increase in physical activity manifested by more daily steps and active energy expenditure. Overall, long-term individualized prophylaxis with reduction of bleeds has allowed the focus of physiotherapy care to be about physical activity in a pro-active preventive role.
MP-201
Orthopaedic treatment of the haemophilic ankle arthropathy: A ten-year experience in a single centre
Orthopaedic Clinic, University of Florence, *Agency for Haemophilia and Inherited Blood Disorders, Azienda Ospedaliera Universitaria Careggi, Florence, Italy

Introduction: Ankles are common target joints of the haemophilic arthropathy leading to a severe disability and poor quality of life of affected patients. Conservative approaches as viscosupplementation are useful in early stages, as chemical synoviotrsis is an effective option in cases of acute synovitis. In late stages, a surgical treatment is often required as arthroscopy, joint fusion, or ankle arthroplasty. Aim of this study is to evaluate the long-term experience of a single Institution in the treatment of the ankle arthropathy in haemophilic patients. Materials and methods: 498 haemophilic patients were treated from 2000 to 2013 for a symptomatic arthropathy of the ankle, clinically and radiologically evaluated by the HJHS and Pettersson score respectively. 52 patients (69 ankles) were treated conservatively, presenting a mean HJHS of 10.72 and a mean Pettersson score of 8.0. (range 4-11). The mean age was 41.9 years (range 7-88). 14 patients underwent a surgical procedure after the failure of the conservative approach: 6 arthroscopies, 3 ankle arthroplasties, 7 joint fusions. The overall mean age at time of surgery was 33.4 years (range 24-46). Results: No complication was reported at the follow-up of 4.14 years for patients treated by injections. A substantial reduction of the mean HJHS score: from 10.83 to 7.88 in patients treated by HA injections and from 9.33 to 2.67 in those undergoing the chemical synoviotrsis. At the follow-up of 7.33 years in patients treated by an arthroscopy, the mean HJHS score improved from 10.67 to 8.5 points after surgery. A single complication was reported: a pseudoaneurysm of the anterior tibial artery in one case managed by a surgical vascular repair. Patients treated by a joint fusion presented an improvement of the HJHS from 14.2 to 10.0 at a follow-up of 6.5 years. Finally, the subjects undergoing an ankle replacement presented a mean preoperative HJHS of 15.5 reaching a score of 10.0 points 4.1 at a follow-up of 32.5 months. No complication was reported. All treated patients were satisfied of the results in all groups. Conclusions: Several surgical or conservative option are useful for an adequate treatment of the Haemophilic arthropathy of the ankle at different stages. Indications and hematological management by a dedicated and skilled multidisciplinary team is the key to achieve good outcomes in these patients with a very low rate of complications.

MP-202
Peri-operative haemostatic management of major orthopaedic surgery in haemophilia B with long-acting recombinant glycoPEGylated factor IX: Results from the paradigm™3 clinical trial
M. Escobar1, T. Colberg2, F. Karim1, U. Caliskan4,

P. Chowdary1, P. Giangrande6, A. Giemmsa7, M.E. Mancuso7, M. Serban7, W. Tsay10, M. Zak1, J. Mahlangu11
1University of Texas Health Science Center and the Gulf States Hemophilia and Thrombophilia Center, Houston, Texas, United States; 2Novo Nordisk A/S, Søborg, Denmark; 3National Blood Centre, Kuala Lumpur, Malaysia; 4Meram Faculty of Medicine, Department of Pediatric Hematology, Konya, Turkey; 5Katharine Dormandy Haemophilia Centre and Thrombosis Unit, Royal Free Hospital, London, United Kingdom; 6Churchill Hospital, Oxford, United Kingdom; 7University of California San Francisco, California, United States; 8Fondazione IRCCS Ca’ Granda, Milan, Italy; 9Ilrd Paediatric Clinic, Timisoara, Romania; 10National Taiwan University Hospital, Taipei, Taiwan, Province of China; 11Charlotte Maxeke Johannesburg Academic Hospital, Johannesburg, South Africa

Background: Key challenges in managing haemophilia B patients undergoing major orthopaedic surgery include the need for frequent bolus injections, monitoring of factor IX (FIX) levels and the increased risk of post-operative bleeding. Nonacog beta pegol, a recombinant glycoPEGylated FIX that offers high trough levels and a prolonged half-life, has the potential to improve the peri-operative management of haemophilia B patients. Aims: To evaluate the efficacy and safety of nonacog beta pegol in haemophilia B patients undergoing major orthopaedic surgery. Methods: The trial was approved by independent ethics committees and patients provided written informed consent. 13 previously treated haemophilia B patients (FIX ≤2%) underwent major surgery. An 80 IU/kg bolus injection of nonacog beta pegol was administered pre-surgery to all patients. Fixed doses of 40 IU/kg were given post-surgery at the investigator’s discretion. Safety assessments included monitoring of immunogenicity, thrombosis and other adverse events. Efficacy was evaluated on a 4-point response scale. In addition, blood loss, need for transfusion, and nonacog beta pegol consumption were recorded. Results: Of the 13 enrolled patients, 9 underwent major orthopaedic surgery (4 patients underwent major non-orthopaedic surgery). On the day of surgery, after pre-operative injection, none of the patients required additional doses. The median duration of surgery was 1.8 hours (range: 0.8–2.5); the median number of days until hospital discharge was 7.0 (range: 4.0–21.0). The median number of post-operative doses was 2.0 (range: 1.0–4.0) for Days 1–6 and 1.5 (range: 1.0–3.0) for Days 7–13. The mean total consumption was 266 IU/kg from the day of surgery to Day 14+. The haemostatic effect was rated as excellent/good in all 9 patients. No thromboembolic events, complications or unexpected bleeding occurred. No patients developed inhibitors. Conclusions: The results indicate that nonacog beta pegol had a good safety profile and was efficacious for major orthopaedic surgery. The low peri-operative consumption and number of injections administered suggest that nonacog beta pegol may offer the advantage of less frequent dosing over currently used standard and extended half-life FIX products, which require frequent bolus infusions or continuous infusion.

MP-203
Analysis of complications in fractures treatment in patient with haemophilia (PWH): Operated vs non operated
H. Caviglia1, M.E. Landro2, G. Cambiaggi2, C. Daffunchio2, Pablo Salgado1, Gustavo Galatro2
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**Introduction**: Indications for surgical management of fractures are the same as in non-haemophilic patients, but certain considerations should be made. The aim of this work is to present our experience of 28 years in a retrospective fashion all fractures that were treated in the Argentinean Foundation of Haemophilia and evaluate its evolution. Materials and Methods: In the period 1986-2013, 151 fractures in 141 PWH were treated, 125 patients type A (88.7%), 12 type B (8.5%) and 4 (2.8%) with von Willebrand’s disease. Fractures were classified according the bone affected. Only 30 fractures were treated with internal fixation. We compared the evolution of the fractures in operated (OP) and non-operated patients (NOP) regarding the complications found: nonunion, delay consolidation, time of consolidation, malalignment. **Results**: The principal bone fractured was the femur 32% (n=48), then tibia 12%, 5% (n=18), fibula 8% (n=12), 11.5% humerus (n=17); 10.5% radius (n=16), 9% ulna (n=13), 6% clavicle (n=9) and 6% phalanges (n=9). The fractures treated surgically were: 2 clavicles, 1 fibula, 1 ulna, 1 radius, 4 humerus, 3 tibia, 12 femur and 6 others. Only one nonunion fracture were found in OP; delay consolidation was seen in 4 of NOP. We can see a decrease in the time of consolidation in almost all the bone fractures in the operated group. Malalignment was found in 40 (33%) NOP and 3 (10%) OP. **Conclusion**: Besides the epidemiological changes, we also observed changed in the surgical approach of fracture treatment because anti-haemophilic concentrates were made available. Many fractures that were previously treated noninvasively were treated with internal fixation, accelerating the consolidation and improving the anatomical alignment of the bone affected without causing complications.

**MP-204**

**Ten year follow-up of total joint replacement in patients with haemophilia A and inhibitors**

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**Introduction**: Total joint replacement is indicated for end-stage haemophilic arthropathy. In patients with haemophilia and inhibitors the possibility of planning major orthopaedic surgery was until few years ago nearly interdicted. This retrospective evaluation was described to describe the long-term outcome of total joint replacement (TJR) in inhibitors patients in our haemophilia centre. **Methods**: From 1997 to 2011, we performed a total of 11 primary arthroplasty in 8 patients affected by severe Haemophilia A with inhibitors: 5 total knee replacement (TKR) and 6 total hip replacements (THR). The median age at the time of surgery was 36 years (range 32 to 59 years). A total of 4 TKR and 5 THR were performed in 6 patients affected by HKR inhibitors, 1 TKR and 1 THR were performed in 2 LR patients. The patients received FVIII plasma-derived concentrates until possible with a level to less than 5 BU: in case the title was more than 5 BU (either at the beginning or following booster dose) patients received rFVIIa. **Results**: The median duration of follow-up was 10 years (range 2 to 18 years): these procedures may be considered successfully for relief of pain and improvement of QoL. Some TJR were characterized by complications: in 1 HR patient the implant was removed (one-stage revision) to treat infection after 2 years from the primary TKR. The result can be considered successful at 9 years follow-up. 1 HR developed late infection of TKR after 10 years from primary procedure. He underwent removal of prosthetic component and replaced the prosthesis. **Conclusions**: In our experience the presence of inhibitors has not represented a limitation in their surgery as haemostasis was under control in all patients because of the availability of safe and effective bypassing agent. All of our patients underwent surgery by using rFVIIa by continuous infusion: this option represents an advantage for cost-saving procedure. Two patients developed late infections (one E. Coli and one Serratia Mercescens). The incidence of infections does not seem higher than infections in not inhibitors patients.

**MP-205**

**Functional outcome of total knee arthroplasty in patient with haemophilia: Experience in a developing world**

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**Introduction**: Total knee arthroplasty (TKA) is the standard procedure in treatment of final stages of hemophilic arthropathy. However, TKA in hemophilic patients has been accompanied by concerns about implant survival, complications including infection, hematoma formation or limited range of motion, and issues around factor supplementation and transfusion. In addition related costs of procedure are of major importance especially in a developing country with limited resources. We conceive this prospective study on TKA in patients with haemophilia to determine the functional outcome and patient satisfaction at our institution. **Material and Methods**: All hemophilia patients who underwent TKA between April 2010 and April 2013 were included in the study. Comprehensive assessment including physical examination, functional scoring and evaluation of quality of life (WOMAC, Knee Society Score, SF36) were done preoperatively. Demographic data, type and severity of hemophilia, concomitant diseases (e.g., hepatitis C, or human immunodeficiency virus infection, diabetes mellitus), and presence of factor inhibitor were registered. Duration of hospital stay and the amount of anti-hemophilic factor used were recorded for each patient. All surgeries were performed using the same routine and by one senior surgeon (SMJM). **Results**: 27 patients (all males, 33 knees) with a mean age 35.8 years (range 25-57 years) were included. All patients have severe type disease with factor levels less than 1 percent of normal. Fifteen patients (60%) were infected with hepatitis C virus (23 knees). One patient had diabetes mellitus as comorbidity. The mean follow-up period was 42.10 months (6-48 months, SD 11.65). The mean admission time was 13.87 days (5-40 days, SD: 9.5). All functional and quality of life score has been improved significantly after the surgery (p value<0.05). Only minor wound complications have been occurred in two patients that were treated conservatively. No patient required transfusion. All patients were highly satisfied with the results of surgery. **Conclusion**: TKA is an effective procedure in the
treatment of HA, revolutionizing the quality of life of the patients. Good functional results and acceptable patient satisfaction can be predicted after TKAs even in developing country, provided that this surgery confines to selected referral centers with high volume surgeries. Definition of standards of care for this procedure, which are tailored for resources of a developing country, can have major impact in improving outcomes and makes it a very cost-effectiveness of this surgery.

**MP-206**

The detrimental effects of iron on the joint: A comparison between haemochromatosis and haemophilia

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**Objectives:** Arthropathy is still a major cause of morbidity in haemophilia. Although the exact pathogenesis has not been fully elucidated, a central role for iron is demonstrated. Likewise, in hereditary haemochromatosis joint destruction is caused by iron overload. A comparison between these types of arthropathy could provide more insight in the influence of iron in inducing joint damage. **Methods:** A literature review was performed to compare both disorders on their clinical and histological characteristics. Moreover, preclinical studies were reviewed on the influence of iron on different joint components. **Results:** Similarities in the features of arthropathy in haemochromatosis and haemophilia are cartilage degeneration, synovial inflammation and proliferation, subchondral bone changes with osteophyte and cyst formation, and osteoporosis. Substantial differences are the age at onset, the occurrence of chondrocalcinosis radiographically and calcium pyrophosphate dihydrate deposition disease in haemochromatosis, and a rapid progression with joint deformity and neovascularization in haemophilia (see figure). Iron deposition in haemochromatosis derives from gradual accumulation of the less catalytic Fe3+ compared to recurrent bursts of exposure to Fe2+ derived from heme together with inflammatory cells in haemophilia. Preclinical studies demonstrate detrimental effects of iron to all components of the joint resulting in synovial inflammation and hyperplasia, chondrocyte death, and impaired osteoblast function. These effects are aggravated in the presence of a pro-inflammatory signal, which is prominent in haemophilic arthropathy and minimal in haemochromatosis. **Conclusions:** A pivotal role for iron in arthropathy in haemochromatosis and haemophilia is demonstrated by clinical, histopathological, animal, and in vitro findings. Based on the present review, the rationale for iron chelation therapy to treat arthropathy in both haemophilia and haemochromatosis remains appealing. As the detrimental effects of iron are enhanced in the presence of an inflammatory signal, so is the treatment aiming at reducing inflammation specifically in the case of haemophilic arthropathy needs investigation.

**MP-207**

Relationship between physical function and joint biomechanics in boys with haemophilia

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**Objective:** The World Federation of Hemophilia recommends joint and muscle health is evaluated using X-ray and magnetic resonance imaging, together with clinical examination scores. To date, inclusion of performance-based functional activities to monitor children with the condition has received little attention. The aim of this study was to evaluate test re-test repeatability of physical function tests and quantify relationships between physical function, lower limb muscle strength and gait patterns in young boys with haemophilia. **Methods:** Timed six-minute walk, timed up and down stairs, timed single leg stance, muscle strength of the knee extensors, ankle dorsi and plantar flexors, together with joint biomechanics during level walking using a 3D motion-capture system, were collected from 17 boys aged 6-12 years with severe haemophilia. **Results:** Measures of physical function and recordings of muscle strength with a hand held myometer were shown to be repeatable (ICC > 0.78). Distances walked in six minutes, time taken to go up and down a flight of stairs and lower limb muscle strength correlated closely to key biomechanical gait parameters, in particular ankle joint range of motion (r = 0.51-0.83; p < 0.005) and ankle (r = 0.61-0.73; p< 0.001) and knee joint moments (r = 0.46-0.69; p < 0.01). Relevance to haemophilia care: Alterations in gait patterns of boys with haemophilia appeared to be associated with changes in performance of physical function and performance seems to be dependent on their muscle strength. Not all key gait parameters in this study were associated with performance of physical activities and muscle strength suggesting that clinical tests of physical function as well as gait analysis data can provide important information on musculoskeletal health outcomes in children with haemophilia. Our findings indicated that timed six minute walk test, timed up and down steps test and muscle strength of the knee extensors correlated strongly with

**FIGURE:** Schematic representation of arthropathy in haemochromatosis versus haemophilia. The structural changes in arthropathy in haemochromatosis are shown on the left, and those in haemophilia on the right. Note the differences indicated in italics.
biomechanical joint function and hence might serve as a basis for physiotherapists to monitor physical function outcomes in children with haemophilia in the clinical setting.

**MP-208**

**Assessment of postural balance during dual tasks in haemophiliacs: Correlation with the HJHS and Gilbert scores**

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**Introduction:** The postural control (PC) has cognitive and automatic control variables. The dual tasks (DT) during the PC have been used traditionally to assess the automatic PC component. This fact could complement the postural balance assessment in patients with hemophilic arthropathy (HA). The aim of this study is to determine the relationship between PC during DT and the joint dysfunction evaluated by the HJHS and Gilbert score.

**Method:** Three repetitions of 30s were measured in three different conditions during bipedal posture: (i) Eyes Open (EO), (ii) Eyes Closed (EC) and (iii) Dual Task + eyes closed (DTEC). The dual task was to counting down from 100 in threes. The sway balance in the medio-lateral (ML) and anterior-posterior (AP) planes was measured with a triaxial accelerometer. Analyzed variables: a) Root Mean Square (RMS) and b) Displacement Center of Mass (DCOM). To simplify the analysis the Gilbert scores were summed, leaving a single value. **Results:** 8 patients with severe hemophilia A were recruited (HJHS mean score 17.3 ± 16.4 and mean age 20 ± 4 years). Significant differences (ANOVA p <0.05) among the three conditions (EO, EC and DTEC) was observed. A high correlation between HJHS score and RMSML and DCOMAP variables during DTEC was found (Table 1). **The relevance and applicability to hemophilia care:** Ours result showed that DT interfering in automatic aspect in PC. Evaluation of PC by DTEC seems to be potential simple and economic options to complement the physical examinations in patients with HA. **The originality of the work:** To date only the DT effect on the PC in patients with central neurological damage has been studied, however, there was not correlated with joint damage in AH patients. **Conclusion:** Automatic CP measured by the RMSML and DCOMAP variables during DT is positive correlated with joint damage. Future studies are needed to assessment the utility of this type of evaluation in AH patients.

**MP-209**

**Functional Impairment, Pain, and Pain Management in US Adult People with Hemophilia (PWH): Initial Lessons from the Pain, Functional Impairment, and Quality of Life (P-FIQ) Study**


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**Objectives:** Hemophilia is marked by frequent hemarthrosis, resulting in acute/chronic joint pain. Surveys in US adult PWH demonstrated suboptimal pain management strategies. The objective of P-FIQ was to assess functional impairment, pain, and pain treatment. Methods: Sequential adult male mild-severe PWH with history of joint pain/bleeding completed a hemophilia/pain history and various patient-reported outcome instruments (completed twice in “retest” population). **Results:** Of 164 PWH (median age 34) in “retest” population, more had hemophilia A (74%) than B (26%); 6% had inhibitors. Most had some college-or-above education (63%), 81% were employed, 61% were overweight/obese, and 61% self-reported arthritis/bone/joint problems. Patient-reported treatments were prophylaxis (42%), on-demand (39%), or mostly on-demand (19%; 25/31 using infusions ahead of activity). Only 32.9% reported unrestricted school/work/recreational activities in the prior 6 months; 31.3% reported using a cane/crutches/walker and 7.6% a wheelchair, and 47.0% reported history of joint surgery (41 knee, 37 ankle, 29 elbow). Patients reported losing an average of 3.7 and 1.8 school or work days in the previous 6 months due to lower/upper extremity problems, respectively. Patients reported that during the prior 6 months, they had experienced acute pain only (24%), chronic pain only (33%), or both (29%); only 15% reported no pain. Acute pain was most frequently described as sharp (77%), aching (66%), shooting (57%), and throbbing (55%), and chronic pain as aching (74%), nagging (49%), throbbing (44%), and sharp (40%). Most common analgesics in the past 6 months for acute/chronic pain were acetaminophen (69%/58%), NSAIDs (40%/52%), hydrocodone-aceaminophen (29%/33%), oxycodone (12%/11%), and oxycodone-aceaminophen (9%/8%). Most common acute/chronic pain non-analgesic strategies in the past 6 months were ice (73%/57%), rest (48%/34%), factor or bypassing agent (48%/24%), elevation (34%/28%), relaxation (31%/23%), compression (27%/21%), and heat (25%/15%). Medical marijuana (17%/9%), alcohol (8%/7%), and illicit drugs (4%/2%) were also reported. While physical therapy was reported by 12%/9%, aqua therapy, acupuncture, biofeedback, and hypnosis were infrequently reported. Faith (9%/8%) and prayer (11%/8%) were also reported. **Relevance and Applicability to Care:** Initial data corroborate the high prevalence of pain and functional disability in adult PWH, and highlight opportunities to address clinical assessment, patient dialogue, and management strategies to improve outcomes.
of the challenges during the transition period from teenager years to young adult are best managed in an interdisciplinary comprehensive care clinic. The study describes the pattern of physical activity levels and vocation choices before and after transition from a pediatric to adult centre in BC. Life stage choices are described in an attempt to provide clinicians with information for establishing clinical guidelines for best practice for educating PWH about exercise and vocation choices. Methods: Retrospective chart review of PWH who transitioned in 2004-2014 using standardized data collection procedures. Transition period encompassed the 2 years prior to, the transition year and 3 years following the transition year. Physical activity and exercise information per year was collected and classified using the NHF “Playing it safe” categories. A similar framework was established in an attempt to classify the vocation choices. Occupational categories were determined based upon the physical demands of standing, walking and lifting; the classification system ranged from safe to challenging. Results: 26 subjects were included (73% severe 19% mod 8% mild). During the 6-year transition period, there was a shift towards exercise and vocation choices that had decreased impact upon patient's joints and easier functional demands. Sport and physical activity choices intensity shifted from 56% to 65% within the safe to moderate categories. By the end of the transition period, no PWH was participating in a dangerous high impact, high risk of injury sport. At transition, 69% of vocation choices involved safe to moderate amount of risk for joint and functional impact. However 30% of PWH continued to work in moderate to challenging areas following transition. Relevance and applicability: Educational programs for exercise and vocation counselling need to start at an early age to provide joint protection and ensure optimal functional ability. Originality of the work: This study is an initial attempt to provide exercise and vocation frameworks. This pilot data shows the feasibility of collecting data to use for establishing activity and vocation guidelines through the transition period.
started secondary prophylaxis with aPCC (50 IU/kg twice weekly infusions), clinical resolution was observed. After three years of follow up, x-ray and clinical findings proceed to normal. He has no pain, nowadays. Case-3 (severe HB, diagnosis age: 9 yr); While on-demand treatment, he admitted with right hip pain while walking. X-ray showed femoral head necrosis. Secondary prophylaxis was started with twice weekly infusions. After eight years of follow up, clinical pain was decreased and disappeared. X-ray findings are correlated with clinical course. Nowadays he has no pain related hip. As a conclusion, hip arthropathy is so rare in hemophilia due to high rate of prophylactic regimes. However, x-ray evaluation should be done for earlier diagnosis if patient had hip pain or limping.

P-113
Vascular remodeling underlies rebleeding In hemophilic arthropathy: A novel hypothesis
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Hemophilic arthropathy is a debilitating condition and develops as a consequence of frequent joint bleeding despite adequate clotting factor replacement. The mechanisms of repeated bleedings are unknown. We investigated synovial, vascular, stromal and cartilaginous changes in response to a single induced hemarthrosis in the FVIII-deficient mouse, and found soft tissue hyperproliferation with marked systemic induction of neangiogenesis. The surprising findings were quick reversibility of soft tissue changes, while vascular changes outlasted the soft tissue response for months, and also occurred in uninjured knees. Vascular changes in FVIII-deficient mice involved pronounced remodeling with expression of α-SMA. We also studied joint tissue obtained from mouse models of rheumatoid arthritis (RA) and osteoarthritis (OA) and patients with the same conditions. Vascular architecture changes and pronounced expression of α-SMA appeared unique to hemophilia. Evidence that vascular changes in hemophilia were significantly associated with bleeding and joint deterioration was obtained prospectively by in vivo imaging of 156 joints (elbows, knees and ankles) in a cohort of 26 patients with hemophilia. These observations support the hypothesis that vascular remodeling contributes significantly to bleed propagation and development of hemophilic arthropathy.

P-114
Total hip revision in Patients with haemophilia
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Purpose: There are very few studies about it and also on revisions. Revisions of total hip replacements in this particularly population should usually caused by: pseudotumors formation, infections, loosening, and fractures. It is important to consider that some patients have also viral infections associated such as HIV and HCV. Aim: The purpose of this work is to describe the results of total hip revision performed in a single centre with a single surgeon in 20 years. Patients and Methods: Eight patients with 9 total hip revisions were performed between 1994-2014, all of them haemophilia type A. Four patients were HIV+ and one patient was HIV+ and HCV+. Revisions were performed because: prostatic hypertrophy fracture, Prosthetic aseptic loosening 3, 3 spontaneous pseudotumor (1 femoral, 2 acetabular), traumatic pseudotumor 1, infections 1. Average age was 48 (28-62). In 6 patients allograft were used for the reconstruction. Results: All patients had good evolution after surgery, even in those with HIV infection. Non dislocations was observed. Infections was present in 22 % of total population and 33,3 % of HIV+ population. Conclusions: Total hip revision performed in a specialised haemophilic centre is a complex procedure with high risk of infection specially in HIV+ patients.

P-115
Knee synovitis, treatment with sinovioangiosis
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Abstract: Haemophilic synovitis is a disabling complication of hemarthrosis that leads to destruction of the articular cartilage and the emergence of hemophilic arthropathy. Produces disability, chronic pain, depression, social and physical limitation. Selective embolization of the knee can prevent joint bleeds and joint damage. Aim: Assess selective embolization in patient with knee synovitis in relation to episodes of bleeding. Material and Method: Thirty four knee embolization in 33 patients were performed. Mean age 20 years old. Thirty one type A, two type A with inhibitors and 2 haemophilia type B. Evaluation of the number/year of bleeding episodes and consumption of factor VIII before and after embolization was performed. Results: Thirty patients (91%) had a satisfactory results. Three patients (9%) needed another embolization, two with favourable outcome, and one need arthroscopic synovectomy for poor outcome. The Average bleeding episodes were 1.21 per month (range 0-3) before the procedure and was reduced to 0 (range 0-1.67, p: 0.001) at three months, 0.17 (range 0-1.67, p: 0.001) at 6 months and 0.33 (range 0-1.67, p: 0.024) at twelve months. Four patients were free of bleeding for more than six months. Also after the procedure there was a significant reduction in the use of factor VIII in the first year. No significant adverse effects were reported. Conclusions: Selective embolization of arteries of the knee, is a safe procedure that prevents repetitive episodes of bleeding, which translates into a better joint function, with decreased cartilage damage and less consume of factor VIII.
Abstracts

P-116
Consumption antihemophilic factor in hemophilic patients with arthropathy and comorbidity in a cohort in Health Facilities Institution (IPS Especializada)
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Introduction: Arthropathy caused by recurrent intra-articular hemorrhages is a common complication of severe hemophilia, hemophilic arthropathy usually occurs in severe patients, which have a higher consumption of antihemophilic factor. In Colombia, there are no studies of antihemophilic factor in patients with arthropathy or comorbidity that allow the implementation of public policies. Objectives: Quantification and differentiation consumption antihemophilic factor in patients with arthropathy and comorbidity in a cohort of hemophilic patients Health Facilities Institution (IPS Especializada) Methods: Design: monitoring and analysis of a cohort of patients with hemophilia between February 2012 and April 2014. Methods: The method used is a univariate analyze of the average patient consumed units, according to the presence of arthropathy and infectious comorbidities. T student test is performed to compare the means of the samples, and find a significance level. Results: In the comparison between groups there are statistically significant differences for each group averages: 22848.5 in patients with arthropathy and infectious comorbidity, 15538.6 arthropathy in patients without infectious comorbidity, 2272 in the group without arthropathy and comorbidity, and 1300 in patients as infectious only comorbidity. A value of p <0.05. Conclusions: The highest average consumption of antihemophilic factor evidenced in patients with hemophilic arthropathy. The presence of infectious morbidity in these patients increases the consumption of antihemophilic factor, with no statistically significant differences in these two groups. These complications can be diminished with a program of comprehensive care in an interdisciplinary group. The relevance and applicability to hemophilia care: Colombia has no studies showing differences in consumption of antihemophilic factor by different groups preventable complications since childhood. It is important for decision making in health care. Besides the establishment of public policies. The originality of the work: We create a proprietary database, and using consumption records of patients in our institution.

P-117
Four years experience with Botulinum Toxin Type A for knee flexion contracture in patients with hemophilia
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Introduction: Knee flexion contracture (KFC) is a common complication of severe hemophilia, patients with haemophilia (PWH), principally in developing countries. This condition alters the normal activities of daily living. Botulinum toxin type A (BTX-A) blocks the release of acetylcholine at the neuromuscular junctions, reducing the contraction of the muscles where it was applied. Objective: Evaluate the effectiveness of conservative treatment of knee flexion contracture with BTX-A in PWH and to compare the clinical outcome with the results of a Functional questionnaire of the Argentine Foundation of Haemophilia Materials and Methods: Twenty four patients were treated, with 30 affected knees, from July 2011 to March 2015 . Mean age was 26 years . The mean follow up was 12 months . We evaluated flexion contracture in the affected knee pre-injection of BTX-A and evaluations were performed after treatment up to a year . The value at 12 months was taken as final data. The application of BTX-A was performed in hamstrings, fascia lata and calf muscles. To assess the function, a questionnaire of the different activities that are affected by knee flexion was performed, and was taken after starting BTX-A treatment. Patients answer comparing their status before and after treatment. Depending on the degree of KFC, patients were divided into 3 groups: Group I: -10º to -30º (n = 17), Group II: -31º to - 45º (n = 8), Group III: > - 45º (n =5) Results: The average KFC improved from - 34 º to -20º. The improvement was 14º (p <0.001). According to the division of groups the average KFC improvement was 10º in group I (p=0.001), group II : 17.5º (p=0.001), and group III: 23º (p=0.051). There is a correlation between post treatment KFC and the total score of the questionnaire R= 0, 77 Conclusion: Treatment of knee flexion contracture with BTX- A improves knee related functional activities, with the advantage of being a low-cost procedure and easy to apply. This questionnaire is useful to evaluate the functional outcome of treatment with BTX-A in KFC in PWH.

P-118
Feasibility of a tissue engineering approach in haemophilic arthropathy
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Haemophilic arthropathy is the hallmark of Haemophilia. Current strategies can only slow its progression and arthropasty is often the only resolute option; however, it can result in several complications up to inhibitor development. Postponing the need of arthroplasty appears highly rewarding; hence, we evaluated a Tissue Engineering (TE) approach to regenerate cartilage focal lesions in Haemophilicics. A composite scaffold was manufactured combining novel chemically modified polyvinyl alcohol (PVA) and a tissue-aspecific extracellular matrix (ECM). Briefly, a PVA solution (16% w/w) was 1% oxidized (1% Ox PVA) by using potassium permanganate. In parallel, Wharton's Jelly (W's J) from human umbilical cord was decellularized and processed obtaining an ECM sheet, which was physically crosslinked with the polymer by freezing-thawing. Resulting scaffolds were characterized for ultrastructure, resilience/stiffness, biocompatibility/biodegradation rate in Balb/c mice. At the same time, before being seeded upon scaffolds, articular cartilage (AC) chondrocytes from Haemophilic patients were
characterized for their morphology, immunophenotype, and specific mRNAs expression. Non-Haemophilic chondrocytes and AC were used as controls for cells and ECM. First, composite scaffold analysis showed that 1% Ox PVA and W’s J can mimic well cartilage tissue for mechanical properties and protein content, respectively. Chondrocytes characterization study demonstrated that Haemophilic cell populations are comparable to healthy controls, exhibiting the typical polygonal shape and being active in the transcription of specific cartilage genes (COL2A1, COL9A3, COMP, ACAN, SOX9). Moreover, both healthy and Haemophilic populations were CD44+/CD49c+/CD49e+/CD151+/CD73+/CD49f+/CD26+. When seeded on composite PVA/W’s J scaffolds, chondrocytes from Haemophilias were able to repopulate completely them, proving not only their chondrogenic activity, but also W’s J singular attitude in sustaining cell adhesion and proliferation. In conclusion, we characterized 1% oxidized PVA as a suitable hydrogel for orthopaedic prosthesis in TE applications. Wharton’s jelly, usually considered a waste product, showed a proper bioactive microenvironment for cartilage restoration even though its a-specific nature. Defining Haemophilic chondrocytes phenotype highlighted the chance for autologous scaffold manufacture, as in vivo exposure to blood seemed not to have altered their potential in matrix-related protein synthesis and cell-cell and cell-matrix interactions.

P-119
Transcriptional profiling in a mouse model of haemophilic arthropathy identifies molecular signatures of bone remodelling, myeloid immune cell infiltration, and increased collagen formation

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Background: The exact mechanisms whereby recurrent joint bleeds cause development of arthropathy in haemophilia patients are not fully understood. To further investigate the molecular regulations involved in this process, we have used transcriptional profiling to identify changes of gene expression by deep sequencing in a F8/-/- mouse model of haemophilic arthropathy. Methods: To trigger development of haemophilic arthropathy in F8/-/- mice, knee bleeds were induced by needle puncture through the patella ligament twice with a 14-day interval. All animals were euthanized 14 days after the second bleed. Knees were collected for either histopathological characterisation (n=10) or mRNA purification followed by next generation mRNA sequencing (n=10). Knees from naïve F8/-/- mice were included as controls. Results: Histopathological evaluation of the affected knees showed a disease incidence of 100%, with no signs of pathology in the contralateral control knees. The pathological findings included synovitis, bone remodelling, haemosiderin deposition, and fibrosis. Cartilage was largely unaffected. Immunohistochemical stainings showed that the synovitis is primarily due to infiltration by myeloid cells, with limited detection of lymphocytes in the joint tissue. Transcriptional profiling of a second set of knees by next generation sequencing showed that there were significant changes in gene transcription when comparing knees with induced haemophilic arthropathy to naïve control knees. The top differentially regulated genes included molecular signatures of myeloid cells, compatible with infiltration by neutrophils and macrophages. In addition, we found increased expression of genes involved in bone remodelling. Finally, transcription of several collagen and matrix metalloproteinase genes was upregulated, suggesting extracellular matrix remodelling and fibrosis as significant players in the pathogenesis of haemophilic arthropathy. Conclusion: Transcriptional profiling of knees from F8/-/- mice with haemophilic arthropathy suggests that myeloid cell infiltration and extracellular matrix remodelling are important mechanisms driving the development of haemophilic arthropathy. This correlates well with histopathological observations.

P-120
Can the prophylaxis change the epidemiology of fractures in patients with haemophilia?

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Introduction: There is very little information on the magnitude and management of fractures in PWH regards the advance on replacement therapy. The purpose of this paper is to present our experience in the past 28 years treating patients with haemophilia (PWH) who suffered fractures and evaluate the impact of access to treatment. Patients and Methods: In the period 1986-2013, 151 fractures in 141 PWH were treated, 125 patients type A (88.7%), 12 type B (8.5%) and 4 (2.8%) with von Willebrand’s disease. As the population of PWH in our centre changed over the years as did the treatment of these patients, we divided the 28 years period in two segments, 1886-2001 and 2002-2013 as in 2001 prophylaxis treatment with Factor VIII and Factor IX was instituted in our country, and divided the fractures in 5 groups: 1986-1990: 25, 1991-1995: 35, 1996-2001: 33, 2002-2007: 31, and 2008-2013: 27; and classified the fractures in lower limb (LL) and upper limb (UL). We also considered the age at which the fractures occurred. Results: Over the 28 year period of the study the incidence of presentation of the fractures of the upper limb and lower limb changed through the years, 76% LL vs. 24% UL in the first period analyzed and 63% UL vs. 37%LL in the latter one. The difference of the UL and LL fracture in the 5 periods analyzed was statically significant (p=0.0168). With regard to the age parameter when we compared the 1986-1990 cohort with the 2008-2013 cohort the 9 year difference observed between groups reached statistical significance (p= 0.035). Conclusion: According to our results, the prevalence of fractures in PWH have changed their pattern, lowering the age at which they occur and being less frequent. We believe that the advent of new and accessibly treatments for PWH decreased the development of orthopaedic complications and favours the improvement in quality of life of this patients.
**P-121**

**Bleeding complications following total knee and hip replacement in patients with inherited bleeding disorders**

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**Objective:** Bleeding complications following total joint replacement are rare in general population. On the contrary, haemophilia is a predisposing factor for postoperative hemorrhatosis. Pseudoaneurysm formation caused by unrecognized intraoperative vascular injury is the most common reason of hemorrhatism in patients with inherited clotting factor deficiencies. Clinical manifestation of this complication may appear both immediately and several months after surgery. One of the major reasons of higher risk of postoperative bleeding in hemophiliacs can be severe joint deformation and intraarticular fibrosis which highly complicate the surgical procedure.

**Methods:** Patients suffering from haemophilia A, B, von Willebrand disease and Factor VII and XI deficiency qualified for total knee replacement (TKR) and total hip replacement (THR) were included in this prospective observational study. Deficient factor substitution with factor concentrate was commenced shortly before the procedure and its appropriate plasma activity level was confirmed. Additionally blood test for inhibitor was performed. TKRs and THRs were performed in typical manner. In postoperative period patients were under strict hematological and orthopedic supervision. All patients were followed up in the 6th, 12th and 24th week after the procedure.

**Results:** Since 2010 till 2014 78 TKRs and 40 THRs were performed. Severe haemophilia A patients formed the majority of the study population (72%). Bleeding complications occurred in 10 patients (8.5%). Hemorrhatosis was observed in 9 patients (7.6%), delayed wound bleeding in 7 patients (5.9%). Pseudoaneurysm formation was diagnosed in 2 patients (1.7%), in one of them in the first 6 weeks and in one of them in the 12th week following surgery. Following methods were used to treat bleeding complications: joint aspiration with hemarthrosis evacuation – 7 patients (5.9%), wound inspections with vessel ligation – 2 patients (1.7%), arthroscopy with hemorrhatosis evacuation – 2 patients (1.7%), ultrasound-guided pseudoaneurysm embolization – 1 patient (0.85%), arteriography with intravascular pseudoaneurysm embolization – 2 patients (1.7%). No recurrences were observed.

**Conclusions:** Proper hematological preparation diminishes but not eliminates the risk of postoperative joint bleeds. Most of bleeding complications occurred in early postoperative period. Ultrasound-guided embolization and angiography with intravascular embolization seem to be least burdensome for patients and most efficacious treatment methods for pseudoaneurysm formation.

**P-122**

**Improve the diagnosis of osteoporosis in patients with hemophilia**

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Because of multiple hemorrhages in patients with hemophilia do not occur rarely severe lesions of the musculoskeletal system, as well as other organs and systems. Destructive bone changes in patients with hemophilia are mostly periarticular and relate to recurrent hemorrhatosis, the development of immune synovitis and hemosiderosis intra-articular tissues. Periarticular osteoporosis is diagnosed in 78% of patients with hemophilia. Osteoporosis, in the terminology of WHO (1994), a progressive systemic disease characterized by low bone mass and structure (microarchitectonics) bone tissue, leading to increased bone fragility and fracture appearance. The defeat of bone in osteoporosis is systemic progressive nature. In this regard, the main objective is early diagnosis it to conduct adequate pathogenetic therapy. So far, there is no single opinion on the incidence of osteoporosis, osteoporotic fractures, prioritization of specific risk factors for their development, the mechanisms of development and progression of osteoporosis in hemophilia. Thus, the diagnosis of osteopenia and osteoporosis in hemophilia is an urgent problem at the present stage of development of medicine. The aim of the study was to examine the levels of bone mineral density (BMD) in patients with hemophilia by ultrasonic bone densitometry. Ultrasonic bone densitometry is based on measuring the propagation velocity of ultrasonic waves on the surface of the bone (this principle work densitometers which measure the density of the bone in the patella or the middle portion of the tibia), and the measuring broadband ultrasonic wave dispersion in the study of bone. As a result, determined by two key parameters: T-score - the number of standard deviations (SD) below the average, typical for the peak bone mass. The value of t-test to -1.0 is the norm, the deviation from -1.0 to 2.5 is regarded as osteopenia (pre-clinical stage of osteoporosis), and the index below -2.5 as osteoporosis, Z-test reflects the value of SD indicators patient from middle age norms. Materials and methods. The study involved 67 patients with hemophilia A and B, aged 10 to 45 years (mean age 27.2 ± 14, 1 year). X-ray diffraction methods were used on the unit Halykry, ultrasound densitometry on the unit Mini Omni. When processing own material adhered to the classification of E.Z. Novikovoy / 19 is based on the clinical - radiological data identifies four stages of the articular process. Method of ultrasound densitometry studied bone mineral density in the middle part of the patella and the tibia in the anterior and middle projections. Discussion. The patients were observed multiple lesions of the joints, and in each of them the process was at a different stage of development. According to X stage I arthropathy installed in 7 (8.9%), II step - 35 (53.7%), III stage in 22 (33.0%) had stage IV disease and three (4.5%) patients. By frequency lesion was in the lead II and stage III arthropathy of the knee (86.7%). Results of the study ultrasound densitometry in 67 patients showed that, of whom 19 (28.3%) had normal levels of t-test within -1.0, Z = 1.4 ± 0.08, 18 (26.8%) patients had less severe fluctuations T-criterion - 1.4 ± 0.09, Z = 1.93 ± 0.14, which indicates severe osteopenia. In 30 (44.7%) patients had marked fluctuations T-test - 2.7 ± 0.14, which is indicative of osteoporosis bone. Conducting osteodensitometry suitable for controlling the level of payment for bone mineral.
Thus, the introduction of effective methods of early diagnosis by densitometry allows to carry out prevention and treatment of osteoporosis in patients with hemophilia.

**P-123**

**Contrast Enhanced Ultrasound Scan (CEUS) for haemophilic arthropathy: A Preliminary experience**

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**Introduction**: In haemophilic patients, recurrent intra-articular bleeding into the same joint results in chronic arthropathy. Radiography, magnetic resonance imaging, Ultrasonography and Power Doppler Ultrasonography remain the most utilized techniques in the diagnosis of this complication. For its ability in identifying and grading the synovial vascularization, contrast-enhanced ultrasonography (CEUS) has been successfully used in the assessment of joints in rheumatoid arthritis and may be a feasible tool in the evaluation of haemophilic articular modifications.

**Objective**: To evaluate the diagnostic value of contrast-enhanced colour Doppler ultrasound scan (CEUS) in the joints of a cohort of haemophilic patients. **Materials and methods**: The ultrasound contrast agent SonoVue (Bragco, Milan, Italy) is a second-generation contrast agent. It demonstrates an elimination half-life of approximately 6 minutes and more than 80% of the compound is exhaled via the lungs in 11 minutes. To date we have evaluated 13 joints in 11 patients: 9 patients were on demand replacement therapy while 2 patients were on secondary prophylaxis. The mean age of the patients was 33 years (range 8 - 69). Irrespective the type of schedule, all patients suffered of persistent pain and/or swelling in the joints considered. CEUS was performed in these joints: 1 knee, 9 ankles, 2 shoulders, 1 elbow. In 7 cases were not detected significant changes in microvascular blood flow. In 4 ankles and in 1 shoulder this technique has been able to detect increased local blood flow. In 2 patients we advised the use of secondary prophylaxis. In 3 patients we used radiosynoviothesis to treat chronic synovitis. **Conclusions**: The use of CEUS is well established in clinical practice, because it has provided enhanced imaging of the tissue microvasculature. CEUS has shown the capability to improve the differentiation of active synovitis from inactive intra articular thickening: in our experience it was important for our therapeutic decision. CEUS is cost-effective (no replacement treatment was used for the technique including the two inhibitors patients) and easy to perform, for a correct and cheap therapeutic approach in the field of haemophilic arthropathy.

**P-124**

**Pseudoaneurysm following total knee replacement in two patients with severe haemophilia A: Diagnosis and conservative or surgery treatment**

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**Objective**: vascular doppler ultrasound (US) in a common evaluation performed after total knee replacement (TKR) in clinical setting. **Methods**: during last 30 months of observation we examined 42 patients with haemophilia A and total knee replacement admitted to our rehabilitation center with lower limb Doppler US. The average time of examination was 8 days after major surgery. **Results**: in two cases doppler US revealed a pseudoaneurysmatic dilatation. The first patient, a 57-year-old man came to our rehabilitation center 6 days after right knee surgery replacement. The patient was under treatment with intravenous Kogenate® 4000 IU daily. Doppler ultrasound examination was performed both for venous assessment of the lower limb and in the area of the knee. A pseudoaneurysm was identified at the level of the upper and medial area of knee. The size was 20x10 mm and it was furnished by a small artery. We decided to begin a conservative approach. It was applied a local pressure with a roll of gauze wrapped tightly. It was a complete spontaneous thrombosis after 8 days of compression. The second patient, a 48-year-old man, was admitted to our rehabilitation center after 7 days from his right TKR. The patient was in treatment with intravenous ReFacto® AF 3000 iu + 2000iu daily. A Doppler ultrasound of the knee region was performed the same day of admission and showed a pseudoaneurysm with a size of 30x25x20 mm. It was furnished by genicular artery. In reason of the relevant size of the hematoma, the patient was therefore referred to a vascular surgery department. An angiographic embolization was performed with BioSphere® injection in a satisfactory and effective way. **Relevance**: The systematic use of ultrasound on the area of the knee could be applied in all cases of total knee replacement.

**P-125**

**Deep vein thrombosis in hemophilic patients undergoing major orthopedic surgery: Experience in a rehabilitation center**

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**Objective**: our investigation is aiming to search the incidence of postoperative deep vein thrombosis (DVT) in patients with haemophilia (PWH) undergoing major orthopedic surgery. **Methods**: from year 2003 to 2014, 151 patients were admitted for a total of 159 hospitalizations following total knee (TKR), hip (THR) and ankle replacement (TAR). No one of them was subjected to pharmacological prophylaxis of venous thromboembolism. 138 patients were studied with ecocolordoppler ultrasound of lower limbs during the first week of hospitalization. **Results**: 6 cases of distal deep vein thrombosis were found and in 100% of the cases they were admitted after TKR (4.3% of all the cohort included; 5.3% of patients undergoing TKR). 3 of them with severe haemophilia A, one with moderate hemophilia A, one with Von Willebrand (VW) disease, one with combined deficiency VIII-V. All patients were treated with graduated elastic compression of class 2 and only one patient (VW) underwent to treatment with low molecular weight heparin. All cases presented a complete resolution. **Relevance**: our experience confirms the possibility of venous thrombotic events in PWH after TKR; we recommend doppler US study for all patients undergoing prosthetic replacement surgery for early recognition of a possible deep vein thrombosis.
P-126
Radiosynovectomy: A suitable treatment for advanced stage haemophilic arthropathy
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Introduction: Although ideal treatment of haemophilia is primary prophylaxis, unfortunately still a proportion of adult patients develop chronic synovitis. In literature the radiosynovectomy (RSO) shows a diminution of hemarthroses in nearly 90% of cases. In Italy RSO is rarely used. In this paper we describe our experience in this technique in a cohort of patients with chronic haemophilic synovitis and end-stage arthropathy. Methods: We have selected 34 patients most of whom were treated on demand, 4 on secondary prophylaxis. 13 patients were affected by haemophilia A (HA), 4 with inhibitor, and 4 were affected by Haemophilia B (HB), 1 with inhibitor. All were suffering of severe pain in the joints or reduce range of motion despite the intensive on demand or prophylaxis treatment. They did not refer severe recurrent haemarthrosis. The mean age of the patients was 38 years (range 9 - 74) and the joints involved were: 55: 14 knees, 17 elbows, 15 ankles, 3 sub-astragals, 4 shoulders, 1 hip, 1 wrist and. The radioactive intra-articular treatment was a single injection with Yttium90 for the knee and Renium186 for the other joints. The mean follow up is now 40 months. The results in terms of recurrent haemarthroses, pain and range of motion were excellent or good in 49 joints treated; in 5 cases the results were unsatisfactory. No side effects procedure-related were observed. Conclusions: Despite recent advances in haemophilia treatment, chronic synovitis may be also present in a small proportion of young patients, and it is a common finding that a larger proportion of adult haemophiliacs suffer of arthrosis. In our cohort pain and reduced range of motion are the main symptoms also in absence of joint recurrent haemorrhages. Our results demonstrate that this treatment may be suitable also in a subgroup with advanced/ end-stage arthropathy reducing pain and postponing, in some cases, the prosthetic procedure. In conclusion, we strongly support RSO and we invite doctors dealing with haemophilia to address frequent logistic difficulties (e.g. legal restrictions, poor appeal) in order to adopt this technique, especially in the current climate of cost-saving and resource limitation.

P-127
Functional ability and joint status in adult patients with hemophilia
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Functional ability and joint health are the main determinants of daily life in people with hemophilia (PWH) and they are related to complications and ageing. Using of standardized assessment method as Haemophilia Joint Health Score (HJHS) is important in order to determine the current principles of treatment identify the main problems and decide the alternative treatment for PWH. Purpose: evaluate functional ability and joint health of PWH. Methods: 21 Lithuanian adults aged 20–51 years (mean 33.48±9.926) with severe or moderate haemophilia A or B were included in the study. Subjects joints were evaluated using HJHS version 2.1, functional ability with Haemophilia Activities List (HAL) and functional independence with Functional Independence Score in Haemophilia (FISH). Results: the analysis showed that the most damaged joints were ankles (10.33±5.825) and knees (10.19±6.361). A moderate statistical correlation was found between the mean of the upper and lower extremity joints HJHS scores (p<0.05). A moderate statistical correlation was found between the low ratings of HAL in lower limbs scores – leisure activities and sport and sitting/kneeling/standing (r=0.571, p<0.05), and functions of legs (r=0.574, p<0.05). The worst component of FISH were Transfers (6.1±1.68), especially Squatting (2.5±1.27), which were usually assessed by 1 score (35% of subjects). Age displayed very weak correlation with the HJHS (r=0.016, p<0.05), HAL (r=0.011, p<0.05), FISH (r=0.002, p<0.05) scores and HJHS with HAL (r=0.013, p<0.05), FISH (r=0.000, p<0.05). Conclusions: the results showed that the most damaged joints were ankles and knees. Joint damage deteriorates functional ability and physical functioning in PWH. Increasing of leg’s functional capabilities leads to improvement of participation in leisure activities and sport. Age influences HJHS, HAL and FISH scores. Joint functional status determines HAL and FISH results.

P-128
Ageing successful with hemophilia: A multidisciplinary program
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Persons with hemophilia born before the 1970 have spent a substantial part of their early life without the benefits of the replacement therapy that became available on a relative large scale only at the beginning of the 1970s. Accordingly, these patients suffer from musculoskeletal and functional problems that are typical of the elderly. We describe herewith a program based principally upon the training by a physiotherapist and an occupational therapist. All PWHs born before 1970 was invited by letter or phone calls to undergo at the Center a comprehensive baseline examination with particular emphasis on musculoskeletal problems. Balance and body load were tested computed from the vertical force of a force platform. According to the results obtained with these baseline exams, PWHs were subdivided in groups homogenous for age, functional capacities and related needs. Then each group started a trajectory of training that took place for 10 months (3 meetings of 4 hours), with regular delivery of information, practical and endorsement sessions. At the end of the 10 months training, each patient underwent again a comprehensive examination, including the tests and measurements obtained at baseline, with the goal to evaluate statistically whether or not the training program yielded general and specific improvement. Of 41 patients with a median age of 54 years, 29 had severe hemophilia A (71%). A history
of inhibitor was present in 7 patients (17%). 25 patients (61%) previously underwent to major orthopedic surgery. 38 patients (93%) completed the whole program. Statistically significant changes were computed using force platform. We are convinced that the early aging of PWHs born before the advent of modern replacement therapy is not sufficiently addressed in the current programs of management of PWHs. We take the liberty to believe that this project has the advantage of triggering the due attention of patients and of their caregivers at the specialized Hemophilia Centre to this issue. This study, focused on a rehabilitation and occupational therapy in patients with hemophilia, is to our knowledge the first.

P-129
Patient-reported fractures in hemophilia
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Background: Recent studies have shown that persons with hemophilia (PWH) have an increased likelihood of clinically significant low bone mineral density (BMD). Multiple studies and meta-analysis have demonstrated decreased areal BMD (aBMD) measured by standard imaging studies, such as dual X-ray absorptiometry (DXA). However, so far it has not been established whether this decrease in BMD translates to an increased risk of fractures in PWH and there is minimal data on fracture rates in this population. Methods: An aggregate of patient-reported fractures including type and location was collected from two studies conducted at our centre investigating low BMD in PWH. One study involves a patient self-assessment survey collecting data on history of fractures; the second is an imaging BMD cohort study and patient-reported fractures were collected as a part of this study. Non-trivial fractures include compression fractures, long bone, wrist and ankle fractures. RESULTS: Data was available on a total of 107 subjects (85 hemophilia A, 22 hemophilia B; 33.6% severe <1%). Mean age 47 (SD±17.5). 50.5% of subjects reported fractures with 34.6% non-trivial fractures. Bone mineral density measurements were available in 81 subjects. 54.3% had osteopenic range BMD (T- or Z-score between -1.0 and -2.5). 7.4% had osteoporotic range BMD (T- or Z-score < -2.5). Conclusions: PWH are known to have higher rates of low BMD. Multiple studies have shown that this decrease in BMD translates to an increased risk of fractures in PWH and there is minimal data on fracture rates in this population. The validity of patient recollection of fracture history. However, this report provides important information and rough estimate on fracture risk as a potential outcome of low BMD in PWH. Prospective studies on fracture rates and correlation to low BMD and activity are needed for true assessment of fracture risk in PWH. Accurate data is needed to guide recommendations on therapeutic and preventative measures for this at-risk population.

P-130
Tool of engagement: Physiotherapy and the use of point of care ultrasound
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Objective: Point of care musculoskeletal ultrasound (MSKUS) imaging is now being implemented into the hemophilia clinics to supplement the physiotherapist’s observational and manual skills and to provide objective visual measurement. Studies have shown that MSKUS is an important reliable and feasible diagnostic tool for evaluating hemarthritic joints. Physiotherapist’s may use MSKUS to assist in physiotherapy assessment, treatment and research, for the purpose of maintaining, restoring or improving function of persons’ with hemophilia and for the promotion of mobility and health. Methods: Description of the use and role of MSKUS over the last 18 months within a single Canadian Hemophilia Treatment Centre. The physiotherapist participated in specific hemophilia ultrasound training programs. A case study demonstrates the practicalities and possibilities of MSKUS role in physiotherapist practice for joint maintenance bleed prevention and joint rehabilitation including education to increase patient knowledge understanding and biofeedback. Results: Over an 18-month period, 78 PWH had at least one joint scanned, 12% have had sequential scans with images saved during their hemophilia clinic visit. Of these PWH, 91% had FVIII, 8% FIX and 1% FVII deficiency with 77% having severe disease, 5% moderate and 18% mild. The majority (94%) were joints with 60% ankle, 19% knee, and 17% elbow joints. During this time period, acute bleeds were seen in 13% of the joint MSKUS images. Each joint ultrasound exam took about five minutes. Relevance and applicability to hemophilia: The hemophilia clinical team has observed the benefits of patient engagement through information sharing from the use of this new technology. Using MSKUS imaging provides the PWH point of care information about their joint status and it appears to initiate increased conversation about most effective methods of managing their joint disease. Originality of the work: MSKUS has the potential to create a foundation for shared decision-making between patient and clinician through increased knowledge and biofeedback for best bleeding disorder management. The next step is research to examine the patient’s perception of the use of this new technology within the hemophilia clinic and to create a patient educational module.

P-131
The challenges of physiotherapy management of children with haemophilia and inhibitors: A case report
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Introduction & Objectives: For children with haemophilia and inhibitors, musculoskeletal management can present significant challenges for physiotherapists. Despite the use of bypassing agents, haemostasis and the resolution of bleeding episodes are more difficult and take longer. Physiotherapy plays a key role in the management and rehabilitation of haemarthrosis in children with inhibitors despite a poor evidence base. The acute stage is focused on immobilisation for pain relief and minimising re-bleeds. Rehabilitation comprises regaining movement, muscle strength and function using exercises, stretching and splints. Decisions on the best approach can be complex, are influenced by many factors and require a multidisciplinary approach (MDT). This case report describes the outcomes of intensive physiotherapy and the use of stretch and cast treatment when managing a knee bleed in an 18 month

**Abstract**

The management of complications following joint surgery in haemophilic patients is crucial to ensure optimal outcomes. This study aimed to evaluate the role of physiotherapy and rehabilitation in preventing complications following joint surgery in haemophilic patients. The study included a retrospective analysis of 100 patients who underwent joint surgery for haemophilia-related arthropathy. The patients were followed up for a period of 2 years to assess the incidence of complications.

**Results**

The results showed a significant reduction in the incidence of complications following joint surgery in patients who received physiotherapy and rehabilitation. The most common complications were pain, stiffness, and decreased range of motion. The use of non-invasive methods such as hydrotherapy, massage, and stretching exercises were found to be effective in preventing these complications.

**Conclusion**

Physiotherapy and rehabilitation play a critical role in preventing complications following joint surgery in haemophilic patients. The use of non-invasive methods such as hydrotherapy, massage, and stretching exercises can significantly reduce the incidence of pain, stiffness, and decreased range of motion.

**Keywords**

Physiotherapy, Rehabilitation, Complications, Joint surgery, Haemophilia.
Muscle strength in the hemophilic patient is of great importance since an adequate muscle tone reduces the joint hemorrhages and provides greater stability to joints. The quality of life of hemophilic patients is directly related to their ability to perform physical activity and sport, and both aspects require and appropriate muscle strength and physical condition.

**Objective:** Evaluate and compare the quadriceps isometric force of mild/moderate and severe hemophilic children with children without hemophilia.

**Methods:** Quadriceps muscle strength in 9 mild/moderate and 9 severe hemophilic children in prophylactic treatment, as well as 9 control children was evaluated using a portable dynamometer. The peak force (kg) was registered 3 times on each leg for 6s. To compare the means of max force obtained in each group, a two-way analysis of variance (ANOVA) was performed (3 groups and 2 levels (left and right leg)).

**Results:** TABLE 1 shows descriptive data, exercise frequency and the mean force, standardized by the subject weight, obtained for each group. Control group has obtained the highest values in both legs. However, results show no significant differences in mean strength between groups (p=0.05). Furthermore, there are no significant differences between the strength of both legs (p=0.80).

**Conclusion:** No significant differences have been obtained in quadriceps muscle strength between groups. Factor replacement therapy in prophylaxis modality allows children with hemophilia to be physically active like their healthy peers. However, the control and maintenance of muscle strength in the hemophilia patient is an essential objective.
objective, qualitative and quantitative evaluation of the UL motion during the simulation of a multiple reaching task while sitting (named: 5Points Test). Methods: A new functional test was designed to carry out kinematic analysis of the UL during a repetitive reaching task through data acquired by a two optoelectronic cameras system (SMART DX BTS Group, Milan, Italy). A plexiglass board (120cmx80cm) was used to place seven different reflective markers on a semicircular track in front of the patient. In this way, the 180° arc was divided in 6 sectors of 30° (Fig.1). In the aim not to cover the seven reflective markers the patient was asked to reach different targets that were placed before than the marker. Patient was placed in a sitting position with knee placed at 90° of flexion and table height was adjusted to let the elbow at 90° of flexion whit the hand palm placed on the starting position on the selected position on the board. The dedicated kinematic analysis for this particular test allows the clinician to collect data about speed of motion, precision of movement, ability to explore the space, trunk compensation and sense of joint repositioning. Limits of the study: reduced number of patients, still to determine the interobserver reliability and ICC in all the several kinematic parameters. The protocol does not allow the correct discrimination of shoulder and elbow contribution during the test. Relevance and applicability to hemophilia care: the protocol offers a global evaluation of UL performance in pwh. In our opinion the kinematic analysis protocol and the global testing procedure and set up can be considered as a highly cost effective procedure to provide a quick and multidimensional evaluation for patients affected by haemophilic arthropathy. Originality of the work: The use of a two optoelectronic cameras and the low number of markers used during the test provides a better accessibility to a higher number of rehabilitation centers and clinicians involved in the management of pwh.

P-213
Intra-articular Hyaluronate injections in severe haemophilia patients with moderate to severe arthritis of the ankle
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Background: One of the most affected joints in moderate and severe haemophilia is the ankle joint. Intra-articular corticosteroid injections may give significant but short term relief. Systematic reviews of the use of intra-articular hyaluronate in patients with degenerative arthritis have shown a small, but significant symptomatic effect lasting up to 26 weeks in comparison to intra-articular saline injections. There is little documented evidence on the use of intra-articular hyaluronate in haemophilia patients with ankle arthropathies. Objectives: To retrospectively determine the effects of hyaluronate intra-articular injections in patients with severe haemophilia and moderate to severe arthritis of the ankle.

Method: 5 severe haemophilia patients (5 Males, age range 26-60, mean 43.6 years) with moderate to severe ankle arthritis received intra-articular 2mLs Hylan G-F20 and 40mg of methyl prednisolone, between Mar 2013 - 2014. One patient had both ankles injected and another patient had a repeat injection 12 months later. All patients had severe pain, 8/10 on the visual analogue scale prior to the injection. The patients were asked to complete a questionnaire (adapted from d’Young et al.) to establish 1) satisfaction with instruction and 2) the impact of therapy on the management of bleeds and pain associated with arthropathy. Results: 35 questionnaires were completed. Use is summarised in table 1. 3 patients had no bleeds and did not use the unit during the follow-up period. Of the remainder 84% noted a reduction in pain and 69% a reduction in swelling. Apart from one patient who found the compression difficult to tolerate, there were no adverse effects. No additional factor was required as a result of using the unit. Discussions/Conclusions: Acknowledging concerns previously expressed it is encouraging that there were no perceived deleterious effects. There is some evidence to suggest that ice can relieve pain temporarily. This audit supports the use of cold therapy to assist with management of pain associated with arthropathy. A number of patients reported using the unit most effectively after the first 48 hours following a bleed rather than in the early period following haemarthrosis. While recommending caution there may still be merit in its use in recovery following a bleed.

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Quality of life and sports activities in children with haemophilia: An observational study

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Objective: The appearance of hemarthrosis since childhood causes the development of degenerative joint damage in patients with haemophilia. Although prophylactic treatments have significantly reduced the frequency of bleeding, we are still haemarthrosis before adolescence. Currently the sports activities are used as part of multidisciplinary treatment in patients with haemophilia. The objective of this study was to assess the incidence of sports activities in the perception of quality of life of children with haemophilia, depending on joint deterioration, compared to healthy controls.

Methods: 53 children with haemophilia from 7 to 13 years of age and 51 healthy children were evaluated. The perception of quality of life for both groups was measured with the CHIP-CE questionnaire. Using a registry the main clinical variables (age, type and severity of haemophilia, medical treatment, presence of inhibitors, etc.) and the frequency of sports activities (days/week) was collected. The joint status of patients with haemophilia was measured with the Spanish version of the questionnaire Haemophilia Joint Health Score (HJHS). Results: There are no significant differences in the perception of quality of life between patients with haemophilia and healthy subjects. In patients with hemophilia, sports activities influenced significantly in a better health satisfaction. The deterioration of knee and elbow joint is correlated with satisfaction with health and wellness.

Relevance and applicability to hemophilia care: It is important to motivate patients with hemophilia to conduct sports activities. The control and individualization of sports practice improves the quality of life of patients, avoiding bleeding risks. The development of specific and controlled sports activities programs, will improve the wellbeing of patients at the same time that allows a correct physical development. Originality of the work: There were no significant differences in the quality of life of children with haemophilia and healthy controls. Despite the disease, it is significant the sports activities in the improvement of the quality of life. Regardless of make or not sport, patients with haemophilia have a quality of life similar to that of healthy controls.

P-215
Impact of regional paediatric haemophilia multidisciplinary out-reach clinics: A case study

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Background: Within the largest geographical region in the UK, covering an area 23,800km2, there is one Comprehensive Care Centre (CCC) based in the north of region. Due to distance, many children with inherited bleeding disorders living within the region were not receiving regular CCC review as recommended by UKHCDO. In September 2012 outreach comprehensive care for children within the region was commissioned. A visiting multidisciplinary team (MDT) consisting of Consultant Paediatric Haematologist, specialist nurse and physiotherapist established clinics to review children together with the support of the local clinical team. A number of children who had no previous CCC involvement had problems identified, one is presented here.

Case: EF was initially reviewed at 9yrs 10mths, with a history of Moderate Haemophilia A, (Factor VIII 4.8%– 1 stage assay). He had a history of joint bleeds treated with DDAVP. Method: EF was assessed by the multidisciplinary team. Findings - Bilateral ankle joint pain at rest and worsening problems with activity. Asymmetry with posture and gait, calf atrophy and weakness and persistent ankle swelling and poor proprioception. CHAQ pain assay – 2 stage Factor VIII 1.4% Discrepant 1 stage/ 2 stage assay – 2 stage Factor VIII 1.4% Reduction in sport and other activities also missed school days. Parents and EF reported needle phobia preventing administration of factor concentrate. Results: Following assessment the resultant problems were addressed – Bilateral ankle joint synovitis treated with steroid joint injections, splinting and physiotherapeutic rehabilitation. Management of needle phobia through the use of topical anaesthetic cream, distraction and play therapy support. Commencement of prophylaxis on an alternate day regime, targeted to activity days, delivered by parents. Outcome: Decreased CHAQ pain score – 13%; Increased PedHAL score – 74.5%;Return to full school attendance, and regular activity within sports of rowing and hockey; Parents and EF feeling empowered to treat both prophylactically and for bleeds. This case study demonstrates the importance of CCC review with a MDT approach to improve patient outcomes.
P-216
Repetitive knee bleeds in a mild haemophiliac due to transient lateral patella dislocation
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Introduction: Transient lateral patella dislocation is a well described knee dysfunction. It is most frequently seen amongst adolescent females. This case involved a 13 year old male with a baseline factor VIII of 9 IU/dL. Presentation: The patient presented with an acute knee haemarthrosis. The mechanism of injury was internal rotation of the femur on a fixed foot during a football tackle. The patient reported brief patella dislocation. Initial Investigations – X-ray – excluded any bony injury, identified patella alta and a shallow lateral trochlear groove. MRI – Identified chondral defects on the articular surface of the patella, acute synovitis and haemarthrosis. No ligamentous injury was identified. Diagnosis: The working diagnosis was traumatic patella dislocation. It was impossible to completely exclude involvement of the passive patella-femoral constraints including the medial patella-femoral ligament. The impact of the injury was compounded by a recent growth spurt, causing significant muscle imbalance within the lower limb, a low lateral shelf to the trochlear groove and patella alta. The final diagnosis was recurrent transient lateral patella dislocation. Management – The acute bleed/s were treated with daily factor VIII concentrate and the patient remains on prophylaxis due to transient lateral patella dislocation. Despite prophylaxis, joint protection and slow progressive physiotherapy led rehabilitation, the patient suffered recurrent bleeds second to repeated joint subluxation. A multi-disciplinary decision was made, including input from an orthopaedic surgeon, to immobilise the joint in a cast for six weeks. The clinical rationale was to fully stabilise the patella whilst the synovitis and haematoma resolved. Outcomes: Following extensive physiotherapy input to improve muscle balance, stability and proprioception the patient returned to full activity at approximately one year. The patient has been advised to avoid contact sport such as football, due to the underlying risk of re-injury. Conclusion: A diagnosis of mild haemophilia when combined with predisposing congenital abnormalities and/or traumatic injury, can place a patient at a high risk of developing a target joint/mono-arthritis. Joint damage can be minimised with haemostatic support and physiotherapeutic intervention. These interventions might otherwise seem unnecessary in a patient with mild haemophilia.

P-217
Prevalence and risk factors of bone mineral density abnormalities in Japanese HIV-infected haemophiliacs
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Background: HIV-infected patients are at high risk for bone mineral density (BMD) loss. The present study was designed to provide information on characteristics of BMD abnormalities in HIV-1-infected haemophiliacs and the risk factors involved in the worsening of BMD. Methods: Sixty-seven Japanese HIV-1 infected haemophiliacs were studied with a dual-energy X-ray absorptiometry scan (DXA) at lumbar spine, total hip and femoral neck. Multivariate logistic and linear regression models were used for comparison of the impact of risk factors on BMD loss. Results: Osteopenia and osteoporosis were diagnosed in 48% and 7% of the patients at lumbar spine, 61% and 18% at total hip, 60% and 23% at femoral neck, respectively. The duration of protease inhibitor (PI) treatment correlated with lower BMD at lumbar spine in logistic analysis [odds ratio (OR) 1.395 per 1 year increase of PI use; 95% confidence interval (CI) 1.116-1.744; P<0.003] and linear regression analysis (Estimate -0.006 for months of PI use, P=0.048). Osteoporosis at femoral neck was associated with physical activity score (OR: 0.391 per 1 score improve, 95%CI: 0.164-0.934, P=0.035) and linear regression analysis (Estimate 0.483, P=0.014). Conclusions: In haemophiliacs, BMD was significantly different between lumbar spine and hips/necks. Because BMD at hip/neck is influenced by physical activity, total body BMD should be assessed at lumbar spine. The use of PI’s is strongly associated with BMD loss at lumbar spine. Treatment for BMD loss should be tailored to BMD measured at each joint in hemophiliacs.

P-218
EXOGEN treatment in two cases of delayed union post tibio-talar fusion
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Two patients with severe haemophilia A who experienced delayed union post tibio-talar fusion, and who were subsequently treated with an EXOGEN device will be presented. Both patients, aged 33 years and 24 years, have been on long acting factor VIII of 9 IU/dL. Presentation: The patient presented with an acute knee haemarthrosis. The mechanism of injury was one of the two patients treated with an EXOGEN device from 1 year post-operatively delayed union post tibio-talar fusion, and who were subsequently treated with an EXOGEN device will be presented. Both patients, aged 33 years and 24 years, have been on long acting factor VIII of 9 IU/dL. Presentation: The patient presented with an acute knee haemarthrosis. The mechanism of injury was an acute knee haemarthrosis. The mechanism of injury was compounded by a recent growth spurt, causing significant muscle imbalance within the lower limb, a low lateral shelf to the trochlear groove and patella alta. The final diagnosis was recurrent transient lateral patella dislocation. Management – The acute bleed/s were treated with daily factor VIII concentrate and the patient remains on prophylaxis due to transient lateral patella dislocation. Despite prophylaxis, joint protection and slow progressive physiotherapy led rehabilitation, the patient suffered recurrent bleeds second to repeated joint subluxation. A multi-disciplinary decision was made, including input from an orthopaedic surgeon, to immobilise the joint in a cast for six weeks. The clinical rationale was to fully stabilise the patella whilst the synovitis and haematoma resolved. Outcomes: Following extensive physiotherapy input to improve muscle balance, stability and proprioception the patient returned to full activity at approximately one year. The patient has been advised to avoid contact sport such as football, due to the underlying risk of re-injury. Conclusion: A diagnosis of mild haemophilia when combined with predisposing congenital abnormalities and/or traumatic injury, can place a patient at a high risk of developing a target joint/mono-arthritis. Joint damage can be minimised with haemostatic support and physiotherapeutic intervention. These interventions might otherwise seem unnecessary in a patient with mild haemophilia.

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technology which activates a biological healing response at a molecular level. It has been used in non-union post ankle arthrodesis in the non-haemophilic population, with one report showing 70% of patients finding it beneficial.

**P-219**

**Comorbidities in patients with hemophilia: Changes in joints and its correlation with bone mineral density**

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**Introduction:** It has been shown that bone mineral density (BMD) may be lower in haemophilia patients. BMD can be also lower in patients who have more severely affected joints or lower activity levels. The main objective of this work is to correlate the BMD data in hip (BMDhip) and spine (BMDspine) with the presence of radiographic abnormalities and arthropathy in load and no load joints in Spanish adult haemophilia patients. **Methods:** The clinical history of 31 haemophilia patients of the Hospital La Fe of Valencia has been analyzed. The Population was divided into two Age Groups (< 35 and ≥ 35 years old (AG1 and AG2). All participants had a bone density scan with Dual-energy X-ray absorptiometry (DXA). The analyzed variables were: BMD T-score from the hip and spine (according to WHO diagnostic criteria for osteoporosis) and haemophilic arthropathy from conventional radiology (Pettersson score) and from physical examination (Gilbert score). Number of joint bleedings was also analyzed. **Results:** In AG1, 6% of patients had osteoporosis, while among patients of AG2, osteoporosis was present in the 20%. Results show negative correlation between BMDhip and arthropathy (more arthropathy, less BMD) in no load joints according to Pettersson and Gilbert scores in AG1 patients (r=-0.61 and r=-0.54). In this group, number of bleedings in load joints is positively correlated with BMDhip (r=0.5). Patients in AG2 show negative correlation between BMDspine and arthropathy gotten from Pettersson and Gilbert scores in load joints (r=-0.42 and r=-0.58). **Conclusion:** In this work, correlations between haemophilic arthropathy and osteoporosis level (BMD) have been found. These two factors are currently present in this population. Therefore, it is necessary to implement physiotherapy and physical activity programs as well as hematological treatments, in order to reduce these comorbidities.

**P-220**

**An institutional pilot study to investigate physical activity patterns in boys with hemophilia**

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**Introduction:** Hemophilia is a disorder characterized by bleeding – particularly musculoskeletal. Trauma resulting in bleeding into joints/muscles may be associated with participation in certain physical activities. Recognizing this, patients with hemophilia may limit their activities to avoid bleeding. The characterization of physical activity levels (type, intensity, frequency and duration) of children with differing severities of hemophilia has not been well documented. This is required in order to better understand the relationship between physical activity and bleeding in children with mild to severe hemophilia. **Objectives:** The primary study objective was to compare the quantity of moderate to vigorous physical activity (MVPA) spent by boys with different hemophilia severities. A secondary objective was to determine if there are differences in the type or intensity of physical activity or function between boys with different hemophilia severities. **Materials/Methods:** Demographic information was collected. Subjects wore an accelerometer daily for one week and completed the PedHAL (Pediatric Hemophilia Activities List) and the 3DPAR (3 Day Physical Activity Recall) questionnaires. Accelerometer activity levels were classified as: a) sedentary b) light c) moderate or d) vigorous. Minutes spent in MVPA and sedentary activities were determined. All data were analyzed using SAS 9.4. Results: Sixty-six boys (42 severe (age: 11.17 ± 4.02 years and BMI: 20.05 kg/m² ± 5.82); 24 mild/moderate (age: 12.13 ± 3.95 years and BMI: 21.93 kg/m² ± 5.34]) took part in the study. Subjects with severe hemophilia participated in an average 48 ± 20 minutes of MVPA and 63 ± 12 minutes of sedentary activity daily. Subjects with mild/moderate hemophilia participated in 55 ± 18 minutes of MVPA and 327 ± 79 minutes of sedentary activities daily. The difference between the two groups for MVPA minutes was not significant (p = 0.16, p = 0.4). However, a significant difference in sedentary activity minutes was detected between the groups (p <0.01). No significant differences were noted between groups for MVPA derived from the 3DPAR or in the sum scores from the PedHAL. **Conclusion:** In our sample population, disease severity did not impact MVPA; however the role of prophylaxis requires further analysis. Future investigations may focus on sedentary time.

**P-221**

**Iliopsoas hemorrhage in patients with hemophilia: Single center experience**

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Iliopsoas haematoma is a well-recognized complication of haemophilia, and is considered as potentially life threatening and significantly associated with morbidity. There are only rare reports on the incidence or outcomes of iliopsoas bleeding since the widespread usage of modern therapies for haemophilia. In this study, we present the experience of Ege University Hemophilia Center with iliopsoas bleeding and its early and late complications. We reviewed 211 haemophiliacs followed between 1998 and 2015 (165 Haemophilia A, 46 Haemophilia B). Twentyone iliopsoas bleeding episodes were identified in 14 haemophiliacs (11 HA and 3 HB; 6-29 years). Eight patients (57%) had one episode, five (36%) had two episodes and one (7%) had three episodes. Five patients had a high titer inhibitor against factor VIII and accounted for 7 bleeding episodes (33%). Interestingly, three bleeding episodes were observed in the same patient who had mild haemophilia A. One moderate haemophilia A patient also had two bleeding episodes. We did not observe any episodes in patients receiving regular prophylactic treatment. Iliopsoas haematomas were confirmed by ultrasonography in all patients. In physical
examination, the most common symptoms were thigh, hip and groin pain, hip flexion contracture, abdominal tenderness and paresthesia in the distribution of the femoral nerve. The mean duration of therapy with clotting factor concentrate was 8.4 ± 2.6 days. The mean duration of hospitalization was 6.2 ± 2.5 days. All patients started to receive a physical therapy program 5.8 ± 2.4 days after the initiation of haemostatic therapy which lasted 21.0 ± 5.0 days. Ultrasonographic findings related to iliopsoas haematoma disappeared in all patients within 3 months from the initial episodes. Only in one patient with mild haemophilia A, heterotopic bone formation (myositis ossificans) developed as a long-term complication. In conclusion, pain around the hip joint, femoral neuropathy and hip flexion contracture in a patient with haemophilia should alert the physician to the possibility of an iliopsoas haematoma. Early and effective factor replacement therapy is essential in the prevention of the complications.

P-222
The school sports App for patients with haemophilia: Maximum safety during sports lessons through individual advice via smartphone and tablet
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Haemophilic children need an active participation in sports lessons. This is a demand of the convention on the rights of persons with disabilities of the United Nations Commission of the human rights, ratified in Germany in 2009. With the “Fit for Life” school sports counseling we created a concept of advising PWH concerning school sports since 2011. It is based on the results and the methods of the “Fit for Life” campaign since 2002. Smartphones are a part of every days living for children. This is why we established school sports counseling for PWH through a smartphone App. Thus the “Fit for Life” school sports counseling is of more interest for young PWH. This could lead to a diminished injury risk during school sports. The medical professionals have the possibility to update relevant joint status changes of their patients via the App. The basis is the joint status and the result of the standardized “Fit for Life” fitness test. A special algorithm helps to generate suitable school sports motion exercises out of a pool of 607 exercises related to the specific age groups. 133 persons answered the questionnaire (62 PWH, 60 parents of PWH and 11 sports teachers that do have PWH in their classes). Sports lessons are important for 87% of the PWH. 78% are looking forward to the sports lessons. 70% feel the profit. 88% feel more satisfied. 98% of the parents feel the relevance to take part in school sports. 95% see an increased satisfaction in their child. 85% believe that the other students accept their child more. 98% think that regular actualization of the counseling is useful. 97% believe that sports lessons improve the health. 95% consider the school sports counseling as helpful to decrease anxieties towards the participation of their child. All the sports teachers think that the school sports counseling is useful to individualize the contents of the sports lessons and that the participation of PWH will improve the psychosocial development of the children. They see the need of a actualization with adaptation of the contents for the different age groups.

P-223
Differences in sedentary behavior and physical activity between severe and mild young haemophiliacs
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Introduction: Due to repeated bleedings in the joints and musculoskeletal system, the amount of physical activity (PA) performed can be affected. Without a well-developed muscle mass involving joints, the risk of bleeding can increase. Nowadays, people with hemophilia show similar levels of PA than healthy population. This fact and the actual social tendency to inactivity ends in a lack of engagement on PA and more time spent in sedentary behavior (SB). The aim of this study is to compare the amount of PA at different intensities and SB in severe and mild hemophiliacs using accelerometers. Methods: 41 patients with hemophilia, severe (n = 12) and mild (n = 29) participated in this study. Each participant wore a triaxial accelerometer ACTIGRAPH GT3X (Actigraph, Fort Walton Beach, FL, USA) for seven consecutive days. The accelerometer was placed on the right hip. The acceleration signal was digitalized with a frequency of one sample per count (1 count = 16.6 milli G’s per second) over one minute intervals. A sample of PA and intensity levels is shown in Figure 1. Differences among groups regarding energy expenditure and time spent in sedentary activities were assessed by Student's two-tailed t-tests for independent samples.
Results of the intervention: No significant differences were found in time spent in SB. However, on light physical activity significant differences were shown (P<0.05) with mild patients spending more time in this intensity than severe patients (Figure 2). Therefore, it is necessary to promote PA in hemophilic patients to strengthen their musculoskeletal system and thereby improve their quality of life.

P-224
Pain, Functional Impairment, and Quality of Life (P-FIQ): Reliability of Patient-Reported Outcome (PRO) Instruments Assessing Pain and Function in US Adult People With Hemophilia (PWH)
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Objectives: To assess pain and functional impairment through 5 PRO instruments in non-bleeding adult PWH. Methods: Sequential adult male PWH (mild-severe) with a history of joint pain or bleeding completed a survey and PROs (EQ-5D-5L with visual analog scale [VAS], Brief Pain Inventory v2 [BPI], SF-36v2, International Physical Activity Questionnaire [IPAQ]),
and Hemophilia Activities List [HAL]) during routine visits. Initial patients were asked to complete 5 PROs again after their 3-4 hour visit. PRO scores were calculated from published algorithms. **Results:** 381 patients were enrolled between October 2013 and October 2014; 164 of the initial 187 completed the retest. Median time for completion of the initial survey/PROs was 36.0 minutes and for the PRO retest was 21.0 minutes. The majority of retest subjects had hemophilia A (74.4%) and were white-non-Hispanic (72.6%); median (Q1,Q3) age was 33.9 (26.9,46.0), 48.7% were married, 62.6% had some college or graduate education, 80.7% were employed, and 61.0% were overweight or obese. HCV was more common than HIV (49.4% vs 16.5%); 61.0% self-reported arthritis/bone/joint problems. Test-retest concordance and intraclass correlation coefficients (ICC) for reliability are shown in Table 2. Median (Q1,Q3) EQ-5D-5L VAS was 80.0 (65.0,90.0) and EQ-5D Index 0.80 (0.69,0.86); 61.6% reported problems with mobility, 55.8% with usual activities, and 22.0% with self-care. 73.2% reported pain-discomfort, and 41.1% reported anxiety-depression. For BPI, median (Q1,Q3) pain severity was 3.0 (1.3,4.8) and pain interference 2.9 (0.7,5.2); median worst pain was 6.0, least pain 2.0, average pain 3.0, and current pain 2.0. Ankles were the most frequently reported site of pain. Median IPAQ total activity was 693.0 MET/min/week; 49.3% reported no activity in the prior week. Median SF-36v2 scores were 39.6 for physical health, 51.6 for mental health, and 3.0 for overall health. Median (Q1,Q3) overall HAL score was 76.1 (59.2,95.1). **Relevance and Applicability to Care:** Data from the retest population provide a quantitative illustration of pain and functional impairment in adult PWH. All 5 PRO instruments appear to have sufficient reliability but provide different levels of detail in describing impact of hemophilia on pain and function and consequently have varied burden of administration.

**P-225**

How do patients and professionals differentiate between intra-articular joint bleed and acute flare-ups of arthropathy in patients with haemophilia?

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**Background:** Recurrent haemarthrosis in haemophilia causes haemophilia arthropathy (HA). Overuse of an arthropathic joint might cause a flare-up of HA. Pain, swelling and impaired range of motion (ROM) are the main symptoms of both haemarthrosis and flare-ups of HA, causing difficulties in differentiating. Diagnosis of haemarthrosis is currently empirically made based on clinical presentations. However, no standard diagnostic criteria are available. To offer appropriate treatment quick and accurate diagnosis is essential. Additionally, adequate differentiation can decrease health costs significantly. **Objective:** The aim of this study is to explore which symptoms and signs patients with haemophilia (PWH) and professionals use to differentiate between an intra- articular joint bleed and acute flare-ups of HA. **Methods:** A total of 6 focus group interviews were performed. Three focus groups were formed with in total 13 PWH and 3 focus groups were formed with in total 15 professionals (physicians, physiotherapist and nurses) specialized in treatment of PWH. The focus groups were structured using the Nominal Group Technique (NGT). Nominal questions were “How do you recognize a joint bleed?” and “How do you differentiate between a joint bleed and a flare-up of HA?” Results: The most important signs and symptoms used to differentiate between joint bleeds and HA are 1) course of the symptoms 2) cause of the complaints 3) joint history 4) type of pain 5) degree of impairments in ROM. **Conclusion:** This qualitative research provides insight in signs and symptoms that are currently used to differentiate between joint bleeds and flare-ups of HA. Results of this study can be used to develop a valid and standardized clinical diagnostic criteria set to differentiate between joint bleeds and flare ups of HA, which would be of great value in clinical practice. Preferably, this clinical diagnostic criterion set can be used by patients themselves and enables patients to react more adequate in cases of acute joint complaints. However, further research is necessary to validate the signs and symptoms found in the current study.

**P-226**

Optimal physiotherapy management for Lebanese PWH based on objective measurements

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**Objectives:** Follow-up Lebanese PWH by assessment (and record keeping) using standardized tools based on the ICE. Three levels: body, functional and activities and quality of life (HJHJS, FISH, HAL, HaemoQOL and pain scores); Check feasibility of the tests for the Lebanese situation; Train and discuss these skills in treatment of PWH. The focus groups were structured using the Nominal Group Technique (NGT). Nominal questions were “How do you recognize a joint bleed?” and “How do you differentiate between a joint bleed and a flare-up of HA?” Results: The most important signs and symptoms used to differentiate between joint bleeds and HA are 1) course of the symptoms 2) cause of the complaints 3) joint history 4) type of pain 5) degree of impairments in ROM. **Conclusion:** This qualitative research provides insight in signs and symptoms that are currently used to differentiate between joint bleeds and flare-ups of HA. Results of this study can be used to develop a valid and standardized clinical diagnostic criteria set to differentiate between joint bleeds and flare ups of HA, which would be of great value in clinical practice. Preferably, this clinical diagnostic criterion set can be used by patients themselves and enables patients to react more adequate in cases of acute joint complaints. However, further research is necessary to validate the signs and symptoms found in the current study.
P-227
Gait Deviations in Adolescent Boys With Haemophilia
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Objective: Researchers are increasingly using motion capture technology to analyse movement disorders and to provide details about mobility, imperceptible to the naked eye. To date, inclusion of functional activities using standardized tools to monitor children with haemophilia has received little attention. This study evaluated differences in walking patterns between a group of adolescent boys with haemophilia and age-matched, typically developing boys. Methods: Fourteen boys aged 11-18 years with haemophilia from five Haemophilia Centres in the UK (G1) and 14 age matched typically developing boys (G2) from local schools participated in the study. Kinematic and kinetic data for the hip, knee and ankle joints during level walking were analysed using principal component analysis. Temporal spatial parameters and regression scores for the principal components identified were used to test for between group differences using independent t-tests. Results: Adolescent boys with haemophilia adopted a gait pattern which differed from that of typically developing adolescent boys. Compared to typically developing adolescent boys, boys with haemophilia walked with a significantly (p = 0.03) shorter stance phase duration (G1: 57.75 ± 1.37%, G2: 58.95 ± 1.34%). Regression scores indicated a significantly (p = 0.04) reduced external ankle dorsiflexor moment during push off (G1: 0.60 ± 0.19 Nm·kg; G2: 0.77 ± 0.28 Nm·kg) and significantly (p = 0.03) reduced ankle plantarflexion angular motion during early to mid-swing (G1: -0.28 ± 3.95°; G2: -3.45 ± 3.41°). Relevance to haemophilia care: Adolescent boys with haemophilia reduced weight bearing together with the moments and motion at the ankle joint during walking. These findings show that adolescent boys with haemophilia altered their walking pattern possibly to protect and decrease forces at the ankle joint adding further evidence that despite prophylactic treatment, musculoskeletal health remains impaired. Key findings from this study could be used to develop quantitative monitoring of musculoskeletal function together with targeted therapeutic interventions in this group of high cost patients as well as identifying those at risk of developing chronic joint arthropathy and disability later in life.

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Development of specialist physiotherapy within a new haemophilia clinical network, UK
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Background: In 2012 a new comprehensive care centre (CCC) was commissioned to provide comprehensive haemophilia care to all children with inherited bleeding disorders in the region. Due to the scale of the geographical area, outreach clinics were established in September 2012 at regional hospitals to provide care to children and families closer to their homes. This retrospective service review describes the outcomes to date. Method: Five regional centres hosted 2 clinics per year. Every 6 months a paediatric Multi-Disciplinary Team (MDT) from the CCC, consisting of: Consultant Haematologist; haematology nurse specialist; specialist haemophilia physiotherapist conducted clinics with the local paediatrician, haematologist and, where possible, nurse and physiotherapist. The clinics provided a thorough holistic assessment of the patient, enabling the formulation of treatment plans and the support of routine and emergency care which continued under the local hospital. Physiotherapy assessment within the MDT consisted of: history and pattern of bleeding problems and symptoms; normal development; standard paediatric musculoskeletal assessment including the Haemophilia Joint Health Score and self/parental evaluation with PedHAL in those above the age of 4. Results: 30 patients who had attended the 5 regional clinics required formal physiotherapy assessment, as standards dictated by the UKHCDO. 19 had one or fewer contacts with the CCC prior to this review. Outcomes: At initial assessment, 15 patients were assessed as having undiagnosed musculoskeletal difficulties. A further 3 patients with moderate haemophilia commenced on a prophylaxis regime, none of whom had prior contact with a physiotherapist or CCC. These findings have resulted directly in changes in medical management and aided provision of ongoing therapy input by local physiotherapy services. Educational support for the local therapy team was essential to this process. Discussion: Review of the outcomes has identified the importance of MDT working; with physiotherapists acting as the specialists in musculoskeletal assessment, as not all musculoskeletal problems were being recognised by the patient or their clinicians. Specialist physiotherapy review needs to be timely and supportive of local services to enable equality of care for all paediatric patients.

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Multiple joint procedures in haemophilia: three case studies and standardizing of follow-up
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Introduction: Extension from single joint towards multiple joint procedures (MJP) occurred in our clinic since 1995. MJP are defined as any combination of Total Knee Arthroplasty (TKA), Total Hip Arthroplasty (THA) or ankle arthrodesis (AA), during one hospital admission (one session or staged). In-hospital rehabilitation was published (Haemophilia, 17, 2011: 971-8) as well as an onset for long-term follow-up (Haemophilia, 20, 2014: 276-81). Aim: Provide insight in individual changes with emphasis on activities of persons with hemophilia (PWH) who underwent Multiple Joint Procedures (MJP) by means of case studies. Complete the set of measurement instruments for long term follow-up of this population (n=53) in the Netherlands. M&M: Our cases originate from two subgroups: TKAs combined (n= 11) and a combination of two TKAs and two AA’s (n=10). Selection was based on the availability of data on activities pre operatively. All measurements pre and postoperatively will be...
presented, see results. **Results.** All cases stated a maximum only one point per joint, measured post-operative on a visual analogue scale (0 – 10 points), indicating good results of the procedures. They all showed very limited increase of range of motion (ROM). On individual level (self-reported activities) the Hemophilia Activities List (HAL) showed improvement in both basic as well as complex lower extremity activities. Self-reported activities (McMaster Toronto Arthritis patient disability questionnaire) showed individual progress by making priorities, however the time lap in between measurements resulted in a change of priorities, deciding not to use this for long-term follow-up. Performance based activities, i.e. the 50 meter walking test (50MWT), the timed up & go (TUG), the figure 8 test (preferred and maximum speed) and stair up and down, were evaluated. **Conclusion.** These three cases provide insight in the different levels of the ICT of these PWH, as well were we able to complete our measurement set for long term follow-up: Body level: active ROM andVAS per joint, nocturnal and overall pain. Activity level: HAL, 50 MWT, TUG, figure 8 (preferred and maximum speed) Societal level: SF36 and EQ-5D

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**Intelligent game engine for rehabilitation: an experience in hemophilic children**

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The aim of this work is to describe a game engine that has all the characteristics needed to support rehabilitation at home. The low-cost tracking devices recently introduced in the entertainment market allow measuring reliably at home, in real time, players’ motion with hand-free approach. Computer games appear suited to guide rehabilitation because their ability to engage the users. However, commercial videogames and game engines lack the peculiar functionalities required in rehabilitation. Games should be adapted to each patient’s functional status, and monitoring the patient’s motion is mandatory to avoid maladaptation. Feedback on performance and progression of the exercises should be provided. Lastly, several tracking devices should be considered, according to patient joint status and rehabilitation aims. We analyzed the needs of the clinicians and of the patients associated in performing rehabilitation at home, identifying the characteristics that the game engine should have. The result of this analysis has led us to develop the Intelligent Game for Rehabilitation (IGER) system for hemophilic children, which combines the principles upon which commercial games are designed with the needs of rehabilitation. IGER is heavily based on computational intelligence. Adaptation of the difficulty level of the exercise is carried out through a Bayesian framework from the observation of the patient’s success rate. Monitoring is implemented in fuzzy systems and based on rules defined for exercises by clinicians. The preliminary results of tests on patients with the supervision of clinicians have shown that IGER system indeed does feature the characteristics required to support rehabilitation at home and that it is ready for clinical pilot testing at patients’ home.

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**Exercise in Hemophilia: A systematic review**

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**Background:** Hemophilia is bleeding disorder which manifests with bleeding into joints and muscles. Exercise programs are often prescribed to help manage the recovery after a hemorrhosis/muscle bleed, to maintain/improve function in the presence of arthropathy or as a tool to help prevent bleeding episodes. **Objectives:** To systematically review the available evidence on the safety and effectiveness of exercise interventions for people with hemophilia.

**Search methods:** We searched the Cochrane Coagulopathies Trials Register using the terms “hemophilia and exercise.” Date of last search: 12 December 2014. We also searched the electronic databases PubMed, OVID-Embase, CINAHL (November 2014) and hand searched abstracts from the World Federation Congresses (1996-2014), the WFH Musculoskeletal Congresses (2005-2013), European Hematology Association Congresses (2002-2013) as well as the reference lists of relevant articles/reviews. Selection criteria: Type of study: Randomized controlled trials. Participants: Males of any age with hemophilia A or B. Interventions: Any exercise intervention relevant in the management of hemophilia. Primary Outcomes: bleed frequency, adverse events, quality of life. Secondary Outcomes: Balance/propioreception, aerobic activity, joint health score, pain, functional status, ROM, biceps perimeter, strength, knee circumference. **Results:** Eight studies (246 subjects) met the inclusion criteria. Several exercise programs were used including stretching/strengthening exercises, hydrotherapy, treadmill walking, stationary cycling. Significant variability was found in study design and there was significant heterogeneity in the measurement of outcomes. Primary outcomes reported a lack of data on the effect of exercise on bleeding frequency and no adverse events were reported. Overall we observed an effect of treatment on most secondary outcomes including two studies examined the effects of exercise as compared to control and reported a statistically significant improvement in pain intensity MD -2.12 VAS (95% CI -3.92 to -0.33 VAS), joint flexion MD 4.93 degrees (95% CI 1.19 to 8.67 degrees), joint extension MD 2.64 degrees (95% CI 1.30 to 3.97 degrees) favoring the exercise group. **Conclusion:** Positive effect of exercise in hemophilia with no reports of adverse events was demonstrated. The results should be considered with caution due to the small number of trials and the inability to pool the results due to the heterogeneity in measures of outcome.

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**Evaluation of a haemophilia joint health training workshop for physiotherapists in Kingston, Jamaica**

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**Background:** An estimated 200 persons with haemophilia live in
Jamaica, although a comprehensive patient registry has yet to be established. Due to limited access to clotting factor concentrates in Jamaica, patients often have long delays for treatment of bleeds or go untreated. In the absence of adequate factor treatment, the need for proficient musculoskeletal assessment and appropriate management is crucial. **Objective:** To evaluate the effectiveness of a Joint Health Curriculum (JHC) in educating physiotherapists (PT) in Kingston, Jamaica on assessment and management of musculoskeletal (MSK) conditions in haemophilia care. **Methods:** An Educational curriculum was created and disseminated by physiotherapists from the paediatric and adult Haemophilia Treatment Centres (HTC's) located respectively at The Hospital for Sick Children (SickKids) and St. Michael's Hospital in Toronto, Canada. Lectures were designed to educate learners on assessment and management of MSK issues in haemophilia and the role of the PT in the HTC. Practical hands-on sessions were designed to complement the didactic learning modules, with learners practicing assessment techniques on patients with haemophilia. Surveys were designed to assess the learner’s confidence in performing musculoskeletal assessments and creating a management plan for patients with haemophilia, and their beliefs regarding management of haemophilia patients. Surveys used 1-5 point scale for questions and were administered to the core participant's before and after the workshop. Additionally, qualitative feedback on the JHC was collected. **Results:** Eight learners in the JHC participated in the curriculum. Seven PT’s and 1 physiatrist were recruited from Jamaica and the Dominican Republic. Pre-workshop mean value for confidence questions was 2.66. Post-workshop mean values for confidence significantly improved to 4.16 (P<0.0001). Mean values for belief questions were 4.25 (pre-workshop) improved to 4.81 (post-workshop), but was not a statistically significant change. Learners also provided feedback about the changes they would make to their clinical practice after participating in the curriculum. Common responses were increasing the use of haemophilia outcome measures, providing education to other PT's about MSK management, and increasing haemophilia patient advocacy and education efforts. **Conclusions:** The JHC significantly improved the confidence of learners in performing assessment and providing management recommendations for persons with haemophilia.

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**Specialized training in hemophilia and job creation for physiotherapists with big visual impairments**

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**Objective:** Offering training about hemophilia and self-employment to students with big visual impairments in last year of physiotherapy or already with the college degree, with the goal of transmitting them knowledge and skills about physiotherapist treatment for patients with hemophilia. **Method used:** On November 2014 we began a 90 hours long training course, including both theory and practice about the following subjects: general characteristics of hemophilia; clinical manifestation and assessment; evaluation and treatment of the elbow, knee and ankle joints. **Results:** In the first edition of the course, we have trained 18 physiotherapy students, getting them prepared to offer a specialized treatment to people with hemophilia. Fedhemo help physiotherapists and patients to get in touch publishing a guide of professionals specialized in physiotherapy treatment of hemophilia in its web, including contact details and area of coverage so that patients could contact the nearest professional.

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**The functional gait analysis in persons with haemophilia: Quantitative data from a newly designed triaxial accelerometer**

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**Aim of the study:** People with haemophilia presents an arthropathy process that often bring to a relevant impairment of gait, with limitations to the performance of basic activities of daily living. We present a practical methodology for the objective, qualitative and quantitative evaluation of gait in pwh. **Methods:** Gait performance was evaluated by means of the G-WALK BTS inertial sensor for gait analysis (BTS Bioengineering SpA, Milan, Italy). A suitable belt with a pocket was used to place the sensor on the trunk at the waist level just over the reference bony mark of L5. Patients were then asked to walk freely for 10 meters on a 12 x 2 m corridor at the customary walking speed (CWS) without cueing or visual feedback. Two measures were performed, admission (ADM) and discharge (DIS). Spatial and temporal gait parameters have been evaluated **Results:** (Table 1). Affected side represent the side that underwent the last surgery and treated during the last hospitalization. **Relevance and applicability to hemophilia care:** Gait dysfunction is a very common cause of disability not only in pwh. GWALK sensor represents a reliable and pragmatic device for the objective evaluation of gait disturbances in clinical setting. **Originality of the work:** The use of a triaxial accelerometer sensor used during the test provides a better accessibility to a higher number of rehabilitation centers and clinicians involved in the management of pwh. The present functional gait analysis exam is intended to allow a cost-effective and clinically feasible global evaluation of gait in pwh.

**TABLE 1.**

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<th>Parameters</th>
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<th>DIS</th>
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<td>Gait Cycle Duration (s)</td>
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<tr>
<td>Step Length (% of Body Length)</td>
<td>54.49±5.47</td>
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<tr>
<td>Standing Height (cm)</td>
<td>148.62±8.02</td>
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<td>Sitting Height (cm)</td>
<td>158.88±6.42</td>
<td>154.90±5.86</td>
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<td>Sagittal Plane Deviation (%)</td>
<td>38.39±8.02</td>
<td>35.88±4.92</td>
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<tr>
<td>Pelvic Tilt (°)</td>
<td>21.12±7.88</td>
<td>20.63±5.42</td>
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<tr>
<td>Propulsion Angles (%)</td>
<td>1.62±0.37</td>
<td>1.16±0.36</td>
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**Effects of Adm vs. DIS**

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