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Abstracts

Physiotherapy Professional Development Workshop

PDW-01
Global Physiotherapy Initiative – an update
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Although the WFH recommends comprehensive care in hemophilia treatment centres (HTC) worldwide, physiotherapists are still rarely involved. This is a problem of both developing and developed countries. Regular WFH grants, to train physiotherapists from developing countries, do not solve these shortcomings.

A Global Physiotherapy Initiative (GPI) was started in 2007. It is based on the principle of training the trainers, in close cooperation with WFH coordinators, regional NMOs, and local medical and paramedical professionals. Emphasis is on training the local trainers, combined with training and implementing basic physiotherapy on the spot. The intention is to set up and stabilize a regional network, in three steps: 1) One-day symposium (attract medical doctors and physiotherapist), and a two- or three-day workshop (for physiotherapists mainly); 2) Site visits, to encourage the role of the physiotherapist inside the HTCs; 3) International course: one-day symposium and two-day workshops, organized by the local trainer for colleagues from that region. Results will be given from two pilot projects (Russia and Egypt) of which only one enrolled into an Arabic physiotherapy network. The Balkans and Baltic region will have their third step later this year. All three existing regions produced trainers, not originating from developed countries, as well as implemented physiotherapy care. Finding tailored solutions for each HTC in this implementation process – with a proper set up, communication, and the cooperation of hematologists and physiotherapists – is still a challenge. But when it works, people with hemophilia (PWH) worldwide will benefit, running towards optimal functional capabilities and, thus, better quality of life.

Session A1 – State of the Art

A1.1
Nuclear factor (NF)-κB and its associated pathways are major molecular regulators of blood induced joint damage in a murine model of hemophilia
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Methods and Results: A sharp-injury model of hemarthrosis that recapitulated the histomorphologic features of both acute hemarthrosis and chronic arthropathy, seen after single- or multiple-articular bleeds, respectively, was used. A global gene expression array on joint-specific RNA isolated 3h post-injury revealed nuclear factor-kappa B (NF-κB) as the major transcription factor triggering inflammation. Since a number of genes encoding various cytokines, growth factors, and hypoxia-regulating factors are known to be activated by NF-κB and many of these are part of the pathogenesis of various joint diseases, we reasoned that NF-κB associated pathways may play a crucial role in blood-induced joint damage. To further understand how the transcriptional potential and activity of this factor is regulated upon bleeding, we did a targeted screening of NF-κB associated pathways between 1h and 90 days after injury. After a single-articular bleed, distinct members of the NF-κB family (NF-κB1/NF-κB2/RelA/RelB) and their responsive pro-inflammatory cytokines (IL-1β/IL-6/IFNγ/TNFα) were significantly up-regulated (>2 fold, p<0.05) in injured vs control joints at the various time-points analyzed (1h/3h/7h/24h). On multiple injury models (day 30/60/75/90), downstream targets of NF-κB, that contribute to hypoxia (HIF-1α, 3.3-6.5 fold), angiogenesis (VEGF-α, 2.5-4.4 fold), and chondrocyte damage (matrix metalloproteinase-13, 2.8-3.8 fold) were significantly (p<0.05) elevated in the injured joints. Many key micro RNAs (miR) with documented roles in NF-κB activation (miRs-9 and 155), inflammation (miRs-16, 155 and 182), and apoptosis (miRs-19a, 155 and 186) were also differentially expressed after joint bleeding (~4 to 13-fold), indicating that the small RNAs could modulate the arthropathy phenotype.

Conclusions: These data suggest that NF-κB associated signaling pathways are involved in the development of hemophilic arthropathy. Further ongoing studies by specific blocking of NF-κB alone or in combination with other key targets such as HIF-1α, VEGF-α, or MMP-13, or modulating the expression of miRNAs (e.g. miR-155) in the hemarthrosis models, will shed further mechanistic insights into this phenomenon.

Keywords: hemophilic arthropathy, hemarthrosis

A1.2
IPSG scoring system
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Abstract unavailable

A1.3
Wound healing in hemophilia
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Our group has been studying how hemostasis affects tissue repair processes in a mouse model of hemophilia B. One of our major goals is to gain information that will assist in optimizing
Osteoporosis

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Bone mineral density (BMD) is determined by peak bone mass and the rate of bone loss. Peak bone mass is reached in the third decade of life and is influenced by genetics, nutrition, body weight, and weight-bearing physical activity. Bone mass remains relatively constant until bone loss begins later in life. Accelerated bone loss can occur resulting in lower peak bone mass if it occurs early in life or progressive bone loss. Osteoporosis is characterized by reduced mass and impaired quality or structural integrity of bone, increasing the risk of fracture. This may be achieved by failure to achieve optimal bone strength (low peak bone mass), excessive bone resorption, or defective bone formation. DEXA is a screening tool for osteoporosis by attempting to measure BMD. Treatment is generally focused on promoting increasing bone mass or anti-resorptive medications. Osteoporosis is an underestimated problem in individuals with hemophilia. Repeated studies have shown a correlation with hemophilia and reduced bone density and/or osteoporosis, compared to controls. Contributing factors in this population may include avoidance of weight bearing physical activity as a child or adolescent, prolonged immobilization, presence of comorbid infections, including HIV and hepatitis C, and the presence of excess iron from intra-articular bleeding. Treatment strategies in this population include weight-bearing physical activity, treating joint disease to maintain mobility, adequate calcium and vitamin D supplementation, and the possible use of antiresorptive medications. Improved screening for early detection in this high-risk population is needed.

Keywords: osteoporosis, bone mineral density, DEXA
A3.1
Avoiding non-union in subtalar joint fusion
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Hemophilic arthropathy of the ankle is often associated with arthropathy of the subtalar joint (STJ). Recurrent bleeding and chronic hemorrhagic synovitis primarily affect the posterior facet. Early involvement is most easily detected at the posterior margin of the posterior facet on lateral ankle X-ray. STJ involvement is evident in about 50% of hemophilia patients who are candidates for ankle fusion. Symptoms of STJ involvement are pain in the region of the sinus tarsi that is aggravated by inversion and eversion. On physical exam, rocking the STJ with the ankle in full flexion, compressing the posterior margin of the posterior facet, will often produce crepitus and reproduce the pain. In these patients, it is important to include fusion of the STJ with the ankle fusion. More rarely, arthropathy of the STJ is present without ankle involvement. The incidence of non-union of the STJ is slightly higher than that for the ankle. In our study, reported at the WFH 2012 World Congress in Paris, the incidence of tibio-talar non-union was 3.7% compared to 5.6% for the STJ. However, these non-unions had stable fibrous union and none required reoperation. Several techniques can be utilized to help facilitate union in STJ arthrodesis. Our approach focuses on the posterior facet. After thorough debridement and curettage, the opposing bony surfaces are “fish-scaled” with a ¼” osteotome to create interdigitating surfaces. Stable fixation and compression of those surfaces is accomplished with two cancellous small fragment screws. When the ankle is included, an anterior plate is utilized with three screws across the STJ. It is essential that the posterior facet be well opposed and compressed prior to placing the anterior plate. Otherwise the anterior screws may actually hold the STJ apart. Immobilization in a short leg cast, non-weight bearing until the x-rays show early consolidation, is important. The time to solid fusion will usually be longer than for ankle fusion alone.

Keywords: hemophilic arthropathy, joint fusion

A3.2
The arthritic knee with flexion contracture: Steps to achieve extension during total knee replacement (TKR)
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Abstract unavailable

A3.3
Hemophilic Chronic Synovitis: Therapy of hemarthrosis using endovascular embolization of knee and elbow arteries

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Purpose: Synovitis in patients with hemophilia is a condition that leads to joint damage and disabled patients. Selective embolization of the knee and elbow arteries can prevent bleeding episodes. The aim of this study is to evaluate the decrease of bleeding in the affected joint before and after selective arterial embolization. Materials and Methods: We performed 30 procedures in 27 hemophilic patients; including 23 knee, and 7 elbow procedures. To evaluate the efficacy of selective embolization of knee and elbow arteries in people with hemophilia, we analyzed the number of bleeding episodes for 12 months before the procedure, compared with the amount of episodes that occurred 3, 6 and 12 months after embolization. Results: Twenty-nine out of 30 procedures were classified as successful. The median of 1.25 episodes per month (range 0-3) observed before the procedure was reduced to 0 (range 0–1.67) (p<0.001) at 3 months, 0.17 (range 0–1.67) (p<0.001) at 6 months, and 0.33 (range 0–1.67) (p=0.024) at 12 months. Three patients remained free of bleeding events for more than six months. Additionally, after the procedure there was a significant reduction in factor VIII usage that sustained up to 12 months after the procedures. No serious adverse events were observed. Conclusions: Selective angiographic embolization of knee and elbow arteries is a feasible procedure that can prevent repetitive bleedings, which would translate into better joint outcomes for these patients.

Keywords: hemophilia, arterial embolization, hemorrhosis, interventional radiology

A4.1
Total knee replacement in patients with inherited bleeding disorders: Early results
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Introduction: The prospective trial aimed at assessing early results of total knee replacement (TKR) in patients with hemophilia A and von Willebrand disease compared to a group operated due to primary degenerative joint disorder (DJD). The evaluation covered postoperative blood loss, pre- and postoperative clinical outcomes, level of pain, and range of motion (ROM). Methods: The study group: 27 patients – (30 knees) operated for hemophilic arthropathy. Hemophilia A – 24 patients, including 1 with high-tither inhibitor. Von Willebrand disease – 3 patients: Routine administration of antithrombotic prophylaxis with nadroparine in patients with additional risk factors for venous thromboembolism (VTE). No thromboprophilaxis administered in inhibitor patient. Discharge was followed by outpatient treatment including physiotherapy. The comparison group: 30
patients (30 knees) – requiring TKR for primary DJD. WOMAC Osteoarthritis Index and Knee Society Score for clinical evaluation and Visual Analogue Score (VAS) for pain evaluation were used. Pre- and postoperative ROM and postoperative blood loss were assessed. Radiographic evaluation was at outpatient visits during follow-up that lasted 12 months. Results: Clinical results in the study and comparison groups were good and satisfactory. Considerable pain reduction was observed. Results were comparable in both groups and its improvement was statistically significant. The mean ROM improvement in the study group was 24° and, in the comparison group, - 13°. Postoperative blood loss was comparable: - 423.67 ml in the study group and 453.50 ml in the comparison group. No symptomatic VTE complications occurred. Conclusion: TKR in patients with inherited bleeding disorders is a very demanding procedure and requires particular surgical and hematological expertise. Early clinical results are promising and comparable to group operated for primary DJD. Pain alleviation and improvement in locomotor abilities were significant despite only minor increase in ROM. Postoperative blood loss was acceptable and comparable in both groups.

Keywords: TKR, hemophilia A.

A4.2

Accelerated discharge programs post total knee replacements (TKR): Are these suitable for people with hemophilia (PWH)? A review of cases at the Haemophilia Comprehensive Care Centre, Belfast, Northern Ireland

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Background: Musgrave Park Hospital, Belfast, operates an accelerated discharge program post TKR for all patients including those with a history of hemophilia, contrasting with reported detail of other hemophilia patients in the UK. Methods: Retrospective review of PWH A or B, post TKR, at Musgrave Park Hospital (July 2002 – July 2012). Information collected using case note review, Belfast Orthopaedic Information System, and patient questionnaire. Results: 15 cases (9 patients): severe hemophilia A (n=8); severe hemophilia B (n=1). Primary n=9; revision n=6. Mean age was 48 years (36-74). Seven patients were Hep C+ve, two of whom were HIV+ve. Two were not affected. Patients received the standard post-operative inpatient care. Factor cover was managed by the Haemophilia Comprehensive Care Team. Mean factor use during the perioperative period was 73,971IU (48,000IU – 107,000IU). Mean length of stay (post-op) was five days (2-12) with 13 discharged directly home. Forty per cent of these were discharged by day 3. Of the two cases transferred to Belfast City Hospital at day 2, one was discharged day 6 postoperatively without further problems. The other had significant co-morbidities and was ultimately discharged home 25 days post-surgery. Overall, patient satisfaction was good. Twelve were very satisfied with surgery in terms of pain relief, ability to return to work and ability to perform their usual leisure activities. There were three early complications. One popliteal artery occlusion requiring further surgery and two bleeds following discharge. Late complications included one popliteal aneurysm, one infection requiring two-stage revisions, and one loss of joint range. Discussion: This review demonstrates that PWH can safely participate in an accelerated discharge program. Recent years have seen a reduction in the mean length of stay required (Fig 1). Multicentre review of current practice, together with previously identified predictors of protracted admission, may help to identify those PWH most suited to this approach.

FIGURE 1: MEAN LENGTH OF STAY (post-op)

Keywords: accelerated discharge, total knee replacement

A4.3

Total ankle replacement in patients with severe hemophilic arthropathy

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Objectives: Arthropathy of the ankle is a frequent complication in hemophilic patients. Therapeutic approaches for surgical interventions in cases of advanced joint destruction include arthrodesis or endoprosthesis. There is only very limited literature data available on total ankle replacement (TAR) in hemophilia patients. The objective of this study is to evaluate the results after TAR in patients suffering from advanced hemophilic...
arthropathy. **Methods:** In a retrospective study, results after TAR (type: Hintegra) were evaluated in 10 patients (11 endoprostheses) with severe (n=8) or moderate (n=2) hemophilia. All patients suffered from severe ankle arthropathy with a Pettersson score of ≥ 10. Nine patients were positive for hepatitis C, five were HIV-positive. Mean follow-up was 2.6 years (range, 1.2 – 5.0 years). Range of motion (ROM), AOFAS ankle-hindfoot score, pain status (visual analogue scale, VAS) as well as patient satisfaction was determined prior to surgical intervention and every six months postoperatively. The data were statistically analyzed using SPSS Version 21.0. **Results:** The 3-year survival rate following implantation was 81.8 %. In two cases, deep prosthetic infection occurred leading to the removal of the implant. In the remaining eight patients (nine implants), the mean AOFAS ankle-hindfoot score improved significantly from 21.5 to 68.0 (p<0.0005), the VAS score decreased significantly from a mean of 7.6 to 1.9 (p<0.0005). ROM did not increase significantly, i.e. from 23.2 to 25.0 degrees. At final follow-up, all patients were satisfied with the surgical result. Radiological controls did not suggest any signs of prosthetic loosening. **Conclusions:** TAR constitutes a therapeutic alternative to arthrodesis in cases of advanced hemophilic arthropathy, providing good pain reduction and high patient satisfaction. Marginal postoperative increase in range of motion may be explained by pre-existing soft tissue scarring caused by repetitive bleeding events in hemophilic arthropathy. Due to the increased risk of infection and a lack of long-term results, TAR in patients suffering from severe hemophilia should be indicated carefully.

**Keywords:** arthropathy, TAR, hemophilia

**A4.4 Outcomes of total knee arthroplasty (TKA) in the hemophilia population: A meta-analysis**

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**Background/Objective:** People with hemophilia (PWH) experience end-stage joint disease due to repeated hemorrhosis. In this review, we examined the available literature on total knee arthroplasty (TKA) outcomes in PWH. **Methods:** A literature review was performed to identify studies with functional outcomes after TKA in PWH published between 1980 and 2012. Inclusion criteria were studies with greater than five TKAs in PWH, reported Hospital for Special Surgery Knee Score (HSSKS), knee range of motion (ROM), and complication rates. Variables such as inhibitor status, hemophilia severity, and HIV status were not criteria for inclusion or exclusion. A meta-analysis was performed on extracted mean and standard deviation data to create a single group effect size and 95% confidence interval for the HSSKS, ROM data, and complication rate with subcategories for infection and revision rate. **Results:** Eleven studies met inclusion criteria; seven of eleven had sufficient data for meta-analysis review. 216 TKAs in 158 PWH were analyzed with a mean follow-up of 5.4 years (SD 1.4). TKA in PWH demonstrated statistically significant ROM improvements: 6.67 degrees improvement of the flexion contracture (-.94 SE, CI -1.34 to -0.54), and 5.10 degrees increase into flexion (.44 SE, CI .22 to .66). HSSKS is a validated outcome tool for the TKA population. 36.8 point increase in the HSSKS score was reported among subjects (4.00 SE, CI 1.99 to 6.00). 20 revisions out of 216 TKAs were reported due to aseptic loosening, infection, and excessive hemorrhaging. **Conclusions:** Total knee arthroplasty is an effective procedure for reducing the effects of hemophilic arthropathy; ROM deficits, and functional deficits. PWH have less ROM gains; however, functional gains reflected via the HSSKS demonstrate TKA improves overall function. This study provides guidelines on expectations post-TKA in PWH based on seven retrospective studies.

**Keywords:** Hemophilia; Total Knee Arthroplasty

**A4.5 Radiosynoviorthesis with three types of radiopharmaceuticals: results in 400 patients**

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Chronic synovitis has major importance in hemophilia care. Radiosynoviorthesis (RS), the intra-articular injection of radiopharmaceuticals (RP), represents an effective and minimally invasive treatment for refractory synovitis. Some characteristics influence RP choice, such as particle size, tissue penetration depth, and availability. Accordingly, yttrium-90 cite (C.90(Y)), yttrium-90 hydroxyapatite (HA-90Y), and samarium-153 hydroxyapatite (HA-153Sm) have been used in Brazil and the objective of this study is to compare the results achieved by these RP. A total of 400 patients with 697 joints were treated in two centres. Six months pre- and post-RS it was compared: number of joint bleeds, range of motion (ROM) and pain (WFL scale). Outcomes were classified as Failure: <50% bleeding reduction; Good: bleeding reduction 50%-75% plus improvement in ROM and pain; and
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Excellent: bleeding reduction >75% plus improvement in ROM and pain. We found statistically significant differences between the three RP in knees, favoring C-90Y. Hence C-90Y compared to HA-153Sm showed OR=9.4 and 7.399, respectively regarding good and excellent outcomes. Differences between the three RP were not statistically significant regarding elbows and ankles. Even properly located inside the joints, RS with 2 mCi of HA-90Y caused cutaneous burn in two ankles (0.5%) of two patients (0.3%), one requiring surgery after five months of evolution; none have presently severe sequelae, eight months post-RS. All three RP achieved reduction of hemarthroses in different percentages. We concluded that 90Y labeled RP, having high tissue penetration depth (mean 3.6 mm, max 11 mm), should be utilized in knees, while HA-153Sm, presenting lower penetration depth (mean 0.7 mm, max 3.1 mm), seems suitable for medium-sized joints. RS is an important therapy for hemophilic synovitis, and centres must count on RP adequate to each case.

Key word: radiosynoviorthesis

A4.6

A fusion protein of IL4 and IL10 (IL4-10 synerkine), is equally effective in protecting cartilage from blood-induced damage compared to the individual components


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Objective: Recombinant human IL4, IL10, or the combination, protects cartilage from blood-induced damage in vitro. To overcome low bioavailability of IL4 and IL10 in vivo, a fusion protein is developed: IL4-10 synerkine. This study investigates whether the IL4-10 synerkine protects against blood-induced cartilage damage similarly as the combination of the individual components.

Methods: Human cartilage explants were exposed to 50% v/v whole blood for four days and simultaneously to a broad concentration range (0-100ng/mL) of the IL4-10 synerkine. Effects of 10 ng/mL IL4-10 synerkine were compared to the individual cytokines, testing the IL4-10 synerkine compared to the individual cytokines, testing the IL4-10 synerkine in an in vivo model of blood-induced cartilage damage is warranted.

Keywords: arthropathy, Synerkine

A4.7

Subchondral cyst in people with hemophilia (PWH) treated with bone substitute (OH apatite coralline)

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Introduction: Subchondral cysts usually can be progressive and lead to joint destruction. Materials and Methods: 37 patients with 49 subchondral cyst were treated. 34 patients suffering from hemophilia A and three from hemophilia B. Four patients presented inhibitors; one was low responder. The mean follow up was nine years (1-18). Most affected bones were the tibia and talus. The lesions were treated when the injury was greater than 15% of the area of the affected joint. The treatment consisted of aspiration of the cyst and filling with coralline hydroxyapatite. Results: 48 cysts cured (p<002); one cyst with extensive tibial lesion recurred at three years and 30% of its original size. The patient underwent surgery and was filled again with coralline hydroxyapatite and finally healed. None of the patients required a TKR in the affected joint. The outcome was similar in patients with and without inhibitors. Relevance and applicability to hemophilia care: This method of treatment has prevented the progression of joint damage. More than 15 years of experience with the method has proven effective and inexpensive. The originality of the work: This is the longest series of subchondral cysts treated with aspiration and filling, using a bone substitute such as coralline hydroxyapatite. This study demonstrates that the coralline hydroxyapatite is an adequate bone substitute; it is suitable for use in patients with hemophilia.

Keywords: subchondral cyst, bone substitute

FIGURE 1: Effect of the IL4-10 synerkine compared to IL4 and IL10 on cartilage proteoglycan synthesis rate (n=8). Median values ± interquartile range are depicted. Hash tags indicate a statistically significant difference compared to 50% v/v blood (p<0.05), asterisks indicate a statistically significant difference compared to control cartilage (p<0.05).
A4.8

Knee flexion contracture treated with botulinum toxin type A in people with hemophilia (PWH)

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Introduction: The knee flexion contracture produces disability in PWH. Objective: To evaluate the effectiveness of conservative treatment of knee flexes with botulinum toxin type A in PWH. Materials and Methods: 13 patients were treated, with 17 affected knees. Eleven patients had severe hemophilia A, two of whom had high response inhibitor, two had severe hemophilia B; mean age was 26 years (9-52). The mean follow-up was seven months (6-12). Depending on the degree of flexion contracture, patients were divided into groups: Group I: - 10° to -30° (n = 9), Group II; -31° to -45° (n = 4) Group III, > -60° (n = 4). The rehabilitation started on the same day of injection. Results: The average pre-operative flexion was 117° and post-operative was 124°. The total increase was 7°. This finding was not statistically significant. The extension improved from -36° to -20°. The improvement was 16° (p<0.001). Group I improved 8°, group II 21°, and group III 28°. The difference was statistically significant in group III (p<0.004).

Relevance and applicability to hemophilia care: This procedure is a low cost, easy application with very good results, which improves the quality of gait in PWH. The originality of the work: It is the only experience using botulinum toxin for flexed knee in PWH.

Keywords: knee flexion; botulinum toxin

A4.9

Orthopedic surgery in patients affected by von Willebrand disease (VWD) and rare bleeding disorders

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Background: Patients affected by VWD and severe rare bleeding disorders (RBD) may suffer from disabling chronic arthropathy as a consequence of recurrent intra-articular bleeding or may require orthopedic surgery independently of their coagulation disorder. Orthopedic surgery in patients with clotting disorders represents a surgical challenge and information regarding the management of orthopedic surgery in such patients is limited. Aim: Description of orthopedic surgery management in patients affected by VWD or RBDs. Methods: Retrospective data collection regarding orthopedic surgery between January 1981 and November 2012. Seventy-one procedures were made in 48 patients affected by VWD (25 patients) or RBDs (23 patients). Results: Of the 71 orthopedic procedures, 12 were minor surgeries (seven hand surgeries, five others) and 59 were major surgeries (19 arthroplasty, 19 arthroscopic procedures, 21 others procedures). The median age of the patients at surgery was 47 years (range: 10-78) and the median follow-up time was 37 months (range: 1-384). The most frequent RBDs were FVII (11/22) and FXI (7/22) deficiency. Bleeding complications occurred in five procedures (7%). No late bleeding problems were recorded. Only three patients received prophylaxis with low molecular-weight heparin (LMWH). Conclusion: Good control of hemostasis can be achieved with an appropriate substitutive therapy in severe bleeding disorders. Mild deficiency replacement therapy can be avoided before surgery in some cases but needs to be available and used in case of excessive bleeding. The control of the bleeding disorder, combined with the surgical technique, is the reason for a high success rate. Post-operative rehabilitation begins immediately after surgery, under treatment coverage when indicated. In conclusion, orthopedic surgery performed in a specialized hemophilia centre is a safe procedure.

Keywords: orthopedic surgery, von Willebrand disease, rare coagulation disorders

A4.10

Cartilage damage biomarkers are increased after a joint bleed; an explorative human and canine in vivo study

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Objective: In hemophilia, a panel of four biomarkers for cartilage degradation (uCTX-II, sCOMP, sc1,C2, scCS846) is associated with overall radiographic joint damage. This study investigates for the first time whether these biomarkers can sense cartilage degradation immediately after a joint bleed. Methods: uCTX-II, sCOMP, sc1,C2, and scCS846 levels were measured in hemophilia patients (n=8) at three time points: within 2 days, after 3-5 days, and about 90 days after a joint bleed (considered as baseline). Similar, a joint bleed was induced in dogs (n=7) by intra-articular autologous blood injections over 5 days. The same biomarkers were measured before the experimental joint bleed, immediately after this bleeding episode, 5 and 90 days later.

Results: In hemophilia patients, the levels of all four biomarkers were elevated 3-5 days after a joint bleed, compared to baseline (p<0.05). A combined score of the four biomarkers, 3-5 days after the bleed, increased compared to levels directly after the bleed (p=0.024). In dogs, 5 days after the bleed, the biomarkers were increased, except for sCOMP; uCTX-II and the combined score were significantly different compared to the levels directly after the induced bleed (p=0.007 and p=0.02). At 90 days, the levels were similar to the pre-bleeding levels. Conclusion: This study demonstrates that joint tissue damage biomarkers increase already after a single joint bleed, both in an experimental and clinical setting. A combined score could be used to detect cartilage degradation immediately after a joint bleed, supporting early cartilage damage after a single bleed.

Keywords: arthropathy, biomarkers
Abstracts

Session B1 – Plenary

B1.1
The World Federation of Hemophilia Research Agenda

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The World Federation of Hemophilia (WFH) has a longstanding history of excellence in supporting the care of persons with inherited bleeding disorders, worldwide. This program of activities has provided access to care in many countries where treatments were not previously available. Alongside these enhancements to global treatment access, the inherited bleeding disorder community has witnessed significant advances in translational initiatives to further improve diagnostic and therapeutic approaches. With this background, the WFH has initiated a new program of activity focused on the support of research into clinical outcomes for inherited bleeding disorders. This program will be supported by new sources of funding, and is intended to run as a complementary program to the existing WFH activities focused on advocacy and clinical care. The new research program will initially comprise two distinct but overlapping foci of investigation: an enhancement of the intramural Global Survey data collection and an extramural grant competition intended to support a small number of projects aimed at novel aspects of clinical outcome evaluation. The initial stages of assessing the current limitations and potential future enhancements of the Global Survey are already underway, and new components of this process are being discussed with the WFH Data and Demographics Committee. The ultimate intention is that this collation of global data could be used by extramural researchers to address specific clinical outcome questions. The second component of the new WFH Research Program will also be launched in 2013, and will provide opportunities for extramural investigators to obtain support for innovative projects whose objective is to provide new information relating to clinical care outcomes.

Session B2 – Crossfire Session: Biological Therapies

B2.1
Biological therapies – The theory

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The standard of care for hemophilia therapy is infusion of coagulation factor protein, using recombinant proteins when possible. This therapy maintains and/or restores the potential for secondary hemostasis. The physiologic effects of hemophilic bleeding are not confined to detrimental anemia or mass effect of unchecked hemorrhage, however. Intra-articular bleeding, in particular, is associated with a cascade of inflammatory and neoangiogenic effects that mediate degradation of joints and bone long after hemostasis has been restored. Evidence is accumulating that even after hemostasis has been achieved, the continued support of thrombin-generating potential helps normalize events in the prolonged period of wound repair. One potential advantage of using complex biological therapies such as virus-mediated or cell-mediated nucleic acid therapies (gene therapy) is the chance to support optimal wound healing, along with optimal prophylaxis via endogenous clotting factor production following transgene delivery. Specific therapies to oppose inflammatory cytokines, including Interleukin 6 (IL-6) receptor antagonists and TNF-alpha receptor antagonists based on engineered immunoglobulins, have become important in the management of inflammatory joint disease, including both childhood and adult rheumatoid arthritis. In mouse models of hemophilia A and B, short-course specific inhibition of these inflammatory cytokines, as an adjunctive approach along with replacement of hemostasis, has been demonstrated to improve the protection from synovitis, when compared to clotting factor alone. These biologics were more effective than non-specific small molecule anti-inflammatory, such as corticosteroids, in these models. Alternative biologic agents that have shown promise in animal models include cytokines that oppose inflammation and neoangiogenesis.

B2.2
Biological therapies – The theory: Why not

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The treatment of hemophilia has progressed significantly since the first written description of the affliction, found during the second century in the Babylonian Talmud, when nothing more than mechanical pressure and hopes for divine intervention were practiced. Later descriptions of the homeopathic remedies used by Leopold and Alexis – who suffered from the “Royal disease” around 1900 – and the injection of a series of ever more pure products to replace missing or defective coagulation factor, beginning in the 1940s. Eight decades later, patients with hemophilia A and B have highly purified concentrates of recombinant factor VIII and IX, respectively available in abundance (in countries willing and able to pay for these drugs). The currently available products are highly effective and able to control hemorrhage with one, or at most, two injections in more than 90% of all bleeding episodes. The products are capable of preventing hemorrhage when administered in the absence of bleeding in virtually all children without existing joint disease, and even in many adolescents and adults with pre-existing joint damage. Importantly, the products are able to prevent hemorrhage during surgical procedures in nearly all cases. In each of these scenarios, the mainstay of treatment is replacement of the missing coagulation factor activity to correct the error of nature. Four very important issues face the hemophilia community today when considering treatment of hemophilia These include: 1) development of new products with sustained duration of action, capable of reducing the frequency of administration; 2) development of therapeutic strategies to circumvent the need for intravenous delivery of replacement products; 3) development of therapies that are less immunogenic; and 4) two items of critical importance to...
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the global hemophilia community: cost and accessibility of the treatments. Herein, each of these issues will be discussed briefly and highlights of the progress made to date in each of these areas will be provided. These achievements underscore the need for caution when considering biological therapies, including gene transfer and use of bioactive molecules, both of which have the potential for serious and considerable deleterious effects on patients with hemophilia. The risks and benefits as well as the costs to the patient and to society must be part of the equation when evaluating any novel therapy. At this time, the evidence argues against the clinical use of biological therapies in patients with hemophilia.

B2.4
Biological Therapies – The reality: Why not

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Nowadays, the most usual surgical procedures for treating articular cartilage defects (cartilage repair) include abrasion chondroplasty, microfracture, mosaicplasty, autologous chondrocyte implantation (ACI), and matrix-induced ACI. In small defects (<2–4cm²), osteochondral autograft or microfracture are the recommended options. In large defects (>2–4cm²), ACI, or osteochondral allograft are indicated. However, so far we have not applied these techniques in hemophilic patients because inflammatory conditions and advanced degenerative change (>50% joint space narrowing) are contraindications for cartilage repair. Thus, prevention of cartilage damage is paramount in hemophilia [1]. Newly developed techniques, mainly those based on cell therapy that use bioreactors, growth factors, mesenchymal stem cells (MSC) and genetically-modified cells, still are under investigation. The aim of cell therapy is restoration of function through the repair of damaged tissue or the stimulation of growth factor synthesis. MSCs hold promise for the repair of joint cartilage given their differentiation capacity and the therapeutic effect induced by a more natural and biologic restoration. The use of bioreactors and growth factors, which stimulate cartilage formation, may optimize such strategies in the context of reimplantation of chondrocytes, differentiated MSCs and cartilage progenitor cells. Implantation of autologous chondrocytes or MSCs was, up to now, able to address only highly localized chondral lesions. Adequate control of the differentiation process, as well as the use of growth factors and appropriate bioreactors, could transform cell-based therapies into a more efficient and longer term treatment, even for patients with hemophilia. We still have a long way to go before use of biological therapies in hemophilic arthropathy. Raising false expectations in hemophilia patients should be avoided [2].

References

Session B3 – Muscle Bleeding

B3.1
Muscle bleeding – Diagnostics: How and when?

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Approximately 20% of all bleeding episodes in individuals with hemophilia occur into muscle. Following joint bleeding, it is the second most frequent consequence of hemophilia and, like joint bleeding, is more common in the lower limb than the upper limb. A recent 12-month study of bleeding patterns in children and adults with severe hemophilia found that the order of muscle bleeding frequency was the forearm, thigh, lower leg, foot, hand, back, groin, upper arm, buttock and iliopsoas, with the forearm and thigh muscle groups accounting for 40% of muscle bleeding episodes (Stephensen et al., 2009). An understanding of the hierarchical macro and microscopic structure, mechanics, and diverse function of human skeletal muscle is key to evaluating muscle bleeding. Whole muscle is composed of bundles of muscle fascicles, which are composed of individual muscle fibres that contain myofibrils arranged side by side in parallel, which are further subdivided into sarcomeres arranged end-to-end in series. Sarcomeres are composed of two sets of overlapping myofilaments, thick myosin filaments, and thin actin filaments that are the basic contractile components of muscle. Detailed clinical examination, together with imaging techniques, can determine the site and extent of bleeding, evaluate the stage of healing and response to treatment, and guide rehabilitation and return to physical activity.

B3.2
Muscle bleeds and low-intensity pulse ultrasound (US) therapy

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The muscles most commonly affected are in the calves, thighs, upper arms, front of the hips, and forearms. Bleeding into the muscle can go unnoticed for some time before discomfort develops. Some bleeds will cause the limbs to swell and become warm and painful to the touch. Bruising can occur if the bleed is near the skin surface. In deeper muscles, the swelling may press on nerves or arteries, which will cause tingling and numbness. Muscle hematomata represents 10–25% of bleeds in patients with severe hemophilia. There is limited consensus on diagnostic or treatment strategies and little knowledge about the natural history of muscle hematomata and optimal treatment goals. Low-intensity
pulsed ultrasound (LIPUS) has gained much attention for patients with musculoskeletal disorders, which occur through a variety of biological and physical mechanisms, include muscle relaxation, reduced swelling, and pain relief. Most knowledge of the effects of US on living tissue has been gained through in vitro studies and animal models, but relatively little in vivo evidence that these effects actually occur has been published. This paper is presented as a literature review of the physiology of muscle bleeds and the influence LIPUS exerts on cells and molecules involved in such bleeding process. **Keywords:** Ultrasound therapy, muscle bleeding, hemophilia

**B3.3**
Compartment syndrome

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Abstract unavailable

**B3.4**
Muscle bleed: Medical management

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Muscle hematomas (MH) represent 10-25% of all bleeds in patients with severe hemophilia. In a cross-sectional survey of current practice in the management of MH, with participation from 22 consultants, the respondents reported 492 MH/year, corresponding to an average of 25/centre, most associated with trauma. Iliopsoas (55%), calf (18%), and thigh (18%) bleeds were scored as most serious. Half of respondents distinguished between contusion and strains, whereas the majority (68.2%) did not categorize bleedings as intra- or inter-muscular, although 77.3% routinely used ultrasound. Although the outcome of treating muscle hematomas has improved in the past 20 years, with fewer patients suffering long-term disability, this has not been paralleled by greater evidence-based understanding of management strategies, nor a treatment consensus among hemophilia treaters. A cross-sectional survey on the management of MH in patients with severe hemophilia, including those with inhibitors, revealed no consensus in diagnosis, timing, type and dosing of treatment, nor in the initiation and appropriate modalities of physiotherapy. Insufficient treatment of MH – or poor response to treatment – can lead to serious and debilitating complications, including re-bleeding, infection, compartment syndrome, joint contractures, pseudotumours, myositis ossificans, functional loss, and decreased range of motion (ROM). In patients with severe hemophilia and inhibitors, MH, such as iliopsoas bleeds, can be life- or limb-threatening. In conclusion, there is a need for further studies on the pathology, diagnosis, and importance of early treatment to achieve rapid control of bleeding, as well as rehabilitation following MH in patients with hemophilia. A prospective international multicentre registry of current management of MH seems desirable to get more data. Optimized and systematic diagnosis may facilitate a better strategy regarding type and timing of physiotherapy.

**B3.5**
Conservative management

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Abstract unavailable

**Session B4 – Free Papers 2**

**B4.1**
Altered muscle strength and architecture influences motor performance in boys with severe hemophilia and ankle joint hemarthrosis

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**Introduction:** It has been shown that the muscles of young hemophilic boys with a history of ankle joint bleeding are smaller and weaker than their unaffected peers. Alterations in balance and gait have also been reported. This study explores the influence of muscle architecture of the lateral gastrocnemius (LG) muscle on ankle plantar flexor (APF) muscle strength and biomechanical walking patterns in 19 typically developing boys (G1), aged 7-12 years, and 19 age and size-matched hemophilic boys (G2).

**Methods:** LG cross-sectional area (CSA), thickness (MT), fascicle length (FL), and pennation angle (PA) using ultrasound imaging. APF strength utilizing an isokinetic dynamometer, and function of the knee and ankle during walking, using a 3D motion-capture system, was recorded.

**Results:** CSA and MT of LG together with strength of the APF were significantly smaller in G2 when compared to G1. Strength correlated most strongly with BMI in G1 (r=0.62, p<0.05) and with age in G2 (r=0.65, p<0.01). Associations between MT and ankle joint motion differed between groups at the beginning (p<0.05, Fig 1) and end of stance (p<0.05). Reduced FL was associated with larger knee flexion moments in G2 but smaller moments in G1 (p<0.05). Relationships between reduced APF strength, ground reaction forces, and knee flexion moments (Fig 2) were significantly stronger in G2 than G1 (p<0.05). Clinical Relevance: Biomechanical function of the ankle and knee joints of hemophilic boys who have a history of ankle joint bleeding appears to be related to APF muscle strength deficits and adaptations in muscle architecture.

**Fig. 1.** Scatter plot showing significantly different relationship (p<0.05) between lateral gastrocnemius (LG) thickness and peak ankle plantar flexion (PF) angle during walking in typically developing boys (G1) and hemophilic boys (G2).
Abstracts

Keywords: muscle strength, ankle joint hemarthrosis

B4.2

Dance-based exercise therapy for patients with hemophilia

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The use of methods derived from creative arts has not been considered in hemophilia treatment. The aim of this study was to investigate the expectations for a dance-based exercise therapy (DbET) for patients with hemophilia (PWH) and the extent of its acceptance. The one-hour DbET was offered to 30 PWH (HI30) (49±11; 30-67 years). For the evaluation of expectations, questionnaires were created and filled out by participants before and after the intervention. Additionally, 19 PWH (HF) and 20 controls without hemophilia (KF), who did not participate in the intervention, were also questioned. The results illustrate that PWH show more experience in dance than controls (HI30:62%, HF:74%, KF:45%). The proportion of those who are currently dancing is higher in controls (HI30:17%, HF:10%, KF:26%). The termination of the dance activity in PWH who were part of the intervention was mainly due to pain (HI30:40%, HF:29%, KF:0%), whereby controls without intervention terminated mainly due to lack of time (HI30:30%, HF:57%, KF:56%). Finally, 24 out of 30 PWH (HI24) completed the DbET. All HI24 met their expectations. Thirty-eight per cent felt limited by hemophilia while carrying out the exercises. Twenty-nine per cent perceived the intervention as moderately difficult or not difficult. The majority were able to follow the exercises well (96%) and did not overstrain physically (92%), nor mentally (87%); also 79% did not have pain and felt comfortable physically. Twenty-three of HI24 (96%) can envision a continuation of the DbET. The experience with the DbET was predominantly positive. It represents an alternative exercise program for PWH.

Keywords: exercise therapy

B4.3

Differences in physical activity and sedentary behavior between young hemophilia patients with and without arthropathy

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Objective of the work: The aim of this study is to compare the amount of physical activity (PA) in people with hemophilia (PWH), with arthropathy (AR) and without arthropathy (NA) both on weekdays and weekends. Methods: 41 patients with hemophilia, 12 with AR and 29 without NA participated in this study. Each participant wore a triaxial accelerometer ACTigraph GT3X (Actigraph, Fort Walton Beach, FL, U.S.A.). Data were saved in a hard disc for subsequent analyses. All the variables complied with the assumption of normality (K–S normality test). Differences among groups regarding energy expenditure and time spent in sedentary activities were assessed by Student’s two-tailed t-tests for independent samples. Bonferroni correction (a/ number of comparisons) was applied to avoid increasing the possibilities of Type I errors. The effect-size (r) was calculated for each comparison. Results of the intervention: No significant differences were found in time spent in SB on weekdays. However, on weekends significant differences were shown (P<0.05) with AR patients spending more time in SB than NA (no arthropathy) patients. Regarding Light PA (LPA), significant differences were found on weekdays (P<0.01), so that participants with healthy joints engaged longer than AR participants (Figure 1). No significant differences appeared in time spent in LPA on weekends. Discussion and conclusions: Both AR and NA accumulated more minutes of LPA on weekdays can be related to the time spent at school. However, no significant differences were found on weekends in LPA level. This may be due to the sedentary lifestyle acquired by young PWH with similar or equal quality of life as their healthy peers. Today, PWH showed a similar quality of life as their healthy peers and this fact may develop SB in these patients as a result of the same lifestyle as the general population.

Keywords: hemophilia and physical activity
B4.4

Associations of quality of life, pain, and self-reported arthritis with bleed rate and hemophilia treatment centre (HTC) and healthcare practitioner utilization: Global results from the Hemophilia Experiences, Results and Opportunities (HERO) Study

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Objective: To examine associations of quality of life (QoL)/pain and self-reported arthritis with bleed rate and HTC/hospital utilization among adults with hemophilia ("adults") in the HERO Study. Methodology: Adults ≥18 years completed a 5-point Likert scale on pain-interference over the prior 4 weeks, a health-related visual analog scale (VAS, 0-100, coded as an 11-point categorical response) and a standard QoL assessment [EQ-5D-3L mobility, usual activities, self-care and pain/discomfort]. Data from 8 countries with home treatment are presented. Results: 515 adults responded, 46% with self-reported arthritis. Adults with self-reported arthritis were older (median 41 vs 35 years); median age increased with worsening EQ-5D disability and pain-interference. Employment and the percentage reporting "good" VAS scores (80-100) declined with worsening EQ-5D, pain-interference, and arthritis. Median annual bleeding rates were higher with more EQ-5D disability/pain, pain interference, and arthritis. Adults with disability/pain reported higher mean number of HTC visits/year. Percentages reporting the greatest pain interference were highest amongst those with more EQ-5D disability and arthritis. Amongst adults without self-reported arthritis, 39% reported moderate/severe pain-interference. Nurse and social worker involvement increased in adults reporting difficulties with self-care (45%-79% and 16%-50%), pain/discomfort (48%-61% and 14%-32%), pain-interference (48%-61% and 14%-28%), or arthritis (45%-61% and 14%-27%). Physiotherapist involvement was moderate (32%-46%) and did not differ with disability, pain-interference, or arthritis. Conclusions: Increased disability and pain were associated with increased age, lower employment, more bleeds, and more HTC visits. Additional physiotherapy involvement/follow-up might be helpful in adults with arthropathy; this could be evaluated in a prospective study.

Keywords: osteoporosis screening, joint score

B4.5

Should osteoporosis screening be a routine standard in hemophilia care: a multi-centre study and review of the literature?

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Introduction: It has been shown that bone mineral density (BMD) may be lower in people with hemophilia. The impact of joint health and activity levels on BMD has not been analyzed thoroughly in the current literature, and a comparison of results to control subjects is needed. Primary objectives: To test the hypothesis that BMD is lower in people with severe hemophilia than in healthy controls and in those people with more severely affected joints or lower activity levels. Method: In this case-control study, 40 patients with severe hemophilia A (aged 18-70) were recruited from 2 hemophilia centres in the U.K. A group of 40 age, sex and ethnicity-matched control participants were recruited. All participants had a bone density scan (DEXA) of the lumbar spine and hip. A musculoskeletal joint score was used to assess joint impairment. Activity levels were assessed using the hemophilia activities list (HAL). Results: 3% of cases were osteoporotic, 42% were osteopenic. No control participants were osteoporotic, 9% were osteopenic. 84% of cases had low vitamin D levels and 86% of controls had low vitamin D. Joint score range 0-56, and activity score range 41.1-100 in case participants. No controls had any joint impairment. Discussion: Results show that people with a higher joint score and a lower activity score have lower BMD. Interestingly, vitamin D levels do not appear to correlate with BMD levels.

Keywords: osteoporosis screening, joint score

B4.6

Correlation of Haemophilia Activities List (HAL) and musculoskeletal physical assessment in a cohort of 95 severe hemophilia patients

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Joint assessment is an integral part of the clinical review of hemophilia patients to monitor joint health and physical function. The self-perceived evaluation of function, as reported by the HAL is also essential in ascertaining the overall musculoskeletal health status in hemophilia patients. A retrospective review of clinic attendances identified 95 individuals (aged 18-83), with severe hemophilia, who had completed a HAL and on whom the Colorado Half-Point Physical Examination joint score had been done. The median, 10th and 90th centile ranges are presented for the scores: Total joint score: 21.5 (0.4, 52), upper limb (UL): 2.75 (0, 15), lower limb (LL): 16 (0, 38.5), total HAL: 76.8 (37.9, 98.1), HAL complex LL: 62.2 (15.6, 100), HAL arms: 80 (35, 100), HAL household: 90 (44.7, 100). The most affected joint in this cohort was the ankle. The elbow and knee were similarly affected. There was a high correlation between the total joint score and total HAL (R=0.67), and between LL and HAL complex LL activities.
of HTC visits/year was generally lower with higher-risk activity for children without inhibitors.

**Keywords**: activity, treatment

## B4.8 Deferasirox prevents cartilage destruction following hemarthrosis in hemophilic mice

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### Introduction

Joint bleedings in hemophilia result in iron-mediated synovitis and cartilage destruction. It was evaluated whether deferasirox, an iron chelator, was able to prevent the development of hemophilic synovitis and cartilage destruction.**

**Methods**: Hemophilic mice were randomly assigned to oral treatment with deferasirox (30mg/kg) or its vehicle (control) (30mg/kg). After two months of pretreatment, the right knees of hemophilic mice were punctured to induce hemarthrosis. The mice were sacrificed after another five weeks of treatment. Post-mortem, knee joints were isolated and sectioned for histology. Hemophilic synovitis and cartilage destruction were determined by two blinded observers, according to Valentino and Glasson, respectively. For hemophilic synovitis, sections of tissue were stained with hematoxylin-eosin and scored for evidence of synovial hyperplasia, vascular hyperplasia, hemosiderin depositions, intra-articular erythrocytes, and synovial villi. For cartilage destruction, sections of tissue were stained with safranin O and the intensity of safranin O staining was scored according to the proteoglycan content in the cartilage, which is a measure of cartilage destruction. The maximum score of the Valentino score is 10, and the maximum score of the Glasson score is 6. An increase in Valentino and Glasson scores represent an increase in hemophilic synovitis and cartilage destruction, respectively. Treatment with deferasirox was compared with control.

### Results

Categorical data were analyzed by loglinear analysis and Pearson Chi-Square.**

**Results**: Treatment with deferasirox (823mg/ml ±56) resulted in a statistically significant (p<0.01) decrease in plasma ferritin levels, as compared to the control group (1220mg/ml ±114). The presence of hemosiderin was statistically lower (p=0.04) in the deferasirox group, compared to the control group. Signs of hemophilic synovitis, as assessed by the Valentino score, were not different (p=0.52) when comparing the control group to the deferasirox group: 1 (12.4% vs 7.7%), 2 (16.7% vs 11.5%), 3 (12.5% vs 38.5%), 4 (29.2% vs 19.2%), 5 (16.7% vs 11.5%), 6 (4.2% vs 7.7%), and 8 (8.3% vs 3.8%). Deferasirox treatment resulted in a statistically significant (p<0.01) reduction in cartilage destruction, as assessed by the Glasson score, when comparing the control group to the deferasirox group: 2 (4.2% vs 65.4%), 3 (4.2% vs 26.9%), 4 (20.8% vs 7.7%), 5 (54.2% vs 0%), 6 (12.5% vs 0%), and 7 (4.2% vs 0%).

### Conclusions

Treatment with deferasirox prevented cartilage destruction following the induction of hemarthrosis in...
B4.9
Healing defects in a hemarthrosis model are improved by extending factor IX activity during healing

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Objective: Wound healing requires interactions between coagulation, inflammation, angiogenesis, cellular migration, and proliferation. We examined healing following hemarthrosis in FIX−/− mice. We also examined whether extended factor IX activity, achieved by glycopegylation of factor IX (N9-GP, NovoNordisk), when compared to recombinant factor IX (rFIX, BeneFIX®, Pfizer) normalizes defects in this wound model. Methods: A unilateral joint hemorrhage was induced in FIX−/− or WT mice by needle puncture of the knee joint capsule. Following wounding, FIX−/− mice were treated intravenously with either normal saline, with N9-GP 250 U/kg, or with rFIX 250 U/kg. Two weeks following induction of hemarthroses joints were collected, the articulating bones evaluated with micro-computerized tomography (MCT), and tissue histology evaluated. Results: Hemarthrosis resulted in severe synovitis in untreated hemophilic mice (Valentino synovitis grade 5.9 on scale of 0 to 10), compared to WT mice (0.87 of 10). A single 250 U/kg dose of rFIX minimally protected the joint (mean synovitis grade 3.7), compared to 250 U/kg N9-GP (mean synovitis grade 1.8). Histologic parameters of healing, including neoangiogenesis, macrophage infiltration/residence, and iron deposition were improved by N9-GP when compared to unmodified rFIX. By MCT, a quantitative calculation of bony degradation at the articular surface demonstrated N9-GP and WT groups to be similar, but significant roughening of bony contours in the other groups. Conclusion: Compared to a single dose of conventional rFIX, extending factor IX activity following the time of wounding significantly improves wound healing in hemophilia B mice, as achieved using an equivalent dose of N9-GP.

Keywords: wound healing, hemarthrosis
institutions, and policy makers. We will discuss the various types of outcomes and the surrogate outcomes that are used to provide estimates of outcomes. Theoretical frameworks will be shared as one way to organize the various types of outcomes and to guide our selection of outcome measures. The presentation will touch on a few relevant frameworks. The session will also describe some of the significant advances in outcome measures in the past decade. The science of disease-specific measures for hemophilia has advanced across the continuum from radiologic measures to assessments of life satisfaction. The session will review these developments so that we can all consider the opportunities they offer us to develop models of best-practices for hemophilia management and care.

Data from several studies will be used to demonstrate what we currently know about quality of life outcomes in hemophilia. This information is important to the interpretation of local data. The final aim is to provoke the discussion of including diverse perspectives in the assessment and interpretation of outcomes.

**Poster Session 1**

**P1.01**

Utility of arthroscopic debridement in chronic arthropathy in hemophilic patients


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**Introduction:** Hemophilia is a blood coagulation disorder that causes recurrent joint bleeding, most often in the knee. This condition causes the destruction of the joint and functional incapacity. For adult hemophilic patients with grade III-IV AH knee arthropathy requiring a total knee arthroplasty that cannot be performed due to the patient’s age, arthroscopic debridement can be of great value. With this procedure, we perform the removal of the meniscal remains of chronic lesions, osteophytes, and intra-articular bodies; shaving of the cartilage; and resection of the hypertrophic synovial and intercondylar sulcus plasty. This increases mobility and walking, reduces pain and bleeding due to mechanic causes, and improves the patient's condition. With this procedure, we perform the removal of the meniscal remains of chronic lesions, osteophytes, and intra-articular bodies; shaving of the cartilage; and resection of the hypertrophic synovial and intercondylar sulcus plasty. This increases mobility and walking, reduces pain and bleeding due to mechanic causes, and improves the patient's performance.

**Objectives:**
- To provoke the discussion of including diverse perspectives in the assessment and interpretation of outcomes.
- To discuss the various types of outcomes and the surrogate outcomes that are used to provide estimates of outcomes.
- To share theoretical frameworks for organizing the various types of outcomes and to guide our selection of outcome measures.
- To describe recent advances in outcome measures and the science of disease-specific measures for hemophilia.

**Keywords:** knee arthropathy, arthroscopic debridement

**P1.02**

Repeated autologous intra-articular blood injections as an animal model for joint pain in hemophilic arthropathy

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**Introduction:** Hemophilic arthropathy following recurrent joint bleeds is one of the major disease-related complications in people with hemophilia (PWH), leading to mostly chronic joint pain. Since many antinociceptive principles interfere with the clotting system, PWH are restricted in treatment options, thereby defining a medical need for novel therapeutic principles. Testing these, however, lacks the availability of an animal model for joint pain in hemophilic arthropathy. **Aim:** In this study, we thus aimed at validating the rat model of repeated autologous intra-articular blood injections for pain-related behaviour. **Methods:** During an observation period of 50 days, groups of animals were injected weekly into one knee joint with either whole blood or cellular/plasma components. **Results:** Injections induced primary hyperalgesia starting after the third injection, accompanied by mild functional gait changes and joint swelling. Secondary hyperalgesia and quantitative gait disturbances were not observed. This phenotype was most prominent in whole-blood injected animals, with effect sizes of cells and plasma being additive. In order to differentiate hemophilia-related arthropathy from traumatic joint bleeding, another group was injected with whole blood only once, which did not cause any alterations. **Conclusion:** Repeated autologous intra-articular injections of blood showed a time course, inflammatory response, and reduction in pain thresholds similar to the signs and symptoms observed in PWH. Therefore, this model may be utilized in the future for testing novel antinociceptive principles in hemophilia-associated joint pain.

**Keywords:** animal models, arthropathy

**P1.03**

Arthroscopic treatment of hemophilic ankle arthropathy

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**Background:** From early childhood, joints are the most common bleeding site in people with hemophilia. Hemarthroses tend to recur at the same site (target joint) causing structural damage that gradually involves synovium, cartilage, and bone, leading to chronic hemophilic arthropathy with crippling and deformities. Although primary prophylaxis has radically decreased the
Abstracts

number of target joints in hemophilic patients, the ankle joint seems to be an exception to the rule, and information regarding the arthroscopic management of hemophilic ankle arthropathy is limited. **Aim:** Description of arthroscopic treatment of hemophilic ankle arthropathy. **Methods:** Retrospective data collection regarding orthopedic surgery between January 1990 and December 2012. Bleeding frequency, radiographic scores, range of motion (ROM) measures, and pain (using VAS) were recorded preoperatively and at follow-up (i.e. at the time of data review). Outcome measures included length of hospitalization, length of follow-up, occurrence of adverse events, need for additional intra-articular intervention, and patient satisfaction. **Results:** Data are reported on 67 procedures performed in 63 patients affected by hemophilia A (59 patients) and B (four patients), three patients with inhibitors at surgery. The median age of the patients at surgery was 20 years (range: nine to 61) and the follow-up time ranges between one to 264 months. Joints showed a bleeding frequency decline. Median arc of motion was stable or improved in the years after surgery. No complications were registered. Radiographic scores worsened slightly or slowly. **Conclusion:** The procedure can be performed safely on an outpatient basis, but an experienced treatment team is of utmost importance in determining a good outcome. **Keywords:** arthroscopy, ankle, hemophilia

**P1.04**

**Standardized ultrasonography of joints and correlation with joint function in children and young adults with hemophilic arthropathy - first results of a clinical pilot trial at a German treatment center**

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**Introduction:** Sonography is used in routine clinical practice to examine joint bleedings or signs of hemophilic arthropathy (HA) with effusion, synovitis, cartilage defects, or subchondral bone damage in patients with bleeding disorders. For the presentation of synovitis or effusions, as a sign of activity and defects of the articular cartilage, or subchondral bone as a sign of progression of HA, standardized sonographic section planes are available. In this study, the sonographic findings are correlated with data from an ultrasonic motion-analysis of the joints and the results of an orthopedic examination. **Materials and Methods:** First experiences were made in a group of 26 young German patients (three to 28 years, median 13.1) with hemophilia A, B, or von Willebrand’s disease. A standardized ultrasonography of the elbow, knee, and ankle joints with a Zonare z.one ultrasound machine (transducer L14-5w) and, simultaneously, a clinical examination and a motion analysis of the knees were performed. Joint ultrasound characteristics were scored. Motion analysis of the knees were done with the Ultrasound-Topometer and scored also. The scores and the results of the orthopedic examination were correlated. **Results:** The results of various studies indicate an age-dependent correlation of ultrasound and motion analysis. Joint sonography shows some changes before detection in clinical examination. **Summary:** Initial studies of correlating a standardized ultrasonography of disease activity, in HA and joint function analysis, showed age-dependent promising results. These results were encouraging to examine the correlation now in a larger group of young patients in Germany (HämarthroSonoPilotTrial). **Keywords:** ultrasound, synovitis, joint function

**P1.05**

**Early complications after total knee replacement in people with hemophilia**

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**Introduction:** Total knee replacement is an accepted method of treatment for hemophilic arthropathy. Nevertheless, the rate of complications in hemophilic patients is still higher than in osteoarthritis. Between 2010 and 2013, 70 total knee replacements (three revisions) were done in patients with severe bleeding disorders. Five complications requiring operative treatment occurred in postoperative months (7.1%). Case 1: Superficial skin necrosis treated successfully with the split skin graft and platelet-rich plasma gel. Case 2: Early joint infection with skin necrosis. In the first stage, early debridement with implant preservation was performed without effect. Secondy, open revision with implants removal and application of spacers with antibiotics was done and was complicated by skin and soft tissue necrosis affecting extensor apparatus. Debridement was performed and the defect was covered with rotation myocutaneous flap from the calf. Case 3: Periarticular pseudoaneurysm. The pseudoaneurysm appeared as a pulsating mass at the lateral aspect of the operated knee. Doppler sonography and arteriography revealed inferior lateral genicular artery bleeding. Intravascular coiling of the pseudoaneurysm was performed with good effect. Case 4: Prolonged intra-articular bleeding after revision surgery with extensive approach and spacer removal. Despite several aspirations in the postoperative period growing hemarthrosis was noted. Sonography and arteriography revealed a group of small bleeding arteries in the popliteal region. Several injections with thrombin were done with partial effect. Vessels that did not respond underwent intravascular coiling that eventually stopped bleeding. **Conclusion:** The risk of early bleeding and infectious complications in patients with hemophilia undergoing total joint replacement remains remarkable. **Keywords:** hemophilia, complications
P1.06
Simultaneous bilateral knee arthroplasty in hemophilia patients: report of two cases
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Introduction: Adult hemophilic patients usually have severe joint destruction due to hemophilic arthropathy, leading to pain and dysfunction of one or more joints, with the need of joint replacement. The knee is the most commonly affected joint but, frequently, multiple joints are affected. Therefore to optimize the use of deficient factor concentrates, to reduce costs, to have a global functional recovery, to facilitate pain control, and to reduce the rehabilitation period, multiple surgical procedures are indicated in the hemophilic patient. The advantages of performing the simultaneous bilateral arthroplasty, in addition of the above mentioned, are the execution of only one surgical event, a maximum of two hours of anesthesia, and the reduction of surgical stress in the patient by accomplishing both joint replacements, with two surgical teams working at the same time, compared with a bilateral arthroplasty in two stages or to perform them in different surgeries. Objective: Report two cases of bilateral total knee arthroplasty performed simultaneously with two orthopedic surgical teams in hemophilia patients.

Methods: Report two cases of bilateral total knee arthroplasty performed simultaneously in the Traumatology Hospital Víctorio de la Fuente Narvaez, México D.F. in two patients with severe hemophilia (one with hemophilia A and VHC infection, one with hemophilia B). There is only one case reported of bilateral total knee arthroplasty.

Conclusion: There is a reduction in hospitalization costs and factor concentrates consumption by performing only one surgical event, as well as a short hospitalization, quick deambulation, opportune rehabilitation, and less psychological impact in the patients.

Keywords: arthropathy, simultaneous bilateral arthroplasty

P1.07
Functionality and quality of life of hemophilic persons undergoing a bilateral total knee arthroplasty
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Subject: Assessing the functionality and quality of life of hemophilic patients undergoing a bilateral total knee arthroplasty.

Material and methods: Analytical and cross-sectional study, with hemophilic patients that underwent arthroplasty at Hospital de Clínicas, Federal University of Paraná, Curitiba, Brazil, in the period from 1997 to 2011. The medical records were analyzed and patients were called for interview and assessment of functionality using FISH, of quality of life using SF-36, and of range of motion.

Results: There were 13 male patients, with mean age 38.91 years (SD 9.20); nine with hemophilia A and four with hemophilia B; 12 were severe and one was moderate. The quality of life assessment resulted in better scores on social functioning, followed by role emotional and mental health; the worst were bodily pain, followed by role physical and physical functioning. The FISH assessment resulted in better performance in activities such as bathing, dressing, eating, and grooming; the worst were running, chair, and stairs (12 to 14 steps). Most patients did not have full extension of knees (0°), staying with attitude in fixed flexion average of 9.23°. (SD 8.86) in the right knee and 8.85°. (SD 8.20) in the left knee. The average range of flexion movement was 88.46°. (SD 21.35) in the right knee, and 79.23°. (SD 18.35) in the left knee.

Keywords: synovectomy, pediatrics, arthropathy

P1.08
Surgical synovectomy in pediatric patients with severe factor VII deficiency
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Background: Severe congenital factor VII deficiency is extremely variable in its presentation and bleeding phenotype. We present the cases of two female siblings with severe factor VII deficiency who developed ankle hemarthrosis, chronic synovitis, and arthropathy. While infusion of recombinant factor VIIa (rFVIIa) was successful in achieving hemostasis acutely, daily prophylaxis did not appear to alter the progression of synovitis and destructive arthropathy.

Case Presentation: The older sibling presented at age four following a left ankle injury. She was subsequently diagnosed with severe factor VII deficiency, due to recurrent swelling of the ankle. Despite daily prophylaxis, intermittently for three years, physiotherapy, and conservative orthopedic interventions, she continued to have progression of bilateral ankle synovitis, with bony changes, and underwent ankle synovectomies at age seven and eight. The younger sibling was diagnosed secondary to oral bleeding. At age 5, she presented with a new gait abnormality not associated with injury or obvious ankle swelling. MRI revealed synovitis in the left ankle without bony changes. She was placed on daily prophylaxis and synovectomy was done within two months.

Conclusion: Arthropathy does occur in congenital factor VII deficiency and established guidelines for treatment and prophylaxis do not exist. Daily rFVIIa prophylaxis did not alter the progression of synovitis and arthropathy in the older sibling. Based on this experience, synovectomy was performed on the younger sibling much earlier. Surgical synovectomy was successful in stopping further bleeding episodes. However, follow-up is required to ascertain if this will arrest the progression of hemophilic arthropathy.

Keywords: synovectomy, pediatrics, arthropathy
P1.09
The economic effect of tandem arthroscopic synovectomy for hemophilic patients

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Objective: Arthroscopic synovectomy is an effective technique for hemophilic articular synovitis, especially in Japan, where synovectomy using radioactive material is not approved. However, orthopaedic procedures, including arthroscopic synovectomy, require expensive drugs. Recently, we devised "tandem" arthroscopic synovectomy in which upper extremity arthroscopy and lower extremity arthroscopy are performed simultaneously to reduce medical cost. The objective of this work is to report the economic effect of our procedure. Method: Four "tandem" arthroscopic synovectomies for 12 joints (two shoulders, two elbows, seven ankles and one metatarsal joint) of four hemophilic patients were performed at our institute. All patients suffered from hemophilia A and two were inhibitor positive. Average operation time was 180 minutes with no perioperative complications. The medical cost for four "tandem" arthroscopic synovectomies, and hypothetical cost for 12 separated arthroscopic synovectomies, were compared. Results: To perform "tandem" arthroscopic synovectomies, 58,500 units of factor VIII concentrate, 46,000 units of factor VIII concentrate, 48 mg of eptacog alpha followed by 32,000 units of anti-inhibitor coagulant complex, and 235 mg of eptacog alpha were needed for patients 1 to 4, respectively. Thus, calculated medical cost reduced by our procedure was 93,071,480 yen, in total. Relevance and applicability: Arthroscopic synovectomy requires expensive drugs, although it is very effective for hemophilic articular synovitis. "Tandem" arthroscopic synovectomy can reduce much medical cost, compared to separated procedures. Originality of the work: To the best of our knowledge, this work is the first report about economic effect of “tandem” arthroscopic synovectomy. Keywords: "tandem" arthroscopic synovectomy, economic effect

P1.10
Radiosynoviorthesis in the treatment of chronic hemophilic synovitis

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Aim: to present our promising results with radiosynoviorthesis in the treatment of hemophilic joints in Hungary. Material and method: Hemophilic hip, knee, and ankle joints have been treated with radiosynoviorthesis method at our department since 2003. Hip and ankle joints are treated with 110 MBq of rhenium-186 sulfide isotope in colloidal suspension, while yttrium-90 isotope, in colloidal suspension is used for knee joints. Isotope implantations are performed in a very sterile environment, in an operating room. Local anesthesia with 1% lidocaine is used for the procedure. There were no cases of injury caused by leakage of the isotope. The patients are admitted to the hospital for three days. Bed rest and immobilization of the joints with brace is prescribed, for the same time period, to reduce extra-articular migration of the radiopharmaceutical. Hip joint is not braced. Results: We observed overall reduction in joint bleeding frequency, from 18.7 to 2.4 per year, post radiosynovectomy. Similar results were obtained in patients with advanced osteoarthritis and in inhibitor cases. There was a significant reduction in pain in all joints. Average range of motion was maintained or increased from five to 15 degrees of motion one year post radiosynovectomy, in most joints. Radiosynoviorthesis was successful in 88% of the patients one year after isotope implantation. Conclusion: Radiosynoviorthesis represents an important alternative for the treatment of chronic hemophilic synovitis, markedly reducing joint bleeding frequency and pain, irrespective of the stage of arthritis and inhibitor status. Keywords: radiosynoviorthesis, inhibitor

P1.11
Our experience with arthroscopic synovectomy of the hemophilic knee joint

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The most frequently observed target joint in hemophilia is the knee. The success rate synovectomy in controlling recurrent bleeding is high; however, significant loss of motion frequently results. Open or arthroscopic knee synovectomy requires an experienced, multidisciplinary collaboration (hematologists, orthopedic surgeons, and physiotherapists) in a dedicated hemophilia treatment centre. Method: Between 1997 and 2012, we performed 72 surgical procedures, of which 30 were knee synovectomies. Among these, 28 were arthroscopic knee synovectomies, combined with joint debridement. Two other knee synovectomies were performed by open surgical procedure. Preoperatively, all patients had experienced an average of three bleeding episodes into the affected joint per month, and had been unresponsive to at least three months of intensive replacement prophylaxis. In parallel to intensive replacement therapy, traditional LMWH prophylaxis was also used in all of the cases. Results: The frequency of bleeding episodes decreased in all cases; however, the average loss of range of motion in the knee was 17 degrees. We have observed five hemorrhagic complications in the postoperative period, but no infections or appearance of new inhibitors occurred after surgery. The average age of the patients at the time of the knee synovectomy was 37 years and the average length of follow-up was 5.65 years (range, one to 16 years). Conclusion: It was concluded from our study that bleeding frequency and the pain associated with persistent synovitis in the hemophilic knee can be effectively influenced by knee synovectomy. All of our patients required less factor replacement to control bleeding after synovectomy, although almost all of our patients experienced a certain degree of loss of motion in the operated knee. Keywords: arthroscopic synovectomy, knee joint
P1.12
Joint distraction results in clinical and structural improvement of hemophilic ankle arthropathy: a series of three cases

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Objective: In ankle osteoarthritis, joint distraction is found to be very effective in diminishing pain and improving joint function and results in actual joint tissue repair. With this treatment, a prosthesis or arthrodesis can be delayed at least five years, which is especially of value for younger patients. In severe hemophilic ankle arthropathy (HAA), the standard surgical treatment options are arthrodesis and total ankle replacement, both treatments having their specific complications. In this study, joint distraction for HAA was explored for the first time.

Methods: Three HAA patients were treated with joint distraction using an Ilizarov external fixator for 10-15 weeks. After 1.7-3.4 years, clinical outcomes were evaluated in retrospect with different questionnaires: hemophilia activities list (HAL), impact on participation and autonomy (IPA), and the Van Valburg pain score. Post-operative ankle joint mobility was measured. Structural changes were assessed on X-ray by the Pettersson score and joint space width (JSW), and on MRI. Results: All patients reported a clear improvement for self-perceived functional health: mean HAL sum score improved from 44±28.4% to 73±17.7% (p=0.04), IPA, and Van Valburg pain score (pre-treatment 80±5.0%; post-treatment 23±15.3% (p=0.016). Partial ankle joint mobility was preserved. The Pettersson score slightly improved in two patients. The mean JSW increased from 2.3±1.8mm to 3.4±1.0mm (p=0.07), and the MRI score improved (pre-treatment 12.0±3.5; post-treatment 8.0±4.4; p=0.020). Conclusion: Although retrospective in nature, this study suggests that joint distraction is a promising treatment for individual cases of HAA, without additional risk of bleeding during treatment. These results warrant further prospective studies.

Keywords: arthropathy, distraction

P1.13
Musculoskeletal status of adult Saudi patients with severe hemophilia

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Background: Arthropathy of various degrees is a common complication of severe hemophilia, due to repeated spontaneous or traumatic bleeding episodes. Regular prophylactic administration of clotting factor concentrates can effectively prevent such complications. Objective: To assess the musculoskeletal status of adult Saudi patients with severe hemophilia prior to the establishment of a comprehensive hemophilia care centre.

Methods: We carried out a full physical musculoskeletal examination, functional assessment, and radiological reporting of knees, ankles, and elbows of five adult male patients, aged 23-42 years.

Results: We found 10 of 30 affected joints, one patient with three affected joints, three patients with two affected joints each, and one patient with one affected joint, all with severely impaired functions. MRI imaging indicated that all affected joints scored 3-5, according to the Arnold-Hilgartner Classification, where zero is normal and five is complete joint destruction.

Conclusion: Adult Saudi patients with severe hemophilia suffer from advanced arthropathy. There is a great need to establish a comprehensive hemophilia care centre, then provide orthopedic surgery and rehabilitation for affected patients, and prophylaxis to patients with severe hemophilia.

Keywords: arthropathy, prophylaxis

P1.14
Peripelvic myositis ossificans in a hemophilic adolescent

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Although intramuscular hematoa is a common manifestation in people with hemophilia, the incidence of myositis ossificans in adolescents with hemophilia is extremely low. The case of a 16-year-old boy with severe hemophilia A, who presented with a 3-month-duration right hip pain and major gait disturbance, is described. Radiographs revealed the presence of an ischiofemoral bony bridge. CT scan with 3D reconstruction not only confirmed the diagnosis of myositis ossificans (MO) but also showed the exact location of the bony mass in the substance of the hip external rotators. Because of the painful and severely impaired motion of the hip joint, urgent surgical resection was performed. Unfortunately, recurrence of the MO, after 10 months, resulted in gradually increased difficulty with walking and the adolescent underwent a second operation. At 10 months
follow-up, the patient presented with a painless full range of motion of the hip joint and the pelvic x-ray showed no signs of recurrence. Juxtaarticular cases of MO in adolescents with hemophilia that severely impair the motion of the adjacent joint should be treated with early surgical intervention, while postoperative maintenance of sufficient levels of factor VIII is of great importance. In order to minimize the risk of permanent stiffness of the joint and disability of the patient, the degree of "maturatıon" of the MO should not be a contraindication.

Keywords: myositis ossificans, heterotopic ossification, hemophilia

P1.15
ACL reconstruction in active athlete with factor VII deficiency: Case report
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Uncontrolled bleeding during or after orthopedic surgery remains a major concern for surgeons, as it may jeopardize the outcome and could require re-intervention to secure hemostasis. This problem is particularly relevant for patients with bleeding disorders. This may raise a fear leading to avoidance of performing elective surgical procedures in those patients. Factor VII (FVII) deficiency is a rare bleeding disorder, which ranges in clinical severity from life-threatening to asymptomatic forms. Surgical bleeding is among the most frequent symptom in this disorder.

A 25-year-old, healthy active athlete was diagnosed with an anterior cruciate ligament (ACL) lesion. Routine preoperative laboratory tests revealed prolongation of prothrombin time (PT). A factor VII (FVII) deficiency was diagnosed (FVII level 8%). Standard, arthroscopic anatomical single-bundle ACL reconstruction using hamstring was performed. The procedure was carried out under hemostatic coverage of activated recombinant factor VII (rFVIIa). RFVIIa was administered in three doses on surgery day and every 12 hours for the next two to seven days. The pre-surgery dose was 30 µg/kg. The subsequent doses were 15µg/kg. Care was taken to limit the procedure time and carry meticulous hemostasis. No excessive bleeding was observed during and after the operation. Standard rehabilitation protocol was introduced. No complication was noted during the procedure and rehabilitation. After six months, the patient returned to the same sport activity level. ACL reconstruction in athletes is possible, in routine surgical protocol, for the factor VII deficient patients.

Keywords: ACL injury, FVII deficiency

P1.16
Surgical and non-surgical management of pelvifemoral bone bridges in patients with hemophilia
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Peripheral heterotopic bone formation (HBF) and its course have been infrequently described in patients with hemophilia. Spontaneous or post-traumatic intramuscular bleedings have been blamed as causative factors since they follow some specific muscle excursions. Sometimes they can extend from one bone to another, form complete or incomplete bone bridges, and block the natural joint motion. We present three cases (one of them previously reported) of HBF, in people with hemophilia, extending from the proximal femur to the pelvic bones. Patients were 15, 17, and 21 years old. Two cases had hemophilia B and one had hemophilia A. The right side was affected in two cases and the left in one. In two cases, HBF was located in the quadratus femoris (QF) muscle (posterior to the hip joint), and in the rectus femoris muscle (anterior to the hip) in the last case. HBFs in the QF did not form a complete bone bridge and caused only limited discomfort without compressing the surrounding soft tissue, particularly the sciatic nerve. In one case, spontaneous regression of HBF occurred within six months. Therefore, management, consisting of regular observation, avoidance of overuse and trauma, and a controlled exercise program, was enough for two QF muscle HBFs. On the contrary, the case with HBF in the RF muscle had a complete bone bridge formation, which completely blocked hip joint motion and was located between the iliac bone and the anterior aspect of the femur. We had to surgically remove the extraarticular bone bridge formation. The patient regained joint motion immediately and almost completely. The perioperative course of the patient was uneventful. The last case is under close observation for the future course. Pelvifemoral bone bridges may be encountered infrequently in people with hemophilia and can be managed by taking into account the patient’s discomfort and the clinical-radiographic course of the HBF.

Keywords: periarticular heterotopic, hemophilia A, hemophilia B

P1.17
Hemostatic management of children with severe hemophilia A, B, and von Willebrand disease (VWD) and high responding inhibitors undergoing orthopedic surgeries
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Hemostatic monitoring of surgical interventions in patients with hemophilia A (HemA), hemophilia B (HemB) and VWD type III and high responding inhibitors is not feasible with replacement therapy. Patients/Methods: Management of five orthopedic interventions in four patients with alloantibodies to FVIII (n=2), FIX (n=1) and VWF (n=1) is presented. Results: Type of surgeries: 1) Chemical synovectomies with rifampicin at three target joints, under bypassing agent infusions. The same procedure was applied for four consecutive weeks to each patient. All synovectomies
resulted in significant reduction of hemarthroses in the affected joints. 2) Drainage of a post-traumatic compartment syndrome of the right forearm, requiring the concomitant use of two bypassing agents in order to control ooze from the surgical site. The outcome was complete recovery after adequate physiotherapy. 3) Excision of a left knee tumor in a boy with alloantibodies to VWF under concomitant use of a bypassing agent and continuous infusion (CI) of recombinant FVIII (rFVIII) devoid of VWF. No drug-related adverse event occurred. A Kaposi-form hemangioendothelioma was revealed in biopsy and the patient followed a physiotherapy course in order to be mobilized under prophylaxis. Details on patients’ characteristics, surgical procedures, inhibitor titres, perioperative management, and outcomes are shown in the following table. **Conclusion:** Hemostatic management of orthopedic surgeries, in children with hemophilia or VWD and high titre inhibitors, is challenging and requires adequate amounts of concentrates in order to attain successful hemostasis and ensure uneventful outcome.

<table>
<thead>
<tr>
<th>Case</th>
<th>Disorder</th>
<th>Age</th>
<th>Inhibitor titre at surgery</th>
<th>Type of intervention</th>
<th>Pre-operative treatment</th>
<th>Day 1</th>
<th>Day 2 onwards</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severe hemA</td>
<td>14y</td>
<td>8 BU 1.2 BU</td>
<td>1) Synovectomy of right knee 2) Synovectomy of left elbow</td>
<td>90μg/kg rFVIIa, 90μg/kg rFVIIa every 2-3-4 hours</td>
<td>90μg/kg rFVIIa every 6-8-12 hours for 2 days</td>
<td>Good post-operative hemostasis</td>
<td>Reduction of joint bleeds</td>
</tr>
<tr>
<td>2</td>
<td>Severe hemB</td>
<td>12y</td>
<td>46 BU</td>
<td>Synovectomy of left knee</td>
<td>90μg/kg rFVIIa, 90μg/kg rFVIIa every 2-3-4 hours</td>
<td>90μg/kg rFVIIa every 6-8-12 hours for 2 days</td>
<td>Good post-operative hemostasis</td>
<td>Reduction of joint bleeds</td>
</tr>
<tr>
<td>3</td>
<td>Severe hemA</td>
<td>4y</td>
<td>7.8 BU</td>
<td>Decompression of post-traumatic compartment syndrome of the right forearm. Symptoms caused by paralysis of median and ulnar nerves</td>
<td>200μg/kg rFVIIa</td>
<td>90μg/kg rFVIIa every 2 hours</td>
<td>90μg/kg rFVIIa every 2 hours and after day 4 tapering for 15 days + pd-aPCC (50UI/kg) every 12 hours for 3 days</td>
<td>Decompression of the right forearm and good hemostasis at surgical site. Full recovery after 3-month physiotherapy</td>
</tr>
<tr>
<td>4</td>
<td>VWD type III</td>
<td>8y</td>
<td>0.6 BU Historical titre 6BU</td>
<td>Excision of left knee tumor</td>
<td>60 IU/kg rFVIIa followed by CI 25IU/kg/h +a single dose of rFVIIa (90μg/kg)</td>
<td>CI of rFVIIa</td>
<td>CI of rFVIIa + rFVIIa every 2-3 h for 2 weeks</td>
<td>Uneventful surgery Mobilization under physiotherapy Biopsy of tumor: Kaposis-form hemangioendothelioma</td>
</tr>
</tbody>
</table>

**Key words:** hemophilia, VWD, inhibitors, orthopedic interventions

### P1.18
**Elective orthopedic surgery in hemophilic patients with inhibitors**

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**Background:** Orthopedic surgery in patients who developed an inhibitor against FVIII/FIX, the most common and most serious complication of replacement therapy in patients with hemophilia A or B, represents a surgical challenge, and information regarding the management of orthopedic surgery in such patients is limited. **Aim:** Description of elective orthopedic surgery in hemophilic patients with inhibitors from a single centre. **Methods:** Retrospective data collection regarding orthopedic surgery between January 1997 and December 2012. Forty-four procedures were performed in 22 patients affected by severe hemophilia A with inhibitor. Outcome measures included length of hospitalization, length of follow-up, occurrence of adverse events, need for additional intra-articular intervention, and patient satisfaction. **Results:** Of the 44 orthopedic procedures, four were minor surgery (surgical treatment of flat foot) and 40 were major surgeries (19 replacement surgeries, 10 arthroscopic procedures, 11 others procedures). Thirty-nine procedures were performed in high-responder patients. Recombinant factor VIIa was used for 36 major surgeries (90%). The median age of the patients at surgery was 32 years (range: 5-70), and the follow-up time ranges between three to 180 months. **Conclusion:** To date, no routine laboratory assay has proven to be helpful for dose optimization of either aPCC or rFVIIa treatment hence careful clinical follow-up is mandatory in order to avoid bleeding complications. Nevertheless, such procedures in hemophilic patients with inhibitors have to be limited to experienced hemophilia centres and surgeons.

**Keywords:** elective orthopedic surgery, hemophilia, inhibitors

### P1.19
**The diagnosis of acute compartment syndrome (ACS) in hemophilia**

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ACS is caused by a restriction of capillary blood flow within a fascial compartment with potential limb-life-threatening
Abstracts

P1.20
Surgical resection of a pseudotumour in Myanmar

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Objective: To showcase a dedicated team's effort in alleviation of severe pain and discomfort of a young boy with severe hemophilia B in a country with minimal hemostatic replacement therapy.

Methods: Myanmar has come out of isolation and is engaging with the rest of the world. The healthcare system is seeing the fruits of the interaction. Donating clotting factor concentrate, and the pharmaceutical companies' showing corporate social responsibility, has made this happen: "Surgical resection of a pseudotumour in a young hemophilia B patient". The methodology is "seizing the opportunity" and the working of a team of paediatricians, orthopedic surgeons, pathologists, and other healthcare professionals. The patient was treated surgically by using both volar and dorsal approach and a pseudotumour was removed without requirement of bone graft. The surgery has been videotaped and the final result of the young boy is shown. It portrays the skills of the surgeons, the dedication of the team, and the capability to work together for the "best care of the patients," as can be given with whatever is available. It also illustrates the need of corporate social responsibility by pharmaceutical companies in helping WFH to close the gap in hemophilia care globally.

Results: At three-month follow-up, normal healing occurred and no recurrence was observed. The patient was completely asymptomatic.

Conclusion: Hemophilia patients, even in places with resource limitations, deserve the treatment needed for them, so that they can have an improved quality of life. This can be made possible when all caring people work together.

Keywords: pseudotumour, hemophilia B

P1.21
A case study of hemophilia: Alfred P.

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A patient with hemophilia has not been recognized for his role in advancing medical care through the application of X-rays. In 1897, Dr. J.E. Shaw of Bristol, England, was first to publish X-rays of hemophilic arthropathy in knees and elbows. The patient was a 30-year-old man named Alfred P. who had previously been reported as a case study in hemophilia. Historical research using original and secondary source material uncovered the family and medical history of Alfred P. along with a copy of the original x-ray of his swollen knee. Alfred P. is due proper acknowledgment as the first person with hemophilia to consent to an x-ray examination of his joints.

Keywords: history, X-rays

P1.22
Factors influencing functional independence score in hemophilia


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Background: Functional independence score in hemophilia (FISH) is a measurement tool to assess disability in patients with hemophilia. Scores ranging from one to four are given for each of eight parameters. Different factors can influence on the function of hemophilic persons after a therapeutic intervention.

Methods and Materials: Demographic data and treatment modalities were collected together with FISH questionnaires in a cross-sectional study on a total of 153 patients, comprising 113 patients with hemophilia A and 32 with hemophilia B. Results: The mean age of patients with hemophilia A and B was 25.1±15.4 and 22.8±11.9, respectively. Furthermore, the mean FISH score of patients with hemophilia A and those with hemophilia B was 27.7±4.6 and 28.1±4.5, correspondingly. No significant difference was observed between hemophilia A and B regarding FISH score (p=0.671), but there was significant difference in FISH score between patients with and without inhibitor (p=0.029). Moreover, there was no significant difference between prophylactic and on-demand groups in hemophilia type A patients regarding FISH score (p=0.977). A significant difference was observed between severe type, and mild and moderate types of hemophilia regarding FISH Score (0.037). As well as this, a wide disparity was detected between patients with and without hepatitis C regarding FISH score (0.000).

Conclusion: FISH score is a simple means of measuring disabilities: the more severe the hemophilia, the more disabled the patient. Furthermore, if factor deficiency can be diagnosed early on and the patient receives prophylactic treatment, the least disability can be predicted for the patient.

Keywords: hemophilia; FISH score
P1.23
Interdisciplinary musculoskeletal clinic for persons with inherited bleeding disorders (PWBD)
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Background: Notwithstanding the progressive adoption of pharmacological prophylaxis, the assessment and management of joint disease remains an integral aspect of comprehensive care for persons with inherited bleeding disorders (PWBD). Given current fiscal restraints, it has been suggested that new models of care may better allow for fiscally responsible health outcomes.

Objective: To develop an interdisciplinary musculoskeletal clinic (IDMC) for PWBD. Methods: An interdisciplinary team, including hematology, orthopedics, physiotherapy, prosthetics/orthotics, nursing, and program administration was created. Patients requiring joint health assessment and management were referred to the bi-annual IDMC at their annual review. Functions provided in the IDMC include orthopedic assessment, recommendations for surgical intervention, factor replacement, intra-articular joint injection, bracing/orthotics, and physiotherapy. Results: The IDMC demonstrated several beneficial outcomes for PWBD including: Interventional procedures were discussed and performed by orthopedic surgery, in the clinic, with factor replacement recommendations provided by hematology and administered by nursing staff; When indicated, goals for physiotherapy and bracing/orthotics were evaluated with the patient and an interdisciplinary team to streamline service delivery and follow-up; Enhanced communication among team members and the PWBD, facilitating accountability, patient self-efficacy, and autonomy. Conclusions/Future Directions: In our experience, the IDMC provided patient-focused care with reduced fragmentation and duplication. Future needs include evaluating the cost-effectiveness of this model of care, the impact on quality of life/disease management for PWBD, provider satisfaction, administrative outcomes, including wait times and the psychosocial/financial impact of joint disease on PWBD with the inclusion of social work as a member of the interdisciplinary team.

Keywords: interdisciplinary care, orthopedics

P1.24
Efficacy and safety of rFVIIa, used as comparator in development of a new rFVIIa analogue: data from a phase 3 trial on vatreptacog alfa in hemophilia patients with inhibitors
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For several decades, rFVIIa has demonstrated a consistent safety and efficacy track record for managing acute bleeds and surgical hemostasis in hemophilia patients with inhibitors. Aim: To report the efficacy and safety of rFVIIa in Adept“2, a phase 3, multi-centre, double-blind, cross-over trial on the treatment of bleeds in inhibitor patients aged ≥12 years. Bleeding episodes were randomized (3:2) to vatreptacog alfa (1-3 doses × 80 µg/kg) or rFVIIa (1-3 × 90 µg/kg). Local standard of care was used if hemostasis was not achieved after three doses. Effective bleeding control was defined as no additional hemostatic medication within 12 hours. Safety assessments included immunogenicity (development of vatreptacog alfa/rFVIIa neutralizing antibodies) and adverse events. A total of 227 bleeds in 57 patients were treated with rFVIIa; 205 were joint or muscle bleeds treated at home. There were 3.98±3.4 (mean±SD; range 1-16) bleeds/patient. Time from bleeding onset to first injection was 1.3±3.8 hours. Effective bleeding control was achieved in 93% of all bleeds treated with 1-3 doses of rFVIIa. Vatreptacog alfa efficacy was also 93%. rFVIIa efficacy was comparable for muscles, joints, and mucocutaneous bleeds. Bleeds treated after two hours responded as well as bleeds treated within two hours. Only 15 AEs (in 6.6% rFVIIa-treated bleeds), of which five were serious AEs (2.2%), were reported. General safety assessments showed no safety signals to rFVIIa. Adept“2, the largest global, randomized trial in inhibitor patients, confirmed the well-established safety and efficacy profile of rFVIIa with a 93% success rate. Late-treated bleeds (>2 hours) responded as well as early-treated bleeds (≤2 hours).

Poster Session 2

P2.01
The effect of a home-based exercise program on postural balance in children with hemophilia: two case studies
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Objective: The objective of this study was to evaluate the effects of a home-based exercise on postural balance in children with hemophilia. Method: Two children with hemophilia A, with a previous history of at least four lower limb joint bleeds over the past six months, participated in this study. The joint condition was evaluated by HJHS 2.1 and the postural control was assessed during quiet standing with (I) eyes-open/stable surface, and (II) eyes-open/foam surface. A (III) condition was assessed using
unexpected perturbation using an external device. Sway area of center of pressure displacement (COP) were analyzed for conditions (I) and (II) and COP-displacement in anterior-posterior (AP) direction for condition (III). Children and parents received a booklet with instructions of a home-based exercise program to be accomplished over a six-week period, three times a week. After this period, they were similarly re-evaluated. Results: Both participants improved the variables analyzed after the 6-week program. Conclusion: These case-reports suggest that a home-based exercise program could improve postural control in children with hemophilia. Applicability to hemophilia care: The understanding of the real effect of exercises can help physiotherapists to improve the already available booklets of home exercise that are distributed in hemophilia centers, especially in developing countries, where the distance between the hemophilia centers and patients’ home is a barrier to optimum care.

Subject 1 (moderate HA, 11 years) Subject 2 (severe HA, 8 years)

<table>
<thead>
<tr>
<th>Condition I swamp area (cm²)</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.06</td>
<td>1.55</td>
<td>-24.7%</td>
<td>0.58</td>
<td>0.47</td>
<td>-19%</td>
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</table>

<table>
<thead>
<tr>
<th>Condition II swamp area (cm²)</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.17</td>
<td>0.93</td>
<td>-57%</td>
<td>2.71</td>
<td>2.25</td>
<td>-17%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition III COP-AP (cm)</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
<th>Initial</th>
<th>After 6 weeks</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>41.4</td>
<td>38.4</td>
<td>-7%</td>
<td>77.7</td>
<td>61.2</td>
<td>-21%</td>
</tr>
</tbody>
</table>

Keywords: postural balance, hemophilia

P2.02
Physiotherapy is an important element of modern hemophilia treatment
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Introduction: Patients with hemophilia suffer from joint bleedings, which can lead to arthropathy. The administration of factor concentrate is primary to prevent these bleeds. Thus, we are investigating if there is an additional benefit by subsidiary measures. We offered these patients physiotherapy in our centre and investigated them systematically. Methods: 44 patients (age four – 62 years) were interviewed about quality of life and their pain sensation before and after one year of physiotherapy. We used also the substitution calendar as a data source. Twenty-nine patients (66%) were treated prophylactically and 15 patients (34%) were treated on demand. For the data analysis, we used SPSS (version 21.0) with algebraic sign test by the scaled sizes and CHI2-test by the dichotomous sizes.

Under physiotherapy, the well-being has increased. Pain could be diminished 2.6 scale points in the mean. Analgesics use was reduced one scale point in the mean. The number of bleeds decreased and additional concentrate administration could be reduced. During the physiotherapy, all kind of injuries were less frequent than before. Conclusions: Individualized physiotherapy can raise the quality of life of a patient with hemophilia through increase of the physical function, prevention of bleeds and injuries, and also pain reduction. Besides, this cost can be reduced as there is less coverage of factor concentrate. These results can only be achieved if the physiotherapy is adjusted on the status of the individual joint.

<table>
<thead>
<tr>
<th>Mean comparison</th>
<th>Number n</th>
<th>1. Survey 2011</th>
<th>2. Survey 2012</th>
<th>Improvement</th>
<th>Equal</th>
<th>Degradation</th>
<th>Significance p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical well-being of children/adolescents (scale-score: 1-5)</td>
<td>22</td>
<td>*4.00 (0.68)</td>
<td>*4.25 (0.64)</td>
<td>10 (45%)</td>
<td>10 (45%)</td>
<td>2 (9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Physical function of adults (Scale-score: 1-5)</td>
<td>22</td>
<td>*3.88 (1.03)</td>
<td>*4.21 (0.79)</td>
<td>11 (50%)</td>
<td>9 (41%)</td>
<td>2 (9%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Pain (maximum scale value: 0-10)</td>
<td>44</td>
<td>*5.84 (2.98)</td>
<td>*2.20 (2.42)</td>
<td>41 (93%)</td>
<td>3 (7%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Analgesics use (0=none – 5=several times daily)</td>
<td>44</td>
<td>*1.45 (1.52)</td>
<td>*0.43 (0.90)</td>
<td>27 (61%)</td>
<td>17 (39%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of bleeds (Jan.-Aug.)</td>
<td>44</td>
<td>*2.95 (3.63)</td>
<td>*0.66 (1.55)</td>
<td>21 (48%)</td>
<td>23 (52%)</td>
<td>0 (0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Additional factor concentrates (Jan.-Aug.)</td>
<td>44</td>
<td><strong>Yes (64%)</strong></td>
<td><strong>No (73%)</strong></td>
<td>16 (36%)</td>
<td>28 (64%)</td>
<td>0 (0%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Events of injuries (Jan.-Aug.)</td>
<td>44</td>
<td><strong>Yes (64%)</strong></td>
<td><strong>No (73%)</strong></td>
<td>16 (36%)</td>
<td>28 (64%)</td>
<td>0 (0%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Keywords: physiotherapy, quality of life
P2.03
Effects of cold application on pain sensitivity in hemophilia knee: Results of a randomized controlled study

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Hemophilic arthropathy is usually accompanied by chronic pain. Cryotherapy is a common procedure in pain treatment, although its practice has hardly been substantiated by studies. The aim of this randomized controlled study was to investigate effects of cold application on pain sensitivity (PS) in hemophilia patients. A total of 51 adults with severe hemophilia A (H) and 20 controls without hemophilia (C) were included. Out of these, 15 H and 10 C underwent a 20-minute cooling of both knees in constant 15°C circulating water using Hilotherm® (with intervention) and were compared to 16 H and 10 C, who had on a room-temperate cuff (without intervention). PS threshold was assessed by means of a force algometer on knees before intervention, immediately after intervention, at two and at 24 hours after intervention. Also, the skin temperature (ST) was examined using an infrared thermometer. ST decreased by 2°C immediately after cold application in both groups with intervention (p≤0.01). In H with intervention, no significant changes were determined in PS in knees (left: 50±15 vs. 49±15 Newton (N); right: 46±13 vs. 49±16N) (p>0.05). In contrast, C with intervention showed a decrease in PS (left: 75±30 vs. 89±29N; right: 78±28 vs. 89±26N) (p≤0.01). Values of groups without intervention did not change regarding ST and PS (p>0.05). The study has shown that the use of cold application on knees lowers skin temperature; however, it does not lower pain sensitivity in hemophilia patients. Therefore, cryotherapy should be reconsidered in the treatment of chronic pain in hemophilic arthropathy.

Keywords: pain, temperature, arthropathy

P2.04
Muscle strength, architecture, and neuromuscular function in adolescent boys with hemophilia following lower limb joint hemarthrosis

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Objective: Muscle strength deficits have previously been reported in young children (seven to 11 years) with hemophilia. To date, muscle strength, along with muscle architecture and neuromuscular function in adolescents, have not been explored. The aim of this study was to evaluate differences in muscle strength, architecture, and neuromuscular function in a group of boys with hemophilia and age and Tanner stage-matched typically developing boys. Methods: Fourteen boys aged 11-18 years with severe hemophilia (G1) were recruited from five hemophilia centres in the U.K. Eight boys had experienced lower limb joint bleeds in the previous 12 months (median: 1, IQR: 0-2 bleeds). Typically, developing boys (G2) were recruited from a local primary school. Maximum isometric and isokinetic muscle strength, muscle architecture, voluntary activation, and surface electromyogram (EMG) parameters of the knee extensors (KE) and ankle plantarflexors (APF) were examined. Results: Preliminary analysis has shown no significant group differences for normalized muscle strength, muscle architecture, and EMG parameters for both the KE and APF (p > 0.05). In G1, muscle strength of the KE (r = 0.70, p < 0.01, Fig. 1) and APF (r = 0.69, p < 0.01, Fig. 2) was significantly associated with six-minute timed walk performance. Conclusion/Relevance: The lack of significant differences in muscle measures may be due to factors such as sample size and the proportion of boys with no recent history of bleeds. The observed significant relationships suggest that strength is still an important indicator in adolescent hemophilic boys. Further planned analysis will address these points.

Keywords: muscle strength, neuromuscular function
P2.05
Effectiveness of joint traction and PNF in hemophilic arthropathy of the elbow

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Objective: Evaluate the effectiveness of joint traction and proprioceptive neuromuscular facilitation (PNF), to improve range of movement (ROM), the perimeter and strength of biceps, and pain perception in patients with hemophilia (PWH) and arthropathy of elbow. Methods: Randomized trial with two groups: one treated with joint traction and PNF (MT group) and a control group (C group). The intervention lasted 12 weeks (two sessions per week, one hour each session), and elbows were evaluated before and after treatment, and after six months. Eighteen PWH participated in this study: nine in TM group and nine in C group, being evaluated 16 and 14 elbows, respectively. Three blind evaluators assessed: ROM (flexion and extension), biceps perimeter (measuring tape), biceps strength (rupture test, 0-5 points), and perception of pain (visual analog scale, VAS). Results: Table 1 shows the descriptive characteristics of PWH in the study, depending on the group. We observed improvement (p <0.05) on the perimeter of biceps, flexion, and pain perception of elbow in MT group. These findings held after the follow-up period. Table 2 shows the statistical data of post-treatment and follow-up period. Relevance and applicability to hemophilia care: Our results provide improvement in the elbow flexion despite advanced joint damage. PNF is achieved with a gradual increase of the strength of the muscles around the elbow. The elbow pain relief, observed in this study, is a valid tool for the management of this symptom of special concern for PWH.

Table 1. Description of the sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>TM group</th>
<th>C group</th>
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<tbody>
<tr>
<td>Age</td>
<td>11.67</td>
<td>12.26</td>
</tr>
<tr>
<td>Weight</td>
<td>83.65</td>
<td>84.45</td>
</tr>
<tr>
<td>Elbow hemarthrosis previous year</td>
<td>0.68</td>
<td>0.71</td>
</tr>
<tr>
<td>Radiological damage (Pettersson score)</td>
<td>1.62</td>
<td>2.90</td>
</tr>
</tbody>
</table>

Table 2. Means and standard deviations of measured variables in three measurements

<table>
<thead>
<tr>
<th>Variable</th>
<th>Assessment</th>
<th>TM group (n=16)</th>
<th>C group (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>0.094</td>
<td>0.134</td>
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</tr>
<tr>
<td>Post-treatment</td>
<td>0.000</td>
<td>0.071</td>
<td></td>
</tr>
<tr>
<td>Follow-up period</td>
<td>0.000</td>
<td>0.181</td>
<td></td>
</tr>
<tr>
<td>Biceps perimeter</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pre-treatment</td>
<td>31.331</td>
<td>32.007</td>
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<td>Post-treatment</td>
<td>31.725</td>
<td>31.857</td>
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<tr>
<td>Follow-up period</td>
<td>30.769</td>
<td>31.686</td>
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<tr>
<td>Flexion</td>
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<td>Pre-treatment</td>
<td>136.130</td>
<td>138.000</td>
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<td>Post-treatment</td>
<td>140.310</td>
<td>138.430</td>
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<td>140.310</td>
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<td>Extension</td>
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<tr>
<td>Pre-treatment</td>
<td>10.870</td>
<td>8.640</td>
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<tr>
<td>Post-treatment</td>
<td>11.730</td>
<td>8.290</td>
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<tr>
<td>Follow-up period</td>
<td>11.310</td>
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<tr>
<td>Pain</td>
<td></td>
<td></td>
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<tr>
<td>Pre-treatment</td>
<td>0.719</td>
<td>0.143</td>
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<tr>
<td>Post-treatment</td>
<td>0.344</td>
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<tr>
<td>Follow-up period</td>
<td>0.125</td>
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</tbody>
</table>

Table 3. Parametric analysis of physical and pain variables in the study groups at 3 measurements

(SD: standard deviation; rd: released degrees; Sig.: significance; ES: effect size).

Key words: joint traction, hemophilic arthropathy
P2.06
Improved ambulation and weight-bearing in hemophilia patients with affected lower limbs using the SmartStep™ Gait System

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Objective: Gait training rehabilitation to improve weight bearing and ambulation on an affected lower limb. The training can be used with hemophilia patients who are post hemarthrosis, pre and post-surgery with joint arthropathy, and joint contractures.

Methods: Using the SmartStep Gait System™, a biofeedback and monitoring device. It records and analyzes key gait parameters during functional activities and provides instantaneous audio and visual feedback. The SmartStep is comprised of a pneumatic insole that is placed in the shoe and is connected to two pressure sensors, which measure and transmit the vertical force under the hind foot and forefoot. The data are received and analyzed by a control unit, which is worn around the ankle and transmitted to computer-running software. For each step, the software provides the peak vertical force over the entire foot, heel and forefoot. Temporal parameters, including the number of strides, velocity, cadence, and timing of the stance and swing phase of each step are also calculated.

Treatment sessions began with a gait assessment. Therapy consisted of strengthening exercises, stretching, the use of electrotherapy modalities, weight shift and balance activities. Training and game modes consisting of weight shifts A-P and lateral were also utilized. Post-treatment assessment was then performed.

Results: A 40-60% improvement was seen in overall weight bearing and, especially, in hind foot placement. A positive learning curve was observed. The SmartStep can also be used in a home environment for continued improvement.

Relevance: Continued improvement of proper gait is an essential aspect of hemophilia care. Due to recurrent bleeds and joint arthropathy, many patients develop gait deviations. These deviations need immediate and exact correction. SmartStep aids the proper steps to gait rehabilitation.

Keywords: hemophilia, physiotherapy

P2.07
Building evidence into practice: proposed evidence-based updates to the Canadian physiotherapists in hemophilia care (CPHC) standards of care

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E-mail: strike@hhsc.ca

Background: Research in the field of hemophilia has played a critical role in the management of the disease. As the practice of physiotherapy becomes more evidence-based, the standards of physiotherapy care must also evolve to ensure that persons with hemophilia receive comprehensive treatment.

Objective: To evaluate and update the Canadian Physiotherapists in Hemophilia Care (CPHC) Standards of Care against current best evidence.

Methods: Medline and Embase were used to identify the current evidence for physiotherapy management of persons with hemophilia. Keywords used were hemophilia and physical therapy, with additional limits restricting results to the English language. Searches of Medline and Embase returned 80 and 265 potential articles, respectively. Articles were reviewed to include only those from which novel standards of care could be developed.

Results: The Hemophilia Joint Health Score (HJHS) has been found to be the assessment most widely adopted by physiotherapists in hemophilia care (CPHC) Standards of Care against current best evidence.

Conclusion: Based on current evidence, it is recommended that the CPHC standards of care include: a) use of the HJHS at annual reviews [1-3]; b) education on appropriate sport selection [4,8]; and c) discussion on levels of physical activity [4-9].

Keywords: hemophilia, physiotherapy

References:
P2.09
Incidence of bone mass deficit in the hemophilic patient: aspects related to physiotherapy and quality of life
F. Querol1, 2, S. Pérez-Alenda1, 2, F. Aparisi3, M. Jaca4, C. Vila5, J.A. Aznar3
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Introduction: In the general population, as well as in patients with hemophilia (PWH), osteoporosis implies: 1) compromise of bone resistance; 2) chronic pain related to age and degenerative process; and 3) fracture risk. Alternatively, the reduction of functional capacity and even invalidity are inevitable. All of these aspects together with those of hemophilia itself represent an increase in the comorbidity of this disease. Objectives: To provide preliminary results of bone mass values in hemophilic patients and their relation to physiotherapy, arthropathy signs, and influence on quality of life. Methods: This is an observational prospective study, in which the inclusion in the different groups is directly linked to socio-sanitary criteria, such as the arthropathy rate that prevents the practice of an aerobic sport, the proximity to a center controlled by a physiotherapist, or the modality of the factor substitutive therapy. Three groups of hemophilic patients (PWH) were evaluated. Group 1) PWH with a physiotherapy and sport controlled guideline; Group 2) PWH with the same guideline of physiotherapy and sport but without any professional control; Group 3) Control group; Group 4) PWH who do not follow any physiotherapy program. Results: PWH n=53 (Chart 1) average age: 30.2 years, median: 33, age range: 10-45.S. Pettersson score and Gilbert score = hemophilic arthropathy (46 PWH). Densitometry (BMD) = abnormally low values of bone mineral density (Table 1). Conclusions: Osteoporosis is a severe problem that mainly affects aging people, and the present life expectancy of hemophilic patients involves socio-economic/sanitary risks not studied so far. The average age of hemophilic patients worldwide is between 30 and 40 years, so that many age-related pathologies are unknown in these patients who have a specific pharmacologic, physical, or surgical treatment. Osteoporosis is associated directly to the age and the abnormally low values found in hemophilic population: young adults may require protocized treatments.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Patients</th>
<th>Clinic Arthropathy</th>
<th>Arthropathy X-r</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Hemophilia A</td>
<td>42</td>
<td>41</td>
<td>41</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Moderate Hemophilia A</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Mild Hemophilia A</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Severe Hemophilia B</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>46</td>
<td>46</td>
<td>8</td>
<td>19</td>
</tr>
</tbody>
</table>

Keywords: physiotherapy, BMD
Abstracts

P2.10
Relation of elbow joint bleed and grip strength rehabilitation

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Objective: To study the changes in grip strength after an elbow bleed and the effects of treatment strategies. Background: Loads of written work is given to students in India. With limited resources, faster recovery strategy is important to cope with writing work. A valid evaluation of handgrip strength is of great importance in determining the effectiveness of different treatment strategies. It is widely accepted that grip strength provides an objective index of the functional integrity of upper extremity. Many treatment protocols compare the strength of the injured limb to the other or compare with normative data. Is there a relation between elbow bleed and hand function? Anatomically, the elbow complex is designed to serve the hand, 15 muscles that cross the elbow complex also act at either the wrist or shoulder, and therefore the wrist and shoulder are linked with the elbow in enhancing function of the hand. Purpose: 1. Does a bleed affect the grip strength? 2. What best strategies improve grip strength. Method: Grip measured before and, periodically, after a bleed by using handheld dynamometer. Group B given isolated elbow exercises; Group B elbow + upper limb exercises. Results: Both groups A+B are significant at 95% confidence, but if you compare T statistics or P value, group B is more significant than group A, faster recovery + better functional outcome. Conclusion + Discussion: Gives biofeedback, goal planning, treatment guidelines and in estimating the severity of force generating impairments in patients.

Keywords: coping strategies, hand grip strength

P2.11
Postsurgical mobility of total knee replacement in patients with hemophilia (PWH) operated without tourniquet

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Introduction: The literature showed that the post-operative ROM in PWH treated with TKR slightly improved with the procedure. Objective: To evaluate the postsurgical ROM in patients with TKR done without tourniquet. Materials and Methods: From 2001 to 2012, 25 TKAs were performed in 18 patients with severe hemophilia A, seven bilateral and 11 unilateral. Mean age at arthroplasty was 47 years, mean follow-up was five years (range one to 11). All the knees were treated with PCS total knee replacement. For surgeries done without tourniquet, the ROM was evaluated preoperatively and postoperatively every six months. Results: The mean knee flexion improved from 67° to 82°, post op. The mean flexion contracture diminished from 26° to 8°. The mean total ROM increased from 40° preoperatively to 74° at the final follow-up. (P<0.0001) Test student paired test. ROM obtained in six months postoperative was maintained up to the final follow-up. The relevance and applicability to hemophilia care: This study shows that patients undergoing TKR without tourniquet, and treated with an appropriate plan of long-term rehabilitation, achieved marked improvement in ROM.

Keywords: ROM (range of motion), TKR (total knee replacement)

P2.12
Fisiocare: a new approach to physiotherapy based on self-treatment

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E-mail: eleforn@libero.it

The objective of the work: The objective of the project is to assess the impact of a new approach based on self-treatment, and also to raise awareness and educate the hemophilic population to the “culture of movement”. Methods: Patients will be included after a multidisciplinary assessment (HJHS, postural analysis, bleeding frequency) in order to plan a tailored rehabilitation program. Twelve weekly physiotherapy sessions of 90 minutes will be dedicated to two groups of five patients (adult and pediatric). Afterwards, a self-treatment program will be carried out at home for three months. Once this period will be completed, a re-assessment will be performed. Results: The first data will be made available at the conference. The relevance and applicability to hemophilia care: The Fisiocare project started in two pilot centres (Turin, Bari) and it will be extended throughout the country, particularly in hemophilia centres without regular access to a physiotherapy service, in order to promote a standardized approach of physiotherapy. Our initiative could be proposed as a model. The originality of the work: The project, Fisiocare, is the first national network of physiotherapists involved in hemophilia. This project provides a model for the organization of collective courses of physiotherapy, held by a specialist, in order to administer and teach specific and tailored exercises that every patient can perform in complete autonomy at home.

Keywords: physiotherapy, hemophilia

P2.13
Effectiveness of training program in open waters, pool, and land exercise in adolescents with hemophilic arthropathy

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* UMAE “Dr. Victorio de la Fuente Narvaez”, Unity of Physical Medicine and Rehabilitation North . ** UNAM “Facultad de Estudios Superiores Iztacala”, ***Hemophilia Federation of the Republic of Mexico, México
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**P2.14**

**Impact of hemophilic arthropathy on quality of life**

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**Abstract**

**Introduction:** Swimming is one of the most recommended sports for people with hemophilia. **Objective:** To evaluate the effectiveness of a training program of swimming in open waters, in the pool, and land exercise. **Material and methods:** After obtaining informed consent, they included five adolescents who performed a training program that included pool, open waters and land exercises for 10 months. Three measurements were made with scale Hemophilia Joint Health Score (HJHS). **Results:** of adolescents included, 80% had hemophilia A (moderate and severe) and 20% hemophilia B (severe). The joints with the most damage were the elbows and ankles. There was a reduction in the HJHS between the second and third measurements, statistically significant difference (p < 0.05). The items that showed significant differences were edema in elbows and muscle strength in ankles. The training program in open waters, pool and land exercise are effective to decrease the severity of hemophilic arthropathy in adolescents. **Relevance:** motivate patients with hemophilia to integrate into supervised sports, showing the results obtained and decreasing the myths. **Originality:** the type of training carried out in Mexican adolescents with hemophilia.

**Keywords:** open waters, exercise in hemophilia.

---

**TABLE 1.** Description characteristics of the sample

<table>
<thead>
<tr>
<th>Joint</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ankle</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>31</td>
<td>35.29</td>
<td>12.87</td>
</tr>
<tr>
<td>Weight</td>
<td>31</td>
<td>82.88</td>
<td>10.945</td>
</tr>
<tr>
<td>Hemarthrosis previous year</td>
<td>56</td>
<td>1.80</td>
<td>0.672</td>
</tr>
<tr>
<td>Radiological damage (Pettersson score)</td>
<td>56</td>
<td>9.95</td>
<td>3.071</td>
</tr>
</tbody>
</table>

| **Knee** | | | |
| Age | 21 | 39.48 | 13.493 |
| Weight | 21 | 83.276 | 12.23 |
| Hemarthrosis previous year | 34 | 1.15 | 0.784 |
| Radiological damage (Pettersson score) | 34 | 9.79 | 2.972 |

| **Elbow** | | | |
| Age | 27 | 34.48 | 12.99 |
| Weight | 27 | 81.6 | 9.71 |
| Hemarthrosis previous year | 46 | 0.96 | 0.96 |
| Radiological damage (Pettersson score) | 46 | 8.61 | 2.80 |

**TABLE 2.** Correlations observed in the study

<table>
<thead>
<tr>
<th>Joint</th>
<th>Variable</th>
<th>PH</th>
<th>TA</th>
<th>JS</th>
<th>JP</th>
<th>TS</th>
<th>TD</th>
<th>EF</th>
<th>MH</th>
<th>SA</th>
<th>Qol</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ankle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.265</td>
<td>0.136</td>
<td>-0.147</td>
<td>-0.164</td>
<td>0.198</td>
<td>0.048</td>
<td>0.209</td>
<td>-0.200</td>
<td>-0.086</td>
<td>-0.058</td>
<td></td>
</tr>
<tr>
<td>Radiological damage</td>
<td>-0.181</td>
<td>-0.008</td>
<td>-0.184</td>
<td>-0.175</td>
<td>0.282</td>
<td>0.122</td>
<td>0.029</td>
<td>-0.230</td>
<td>-0.211</td>
<td>-0.106</td>
<td></td>
</tr>
<tr>
<td>Flexion</td>
<td>0.166</td>
<td>0.041</td>
<td>0.389**</td>
<td>0.265**</td>
<td>-0.114</td>
<td>0.016</td>
<td>-0.246</td>
<td>-0.058</td>
<td>-0.087</td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>Extension</td>
<td>0.381</td>
<td>-0.153</td>
<td>-0.034</td>
<td>-0.191</td>
<td>-0.295**</td>
<td>-0.401*</td>
<td>-0.358*</td>
<td>-0.069</td>
<td>0.017</td>
<td>-0.148</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>-0.502*</td>
<td>-0.380*</td>
<td>-0.341**</td>
<td>-0.301**</td>
<td>0.028</td>
<td>-0.030</td>
<td>-0.343*</td>
<td>-0.493*</td>
<td>-0.424*</td>
<td>-0.461*</td>
<td></td>
</tr>
<tr>
<td><strong>Knee</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.364</td>
<td>-0.093</td>
<td>0.210</td>
<td>-0.120</td>
<td>0.117</td>
<td>0.108</td>
<td>-0.011</td>
<td>-0.382</td>
<td>-0.195</td>
<td>-0.145</td>
<td></td>
</tr>
<tr>
<td>Radiological damage</td>
<td>-0.454**</td>
<td>-0.003</td>
<td>-0.384</td>
<td>-0.206</td>
<td>0.298</td>
<td>0.257</td>
<td>-0.033</td>
<td>-0.272</td>
<td>-0.248</td>
<td>-0.19</td>
<td></td>
</tr>
<tr>
<td>Flexion</td>
<td>0.159</td>
<td>-0.286</td>
<td>0.235</td>
<td>0.062</td>
<td>-0.247</td>
<td>-0.413**</td>
<td>-0.248</td>
<td>0.021</td>
<td>-0.018</td>
<td>-0.016</td>
<td></td>
</tr>
<tr>
<td>Extension</td>
<td>0.103</td>
<td>0.405**</td>
<td>0.069</td>
<td>0.154</td>
<td>0.061</td>
<td>0.199</td>
<td>0.242</td>
<td>-0.014</td>
<td>0.114</td>
<td>0.235</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>-0.387**</td>
<td>-0.009</td>
<td>-0.270</td>
<td>-0.491*</td>
<td>-0.103</td>
<td>-0.009</td>
<td>-0.222</td>
<td>-0.453*</td>
<td>-0.266</td>
<td>-0.342**</td>
<td></td>
</tr>
<tr>
<td><strong>Elbow</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.179</td>
<td>0.219</td>
<td>-0.056</td>
<td>-0.041</td>
<td>0.192</td>
<td>0.058</td>
<td>0.290</td>
<td>-0.137</td>
<td>0.004</td>
<td>0.042</td>
<td></td>
</tr>
<tr>
<td>Radiological damage</td>
<td>-0.211</td>
<td>0.166</td>
<td>-0.155</td>
<td>0.075</td>
<td>0.321</td>
<td>0.437**</td>
<td>0.207</td>
<td>-0.103</td>
<td>-0.213</td>
<td>0.051</td>
<td></td>
</tr>
<tr>
<td>Flexion</td>
<td>0.246</td>
<td>-0.02</td>
<td>0.251</td>
<td>0.047</td>
<td>-0.146</td>
<td>-0.119</td>
<td>-0.105</td>
<td>0.149</td>
<td>0.171</td>
<td>0.091</td>
<td></td>
</tr>
<tr>
<td>Extension</td>
<td>-0.136</td>
<td>-0.169</td>
<td>-0.141</td>
<td>0.075</td>
<td>0.228</td>
<td>0.228</td>
<td>0.202</td>
<td>-0.028</td>
<td>0.068</td>
<td>0.057</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>0.09</td>
<td>0.024</td>
<td>-0.115</td>
<td>-0.071</td>
<td>0.074</td>
<td>0.093</td>
<td>-0.064</td>
<td>-0.002</td>
<td>-0.028</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

(Ph: physical health; Ta: treatment adherence; JS: joint state; JP: joint pain; TS: treatment satisfaction; TD: treatment difficulties; EF: emotional functioning; MH: mental health; SA: social activities; QoL: total perception of quality of life)

* Correlation is significant at the 0.01 level (bilateral) ** Correlation is significant at the 0.05 level (bilateral)

**Keywords:** hemophilic arthropathy, quality of life
P2.15
Characteristics of orthopedic status and impact on the quality psychosocial functioning of persons with hemophilia

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Research on the relationship between (poor) body conditions of persons with various physical disabilities and their psychosocial functioning are not always unambiguous. While on the one hand, research shows a negative correlation between the degree of disability and the mentioned areas, the other refers to the so-called “disability paradox,” or high quality of life despite the poor state of the body. Therefore, we wanted to investigate the nature the relationship between quality orthopedic status and psychosocial functioning of persons with hemophilia. An empirical survey among adults with hemophilia was conducted in Croatia (N=135). To determine orthopedic status we used: the scale of bleeding frequency in individual joints (elbow, knee, and ankle); the scale of damage levels of each joint; the scale of pain frequency, the scale of average pain intensity and the scale of physical mobility. The quality of psychosocial functioning was measured by using the Life Satisfaction Scale, the Emotional Functioning Scale the Mental Health Scale, and the Relationships and Social Activity Scale. We also used a variety of socio-demographic variables. The results show a significant correlation of all analyzed orthopedic status domains with psychosocial functioning. Frequent bleeding in joints, greater damage to joints, greater problems with mobility, and frequent and intense pain were negatively correlated with emotional functioning, mental health, relationships and social activity, and life satisfaction. It is interesting to note that the highest correlation was found in relation to knee damage and it seems that knee problems are precisely the biggest problems for people with hemophilia. It is also interesting to note that the worst results (in all forms of psychosocial functioning) were obtained from respondents who were between 40 and 50 years old. The results, among other things, show that the poor orthopedic status of hemophilia patients is not only an indication of major problems with regard to physical functioning, but that this greatly impacts other domains of human life. Therefore, to preserve the quality of psychosocial functioning, it is extremely important to receive quality medical care to ensure health of the musculoskeletal system. Moreover, the implementation of counselling for patients about the easiest ways of coping with these problems is also necessary.

Keywords: psychosocial, hemophilia, quality of life

P2.16
Safety concerns for small children in radioisotope synovectomy for hemophilia: 12 years of experience from a single center

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E-mail: kaan.kavakli@ege.edu.tr
Radioisotope synovectomy (RS) is defined as intra-articular injection of radioisotopes for target joints. Safety concerns related to exposure to radiation have arisen, especially for small children. We aimed to evaluate safety records for 12 years in young children aged <10 years (20% of all patients) (38 patients and 85 joints). Mean age was 8±2 (three to 10 years). All were male 33 had hemophilia A and five had hemophilia B. RS was used for 36 knees, 26 elbows, and 23 ankles. Only four cases had inhibitor (10%). All patients had prophylaxis-resistant synovitis. Target joints per patient were 1.8 (1–3). By 2005, Yttrium 90 (Y-90) was used for all joints, as of 2005, Rhenium 186 (Re-186) started for elbows and ankles, Y-90 continued for knees. Children dose for Y-90 was 2.5-3.0 mCi and 1-1.5 mCi for Re-186. Mean RS count was 2.2 per patient (1–6). Two consecutive RS (with six-month duration) were used for six patients. Three RS in the same joint were used for three patients. During 12 years of observation, we have not had any single patient with malignancy (0/38 patients). One patient, aged six years, with HA and inhibitor was diagnosed severe aplastic anemia after eight months of RS (Re-186 for ankle) (1/38; 2.6%). He was evaluated as co-incident due to short time of duration. Radioisotope leakage to skin has not been seen in children. Acute inflammatory reaction was observed in two patients with inhibitors. Y-90 was used this four-year-old boy with HA (1/38; 2.6%). After 12 years of observation serious safety problems were not observed. RS has also evaluated as safe procedure for children. No doubt, firstly prophylaxis must be tried for children. Radioisotope synovectomy should be preserved for resistant cases.

P2.17
Thermographic and clinical comparison of children with hemophilia and healthy age-matched children

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The objective of the work: Children with hemophilia have silent bleeds, often recognized too late by structural changes in MRI. They cause silent, joint-associated symptoms associated with inflammation. Inflammation increases local blood flow and heat is a cardinal symptom. This can be measured by infrared based thermography. This non-invasive sensor method could be a basic instrument for early detection of silent bleeds. Material and Methods: 10 symptom-free children with severe hemophilia, no reported joint bleeds within the last two years, age four to 17 years (10.3y) and 12 healthy boys age 10 to 14 years (11.75y). Digital Thermografic camera (Vario-Scan High Resolution 3201 ST, Jenoptik Laser, Jena, Germany). Room temperature: 21.9°C (21.7–22.2°C), humidity: 62.3% (59–63.7%). Digital RGB-photos for anatomic right-left comparison. Physical examinations: silent pressure points, were compared with Hemophilia Joint Health

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P2.18 Obesity and metabolic syndrome in Mexican children with hemophilic arthropathy

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Overweight and obesity and hypertension among people with hemophilia are a well-known problem; these are core components of the metabolic syndrome (MS). There are no studies about MS in children with hemophilia. Objective: To establish the prevalence of overweight-obesity and metabolic syndrome in pediatric patients with hemophilic arthropathy (HA). Methods: The Cook pediatric criteria for MS includes: waist circumference (WC, adjusted for age and sex, >90th percentile), high blood pressure (BP, adjusted for age and sex, >90th percentile), triglycerides (TG, >110mg/dL), HDL cholesterol (HDL-c, <40mg/dL) and fasting glucose (Glu, >100mg/dL), requiring at least three criteria to establish MS. Results: 26 children with HA were studied, mild form in three (12%), moderate 10 (38%), and severe 13 (50%), the mean age was 11 ± 3. The prevalence of overweight and obesity (according to Z score CDC-NCHS reference values) was 12% and 31%, respectively. The MS criteria distribution was: high TG 46%, low HDL-c 34%, high BP 23%, high WC 15%, high glucose 0%. Finally the prevalence of MS was 8%. Obese children had statistically significant higher WC ratio (0.91 ± 0.07 vs. 85 ± 0.03; p = 0.018) and LDL-c levels (95.6 ± 16 vs. 62.5 ± 16; p = 0.007) than non-obese children. Conclusions: Overweight and obesity are common in our pediatric patients with HA, our obese/overweight children had a lipoprotein profile of cardiovascular risk, and additionally obese/overweight children could damage earlier weight-bearing joints, affecting the range of motion, physical functioning, sports, and quality of life. Early detection allows appropriate intervention.

Keywords: Obesity, pediatrics, arthropathy

P2.19 Joint health and functional ability in children with hemophilia in Bosnia and Herzegovina

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Introduction: Currently there is growing interest in objective measurement of health outcome in patients hemophilia. Evaluation of joint health in hemophilia patients and their limitations in performing activities of daily living are very important. This is of particular importance in Bosnia and Herzegovina, where in the last five years, great efforts were made to provide prophylactic treatment for children suffering from hemophilia. Aim: The aim of this study was to determine the status of the joint function and functional ability of children with hemophilia and compare it with the degree of severity of hemophilia, age of the patient, therapy (on demand, primary or secondary prophylaxis). Methods: This study is based on data that were collected by phone interviews with patients and their parents and data from the National Register for people with hemophilia, which is currently in the process of forming. Joint check list and questions about functional ability are made by joint HSPH and Pediatric Hemophilia Activity List and adapted for the telephone survey. Results: 26 children with HA were studied, mild form in three (12%), moderate 10 (38%), and severe 13 (50%), the mean age was 11 ± 3. The prevalence of overweight and obesity (according to Z score CDC-NCHS reference values) was 12% and 31%, respectively. The MS criteria distribution was: high TG 46%, low HDL-c 34%, high BP 23%, high WC 15%, high glucose 0%. Finally the prevalence of MS was 8%. Obese children had statistically significant higher WC ratio (0.91 ± 0.07 vs. 85 ± 0.03; p = 0.018) and LDL-c levels (95.6 ± 16 vs. 62.5 ± 16; p = 0.007) than non-obese children. Conclusions: Overweight and obesity are common in our pediatric patients with HA, our obese/overweight children had a lipoprotein profile of cardiovascular risk, and additionally obese/overweight children could damage earlier weight-bearing joints, affecting the range of motion, physical functioning, sports, and quality of life. Early detection allows appropriate intervention.

Keywords: Obesity, pediatrics, arthropathy
Conclusion: Treatment of hemophilia should be more than the use of clotting factor. Joint physical examination must be performed by hemophilia joint score and provide adequate physiotherapy and surgical treatment for patients.

Keywords: joint health

P2.20
Using the PedHAL to measure functional abilities in children with hemophilia

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Clinical outcomes are important aspects of hemophilia care; these include disease-specific tools evaluating medical and social consequences. The Paediatric Hemophilia Activities List (PedHAL) is a self-reported functional outcome questionnaire, measuring the impact of hemophilia on activities of daily living. This study reports the largest cohort to date using the PedHAL in a single U.K. hemophilia centre. Questionnaires were completed by patients with all severities of hemophilia A or B when attending hemophilia reviews. The PedHAL has 53 questions in seven subsections and is completed by children and/or parents. All scores are normalized, with a score range of 0 – 100 (worst to best function). 95 questionnaires were completed. Results were analysed looking at three groups: parent only (n=33, median age six years), child only (n=8, median age 14.5 years), child parent dyads (n=54, median age 11 years). The parent only group had the highest median total score (100, 50.6-100). The child only group had the lowest median total score (82.7, 48.8-100). 3 joints or and more

Joint loss/impairment function

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<th></th>
<th>Severe</th>
<th>Moderate</th>
<th>Total</th>
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<tr>
<td>Primary prophylaxis</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>Secondary prophylaxis</td>
<td>16</td>
<td>8</td>
<td>24</td>
</tr>
<tr>
<td>No joint problems</td>
<td>4</td>
<td>4</td>
<td>8</td>
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Functional ability score

1. joint

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</thead>
<tbody>
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<td>Excellent (5)</td>
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<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Good (3-5)</td>
<td>10</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>Bad (0-3)</td>
<td>12</td>
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<td>12</td>
</tr>
<tr>
<td>Regular physiotherapy</td>
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<td>0</td>
<td>4</td>
</tr>
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<table>
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<td>10</td>
<td>2</td>
<td>12</td>
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<tr>
<td>Leg function</td>
<td>10</td>
<td>0</td>
<td>10</td>
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<tr>
<td>Leisure and sport</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

Conclusion: Treatment of hemophilia should be more than the use of clotting factor. Joint physical examination must be performed by hemophilia joint score and provide adequate physiotherapy and surgical treatment for patients.

Keywords: joint health

P2.21
Are age, prophylaxis, history of high-titre inhibitor and recent bleeding variables that affect HJHS in children with severe hemophilia?

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Many variables may influence the frequency and severity of bleeding leading to joint damage and physical limitations in people with hemophilia. The variables age, prophylaxis, history of high-titre inhibitors (HTI), and recent bleeding events were evaluated to see if they influenced the Hemophilia Joint Health Score (HJHS) in children. In boys with severe hemophilia, aged 4-18 years, medical and physiotherapy were reviewed to collate information about the possible variables associated with increased HJHS. Total HJHS zero scores were seen in 44/83 (53%) of boys whose median age was 11 (range 0-25). The median HJHS was 0 (mean 2.6). Variables: age, number of recent bleeds, and tolerized status were all significant. History of a HTI demonstrated higher HJHS than those boys in the non-HTI group. A significant relationship was identified with number of recent bleeds, tolerized status, and age. The score rose on average by 28% for every year of age and by 76% for non-tolerized boys. In the non-HTI group, the HJHS for boys on late prophylaxis was 2.68 times higher than those who started early; the HJHS was on average 10% higher for every additional recent bleed. In this group, the odds of having a zero score fell by 30% for every year increase in age. Early prophylaxis and immune-tolerance are important outcome variables as evidenced from this study. Monitoring joint scores is essential to clinical management; the HJHS offers such an outcome measure. Advances in hemophilia care may pose challenges to understanding the HJHS given the likely rise in zero scores.

Keywords: HJHS and children

P2.22
Long-term follow-up of boys with severe hemophilia in one hemophilia centre

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The Hemophilia Joint Health Score (HJHS) is one method of evaluating long-term joint status in people with hemophilia, which is important for management. HJHS (v2.1) scores at transition to adult care from Great Ormond Street Hospital were
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P2.23

Hemarthrosis in hemophilic mice results in alterations in M1-M2 monocyte/macrophage polarization

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Background: Joint bleedings result in iron-mediated synovitis and cartilage destruction. Monocyte/macrophage polarization affects their role in iron homeostasis: M1 cells have limited iron recycling capacities, whereas M2 cells have effective iron recycling capacities. Objective: The aim of this study was to evaluate the effects of hemarthrosis on monocyte/macrophage polarization. Methods: Using a murine hemophilia model of acute joint bleeding and flow cytometry, we evaluated monocyte/macrophage polarization in blood, spleen, synovium, and knee lavage at day 1, 2, and 7 following the induction of hemarthrosis. Results: Induction of hemarthrosis resulted in a transient shift of blood monocyte/macrophage polarization in blood, spleen, synovium, and knee lavage at day 1. No significant alterations in synovial macrophages were noted. In the joint lavage, a temporary increase in M1 monocytes (control 2841 vs. 1086 counted cells at day 1; p=0.02) and a sustained decrease of spleen M2 red pulp macrophages (control 1853 vs. 673 counted cells at day 7; p=0.01). In addition, an increase in M1 (control 119 vs. 592 counted cells at day 1; p=0.04) and M2 (control 247 vs. 650 counted cells at day 1; p=0.02) synovial macrophages was noted. In the joint lavage, a temporary increase in M1 monocytes (control 20 vs. 125 counted cells at day 1; p=0.04) and a more sustained increase in M2 monocytes (control 73 vs. 186 counted cells at day 2; p<0.01) was observed. Conclusion: This study demonstrates for the first time alterations in monocyte/macrophage polarization, following hemarthrosis, resulting in a blood monocyte M1 phenotype and a combined M1-M2 monocyte/macrophage phenotype in the joint. Based on the different capabilities of M1 and M2 cells in iron homeostasis, modulating polarization of distinct monocyte/macrophage populations might represent interesting prophylactic or therapeutic approaches for joint bleedings.

Keywords: HJHS

P2.24

Antiplasmin, but not amiloride, prevents synovitis and cartilage destruction following hemarthrosis in hemophilic mice

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Introduction: In this study, we evaluate the alterations in synovitis and cartilage destruction following the induction of a joint bleeding in hemophilic mice treated with placebo, amiloride (a specific inhibitor of uPA), or antiplasmin. Methods: The right knees of hemophilic mice were punctured to induce hemarthrosis. Hemophilic synovitis and cartilage destruction were determined by two blinded observers according to Valentino and Glasson. An increase in Valentino and Glasson score represents an increase in hemophilic synovitis and cartilage destruction, respectively. Treatment with amiloride or antiplasmin was compared with control. Categorical data were analyzed by loglinear analysis and Pearson Chi-Square. Results: No significant alterations in synovitis and cartilage destruction were found when comparing the oral amiloride group with the oral control group, and when comparing the intra-articular amiloride group with the intra-articular control group. In contrast, intra-articular treatment with antiplasmin resulted in a statistical significant (p<0.01) reduction in synovitis, as assessed by the Valentino score, when comparing the intra-articular control group to the intra-articular antiplasmin group: 1 (0% vs. 11.1%), 2 (4.2% vs. 11.1%), 3 (16.7% vs. 61.1%), 4 (29.2% vs. 5.6%), 5 (20.8% vs. 11.1%), 6 (8.3% vs. 7.7%), 7 (8.3% vs. 0%), and 8 (12.5% vs. 0%). Conclusions: Intra-articular treatment with antiplasmin following the induction of a joint bleeding prevented synovitis and cartilage destruction in hemophilic mice. Oral and intra-articular treatment with amiloride failed to attenuate synovitis and cartilage destruction. Given that complete prevention of joint bleeds in hemophilia is not feasible at the moment despite the prophylactic use of factor replacement, the data presented herein offer promise for the use of antiplasmin as a new therapeutic intervention.

Keywords: synovitis, antiplasmin