WORLD FEDERATION OF HEMOPHILIA

10TH MUSCULOSKELETAL CONGRESS

Stresa, Italy
May 3–6, 2007

FINAL PROGRAM AND ABSTRACTS
GREETINGS

Benvenuti a Stresa and the 10th Musculoskeletal Congress of the World Federation of Hemophilia.

The Musculoskeletal Committee began as the brainchild of a small group of forward-thinking orthopedists in 1980 and has been recognized as an official committee of WFH for nearly twenty years. One of the first chairs of the group was Dr. Vincenzo Pietrogrande of Milan. It is very fitting that the 10th MSK Congress is being held in his back yard.

The theme of this congress reflects the mission of the MSK committee: “Bringing together orthopedic surgeons and physiotherapists”. Of course, we also welcome colleagues with expertise in many other areas such as rheumatology, physical medicine, cellular biology, radiology and hematology. The program was designed to include diverse topics and lively debate so that all disciplines can learn from each other. The planning committee has also arranged for delegates to sample some of the scenery and cuisine for which the Italian Lake District is noted.

Musculoskeletal complications of hemophilia continue to be prevalent despite advances in hematologic therapies. We hope you are able to take home knowledge that will make a difference in the lives of people with hemophilia around the world as we move toward the goal of the WFH: Treatment for All.

Best wishes,

Kathy Mulder  
Chair

Adolfo Llinas  
Senior Vice-Chair

Pierluigi Solimeno  
Junior Vice-Chair
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Committees

WFH MUSCULOSKELETAL EXECUTIVE COMMITTEE

Ms. Kathy Mulder – Canada – Chair

Dr. Adolfo Llinas – Colombia - Senior Vice Chair

Dr. Luigi Solimeno – Italy- Junior Vice Chair

Ms. Rachel Tiktinsky - Israel – Secretary

MEMBER AT LARGE

Dr. Tariq Sohail – Pakistan

HONORARY PRESIDENT

Mrs. Brenda Buzzard UK
Acknowledgements

The World Federation of Hemophilia Congress organizer of the Musculoskeletal Congress 2007 would like to thank the following companies for their significant contributions:

Congress Sponsors

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Congress Information

Congress Venue
The WFH 10th MSK Congress is being held at the Regina Palace Hotel which is located at Corso Umberto I, Stresa, Italy
www.regina-palace.it

Badges
Delegates, Speakers and exhibitors must wear their name badges. Entrance to the Lunch area and social even of Saturday night is limited to badge holders only.

Duplication/Recording
Photography, audio-taping, videorecording, digital taping or any other for of duplication is strictly prohibited in the session’s halls.

Cellular Phones and Pagers
As a courtesy to all congress attendees and speakers, cellular phones, pagers and other electronic devices must be operated in the silent/vibrate mode within educational sessions. Devices that beep and ring are strictly prohibited. No cellular phone conversations are permitted within the meeting rooms.

Smoking Policy
Please note that it is not allow smoking inside the Hotel Regina Palace.

Registration
Registration on Thursday, May 3 located in the lobby area of the Regina Palace Hotel
Registration on Friday, May 4 and Saturday May 5 located in the Exhibit area

Thursday, May 3: 13:00 – 17:00
Friday, May 4: 07:45 – 17:00
Saturday, May 5: 07:45 – 16:00
Sunday, May 6: 07:45 – 12:00

About Stresa

The pearl of Lake Maggiore, the beautiful Stresa, known throughout Europe for its great inclination of tourism and its ability to attract great events and famous personalities every year.

Apart from the lake, Stresa offers a full array of fantastic touristic opportunities, including the Borromeo islands. On the first island, Isola Bella, you can find an insurmountable amount of Borromeo construction in the Baroque Palazzo Borromeo, where Napoleon was once a guest.

Isola dei Pescatori, has a unique skyline of the old town has a unique skyline of the old town. Unchanged over the years, Isola dei Pescatori certainly is the most picturesque amongst the Borromeo Islands. The sharp bell tower stands out above the red pantiles of roofs, the houses with low porches overlook the lake showing their pergolas and roof-terraces and the shore is always full of boats.

The island, also called Superiore for its northern position in comparison with the other two “sisters”, is named after the main activity, which over the centuries has characterized this fishermen town. Although only a few families still continue to fish, the identity of the small community appears still intact. Tourists are fascinated by its simple houses, the narrow lanes, the stone portals and the attractive underpasses.

We look forward to welcome you in Stresa!

Climate & Clothing
Day time temperature in May is around 22 degrees Celsius. Evenings can be cool, about 14 degrees so it will be handy to have a light jacket.

Social Program

Opening Ceremony & Welcome Reception
Date: Thursday May 3, 2007
Time: 18:30–19:30
Venue: Regina Palace Hotel
Dress: Business Attire
Cost: Complimentary

Cultural event and Farewell dinner
Date: Saturday, May 5, 2007
Time: 16:30–22:00
Venue: Isola Bella & Isola dei Pescatori
A 45 minutes visit to the Borromeo Palace in Isola Bella, followed by dinner at Isola dei Pescatori
Dress: Casual Chic (Make sure to wear comfortable shoes—we will walk in the sand and stones)
Cost: 120 Euros. Complimentary for full registrations.
## WFH 10th Musculoskeletal Congress
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Chairman: K. Mulder (CAN)
Demonstrators: M. Perja (ALB)   Presenters:  G. Pasta (ITA)
D. Stephensen (UK)    F. Querol (SP)
F. Aparisi (ITA)

15:00–16:00 Deep infections after TKR: Diagnosis and treatment
Chairman: J. Wiedel (USA)
Deep infections after TKR in hemophiliacs
O. Perfetto (ITA)
Diagnosis and treatment: guidelines
E. Meani (ITA)

16:30–18:00 Physiotherapy Standards Meeting
Chairman: K. Beeton (UK)

16:30–18:00 Peri-operative management in inhibitor patients
Chairman: E. Santagostino (ITA)
Peri-operative management in inhibitor patients
C. Negrier (FRA)
Orthopedic treatment in inhibitor patients
C. Rodriguez-Merchan (SPA)
C.I. versus bolus treatment in inhibitor patients
M. Morfini (ITA)
EUREKA project
N. Goddard (UK)

18:30 Opening ceremonies
K. Mulder (CAN) WFH
Paul Giangrande (UK) WFH
P.M. Mannucci (ITA)
R. Facchini (ITA)
G. Torri (ITA)
08:00–08:20  Session 1-1
The history of the MSK Committee
Chairman: Brenda Buzzard (UK)

The history of MSK
M. Gilbert (USA)

08:20–9:10  Session 1-2
Synovitis
Chairman: F. Fernández-Palazzi (VEN)

08:20  Medical management of synovitis
P. Giangrande (UK) WFH

08:30  Physiotherapy treatment: guidelines
N. Zourikian (CAN)

08:40  Surgical treatment: guidelines
A. Linhas (COL)

08:50  Discussion panel:
08:50  M. El-Ekiaby (EGY)
08:55  G. Tagariello (ITA)
09:00–09:10  voting

09:10–10:00  Session 1-3
Cartilage and bone defects
Chairman: H. Caviglia (ARG)

09:10  Cartilage damage: state of the art
V. Mascolo (ITA)

09:20  Bone defect
M. Silva (USA)

09:30  Discussion panel
09:30  M. Gilbert (USA)
09:35  T. Sohail (PAK)
09:40  A. Abatangelo (ITA)
09:45  G. Roosendaal (NED)
09:50–10:00  voting

10:00–10:20  Coffee break

10:20–11:05  Session 1-4
Total knee replacement
Chairman: F. Benazzo (ITA)

10:20  TKR in PWH: state of the art
G. Pasta (ITA)

10:35  Discussion panel
10:35  M. Innocenti (ITA)
10:40  N. Goddard (UK)
10:45  A. Forsyth (USA)
10:50  J. Wiedel USA
10:55–11:05  discussion
11:05–12:30 Session 1-5
Free papers I
Chairman: C. Rodriguez-Merchan (SPA)

11:05 Long-term results of primary total knee replacement (TKR) in patients with hemophilia
GL Pasta

11:15 Treatment algorithms for target joints and chronic synovitis in children with hemophilia: Izmir experience
K Kavakli

11:25 Early- to mid-term results of total knee arthroplasty in hemophilic knees: a review of 34 cases
O Guyen

11:35 Physical fitness, functional ability in children and adolescents with hemophilia: a cross-sectional study
JJ Van Der Net

11:45 Protective abilities of interleukin-10 in blood-induced cartilage damage
N Jansen

11:55 Adeno-Asssociated Virus (AAV) mediated intra-articular expression of clotting factor IX protects from hemophilic arthropathy
PE Monahan

12:05 Water rehabilitation after knee replacement in hemophilic arthropathy: short-term and long-term effects
W Passeri

12:15 Orthopedic Evaluation of Children with Severe A and B Hemophilia Submitted to Primary Prophylaxis at Centro de Tratamento de Coagulopatias do Distrito Federal (CTCDF) in Brasília, Brazil
DP Haje

12:25 Discussion

12:30–13:45 Lunch

13:45–17:00 Concurrent Sessions 1-6

Session 1-6-A
Live surgery
Surgeon: P. Solimeno (ITA)
Moderator: A. Llinás (COL)

Session 1-6-B
Physiotherapy workshop
Chairmen: G. Blamey (CAN) and W. Passeri (ITA)

Topics will include physiotherapy for muscle bleeding, postural analysis, joint assessment, the use of foot orthoses for patients with hemophilia, water rehabilitation and post-operative rehabilitation
17:00–18:00  Session 1-7
Free papers II
Chairman: P. Narayan (IND)

17:00  Degenerated cartilage is as vulnerable to blood-induced cartilage
damage as healthy cartilage is
N. Jansen

17:10  The rehabilitation after surgery in hemophilic arthropathy
W. Passeri

17:20  Consensus protocol for the use of recombinant Factor VIIa
(NovoSeven™) in elective orthopedic surgery in hemophilic patients
with inhibitors
P. Giangrande

17:30  Successful surgical treatment of a hemophilic pseudotumour of the
distal radius and ulna: a case report
S. Shaheen

17:40  Ultrasound diagnosis of acute joint pain may lead to more effective and
efficient use of hemophilia therapy
D. Stephensen

17:50  Local intra-articular factor IX protects hemophilia B mice from bleeding-
induced in the absence of circulating factor IX
P.E. Monahan
08:00–09:30 Session 2-1
Arthropathy of the ankle and the elbow
Chairman: M. Heim (ISR)

08:00 PT approach to the stiff ankle
A. Forsyth (USA)

08:10 From arthroscopic debridement to ankle fusion
G. Pasta (ITA)

08:20 Pan talar arthrodesis: blessing or curse?
M. Heim (ISR)

08:30 Rehabilitation protocol after ankle arthroplasty
B. Buzzard (UK)

08:40 Surgical treatment of stiff elbow
M. Silva (BRA)

08:50 Elbow arthroplasty: surgical indications and technique
L. Celli (ITA)

09:00 Rehabilitation after elbow arthroplasty
G. Blamey (CAN)

09:10–09:30 Discussion

09:30–10:40 Session 2-2
The management of children with hemophilia in the 3rd millennium
Chairman: P. Giangrande (UK) WFH

“North of the border” = countries who can afford factor concentrate and/or who use factor for prophylaxis
“South of the border” = countries who do not have easy access to factor

09:30 The hematologist’s role
North of the border  E. Santagostino (ITA)
South of the border  M. El Ekiaby (EGY)

09:50 The physical therapist’s role
North of the border  D. Stephensen (UK)
South of the border  P. Narayan (IND)

10:10 The surgeon’s role
North of the border  R. Facchini (ITA)
South of the border  F. Fernández-Palazzi (VEN)

10:30 Discussion

10:40–11:00 Coffee break

11:00–12:00 Session 2-3
Anesthesia and pain management
Chairman: J. Wiedel (USA)

11:00 Which kind of anesthesia in PWH?
D. Subacchi (ITA)

11:10 Client satisfaction following THA or TKA
A. Buzzi, I. Moravero (ITA)

11:30 Discussion
Saturday, May 5, 2007
Congress Day 2

12:00–13:30  Lunch

13:30–14:30  Session 2-4  
**Current topics in rehabilitation**  
Chairman: L. Heijnen (NED)

13:30  **Global postural approach to PWH**  
*E. Boccalandro (ITA)*

13:45  **Back pain in hemophilic patients**  
*A. Seuser (GER)*

14:00  **Immobilization: use and abuse**  
*B. Buzzard (UK)*

14:15  Discussion and voting

14:30–16:00  Session 2-5  
**Muscle bleeds**  
Chairman: K. Beeton (UK)

14:30  **Early identification and management**  
*N. Zourikian (CAN)*

14:45  **Psoas bleeds: pitfalls in management**  
*P. de Kleijn (NED)*

15:00  **Nerve compression and management**  
*M. Heim (ISR)*

15:15  **Heterotopic ossifications**  
*S.J. Mortazavi (IRAN)*

15:30  **Pseudotumours**  
*H. Caviglia (ARG)*

15:45  Discussion and voting

16:30-  Dinner off site
08:00–09:10  **Session 3-1**  
**Free papers III**  
Chairman: G. Torri (ITA)  
08:00  **Experience of surgical treatment of hemophilia patients with inhibitor**  
V. Zorenko  
08:10  **Ultrasound prognostic signs of hemophilic arthropathy**  
G. Pasta  
08:20  **Autologous cultured chondrocyte implantation in hemophilic arthropathy**  
V. Mascolo  
08:30  **Predicting parameters for fitness in children with hemophilia**  
A. Seuser  
08:40  **Total knee arthroplasty in hemophilic arthropathy: long term follow-up**  
C. Ruosi  
08:50  **Spectrum of bleeding in hemophiliacs presenting at Haemophilia Treatment Center, Pakistan Institute of Medical Sciences(PIMS), Islamabad over a one-year period**  
T. Zafar  
09:00  Discussion  

09:10–10:20  **Session 3-2**  
**Free papers IV**  
Chairman: T. Sohail (PAK)  
09:10  **Static posturographic analysis in hemophilic patients: a case report**  
F. Querol  
09:20  **Synoviorthesis with Yttrium 90 in the hemophilic synovitis: 24 months of follow-up in 53 joints and 177 patients submitted**  
S. Thomas  
09:30  **Long-term results of total knee replacement in hemophilic patients: 19-year single-institution experience**  
G. Tagariello  
09:40  **Musculoskeletal assessment: the joint and beyond...**  
F. Van Genderen  
09:50  **Blood-sparing surgery: the use of hemostatic sealant**  
L. Solimeno  
10:00  Discussion
10:20–11:30  **Session 3-3**  
**Free papers V**  
Chairman: P. de Kleijn (NED)

10:20  **Total ankle replacement for end-stage arthropathy in hemophiliacs: report of two cases**  
G. Tagariello

10:30  **Clinical, radiologic and magnetic resonance findings following 32P synoviorthesis in hemophilia**  
S.M. Mortazavi

10:40  **Musculoskeletal status of the Canadian Hemophilia Prophylaxis Study cohort after 10 years**  
P. Hilliard

10:50  **Primary knee arthroplasty using recombinant factor VIIa (rFVIIa) as first-line therapy in hemophilia patients with high responding inhibitors**  
A. Kurth

11:00  **Assessment of physical performance in adult hemophilia patients: development of a subjective measure (HEP-TEST-Q)**  
S. von Mackensen

11:10  **Hemophilic Intraosseous Pseudotumour of the talus in children**  
H. Pergantou

11:20  Discussion

11:30–13:00  **Annual General Meeting of Musculoskeletal Committee of World Federation of Hemophilia**
Deep infections after TKR: diagnosis and treatment
Chairman: J. Wiedel

DEEP INFECTION AFTER TKR IN HEMOPHILIC PATIENTS: RISK FACTORS AND TREATMENT

O.S. PERFETTO1, G. PASTA2, C. CASADEI3 AND L. SOLIMENO1
1 Haemophilic Arthropathy Treatment Center “Maria Gatti Randi,” CTO, Milan; 2 Traumatology Department and Angelo Bianchi Bonomi Hemophilia Center, IRCCS Maggiore Hospital Foundation; 3 Department of Orthopaedics, CTO, Milan, Italy

Aim of this study is to evaluate risk factors for infection after TKR in hemophiliacs and to describe the relationship with the outcome. We reviewed retrospectively 100 consecutive total knee replacements performed on 87 patients at our institution from 1994 to 2005. The mean age at the time of surgery was 38.5 y, 81 pts had hemophilia A, 5 had hemophilia B and 1 patient had a FVII deficiency; 6 patients had an inhibitor against factor VIII and 27 pts were HIV positive. The CD4 counts were determined for all HIV+ pts. Eight knees in 8 patients had a deep infection after surgery; 3 patients had early post-op infections and 5 late chronic. The mean follow-up of infected arthroplasty was 7.11 y (range: 4.4 to 11.6).

PREVENTION, DIAGNOSIS AND TREATMENT OF INFECTED TOTAL KNEE ARTHROPLASTIES

E. MEANI AND O.S. PERFETTO
Department for Osteoarticular Infection Surgery, G. Pini Institute, Milan, Italy

The purpose of this symposium is to focus on the recent trends in prevention, diagnosis and treatment of total knee arthroplasty infections. Deep infection after knee arthroplasty can present a diagnostic challenge. No pre-operative tests are consistently 100% sensitive and specific. Different options for antibiotic prophylaxis and treatment of the infection were analyzed. The authors also consider the management of early infection. Focusing on late chronic infections, we compared advantages and disadvantages of one-stage or two-stage surgical revision techniques. In selected cases, knee fusion could be considered.

Peri-operative management in inhibitor patients
Chairman: E. Santagostino

PERI-OPERATIVE MANAGEMENT IN INHIBITOR PATIENTS

C. NEGRIER
Centre Régional de Traitement de l’Hémophilie, laboratoire d’Hémostase, Hopital Edouard Herriot, Place d’Arsonval, 69003 Lyon, France

The development of inhibitory antibodies to factor VIII (FVIII) or IX (FIX) is one of the most serious complications for the management of patients with hemophilia. It is estimated that as many as 20 to 30% of patients with hemophilia A and 3% of patients with hemophilia B develop inhibitory antibodies. Inhibitors represent a particular therapeutic challenge as they induce relative or complete refractoriness to conventional replacement therapy. Different therapeutic options are currently available for treatment and prophylaxis of bleeds during surgical procedures. High doses of FVIII/FIX may achieve hemostasis with a rather predictable manner if the inhibitor titre is below 5 Bethesda units. If this titre is higher or if the clinical response is not obtained with FVIII/FIX or if the anamnestic response to the clotting factor infused is harmful, two types of activated coagulation factors (bypassing agents) can be used, i.e., activated prothrombin complex concentrates (aPCCs) and recombinant activated factor VIIa (rFVIIa).

Data have revealed that both products were able to achieve hemostasis in various clinical situations.
ORTHOPEDIC SURGERY FOR INHIBITOR PATIENTS: A SERIES OF 27 PROCEDURES (26 PATIENTS)

E. C. RODRIGUEZ-MERCHAN1, M. QUINTANA2, V. JIMENEZ-YUSTE2, F. HERNANDEZ-NAVARRO2
1 Department of Orthopaedics and Haemophilia Unit, 2 Department of Haematology and Haemophilia Unit, La Paz University Hospital, Madrid, Spain

We report on a series of 27 orthopedic surgical procedures. It includes 20 radiosynoviortheses and 7 major orthopedic procedures performed on 26 patients. The average age of patients was 36 years (range: 8–53), and the average follow-up time was 2.5 years (range: 1–5). There were 23 good results and 4 fair. In the synovectomy group (20 patients, 20 synoviotheceses), the average age was 13.5 years (range, 9–26) and the average follow-up was 4.5 years (range, 1–7). There were 19 good results and 1 fair. All synoviecstheses were done with aPCCs (FEIBA); all responses were good except in one case (which had the final fair result). The total dose of FEIBA used was 600 IU/kg except in a patient that had a hemorrhagic complication. In fact, he required a prolongation of treatment up to a total dose of 2000 IU/kg.

C.I. VERSUS BOLUS TREATMENT IN INHIBITOR PATIENTS

M. MORFINI1, G. TAGARIELLO2, M. INNOCENTI3, P. RADOSSI2, R. GIVENNI1 E R. SARTORI2
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Seventeen patients with hemophilia A and FVIII inhibitor underwent orthopedic surgery in HC of Florence and Castelfranco Veneto, under treatment with rFVIIa. Twenty surgical procedures were performed: 13 total knee and 4 hip prosthesis, 2 arthrodeis of ankle. In most patients, a single dose (90µg/kg) of pharmacokinetics immediately before surgery was used in order to evaluate the individual clearance of rFVIIa. The mean values of Clearance and Terminal Half Life were 35 ml/h/kg and 2.85 hours, respectively. These kinetic characteristics vary from case to case and short half-life make continuous infusion much more suitable to spare the drug needs than intermittent bolus administration by cutting the very high and unnecessary peaks. Two or three bolus (90–120 µg/kg) of rFVIIa were administered during the first 2–3 hours in the peri-operative period. Soon after the wound closing, continuous infusion (CI) started at 50–30 µg/kg/h. The infusion rate was adjusted in the following days according to the FVII:C level up to 15–10 µg/kg/h. CI was maintained at least for the first 14–18 post-operative days, when intermittent bolus was administered daily before each physiotherapy session. rFVIIa clearance was evaluated daily from FVII:C plasma level. All patients were maintained at a FVII:C level higher than that recommended by S. Schulman (15U/ml). A definitive increase of rFVIIa clearance was observed during surgery but in the following days, the values declined to the pre-surgery ones. In some patients, clearance decreased significantly, allowing the treaters to reduce the infusion rate. In this way, a very large amount of drug was saved. No bleedings or adverse event occurred during surgery and all patients recovered very well in about three weeks. Even though, FVII:C assay cannot be regarded as a specific test for monitoring rFVIIa plasma levels, it was a valid and helpful surrogate test. CI definitively shows some advantages in terms of patient management provided that a central line (CVC) is available. No heparin, but only infusion of saline 20 ml/h, was used to keep the line open. Tranexamic acid was always added at 1g/8 hours for the first three weeks of treatment.

PRIMARY KNEE ARTHROPLASTY USING RECOMBINANT FACTOR VIIa (RFVIIa) AS FIRST-LINE THERAPY IN HEMOPHILIA PATIENTS WITH HIGH RESPONDING INHIBITORS: THE EUREKA STUDY


Haemophilia centres from France, Italy, Spain, Germany, and UK.

Clinical report forms have been developed with a clinical research organization to collect data on primary knee arthroplasties (KA) performed with rFVIIa as first-line therapy. To date, 27 KAs (13 right, 14 left) have been reported in 26 patients (21 severe HA, 3 severe HB, 1 mild HA) with an average age of 37 yr (17–70 yr) from 12 European hemophilia centres. Prior to KA, inhibitor titres were 0–400 BU (median: 5 average age of 37 yr (17–70 yr) from 12 European patients was 36 years (range: 8–53), and the average follow-up time was 2.5 years (range: 1–5). There were 6 good results and 1 fair. Post-operative bleeding complications occurred in 1 of the 7 major orthopedic procedures performed (arterial pseudoaneurym after a total knee arthroplasty). Despite this complication, which had a final fair result, our study has shown that hemophilic patients with high inhibitor titres requiring orthopedic surgery can undergo such procedures with a high expectation of success. In other words, orthopedic surgery is now possible in hemophilia patients with high-titre inhibitors, leading to an improved quality of life for these patients.

In the group of major orthopedic procedures, the average age of the 6 patients was 30.5 years (range: 11–53), and the average follow-up was 2.5 years (range: 1–5). There were 6 good results and 1 fair. Despite this complication, which had a final fair result, our study has shown that hemophilic patients with high inhibitor titres requiring orthopedic surgery can undergo such procedures with a high expectation of success. In other words, orthopedic surgery is now possible in hemophilia patients with high-titre inhibitors, leading to an improved quality of life for these patients.

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Session 1-1: The history of the MSK Committee
Chairman: B. Buzzard

THE HISTORY OF MSK
M. GILBERT

Abstract not submitted

Session 1-2: Synovitis
Chairman: F. Fernández-Palazzi

MEDICAL MANAGEMENT OF HEMOPHILIC SYNOVITIS
P. GIANGRANDE
Oxford Haemophilia Centre and Thrombosis Unit, UK

Primary prophylaxis clearly prevents development of hemophilic arthritis and synovitis. At the other end of the spectrum, surgical, chemical and/or radionuclide synovectomy all have a place in the management of established synovitis. Conservative medical options include injection of steroid or hyaluronic acid into an affected joint. Both treatments can reduce pain for up to a year after treatment although the effect is not sustained. Angiography may identify a “blush” or microaneurysms in associated with frequent bleeding. Selective microcatheterization and embolization with microcoils can stop the bleeding and control associated synovitis (Mauser-Bunschoten EP, Blood 2005). Physiotherapy is important to maintain muscle power and range of movement as well as to prevent the development of contractures. The use of COX-2 inhibitors such as etoricoxib remains controversial. These agents are undoubtedly of great benefit to many hemophilic subjects. Their continued use to control pain when a patient has many joints affected is probably justified in the absence of cardiovascular risk factors, although the lowest dose should be used and the duration of treatment restricted. Looking to the future, it may prove useful to explore the value of monoclonal antibodies such as etanercept, which antagonize the effect of inflammatory cytokines, and which are of great benefit in conditions such as rheumatoid arthritis. Identification of patients at particular risk may also be possible. One study has suggested a strong link between predisposition to hemophilic synovitis and HLA B27 (Ghosh K, Lancet, 2003) with the implication that some patients might benefit from early and intensive prophylaxis.

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PHYSIOTHERAPY TREATMENT GUIDELINES
N. ZOURIKIAN

Abstract not submitted
A person with hemophilia will require treatment for synovitis that is refractory to medical treatment in one of three circumstances: a) synovitis developed while on primary prophylaxis, b) synovitis developed without prophylaxis that did not respond to treatment with secondary prophylaxis or c) synovitis developed in the absence of access to primary or secondary prophylaxis. Invasive treatment of synovitis is staged in three levels of complexity. A) The first step in treatment is to attempt inactivation of the synovium with substances injected percutaneously. There is a strong trend toward agreement that radioisotopes (yttrium, disoproium, rhenium or phosphorus) achieve this goal quicker and more reliably than chemical agents (rifampin or oxytetracycline). Considerations such as regional availability, cost, and complexity of the institution and accessibility of persons with hemophilia to the treatment centre will influence the choice of methodology and therapeutic agent. Up to three applications of radioisotope (three-month intervals) and up to 7 of chemical agents (at weekly intervals) with incremental clinical response are appropriate before considering moving on to the next level of invasiveness. B) Arthroscopic synovectomy is recognized as an effective method of synovial deactivation. While its use as a first line of attack has some advantages, there is general consensus that it is best used as a second level of defence. On rare occasions upon failure of arthroscopy and when confronted with the need to perform posterior releases of the joint or osteotomies to correct flexion deformities one may need to progress to the third level of invasiveness; c) open synovectomy. The success rate of open synovectomy in controlling recurrent bleeding is over 80%. However, open synovectomies have a lengthy post-operative course that require surgical amounts of concentrate for prolonged periods since they are remarkably difficult to rehabilitate. The objectives of treatment are to de-activate the synovium immediately returning the joint to a state where physiotherapy may work toward complete range of motion, muscle strength and joint speed, and prophylaxis are effective in preventing articular bleeds.

Thursday, May 4, 2007, 9:10–10:00

Session 1-3: Cartilage and bone defects
Chairman: H. Caviglia

CARTILAGE DAMAGE: STATE OF THE ART
V. MASCULO
Abstract not submitted

BONE DEFECT
M. SILVA
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About 6 million fractures occur every year in the United States and, of those, about 250,000 will require further treatment for compromised healing or to repair skeletal defects. The availability of osteoinductive signals, an osteogenic cell capable to respond to these signals, an appropriate osteoconductive matrix, and sufficient blood supply are key factors in the process of repairing skeletal defects. Traditional approaches to the repair of bone defects have included the use of autogenous bone grafts, allografts, demineralized bone matrices, and calcium phosphate ceramics. Autogenous bone grafts provide osteogenic cells, inductive signals, and an osteoconductive matrix, but lack vascularity. The ideal bone grafting material is probably one that replicates or improves upon autogenous bone graft, providing osteogenic cells, osteoinductive signals and an osteoconductive matrix, but with an unlimited supply, and without the secondary effects usually associated with the retrieval of autogenous bone grafts. In the search for this ideal grafting material, multiple elements have been used, including growth factors, bone marrow cells, mesenchymal stem cells, genetically modified mesenchymal stem cells, and scaffolds. It is likely that a combination of modalities, an optimization of vectors, growth factors, delivery methods, cell types, and carriers used for the genetic modification of mesenchymal stem cells, and an improvement of vascular supply will be required in the future to obtain rapid tissue regeneration. Further research, including clinical trials, is necessary to determine the safety and efficacy of these newer techniques.
TKR IN HEMOPHILIC PATIENTS: STATE OF THE ART

L.P. SOLIMENO1, O.S. PERFETTO1 AND G.PASTA2
1Hemophilic Arthropathy Treatment Center “M.G. Gatti Randi,” CTO Hospital, Milan; 2Traumatology Department and Angelo Bianchi Bonomi Hemophilia Center, IRCCS Maggiore Hospital Foundation, Milan, Italy

The knee is the most common joint affected in hemophilia. Despite prophylactic treatment that has improved the life style of hemophiliacs over the last years; there are still patients who have a severe degree of joint destruction as a result of repeated articular bleeding episodes. Even though replacement surgery on hemophiliacs started in the 70s, some questions remain cause for concern. We reviewed the literature about surgical indications, peri-operative management, surgical technique and septic complications. The early literature was pessimistic, reporting poor results and in particular, a high incidence of infection. In recent years, significant changes in hematological management, patient selection and surgical devices have led to better results.

NEW BIOMATERIAL IN TOTAL KNEE ARTHROPLASTY FOR HEMOPHILIC ARTHROPATHY

M. INNOCENTI; R. CIVININI R.; M. VILLANO; C. CARULLI
Second Orthopaedic Clinic, University of Florence, Firenze, Italy

Total knee arthroplasty in hemophilic arthropathy is usually performed at a younger age. It is a technically demanding procedure due to bone loss, altered anatomy, soft tissue fibrosis and flexion contracture. Two main strategies are relevant for the long-term success of a total knee arthroplasty in the hemophilic patients: the surgical technique and the tribology of the material. Dedicated approaches, accurate bone resections and ligament balancing are the prerequisite for a good knee cinematic and range of motion. Femoral and tibial modular metal augments are used to fill bone deficiencies and to aid in restoring the joint line. Femoral cams and tibial inserts with various levels of constraint are chosen for managing instability. Fixation was further enhanced by modular stems that are also available with offset option. However, recent advances in the metallurgy have led to the introduction of new materials that offer several advantages over traditional implants. Tribology was enhanced by new material like oxidized zirconium (Oxinium) that had shown in mechanical and clinical testing a decrease in adhesive and abrasive wear compared with CoCrMo, suggesting that its use in younger patients could be beneficial. For fixation, a new porous biomaterial made of tantalum has recently been developed for application in reconstructive orthopedics. The porous architecture of this material (Travecular Metal) has been shown to facilitate growth in bone and a monoblock tibial base plate has been created. When used in younger patients, like the hemophilic population, it allows a greater initial stability and rapid and extensive bone in-growth, without the use of bone cement that could be detrimental for future revisions. We prospectively reviewed the results of 22 modular total knee arthroplasties performed in 20 patients with hemophilia, with new biomaterials. In 18 knees we implanted a Genesis II TKA with an Oxinium femoral component, and in 4 knees a NexGen TKA with a trabecular metal monoblock Tibial Components. The mean age at the time of surgery was 34 years (25–42). At the final follow-up the knee score improved from an average of 27 points to 84 points. The mean knee flexion contracture improved from 18° to 4°. The mean total flexion arc improved from 72° to 94°.

The results of our study confirm that the introduction of new biomaterial may improve the functional results of TKA in hemophilic arthropathy, providing for a better range of motion and lower flexion contracture.
LONG-TERM RESULTS OF PRIMARY TOTAL KNEE REPLACEMENT (TKR) IN PATIENTS WITH HEMOPHILIA

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1 Traumatology Department and 2 Angelo Bianchi Bonomi Hemophilia Center, IRCCS Maggiore Hospital Foundation, Milan; 3 Hemophilic Arthropathy Treatment Center "M.G. Gatti Randi," CTO Hospital, Milan, Italy

Introduction: TKR represent the treatment of hemophilic arthropathy not responding to conservative approaches. Methods: Clinical data on 106 primary TKRs performed at a single centre in 84 patients with hemophilia A or B (7 with inhibitors) were reviewed. Adult hemophiliacs were eligible if they had pain, poor functional range of motion and/or axial deviation. The Hospital for Special Surgery knee-rating scale (HSS), data on knee flexion contracture and range of motion (ROM) were collected before, after surgery and during a long-term follow-up. Results: The median duration of follow-up per implant is 4.7 years (range 0.2–13.2). Four patients died at a median of 6.8 years (range 5.7–9.2) after surgery for causes unrelated to TKR. Thirteen prostheses have been removed after a median of 4.3 years (range 0.7–10.8). The median HSS score were 39 (range 10–72) and 91 (range 60–96) before and at last follow-up visit, respectively. Deep infection occurred in 9 implants (8.5%). Three of 9 patients with TKR infection and 4 of 75 without implant infection had inhibitors (33% versus 5%; p=0.004). Three of 9 patients with TKR infection and 27 of 75 without implant infection had HIV infection (33% versus 36%; p=0.9).

Conclusions: In this series, followed-up for a prolonged period, the presence of inhibitors is associated with a high risk of infectious complications.

Key words: total knee replacement, hemophilia

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TREATMENT ALGORITHMS FOR TARGET JOINTS AND CHRONIC SYNOVITIS IN CHILDREN WITH HEMOPHILIA: IZMIR EXPERIENCE

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Recurrent hemarthroses cause chronic synovitis in hemophilia. If synovitis cannot be controlled, progressive arthropathy ultimately develops. Our aim was to compare the outcome with different regimens as continuation of episodic therapy, secondary prophylaxis (SP) and radioisotope synovectomy (RS) for target joints and chronic synovitis. Since 2000, study group comprised 51 children with severe hemophilia (HA=40, HB=11) and 73 target joints (knee=32, elbow=18, ankle=23). Mean age was 13.5±5.5 years (range: 3–22). Synovitis was diagnosed by clinical findings and MR. With episodic factor replacement, target joints were successfully treated only in 7 patients (10 joints) (13%). The best outcome was in elbows (28%) and worst in knees (3%). All untreated cases (44 patients/63 joints) were directed for SP (20–50 IU per kg; twice-weekly infusions at least 6 months). However, only 28 patients were able to be treated due to social security problems. Others were directed to RS. After the end of SP success rate was 46% (14 patients/19 joints). The best results were in ankles (58%) and were similarly in knees and elbows (37%). Untreatable patients with SP (16 patients and 22 joints) were directed to RS for synovitis and were completed in 20 cases. Success rate was 80% in RS (zero bleeding in 16 cases).

To conclude, for target joints and chronic synovitis, medical treatment was not satisfactory and the best treatment approach was evaluated as radioisotope synovectomy. This procedure is a simple, inexpensive, outpatient procedure and should be the first choice if it is available.

Table 1. Treatment modalities in severe hemophilia with target joint and synovitis

<table>
<thead>
<tr>
<th>Treatment Modalities</th>
<th>Joints (n)</th>
<th>Success rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home Treatment (Regular episodic treatment)</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>Secondary Prophylaxis (twice weekly)</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>Radioisotope Synovectomy</td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Key words: chronic synovitis, target joint, radioisotope synovectomy

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Results: BMI in 75% of children with mild type hemophilia Z- and differences between subgroups were analyzed. Compared to reference groups. Correlations between variables (physical activity diary). Performance level was calculated and PA questionnaires (revCHAQ-38, MAQ and a Bouchard maximal exercise test to volitional exhaustion (AF), three FA VO\textsubscript{2peak} was 0.1. AF in 6% of children showed Z-scores below -2 on VO\textsubscript{2peak}, whereas 30% showed Z-scores below -2 on VO\textsubscript{2peak/kg}. AF was more impaired in mild hemophilia. Obese participants had lower VO\textsubscript{2peak/kg} compared to the normal population. FA was normal, revCHAQ-38; median 0 (IQR 0-1). Patients with higher PA-scores on MAQ and the Bouchard questionnaire requiring a re-operation (one case). Mid-term results showed an improvement of the IKS score (mean increment of 80 points) and a dramatic relief of pain. Regarding the knee mobility, pre-operative flexion contracture significantly improved while improvement of the flexion remained limited (mean increment of flexion of 8 degrees).

Conclusion: The main advantage to be gained from TKA in hemophilic arthropathy appears to be relief of pain. The restoration of joint movement appears to be of secondary consequence and variable in its achievement. The functional gain outweighs any loss of mobility.

Because of the increased potential for intra and post-operative complications, knee replacement in hemophilic arthropathy should be performed only in properly equipped and experienced centres.

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PHYSICAL FITNESS, FUNCTIONAL ABILITY IN CHILDREN AND ADOLESCENTS WITH HEMOPHILIA: A CROSS-SECTIONAL STUDY

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Objective: Current Dutch prophylaxis regimes allow children to be physical active. The aim of this study was to investigate the level of aerobic fitness (AF), muscle strength (MS), functional ability (FA) and amount of physical activities (PA) of a Dutch hemophilia population between 8 and 18 years characterized by type, severity and joint health (HJHS).

Methods: Forty-seven boys, on prophylactic treatment, participated in this study. Measurements: body mass index (BMI), Joint Health (HJHS), handheld-myometry (MS), maximal exercise test to volitional exhaustion (AF), three FA and PA questionnaires (revCHAQ-38, MAQ and a Bouchard physical activity diary). Performance level was calculated compared to reference groups. Correlations between variables and differences between subgroups were analyzed.

Results: BMI in 75% of children with mild type hemophilia Z-score was > 2. HJHS median score: 0 (IQR: 0-1.7). Obese participants had slightly worse HJHS. The mean Z-score of MS was 0.1. AF in 6% of children showed Z-scores below -2 on VO\textsubscript{2peak}, whereas 30% showed Z-scores below -2 on VO\textsubscript{2peak/kg}. AF was more impaired in mild hemophilia. Obese participants had lower VO\textsubscript{2peak/kg} compared to the normal population. FA was normal, revCHAQ-38; median 0 (IQR 0-1). Patients with higher PA-scores on MAQ and the Bouchard questionnaire had a better AF (Rp: 0.5). Children with higher MS had better AF (Rp: 0.57).

Conclusion: Overall MS, AF, FA, PA level and joint health of the participants in this study were comparable with healthy peers. Obesity was positively correlated with mild hemophilia and parameters of poorer health.

Key words: Physical fitness, hemophilia

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PROTECTIVE ABILITIES OF INTERLEUKIN-10 IN BLOOD-INDUCED CARTILAGE DAMAGE

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Background: One of the major problems in hemophilia is the arthropathy induced by joint bleeds. In search of possible interventions to prevent or limit the deleterious effects of joint bleeds, we tested interleukin-10 (IL-10) as an inflammation-controlling cytokine on blood-induced cartilage damage.

Methods: Healthy human articular cartilage tissue explants were cultured in the presence of 50% blood for 4 days, followed by a recovery period of 12 days. IL-10 was added in 0.1, 1 or 10 ng/ml. The effect on cartilage matrix proteoglycan synthesis rate, release, and content were determined.

Results: IL-10 was able to prevent the decrease in proteoglycan synthesis and increase in proteoglycan release of cartilage exposed to blood dose dependently. As a consequence, the decrease in proteoglycan content after blood exposure could be prevented dose dependently, with 10 ng/ml IL-10, which is still a low dose for local therapeutic treatment, at least 50% reduction in adverse effects was observed. Conclusions: The present results show that interleukin-10 prevents the direct harmful effects of blood on articular cartilage. This effect of IL-10, in addition to its anti-inflammatory properties, may add to prevention of irreversible degenerative joint damage as a consequence of joint hemorrhages. Future treatment studies in addition to this prevention study are needed to further investigate the role of IL-10 in treatment of blood-induced arthropathy.

Key words: arthropathy, interleukin-10

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ADENO-ASSOCIATED VIRUS (AAV) MEDIATED INTRA-ARTICULAR EXPRESSION OF CLOTTING FACTOR IX PROTECTS FROM HEMOPHILIC ARTHROPATHY

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1Gene Therapy Centre, University of North Carolina at Chapel Hill, Chapel Hill, NC, 2 Rush University Medical Center, Chicago, IL, USA

Objective: Maintaining adequate circulating plasma factor IX activity to prevent hemophilic arthropathy (HA) is challenging and costly using factor replacement, and has not been achieved with systemic gene therapy. We investigated potential protection by expressing genes directly in the hemophilic joint.

Methods: Serotype AAV1, AAV2, AAV5, AAV8 and chimeric AAV2.5 vectors were used to transduce joint tissues in vitro, or to transduce mouse joints in vivo via direct injection to the knee of vectors expressing firefly luciferase. Luciferase expression was quantified in vivo using serial Xenogen CCD bioluminescence imaging. Under hemostatic coverage with I.V. factor IX concentrate, factor IX knockout (FIXKO) mice were injected in the left knee with either lower dose AAV2 or AAV5 (2.5 x 108 vg), or with higher dose AAV1, AAV2, AAV5, AAV8 (1 x 109 vg); right knee injected with normal saline was control. After 4 weeks, bilateral knee bleed was induced by needle puncture, with joint tissues collected two weeks subsequently and scored with an established mouse hemarthropathy histopathology scale.

Results: Cell culture and bioluminescence imaging established that AAV serotypes differed in patterns of transduction of cell types within and outside the joint, with greater than 100-fold differences in levels of expression. 100% of control knees demonstrated subacute joint damage. Most joints receiving the higher dose of AAV2 or AAV5 were completely protected, with efficacy in all AAV groups.

Conclusion: Intra-articular hemostasis and joint-directed gene therapy may ameliorate the events that lead to hemophilic joint destruction.

Key words: Gene therapy, synovitis

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ORTHOPEDIC EVALUATION OF CHILDREN WITH SEVERE A AND B HEMOPHILIA SUBMITTED TO PRIMARY PROPHYLAXIS AT CENTRO DE TRATAMENTO DE COAGULOPATIAS DO DISTRITO FEDERAL (CTCDF) IN BRASÍLIA, BRAZIL

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Objective: The main objective of this study was to check the results of orthopedic evaluation in severe hemophiliacs submitted to primary prophylaxis (PP), as performed by a multidisciplinary team at CTCDF. We also aimed to show the pitfalls found when performing PP and managing the patients who took this prophylaxis in a developing country.

Methods: A number of 19 hemophiliac patients were prospectively evaluated; inclusion criteria for PP initiation included having severe hemophilia A or B; the absence of more than one joint bleeding, regardless of age; and fulfillment of family pre-established social and psychological criteria. PP was performed using a dose of 20 to 40 IU/kg of factor VIII or factor IX, three or two times a week, respectively. Patients were followed by a multidisciplinary team, with orthopedic and radiological evaluation, as documented according to recommendations from the Orthopedic Advisory Committee of the WFH, when the following were evaluated: pain, bleeding, physical examination and radiological examination (Pettersson’s Joint Score). Magnetic resonance imaging was suggested for bleeding joints. PP regularity was checked. Results: When PP was done with regularity the results were better (Table 1). The relevance and applicability to hemophilia care: Preliminary PP results point to effectiveness in prevention of joint bleeding. Socioeconomic factor difficulties did not preclude the performance of PP due to the effort of a Brazilian multidisciplinary team. The originality of the work: This was the first study of this kind in Brazil, approved by National Review Board of Ethics and Research.

Table 1. Hemophiliacs submitted to PP: Type of hemophilia; age at first and last consultation; age at PP initiation; time of interruption (mos); PP total length; PP regularity; pain (0-3), bleeding (0-1), physical examination (0-12); PETT (0-78); changes at last physical examination.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Type</th>
<th>Age at 1st and last consultation (mos)</th>
<th>Age at PP initiation (mos)</th>
<th>Time of interruption (mos)</th>
<th>PP total length</th>
<th>PP regularity</th>
<th>Pain (0-3)</th>
<th>Bleeding (0-1)</th>
<th>Physical examination (0-12)</th>
<th>PETTerson’s score/SRI (0-78)</th>
<th>Changes at last physical examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVS</td>
<td>PWH</td>
<td>11 / 116</td>
<td>60</td>
<td>96</td>
<td>Regular</td>
<td>0,1,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>MDF</td>
<td>A</td>
<td>6 / 78</td>
<td>48</td>
<td>Regular when performed</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Right elbow with deficit of 17° flexion and 10° of extension</td>
</tr>
<tr>
<td>ALSV</td>
<td>A</td>
<td>9 / 47</td>
<td>23</td>
<td>Regular</td>
<td>0,1,0</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Last ankle with 10° dorsiflexion deficit</td>
</tr>
<tr>
<td>ECR</td>
<td>A</td>
<td>6 / 108</td>
<td>84</td>
<td>Irregular twice a week for the first month, regular thereafter</td>
<td>1,2,4</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>0</td>
<td>Knee flexion deficit</td>
</tr>
<tr>
<td>PECS</td>
<td>A</td>
<td>4 / 48</td>
<td>28</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Right knee with 10° dorsiflexion deficit</td>
</tr>
<tr>
<td>VIAD</td>
<td>A</td>
<td>18 / 190</td>
<td>76</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>PARM</td>
<td>MGL</td>
<td>5 / 29</td>
<td>23</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Right ankle with 10° dorsiflexion deficit</td>
</tr>
<tr>
<td>MGL</td>
<td>A</td>
<td>5 / 62</td>
<td>49</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>GCF</td>
<td>B</td>
<td>2 / 22</td>
<td>20</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>CEVC</td>
<td>A</td>
<td>8 / 70</td>
<td>12</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Foot deformity of 2°</td>
</tr>
<tr>
<td>GIMS</td>
<td>A</td>
<td>0 / 73</td>
<td>27</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>CIG</td>
<td>B</td>
<td>7 / 79</td>
<td>28</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>LGVS</td>
<td>A</td>
<td>5 / 66</td>
<td>54</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>BECM</td>
<td>A</td>
<td>3 / 66</td>
<td>42</td>
<td>Irregular twice a week for the first 16 months, regular thereafter</td>
<td>0,1,0</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>0,0,0</td>
<td>5-degree extension deficit of right elbow</td>
</tr>
<tr>
<td>BCRM</td>
<td>A</td>
<td>5 / 105</td>
<td>69</td>
<td>Regular</td>
<td>0,1,0</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>BSM</td>
<td>A</td>
<td>2 / 96</td>
<td>94</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>EBRP</td>
<td>A</td>
<td>12 / 78</td>
<td>16</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>WPL</td>
<td>A</td>
<td>6 / 16</td>
<td>0 (4) interruption on the second month of pp</td>
<td>Regular, when performed</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>DMS</td>
<td>A</td>
<td>13 / 40</td>
<td>24</td>
<td>Irregular twice a week for the first 10 months, regular thereafter</td>
<td>0,0,0</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
<tr>
<td>TOTAL</td>
<td>MEAN</td>
<td>7 / 62</td>
<td>17</td>
<td>Regular</td>
<td>0,0,0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0,0</td>
<td>Slight pain on knee motion</td>
</tr>
</tbody>
</table>

* Not performed yet due to financial constraints of the public health system.
JOINT ASSESSMENT IN INDIA

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In a developing country like India, there is not much awareness about hemophilia. Factor availability is almost nil and so systematic recording and planned management program is important or else it sets a vicious cycle of poor musculoskeletal structure, leading to instability, increased bleeding episodes and further joint and muscle destruction. By using simple low-cost devices and techniques in the rehabilitation, the number of bleeding episodes has reduced and quality of life improved. Parameters monitored: number of bleeding episodes, factor usage and its cost, girth measurements, range of motion, strength, gait analysis and functional improvement. Treatment Protocols: Initially non-weight bearing exercises followed by weight bearing exercises were done along with strength and endurance and stretching programs. Total 29 patients were assessed; involving joints included knee, elbow, hip, ankle and shoulder: 15 patients had knee joint disorder, sub acute stage; 2 patients had elbow joint involvement; 2 patients had hip joint involvement; 4 had ankle bleeds; 2 shoulder bleeds.

<table>
<thead>
<tr>
<th>Joints</th>
<th>Swelling reduced</th>
<th>Range of motion</th>
<th>Strength</th>
<th>Girth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee</td>
<td>7 Patients</td>
<td>14 patients</td>
<td>8 patients</td>
<td>8 patients</td>
</tr>
<tr>
<td>Elbow</td>
<td>6 Patients</td>
<td>Improved</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>Hip</td>
<td>2 Patients</td>
<td>Same</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>Ankle</td>
<td>4 Patients</td>
<td>Improved</td>
<td>Improved</td>
<td>Improved</td>
</tr>
<tr>
<td>Shoulder</td>
<td>Same</td>
<td>Improved</td>
<td>Improved</td>
<td>Same</td>
</tr>
</tbody>
</table>

Conclusion: In 18 months with regular physiotherapy, the tone improved and the number of bleeding episodes reduced from 20 bleeds per year to 3. Range of motion improved the knee and so the gait improved, strength improved considerably from grade 2 to 5 in many knee cases and so functional activities like the staircase and easy toilet activities improved. Girth improved much more in calf then in the thigh. Endurance training also has improved the quality of a patient with hemophilia. There have been advantages of coordinated exercises and treadmill walking.

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A 7-YEAR FOLLOW-UP STUDY: THE USE OF FOOT ORTHOSES FOR PATIENTS WITH HEMOPHILIA

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Specific Aims/Objectives: 1. Re-evaluate the efficacy of using foot orthoses in patients with hemophilia to reduce the number of breakthrough bleeding at the ankle joint; 2. Evaluate the mechanism of the foot orthoses via motion analysis in a patient with hemophilia.

Methods: A retrospective chart review of the Hemophilia Clinic visit progress notes and the Rehabilitation division records over the past 7 years will be conducted. The same criteria will remain in evaluating the control group and treatment group from the original data to the present day. The frequency of bleeding episodes in the ankles, as well as factor usage will be tracked from the original data in 2000 through 2007. A motion analysis study with foot pressure analysis will be conducted. A patient with hemophilia will participate in the gait study with and without the foot orthoses. Kinematics and kinetic data will be collected as well as data from the foot pressure analysis.

Discussion: A long-term study looking at the efficacy of using the foot orthoses in patients with hemophilia to reduce the number of breakthrough bleeding at the ankle joint would only further support our original data. We have proven the foot orthoses to be a significant factor in the short term. We are hypothesizing that the long-term data will be significant as well. The cost-benefit analysis will demonstrate the relevance of the inexpensive foot orthoses in relation to the factor usage with breakthrough bleeding episodes. The use of motion analysis will give objective data when comparing the kinematics and kinetics of a person with hemophilia with and without the foot orthoses. The foot pressure analysis will support our theory that by capturing the calcaneus and aligning it to a neutral position, over pronation during the gait cycle will not occur and therefore breakthrough bleeding at the ankle will be significantly reduced.
WATER REHABILITATION AFTER TOTAL KNEE REPLACEMENT IN HEMOPHILIC ARTHROPATHY: A POSSIBLE REHABILITATION

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1Domus Salutis Rehabilitation Hospital, Brescia; 2CTO Traumatological Hospital, Milan, Italy

Aim of the study: The targets of hemophilia care, given by the WFH, are "to reduce disability, to prolong life, to make easier to get a social and physical well-being, and finally to help every patient to achieve his own potential without damage." Total knee rehabilitation (TKR) produces reduction of pain, improvement of ROM in flexion/extension, and muscular trophism. Aim of this study is to show the importance of water rehabilitation (WR) after TKR to keep good results of joint ROM, of muscular trophism, reduction of pain and hemarthrosis; finally, best quality of life (QoL).

Methods: We treat PWH with standard rehabilitation and WR. The protocol treatment is subdivided in 3 steps: the first in gymnasium, the second in water, the third in and out of water, to keep the best results of physiotherapy.

Furthermore WR is an alternative instrument, if not elective, for effective hemophilic arthropathy rehabilitation because our body is more light in water; WR is soft and don't help bleeding.

Results: from July 2003 until December 2006, we treated 40 patients; everyone was able to walk on their own, with high independency in ADL.

Relevance for hemophilic care: these benefits, produced by standard and WR methods, make us say that WR improves QoL in PWH.

Key words: hemophilia, water rehabilitation

ECHOGRAPHIC EVALUATION OF HEMARTROHESIS IN INHIBITOR HEMOPHILIC PATIENTS TREATED WITH RFVIIA (PRELIMINARY REPORT)

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Universidad de Valencia. Unidad de Coagulopatías, Hospital La Fe, Valencia, Spain

Hemophilic patients with inhibitor usually suffer significant joint damage when assessed from either radiologic or clinic points of view. The rFVIIa is a useful treatment for hemarthrosis, but there are very few cases in which joint recovery is actually re-established. To assess joint healing, echographic evaluation of the hemarthrosis treatment, controlling the evolution of the spillage and the modifications of the synovial membrane. We have selected patients suffering from hemophilia and inhibitors, exhibiting joints with less than three reported hemarthrosis. A basal echography was made. Patients were asked to self-administer an early dose of rFVIIa (90 µg/Kg) in case of injury, not exceeding 3 hours after the damage is actually produced, and were also asked to visit the hospital for echographic diagnosis. The treatment should continue every 2–3 hours until the end of the pain. Once the pain is finished, a new echography should be made, and treatment of a single dose of rFVIIa daily (every 24 h) should continue until the ultrasound image returns to a evident basal status.

New echographic studies will be made performed 6 months and 12 months after this damage episode, including Gilbert’s score and Pettersson’s score. The protocol has started in February 2007, and 4 patients have been included so far. Thirteen joints have been studied and considered normal from an echographic and clinic point of view. Two joints (in two different patients), have suffered damage evolving positively. Six month and 12 month studies still remain undone.

PHYSIOTHERAPY FOR MUSCULAR BLEEDINGS IN HEMOPHILIC PATIENTS

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The muscle hematoma in hemophilia affects 10–20% of all patients. Characteristics of this bleeding are pain, swelling, force reduction, difficulty or incapacity of gait. The aim of this study was to evaluate the rehabilitation effectiveness in hemophilic patients with muscle bleedings controlled by using appropriate factor. We analyzed 14 hemophilic A and B with muscle hemorrhage. Of these, 7 were iliopsoas, 5 quadriceps femoris, and plantar flexor muscles. All without neurovascular function complication compromising the neurovascular function. In initial evaluation, 8 patients had force degree 1 in the affected muscle, 3 patients had force degree 2, and 3 hemophiliacs could support the proper weight of the affected member, which is force degree 3. All the patients were in antalgic position and with incapacity of gait. The rehabilitation program consisted in daily application of ultrasound and aquatic physiotherapy. The medium time of hospital care was 19 days. At the end of the program, all the patients had force degree 5, with normal gait and range of movement. In that way, we could suggest that ultrasound with aquatic physiotherapy could be beneficial in the treatment of muscular bleedings in hemophiliacs treated with coagulation factor.
DEGENERATED CARTILAGE IS AS VULNERABLE TO BLOOD-INDUCED CARTILAGE DAMAGE AS HEALTHY CARTILAGE IS

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Background: Joint bleeds lead in time to severe joint destruction. Research has shown that healthy cartilage is severely damaged upon blood-exposure and that this effect is caused by apoptosis of chondrocytes. Degenerated cartilage, as in osteoarthritis, is characterized by disturbed matrix turnover and has been associated with chondrocyte apoptosis. Therefore, degenerated cartilage might be more susceptible to blood-induced damage than healthy cartilage is.

Methods: Healthy, degenerative, and osteoarthritic human cartilage explants were cultured in the presence of 10% blood for 2 days, followed by a recovery period of 12 days. The effect of blood exposure to cartilage was determined by its effect on matrix synthesis, release, and content, and on the activity of matrix metalloproteinase (MMP).

Results: When healthy cartilage was exposed to blood, this resulted in a direct decrease of the matrix synthesis (-72%), an increase in release of matrix components (+134%) and an increase in MMP activity (+267%). These effects were still present after the recovery period and at that time proteoglycan content of the matrix was decreased (-18%). Degenerated and osteoarthritic cartilage were at least as susceptible to this blood-induced cartilage damage as healthy cartilage was.

Discussion: Although these are in vitro findings, these results suggest that although degenerated cartilage is not explicitly more susceptible to blood-induced cartilage damage, degenerated cartilage is as least as vulnerable to blood-induced damage as healthy cartilage is. Therefore, it is of great importance to prevent joints bleeds in already affected joints and when they do occur, to treat them adequately.

Key words: arthropathy, cartilage

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THE REHABILITATION AFTER SURGERY IN HEMOPHILIC ARTHROPATHY

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Aim of the study: to evaluate rehabilitation effects after surgery in people with hemophilia (PWH) and to propose a clinical tool to record the rehabilitation program.

Methods: 36 PWH (46 different admissions) have been treated from July 2003 to Dec 2006. Joint ROM and pain (VAS, 0-100) were used to determine impairment, FIM for disability assessment. Treatment was recorded through a specific clinical report to allow a stratification of performed activities.

Results: mean age was 45.3±17.8yrs, 2 patients had three admissions and 6 had two. Thirty-nine were for knee replacement (TKR), 6 for hip replacement (THR) and 1 for ankle arthrodesis. 66% were PWH-type A (2 with inhibitor) and the remainder had type B hemophilia or factor V, VII and XI lack. Patients obtained a relevant reduction of disability (+30% in FIM score, Table1); 90% of PWH were able to walk without assistance at the time of discharge (at least 6 points at FIM).

Rehabilitation activities showed in Graphic1. Statistical analysis revealed a sufficient correlation with the initial evaluation (mean Pearson CC of 0.40).

Relevance for Hemophilic care: rehabilitation after surgery was effective in obtaining a high independency in daily life; the proposed clinical report represented a valid clinical tool to depict the rehabilitation activities and to eventually support multicentre studies.

Key words: surgery, rehabilitation, hemophilia
CONSENSUS PROTOCOL FOR THE USE OF RECOMBINANT FACTOR VIIa (NOVOSEVEN™) IN ELECTIVE ORTHOPEDIC SURGERY IN HEMOPHILIC PATIENTS WITH INHIBITORS

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Objective: The objective of this work was to reach a consensus of opinion from a group of experts in hemophilia care with experience of elective orthopedic surgery (EOS) in hemophilic patients with inhibitors, on the optimum management strategy in such patients undergoing EOS with NovoSeven as hemostatic therapy.

Method: A group of hemophilia consultants and one consultant orthopedic surgeon from the UK convened in London on 30 October 2006 to discuss the optimum treatment strategy for the management of hemophilia patients with inhibitors undergoing EOS under hemostatic cover of NovoSeven. The group’s meeting was chaired and facilitated by Professor Jørgen Ingerslev, who has himself extensive documented experience in EOS in this group of patients. The group felt that by sharing its own experiences it could develop a “best practice” approach to the overall management of these patients from the pre-operative planning phase through to hospital discharge.

Results: The Expert Group reached a consensus on the protocol for the management of hemophilic patients with inhibitors undergoing EOS. This protocol encompassed the planning of the surgery and pre-operative tests; the surgery itself (dosing schedule of boluses of NovoSeven, the concomitant use of antifibrinolytics, and the use of fibrin sealant); post-operative dosing of NovoSeven until discharge; and a section on “trouble shooting” in case of bleeding complications.

Conclusions: It is hoped that this consensus protocol will offer guidance to a consultant planning EOS for a hemophilic patient with inhibitors, thereby ensuring the adoption of a consistent approach to managing the course of surgery and ultimately leading to an optimization of care and improved outcome.

Key words: recombinant Factor VIIa (NovoSeven™), Surgery

SUCCESSFUL SURGICAL TREATMENT OF A HEMOPHILIC PSEUDOTUMOUR OF THE DISTAL RADIUS AND ULNA: A CASE REPORT

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This case report was published in the JBJS the American volume in November 2005. J Bone Joint Surg Am. 87:2546 – 2549, 2005

Bleeding into joints and muscles is a known complication of hemophilia. Pseudotumours and cysts are rare, occurring in 1–2% of severe hemophilia patients. It may lead to destruction of muscles, nerves, vessels and bone. From 1856 to 1994, 34 cases were reported. The frequency and severity of hemophilic pseudotumours have decreased with the use of factor VIII replacement therapy. However, they may still occur in developing countries where facilities for diagnosis and treatment of hemophilia are not available.

We report a case of pseudotumour affecting the distal left radius and ulna in a 16-year-old patient. The diagnosis of hemophilia was made at the age of 12 years. He was misdiagnosed as osteosarcoma and had an amputation right below the elbow at the age of 10 years.

He presented with open wound on the volar surface of the left distal forearm (Fig.1). Condition started as a painful forearm swelling that spontaneously opened and drained 10 days prior to presentation. His fingers were contracted and active finger motion was limited. He had features of pressure on the median nerve. X-ray showed erosion of distal radius and ulna with periosteal reaction (Fig.2). Hemophilic pseudotumour was diagnosed. Surgical excision was done under factor VIII (Fig.3). After wound healing, physiotherapy was instituted. He was followed up for two and a half years. Finger’s contractions responded to physiotherapy (Fig.4). Radiology showed full bone recovery (Fig.5). In conclusion: Hemophilic pseudotumours can be successfully and safely treated by surgical resection and factor VIII cover.

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ULTRASOUND DIAGNOSIS OF ACUTE JOINT PAIN MAY LEAD TO MORE EFFECTIVE AND EFFICIENT USE OF HEMOPHILIA THERAPY

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Severe hemophilia is characterized by spontaneous bleeding into joints and muscles and medical intervention involves the use of high-cost clotting factor concentrates, thus, an accurate objective diagnosis of the presence of bleeding is essential. Traditionally a diagnosis of bleeding is suspected using clinical assessment of pain, swelling and stiffness. Symptoms of pain, swelling and stiffness are not limited to hemarthrosis and can be the result of synovitis, inflammation and other musculoskeletal pathology where treatment with clotting factor concentrates may be inappropriate. Ultrasound imaging provides objective information regarding location, state and severity of bleeding and inflammation in joints and muscles. It can be performed quickly and easily in the outpatient clinic and compared to other imaging modalities is relatively inexpensive. This paper reports on 45 patients with spontaneous acute joint pain and stiffness (10 ankles, 21 knees, 14 elbows) and a known diagnosis of hemophilia (36 hemophilia A, 9 hemophilia B) who presented to the Haemophilia Centre between July and December 2004. All patients underwent ultrasound imaging (Sinosite 180 Plus) in the longitudinal and transverse planes. No evidence of bleeding was found in 33.4% of patients; acute intra-articular hemarthrosis was found in 31.1%; acute muscle bleeding was found in 17.8%; bleeding in the subcutaneous tissues was found in 15.6%. Synovitis was diagnosed in 22.2% of patients and 11.2% were diagnosed with musculoskeletal pathology unrelated to hemophilia. These data indicate that a diagnosis of hemarthrosis may not be accurate when based on the symptoms of pain, swelling and stiffness. Ultrasound imaging may enable clinicians to non-invasively evaluate bleeding in this patient group rather than relying on clinical signs and symptoms and may inform clinicians regarding the use and response to high-cost treatment.

Key words: Ultrasound, Hemarthrosis

LOCAL INTRAARTICULAR FACTOR IX PROTECTS HEMOPHILIA B MICE FROM BLEEDING-INDUCED JOINT DETERIORATION IN THE ABSENCE OF CIRCULATING FACTOR IX

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Objective: Improving circulating plasma factor IX level is the mainstay of treatment of hemophilic joint bleeding. The capacity of factor within the joint space to contribute to local hemostasis and protection from joint deterioration is not known.

Methods: A reproducible needle puncture injury of the hind knee joint of factor IX knockout (FIXKO) mice was developed, which results in acute bleeding and histopathologic changes to the injury. Groups of FIXKO mice received unilateral hind knee puncture with a 30 gauge needle and human factor IX (hFIX) doses consistent with hemophilic synovitis in > 90% of injured knees, ranging from the equivalent of 0 IU/kg to 20 IU/kg. Synovitis scores in mice treated with 10 IU/kg were low and better than mice treated with 100 IU/kg I.V. factor IX. Intraarticular treatment at the highest dose (20 U/kg) did not result in detectable circulating factor IX activity in the first two hours after treatment that could account for the hemostatic protection. Two week later, joints were harvested. Joint deterioration was scored with a standardized murine hemophilic synovitis grading system. Results: Intraarticular factor IX contributed in the joint. Comparison groups received the same injury and intravenous hFIX doses ranging from 25 IU/kg to 100 IU/kg. Conclusion: Factor IX in extravascular sites may contribute to significant protection against subacute joint deterioration from coagulation by mechanisms that warrant study. Strategies to take advantage of factor IX local hemostasis may have an adjuvant role in avoiding blood-induced joint destruction.

Key words: factor IX, intraarticular

Figure 1: Histopathology scores from joints graded 14 days after joint puncture injury and factor IX delivered either intravenously (right) or intraarticular dose.
PT APPROACH TO THE STIFF ANKLE: COMPILATION OF US PHYSIOTHERAPISTS’ PERSPECTIVES

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The ankle joint is a common target area for those with hemophilia. To promote the best functional status possible, it is important to recognize stiffness and offer physiotherapy interventions to address this common complication of bleeding disorders. What is the cause of the stiffness? Is the joint stiff due to soft tissue, muscular, or capsular restrictions? Is the joint stiff due to repeated bleeds causing a change in the integrity of the articulating bones? In the US, we are fortunate to have diagnostic imaging, such as radiography, CT and MRI, available to help with this differentiation. These tools may be used to detect early arthritic changes that may interfere with joint articulation and biomechanics, giving us information on the prognosis expected with joint range of movement. However, these scans are not used as a standard, so physiotherapists must rely on their clinical examination and evaluation skills. If the joint is stiff due to restrictions in the soft tissue structures, and the integrity of the bones of the ankle joint are not involved or minimally affected, we can expect an improvement of range of movement with applied therapy techniques. These interventions could include manual physiotherapy techniques, stretching and home exercises, dynamic splinting or serial casting. If the joint is stiff due to restrictions in the bony structures, depending on the severity and location affected, we can expect that range of movement with applied therapy techniques will have little or no improvement. Physiotherapy interventions could include manual techniques, stretching and home exercises to maintain soft tissue flexibility, or supportive splinting, orthotics, and bracing to support the degenerating joint. Physiotherapy treatments can be designed to gain and maintain range of movement or accommodate and support a severely damaged joint.

FROM ARTHROSCOPIC DEBRIDEMENT TO ANKLE ARTHRODESIS

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Introduction: Although the ankle arthropathy remains a frequent source of disability in hemophilic patients, its treatment is still controversial. Methods: Clinical and radiological data on 27 ankle arthroscopic procedures and 6 ankle arthrodeses performed at a single centre in 26 and in 6 patients with hemophilia A and B (1 with inhibitor) respectively, were reviewed. Hemophiliacs were eligible if they had recurrent bleedings, pain, and poor functional range of motion and radiological signs of arthropathy. Functional (Gamble) and radiological (Pettersson) scoring systems were used before and after surgery and during long-term follow-up. Results: The median duration of follow-up for the arthroscopic procedures was 49 months and we assessed a median functional score of 34 (range 14–71) and 82 (range 34–100) before and at last follow-up visit, respectively. The 86% of patients with a pre-operative Pettersson score >5 had a post-operative functional score <60. The median duration of follow-up for the 6 ankles that underwent arthrodesis was 22.5 months and we attained fusion in all cases without any complication. Conclusions: In this series, arthrodesis is a suitable surgical option in hemophilic patients with advanced stages of ankle arthropathy. Key words: ankle arthropathy, arthroscopy, arthrodesis, hemophilia

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PAN TALAR ARTHRODESIS: BLESSING OR CURSE?

M. HEIM

Abstract not submitted
PHYSIOTHERAPY FOLLOWING TOTAL ANKLE REPLACEMENT (TAR)
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Hemorrhage into the ankle joint in people with hemophilia accounts for 14.5% of all bleeding episodes. Repeated bleeding, into the joint, leads to gradual deterioration of joint function, increased pain, loss of movement and reduction in quality of life. Conservative methods of treatment are advocated initially such as regular prophylaxis, short-term orthotics, exercise programs and in some circumstances a change of lifestyle is recommended. When these options fail, other, more invasive procedures may be undertaken, i.e., synoviothrosis, cheillectomy or joint debridement. Most of these interventions have limited benefits and to date, ankle and subtalar joint arthodesis have been most effective for those with end-stage hemophilic arthropathy. Total ankle replacement (TAR) in people with hemophilia is rare, the literature reveals very little evidence of its benefit, and even in the non-hemophilic population the success rate of TAR is questionable. However, TAR prostheses have been developed and are now evolving as a potentially viable option for the management of end-stage arthropathy. Within our Trust our foot and ankle specialist consultant has performed a number of TARs using the mobility total ankle system. As there was no previous rehabilitation protocol for this procedure we are currently trialing two post-operative rehabilitation programs, Immobilization in POP, and no immobilization in plaster. The results will be presented at the Musculoskeletal Congress.

SURGICAL TREATMENT OF STIFF ELBOW
M. SILVA

Abstract not submitted

ELBOW ARTHROPLASTY: SURGICAL INDICATIONS AND TECHNIQUE
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Over the past decade the indication for total elbow arthroplasty performed for the treatment of post-traumatic, degenerative and inflammatory arthritis, as well as for selected intra-articular fractures of the distal humerus in the elderly population, has increased markedly in subsequent years, we can therefore expect an increase in the number of complications. The complications following total elbow arthroplasty can be divided into three different groups, according to their management: complications requiring revision surgery, those requiring additional surgery but not replacement of the components, and those that increase morbidity but do not require additional surgery. The outcomes of total elbow arthroplasty are correlated to the primary indications, to the surgical technique used, to implant design and to the daily living activities performed by the patients with the replaced elbow. The aims of our oral presentation will be to describe the design evolution of the elbow prosthesis, the surgical techniques and the outcomes that can be expected from this procedure.

PHYSIOTHERAPY POST TOTAL ELBOW ARTHROPLASTY
G. BLAMEY

This presentation will address the role of physiotherapy during both the pre- and post-operative phases of this surgical procedure. Emphasis will be placed on the necessity to prepare remote joints for the increased physical burden after joint replacement, as well as on techniques and exercise progressions to restore elbow joint motion and function. The important role that the elbow plays in overall function and quality of life will be discussed.
To ensure a high quality of care, children with hemophilia should undergo a regular and frequent follow-up program allowing musculoskeletal assessment, inhibitor detection and treatment monitoring. For boys with severe hemophilia and no evidence of inhibitors, arthropathy development can be effectively prevented by the early initiation of a long-term prophylaxis program. In order to achieve a normal musculoskeletal status for age, prophylaxis should be started before the onset of joint damage (primary prophylaxis). The gold standard primary prophylaxis regimen was pioneered and tested in Sweden and involves the infusion of 20–40 U/Kg of factor VIII at least thrice weekly or 20–40 IU/kg of factor IX twice weekly. This protocol is, however, demanding on peripheral veins and very expensive. Modified prophylactic regimens involving early start with once weekly infusions via peripheral veins followed by rapid escalation to full-dose prophylaxis or dose escalation based on bleeding frequency have been recently implemented. These individualized approaches decrease the need for central venous access devices that carry the risk of infection and thrombosis. A further advantage of tailored prophylaxis is that it permits an effective outcome at reduced cost. Inhibitor development occurs in 28–30% of children with severe hemophilia A and it represents the major obstacle to arthropathy prevention strategies. Immune tolerance induction (ITI) is a highly demanding and expensive treatment; however, it is the only approach able to eradicate inhibitors. ITI should be offered to patients with high-responding inhibitors within 1–2 years from diagnosis. Concomitant treatment with bypassing agents is often required in these children to control bleeding episodes limiting the development of joint damage.

Shabrawishi HTC, Cairo, Egypt

The main sites for bleeding in hemophiliacs are the joints and muscles. Repeated untreated bleeds in these sites will eventually lead to variable degrees of morbidity, disability and probably fatal outcome. During the last two decades several developments have contributed to a remarkable improvement in the management of patients with hemophilia in the developed world. These developments included virus inactivation of human derived clotting factor concentrates; recombinant clotting factor concentrates, which both dramatically improved the safety of these treatment products and paved the way for the introduction of primary prophylaxis therapy into the previously untransfused hemophilia children. These developments have proved very effective in offering an almost normal life to those hemophiliacs with very good integration in society. On the other hand these products as well as the primary prophylaxis program are too expensive to be adopted by developing countries. Consequently, musculoskeletal complications, transfusion transmitted infection, which is now history in the developed world, are still the reality among hemophiliacs in the developing world. The hematologist south of the border is still prescribing anti-hemophilic agents upon demand, striving to implement home-treatment protocols to decrease the musculoskeletal complications of the bleeds. Unsafe blood products like cryoprecipitate and FFP are still used, which results in a high prevalence of transfusion-transmitted infections among these patients. Coordination with orthopedists and physiotherapists to treat these complications and apply different protocols like chemical or radioactive synovectomy, surgical correction of joint and muscle deformity are among the main tasks of the hematologist south of the border.
NORTH OF THE BORDER: THE PHYSIOTHERAPIST’S ROLE

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Prophylaxis has significantly reduced the number of bleeding episodes experienced by children with hemophilia, changing their lifestyle and long-term outcome. Fewer joint bleeds per year, improved clinical scores, improved radiological scores, less pain and improved quality of life have been reported. It had been assumed that prophylaxis with clotting factor concentrates during childhood would result in the development of normal joints and muscles, eliminating the disabling joint damage and muscle weakness so characteristic of hemophilia. However, physical function and general health in patients receiving prophylaxis is still significantly lower than normative values.

Sub-clinical bleeding leading to joint damage has been observed in children on prophylaxis and there appears to be only modest correlation between bleeding frequency and MRI outcomes. Furthermore, abnormal gait patterns have been observed in children with hemophilia despite a regime of prophylaxis. Therefore it is clear that in some children with hemophilia the potential for chronic joint damage remains, despite prophylaxis. Further understanding of the underlying physiological and biomechanical mechanisms of joint damage is required. In addition, knowledge of the impact of physiotherapy on these mechanisms is essential. Are activity levels inappropriate? What is the most effective and optimum rest and rehabilitation program required following a joint haemarthrosis? What is the influence of pre-existing biomechanical abnormalities on bleeding frequency and sub-clinical bleeding? These are just some of the challenging questions facing physiotherapists who have been involved in hemophilia care in the 3rd millennium.


THE PHYSICAL THERAPIST’S ROLE (SOUTH OF THE BORDER)

P. NARAYAN

This year, 2007, the focus of the World Hemophilia Day is to be physical therapy and exercise. In developing countries, treatment of hemophilia is still largely oriented around factor therapy; there being a great deal of skepticism about exercise and its role in the treatment of affected joints. In the past, similar attitudes to exercise prevailed in the industrialized countries out of fear that exercise could induce or increase the risk of hemarthroses. (Broderick et al, 2006). Ironically where factors are scarce, exercise may be the only practical solution available to help reduce the incidence of repetitive musculoskeletal bleeds. In such situations, these negative attitudes make it more difficult to treat the child with hemophilia. Substantial efforts are required to sensitize children with hemophilia and their families to the benefits of exercise. The physical therapist’s role is therefore a very important one particularly in the developing country scenario. The role of the physical therapist may involve being an educator, an agent of change (treater) and a counsellor for PWHs and their family. There is some evidence in literature supporting the idea that appropriate exercise and physical activity early in life can reduce the tendency to develop target joints. This is probably because appropriate exercise therapy can help developing bodies calibrate themselves thereby enabling them to effectively face environmental challenges to their system without injury. This presentation will discuss the various roles of the physical therapist in the developing country scenario with clinical examples as appropriate. Strategies on how to develop tailor-made exercise programs with limited or no factor cover will also be discussed as part of this presentation.

THE ORTHOPEDIC SURGEON IN DEVELOPED COUNTRIES

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Hemarthrosis and the consequential musculoskeletal complications are the most common and most disabling manifestations of hemophilia. The availability of intensive treatment with factor concentrate from early childhood has dramatically improved the clinical history for patients with hemophilia in developed countries. Today, prophylaxis can prevent hemophilic arthropathy or postpone it until later in life. The orthopedic surgeon’s role in hemophilic patients’ management is still to prevent deformities related to hemophilia but more frequently to treat musculoskeletal diseases (i.e., Perthes osteochondritis, flat foot, scoliosis and sports traumatology) as in normal population patients.

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THE SURGEON: SOUTH OF THE BORDER
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Is the treatment of children with hemophilia different in developing countries than in developed countries? Definitely, the answer to this question is YES. The professional knowledge and formation of the pediatric orthopedic surgeon, is similar in developing and developed countries, but the practice of orthopedics in hemophilia differs greatly between the two. Many special circumstances in developing countries compel the surgeon to improvise techniques to apply and use non-conventional implants to solve these fractures. We must realize that 33% of the world population lives in underdeveloped countries. Apart from the economic situation, which is, the most important consideration and that often interferes with the possibility of obtaining equipment or up-to-date materials, surgeons providing care for people with hemophilia in developing countries must be aware of religious, cultural, and social considerations. They must also be aware of hospital structure, idiosyncrasy, and—a very important reality—corruption! This work presents cases of frequently encountered orthopedic problems that require the surgeon to solve them creatively by analyzing causes and consequences. Examples are given of critical situations during surgery that need to be solved, for example, by wrapping non-sterile instruments with sterile gauzes. Or treating fractures without the benefits of X-rays because there were no machines, or being unable to follow the patient post-surgery because of social and economic realities, or working in hospitals with deficient situations due to their infrastructure. Other considerations include the need to use a non-standard tool for a surgical procedure because the hospital does not have the proper one, or the need to use an inappropriate implant because it was the only one available. Sometimes possibilities are limited by religious ideas or considerations. All these situations make the treatment of hemophilic patients in developing countries somewhat unusual and require the surgeon, at times, to use methods that are not completely accepted by all surgeons. Examples of these are given.

WHICH KIND OF ANESTHESIA FOR THE PWH?
D. SUBACCHI

Anesthesia in the PWH is controversial since there are no guidelines to be applied to this problem. In the past only general anesthesia (GA) was applied, since there were no safe techniques in local regional anesthesia (LRA). Now, following the introduction of electro neural stimulators (ENS), the LRA is receiving more consideration in orthopedic anesthesia. As our hospital is one of the most important centres for the treatment of PWH, we've been evaluating these more recent techniques. We have ruled out central block (epidural and spinal anesthesia) since they could cause damage post-operatively and prefer to treat these patients with peripheral nervous system block, to be used both as anesthesia and analgesia. Since 2002 we have treated 175 PWH, 81 of whom were subjected to major operations (knee and hip prosthesis). GA was applied in all cases without any problem. A peripheral block was used on 43% of these patients, as single-shot or continuous, which proved to be a very efficient anesthesia for post-operative care. We also treated 82 patients in minor orthopedic operations (arthroscopy of shoulder, elbow, knee and ankle) and 65% of them received LRA with peripheral nervous system block. Complications were not noticed in any of these cases. In our experience, LRA was applied with success on PWH, without any discrimination between grade or light pathologies. Our opinion is that this technique can be considered a very good alternative to the GA for minor orthopedic operations and can be a perfect solution for post-operative analgesia in major surgery.
POSTURAL ANALYSIS AND GLOBAL FASCIAL TREATMENT IN PATIENT WITH HEMOPHILIC ARTHROPATHY

E. Boccalandro

By using postural analysis it is possible to focus on the mechanical musculoskeletal causes that contribute to hemarthrosis. Global fascial treatment includes osteopathic manual techniques that concentrate on and rebalance two aponeuroses to reinstate fascial elasticity and increase articular mobility. The results include a positive postural analysis, a positive global facial treatment, and useful advice for patients; to follow that will improve their elasticity and functional ability, and help to prevent abnormal strain. The methods are mild and do not impair the patient. We start from the consideration that there is no such a thing as (spontaneous) target-joints, rather, that a musculoskeletal mechanical involvement impairs the system and results in bleeding.

Key words: Posture; fascial system

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BACK PAIN IN HEMOPHILIA

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A literature research for back pain in hemophilia (1990 to 2007), showed only five papers describing three children with factor 9 deficiency, two children with factor 8 deficiency and one elderly patient with factor 8 deficient and lumbar sciatic pain or low back pain. All of them were due to bleeding. Reasons are infraspinal hematomas, hematoma of iliopectineus muscle, retroperitoneal hemorrhage and two epidural hematomas. All symptoms responded to factor replacement. A literature review looking for back pain in a normal population revealed over one hundred findings with hundreds of thousands of patients and the same data throughout the world. We have a lifetime prevalence of back pain of about 80% and about 30% of the subjects reported having back pain in the last week. Thirty per cent of these patients need medical care and can end up in chronic spinal pain, which is physically debilitating and emotionally demoralizing.

Empirical estimates reveal that chronic spinal pain costs society close to $50 billion a year in direct health care costs, disability compensation and lost productivity. In our own pain survey, we discovered that hemophilic patients are silent sufferers. Our data in children shows that as in the non-hemophilic population there are risk factors for low back pain starting in childhood (18% back ache in a Swedish population of school age children).

In literature back pain is associated with the ability of coping. We assume that patients with hemophilia have learned to live with their pain and are focused on the pain in their major joints after bleeds.

There is enough evidence that patients with hemophilia should have the same risk of having back pain as the normal population. Doctors should learn to ask for this and help their patients to establish an even better quality of life.

IMMOBILIZATION: USE AND ABUSE

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For those with hemophilia, acute bleeding into a joint or muscle requires appropriate treatment with replacement blood products (if available), rest and +/- immobilization. Immobilization is a means of preventing movement to allow natural healing to take place. Immobilization with casts, splints or braces is common for fractures but may be used for other injuries or conditions as well. Functional casts or braces allow limited or controlled movement of some joints. Immobilization can also help to reduce pain, a major consideration for those with acute bleeding or even chronic arthritic joints. The treatment of hemophilia and related bleeding disorders has rapidly progressed over the past two decades and the use of immobilization is becoming less common in developed countries. However, in developing nations there is still a need for immobilization of acute bleeding episodes in the absence of clotting factors. Those who have splints, casts or braces on their limbs for any period of time will experience decreased muscle tone and muscle atrophy as a result of non-use of the affected limb. Rehabilitation can restore this muscle imbalance once healing has occurred. Immobility can also cause psychological stress, especially in children. They may become bored, frustrated, irritable and withdrawn from a lack of contact with their peers. Current opinion is that there is a place for immobilization in hemophilia but it should be limited and closely monitored.
EARLY IDENTIFICATION AND MANAGEMENT OF MUSCLE BLEEDS

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Muscle bleeds account for approximately 10–30% of all musculoskeletal bleeds in PWH. Since they occur less frequently than joint bleeds, PWH may be less familiar with the early recognition, treatment and potential complications related to these bleeds. “Muscle bleeds” are often classified as a generic, single entity but they can effectively range from a very mild strain of only a few muscle fibres, to an extensive, deep, intra-compartmental muscle lesion. Muscle bleeds are not necessarily accompanied initially by visually “impressive” signs such as significant swelling or bruising, thereby possibly contributing to a sense of inoffensiveness, as the potential consequences are unknown. Knowledge and early recognition by the PWH of the key initial signs and symptoms of muscle bleeds, such as muscle pain, stiffness, discomfort or weakness, are paramount. Decreased range of motion or an antalgic posture of the involved muscle group may also be present. Appropriate early management involves factor replacement, adequate rest, protection and observation. The treatment team hematologist should be swiftly consulted should extensive pain, movement limitations, neurological signs or swelling appear. Guidance of an experienced hemophilia physiotherapist throughout the management of the muscle bleed can be instrumental to a favourable outcome. Following a thorough evaluation to identify the possible cause(s) of the muscle bleed, the physiotherapist can then help decrease the risk(s) of re-bleeds. Fundamental advice, suggestions and adequate muscle protection are provided throughout the rehabilitation process, which should emphasize a progressive (as opposed to a hastened) return to pre-injury activity levels and function.

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PITFALLS IN THE MANAGEMENT OF PSOAS BLEEDS

P. DE KLEIJN

Psas bleeds occur quite commonly in PWH. They can be very painful and cause immobilization for a longer period. Delay of medical treatment and insufficient functional recovery may lead to a lifelong disability. These topics, observed from the literature, daily practice and personal communication will be discussed:

- Already in 1967, in the British JBJS had an article, “Iliacus haematoma, a common complication in hemophilia.” Where is this “Psas bleed” localized?
- Hematological treatment is described, but does any consensus on rehabilitation exist? In the literature, advice on bed rest and/or hospital stay varies.
- Much is written on femoral nerve palsy, but less on the consequences for the psas muscle itself.
- In the literature the rate of recurrent bleeding is variable.

- Is the use of echography helpful for diagnostic reasons or follow-up purposes?
- During which age span do psas bleeds occur most?
- What causes psas bleeds, are there factors unclear or unspoken?
- Do preventive measures exist?

Recurrent bleeding episodes in the m. iliacus and/or m. iliopsoas can cause severe functional problems and slowly progressing pseudotumours can eventually even lead to death. It seems evident that a more protocollized treatment and follow-up could be of benefit for PWH worldwide. Could it be a task for the musculoskeletal committee to develop this? Could it be a common task for the WFH and MSK to help hemophilia centres to implement this?

CONDITIONS POTENTIALLY AFFECTING THE PERIPHERAL NERVES IN PERSONS WITH HEMOPHILIA

MICHAEL HEIM
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This lecture will consider the etiology, pathogenesis and outcome of hemorrhage and their effect upon the functioning of peripheral nerves. Problems of radiculopathies and neuropathies will be dealt with. Spinal or foraminal bleeds are very rare, while compartment syndromes are common. Local trauma may produce neural damage owing to the extensive expansion of haematomata or local ischemia. The ability to measure compartment pressure becomes an essential requirement. Joint deformities, so frequently found in persons with hemophilia, sometimes produce conditions of nerve traction with resulting paresthesia. Neural tissue is exceedingly sensitive and recovery may be timely and problematic. Sensory and motor functional losses may continue for months post neurolysis and these pathologies may become permanent. Timely intervention is of the essence for “he who hesitates is lost.”
HETEROTOPIC OSSIFICATION IN PATIENTS WITH HEMOPHILIA

S.J. MORTAZAVI

Heterotopic ossification is the formation of mature, lamellar bone in extra-skeletal soft tissues where normally bone does not exist. This pathologic process may occur in sites such as skin, subcutaneous tissue, skeletal muscle, and fibrous tissues adjacent to the joints. Although there is no clearly defined mechanism for its occurrence, the main pathology seems to be an alteration in the normal regulation of skeletogenesis. The formation of bone ranges from clinically no significant coincidental radiographic findings to devastating clinical conditions that dramatically affect quality of life. Contrary to bleeding diathesis seen in patients suffering from hemophilia and a relatively frequent incidence of intramuscular hematomas, heterotopic bone formation has not been reported as a common condition in this group of patients. Few case reports have addressed this entity in English language literature, most of them being instances of heterotopic bone formation around pelvis. The true incidence might be higher.

Some reports indicate that heterotopic bone formation could be present in up to 15 per cent of patients with hemophilia. Persistent symptoms after the acute phase might help to reach the diagnosis using radiological assessment. On the other hand, as most of hemophiliacs’ muscular bleeding is spontaneous and trauma has been known as a crucial part of ectopic bone formation, most of muscular hematomas would not lead to ectopic bone. Similar to non-hemophilia patients, treatment of myositis ossificans is mainly conservative in patients with hemophilia. Surgical excision of heterotopic bone might be indicated if it causes severe limitation of joint motion and functional impairment that does not respond to conservative treatment. However, surgical excision is recommended to be withheld until bone maturation occurs. When all surgical prerequisites for resection of heterotopic ossification are taken into account, the favourable prognosis might be anticipated.

PSEUDOTUMOURS

H. CAVIGLIA

The hemophilic pseudotumour is a truly encapsulated hematoma, which tends to progress and produce clinical symptoms in relation to its anatomic location. Therefore, this is a clinical entity rather than a specific pathological injury. The behaviour of the pseudotumour is different in children than in adults. In children it generally appears at distal bones such as in hands or feet, and responds to replacement treatment with factors VIII or IX. But, in adults, they are usually observed at proximal bones, and do not respond to replacement treatment. Each patient without inhibitor requires a six week replacement treatment, with a 50 to 100UI/kg daily dose of factor VIII or IX.

After six weeks, the pseudotumours must be monitored through nuclear magnetic resonance to determine the extent of its involution. If it is lower than 50%, surgery is necessary, it is higher, replacement therapy must continue for another period of 6 weeks. After these last 6 weeks, a new nuclear magnetic resonance must be performed to re-evaluate the pseudotumour. If it has not involved another 25%, the corresponding surgery must be carried out. However, if is has involved more than 25%, replacement treatment must continue, with a new monitoring after another 6 weeks. If the pseudotumour persists, surgery is indicated.
EXPERIENCE OF SURGICAL TREATMENT OF HEMOPHILIA PATIENTS WITH INHIBITOR

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Introduction: We present 16 years (1990–2006) of experience of surgical treatment of hemophilia patients with inhibitors. Patients and Methods: There were patients with severe hemophilia and inhibitor aged from 6 to 49 years. Sixty-eight per cent of them were patients with high responding inhibitors, usually greater than 10 BU. All of them were HCV (+). During this period, 67 surgical operations were performed on these patients. These included total knee replacements (5), hip replacements (1), extirpation of pseudotumour (10), osteosynthesis (6), synovectomy (16: 13 knee, 3 elbows), oseteotomy (4), ectomy of hematic abscess (3), achillotomy (4), ectomy of iliopsoas hematomas with intra-abdominal bleeding (3) and others. We used different hemostatic treatment: high dozes of cryoprecipitate, high dozes of concentrates FVIII, activated protrombin complex concentrate (FAIBA) and recombinant activated factor VII (rFVIIa-NovoSeven). For patients with a high titre of inhibitor before surgery we carried out plasmapheresis until the titre of inhibitor was reduced to 2 BU or lower. Additional means also use glucocorticoids.

Results: In 8 cases surgery and the post-operative period were accompanied by recidivating bleedings. It has been connected with insufficient hemostatic treatment and the expressed local inflammation. These patients needed repeated surgical interventions. In 75% of cases there were good results (positive functional and anatomic results). Conclusion: Modern hemostatic therapy carried out in a complex with additional methods allows the hemophilia patient with inhibitor to have surgical operations of any complexity. Full rehabilitation of patients is possible.

Key words: hemophilia, inhibitor, surgery

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ULTRASOUND PROGNOSTIC SIGNS OF HEMOPHILIC ARTHROPATHY

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Objectives: The aim of the study was to evaluate the correlation between specific ultrasonographic signs and evolution of hemophilic arthropathy. Materials and methods: fifteen patients with severe hemophilia A were included in the study. Data on general clinical conditions and frequency of hemarthrosis in examined joints were collected. Several ultrasonographic signs were considered: increase of synovial liquid, hemarthrosis, synovial hypertrophy, articular capsule thickening, articular cartilage damage and soft tissue calcification. Results: The median age of the patients was 16 years (range 2–40). In all patients with severe hemophilic arthropathy of the knee a synovial hypertrophy, suprapatellar pouch relaxation with thinning of the patellar ligament and hyperechoic formations in posterior condylar area were detected. Conclusions: The synovial hypertrophy, suprapatellar pouch relaxation with thinning of the patellar ligament and hyperechoic formations in posterior condylar area are present in severe hemophilic arthropathy.

Key words: ultrasound, hemophilic arthropathy

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INTRODUCTION: Hemophilia is a congenital disorder that results in frequent bleeding into joints, in which a chronic and debilitating arthritis develops. The presence of blood evokes an inflammatory and proliferative synovial reaction. Up to now, the molecular mechanisms and biochemical pathways that underlie this disorder were not known. METHOD: In order to better understand and correlate cellular behaviour of hemophilic chondrocytes in view of their use either in tissue engineering or in clinical application, their in vitro behaviour was studied in the present work. Chondrocytes obtained from normal and hemophilic patients were isolated and cultivated either in monolayer or 3D conditions. For three-dimensional cultures, cells were cultured onto non-woven meshes made with the benzyl ester of Hyaluronic acid (Hyalit materials obtained from Fidia Advanced Biopolymers- Abano T.Italy). Proliferation test and rt-PCR analysis for extracellular matrix molecules such as collagen type I and collagen type II were performed in all cell cultures at day 28. MTT test performed to

RESULTS: Semi-quantitative RT-PCR analyses of collagen types I and II showed a greater synthesis of collagen type II (typical marker of adult chondrocytes) than collagen type I. These findings confirm that in vitro conditions, hemophilic chondrocytes maintain their unique phenotype and are able to synthesise a cartilage-like extracellular matrix. This might reflect in a possible application of these chondrocytes in a transplantable engineered cartilage for the regeneration of chondral lesions in hemophilic patients.

Key words: Autologous cultured chondrocyte implantation, hemophilic arthropathy

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TOTAL KNEE ARTHROPLASTY IN HEMOPHILIC ARTHROPATHY: LONG-TERM FOLLOW UP

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Severe hemophilia is complicated by recurrent spontaneous joint bleedings, which lead to severe secondary arthrosis, defined as hemophilic arthropathy. Joint pain, unresponsive to medical treatment and impaired function are indicators for total knee replacement. A well-balanced homeostasis is the basic requirement for successful operative interventions. The aim of our study is to evaluate the results of a combined series of total knee replacements in 25 patients with severe hemophilia A and 1 patient with severe hemophilia B, treated at University Orthopaedic Departments of Naples and Bari from 1992 to 2006. We evaluated patients according Knee Score. Review of the patients over a period of 85 months (12months) after operation showed dramatic reduction of pain and maintenance of a satisfactory range of movement. The frequency of hemarthrosis was also markedly reduced and the requirements for replacement FVIII/IX concentrate in the years after operation fell substantially. On the whole, an improvement of the Knee Score from 37 (pre-operative) to 87 (post-operative) has been recorded. In our experience total knee replacement led to a significant clinical improvement in all the patients, with relevant impact on quality of life.

Key words: Total knee arthroplasty, hemophilia
SPECTRUM OF BLEEDING IN HEMOPHILICS PRESENTING AT HEMOPHILIA TREATMENT CENTER, PAKISTAN INSTITUTE OF MEDICAL SCIENCES (PIMS), ISLAMABAD OVER A ONE-YEAR PERIOD

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Objective: The study was done to evaluate bleeding episodes and sites of involvement in patients presenting to a hemophilia centre in a developing country to highlight the problems so that measures can be taken to improve care.

Methods: Patients presenting to the centre were evaluated by the medical officer. A detailed Performa was filled noting the details of bleeding and the time between the bleed starting and arrival at the centre.

Results: There were a total of 1641 visits to the centre in 2006. Most (894) of these were due to a bleeding episode. Joint bleeds were 554 (61.96%), gingival (8.85%), muscle 73 (8.16%), nose 51 (5.71%) and tongue and intracranial. The average time taken to reach hospital was 24 hrs.

Relevance to hemophilia care: The study highlights that in developing countries joints bear the brunt of bleeding. It also points out the delay in reaching a centre. In view of this, counselling of patients on the importance of reporting early and educating parents about home care and regular physiotherapy assessment has been included in the care program. It is also planned to open treatment centres in far-off areas so that the delay in treatment can be minimized.

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Session 3-2: Free Papers IV
Chairman: T. Sohail

STATIC POSTUROGRAPHIC ANALYSIS IN HEMOPHILIC PATIENTS: A PILOT STUDY

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The stability of the body performs maximum importance in the activities of the daily life. The osteoarthritis and the hemophilic arthropathy of ankle and knee influence the musculoskeletal, joint mobility, forces and stability. Physical therapy and orthosis can bring improvements of the arthropathy, which can be evaluated by means of the stability analysis. The aim of this study is to describe the static balance in hemophilic patients and to establish the possible relations of the arthropathy with postural stability.

Eleven patients with severe hemophilia have taken part in the study. The standard clinical exploration includes Gilbert’s score and Pettersson’s score. The measurement of the stability has been realized in a platform of force Kistler

SYNOVIORTHESIS WITH YTTRIUM 90 IN THE HEMOPHILIC SYNOVITIS: 24 MONTHS OF FOLLOW-UP IN 53 JOINTS AND 177 PATIENTS SUBMITTED


Joint disease is a major morbidity in hemophilia. A hypertrophic synovium leads to recurrent bleeding; the aim of treatment is to remove it. Radiosynoviorthesis has been considered the best choice once conservative approaches fail. Since April 2003, as an ongoing study, authors injected Yttrium 90 in 308 joints of 177 patients referred by 17 states in Brazil. Election criteria were diagnosis of hemophilia or VWD, at least 3 hemarthroses on a 6-month interval, clinical evidence of synovitis and US, MRI or Scintigraphy. Factor VIII / IX were raised to 80% and 30% before and after arthrocentesis, respectively, using factor concentrates. Patients with inhibitors received aPCC or rFVIIa. Doses of 3 to 5mCi of Yttrium 90 Citrate were used for knees, 1 to 3 mCi for ankles, elbows and shoulders, depending on the size of the joint. Mean age was 12 years. Criteria of evaluation were: n. of hemarthroses, pain (WFH scores) and ROM, at intervals of 12 months before and after. Results: In 53 of treated joints at 24 months of follow-up was obtained. In 54.7%, results were excellent (100% of cessation of bleedings) and in 39.6% there was a reduction of at least 75% (“good”). There were no significant complications, including the 19 patients with inhibitors. Patients submitted to a regular physiotherapy program after procedure had a better outcome, in relation to ROM. The authors concluded that the treatment was safe and effective, significantly improving the lives of these patients. Outcome did not depend on Pettersson scores.
LONG-TERM RESULTS OF TOTAL KNEE REPLACEMENT IN HEMOPHILIC PATIENTS: 19-YEAR SINGLE-INSTITUTION EXPERIENCE

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End stage hemophilic arthropathy of the knee, the most commonly involved joint in hemophilia, causes severe pain and disability: in this circumstance, total joint replacement is recommended. From 1987 to 2005, 50 primary total knee replacements (TKR) were performed in 39 hemophilic patients at our institution. The median age of the patients at the time of surgery was 42.7 years (range 22 to 62 years). The mean follow-up was 6 years (range 19 years to 12 months). Thirty-seven patients had severe FVIII deficiency (HA), 1 severe FIX deficiency (HB), 1 Von Willebrand Disease type III. 2 showed high titre anti FVIII inhibitors while one had low titre inhibitor. All patients were HCV positive, 6 were HIV coinfected. The patients without inhibitors received plasma-derived FVIII replacement therapy via bolus injections or continuous infusion while those with anti FVIII inhibitors received rFVIIa by continuous infusion. Antibiotics were administered for ten days; no antithrombotic prophylaxis was utilized and antiphibrinolytic treatment was used in all. Four patients underwent two knee replacements during different operative sessions. Three patients had died at a mean of 8 years after the surgery for cirrhosis and complications of AIDS. One patient was lost to follow-up. One knee required partial removal because of aseptic loosening. The survival rate of TKR (with revisions at any reason as the end point) was 87%. In total knee replacement performed in our cohort of patients there were a high rate of infections as some authors have already reported in the literature. Orthopedic surgeons and hematologist should consider carefully risks and benefits of these procedures as they can carry a high rate of complications and they should be suggested for a very selected proportion of patients with hemophilia.

Key words: knee prosthesis, hemophilia

MUSCULOSKELETAL ASSESSMENT: THE JOINT AND BEYOND...

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Many instruments are available for musculoskeletal assessment in hemophilia. Some of these may be more appropriate then others, depending on the information needed and resources available. The present study addresses the association between two frequently used, though rather different outcome measures for joint status (i.e., radiological damage (Pettersson score) and mobility (AROM) and their association with activities and participation. Retrospective data were available for thirty-six patients with severe hemophilia; aged 18–62 (mean 37). Seven patients had a history of orthopedic surgery. Associations between radiological damage and joint mobility were strong: ranging from r=0.69 for the ankle joints, to r=0.91 for the sum of all joints (p<0.001). However, these measures are not interchangeable, especially not after orthopedic surgery, as a Pettersson score cannot be given after orthopedic surgery. Regression analysis confirmed that the impact of AROM on activities was much stronger than of Pettersson score. Whereas joint mobility of both the upper and lower extremities explained 62% (p<0.001) of the activity outcomes, Pettersson score had no significant contribution to the model (p=0.67). Similar results were found for participation (45% (p<0.001) vs. p=0.24).

Key words: Assessment, joint status

BLOOD SPARING SURGERY: THE USE OF HEMOSTATIC SEALANT

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Orthopaedic surgery in haemophilic patients is surely related to higher risk of bleeding complications. Generally, even in surgery performed on patients without bleeding disorders, is correct the use of blood sparing techniques in perioperative period like: general anesthesia under controlled hypotension, preoperative autologous blood donation, intra and post op autologous blood transfusion device. At surgery time the use of hemostatic agents and intra op devices should be recommended. We present preliminary results of the use of Flo-Seal matrix hemostatic sealant in replacement surgery on hemophiliacs.
TOTAL ANKLE REPLACEMENT FOR END-STAGE ARTHROPATHY IN HEMOPHILIACS: REPORT OF TWO CASES

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Standard conservative treatment for ankle arthropathy includes primary and secondary prophylaxis, physical therapy, modification of footwear and orthosis. In chronic hemophilic synovitis causing recurrent hemorrhrosis, synoviorthesis may be considered, the intra-articular injection of radioactive \( \text{Rodriguez-Merchan, Haemophilia 2006, 12, 337–344} \) or chemical substances \(( \text{Radossi et al. Haemophilia 2003, 9: 60–3} \)). These procedures are effective in reducing joint pain and improving range of motion (ROM), but are not able to modify the natural course of the degeneration.

Advanced ankle arthropathy is common in severe hemophiliacs and the standard surgical treatment is represented by arthrodesis. Total ankle replacement is a well-established approach in rheumatoid arthritis and post-traumatic arthritis but in the literature, only few cases are published in end-stage ankle hemophilic arthropathy. Between 2000 and 2002 we implanted two total ankle prostheses in two severe hemophilia A patients: the indications for surgical operation were persistent pain and severe reduction in ROM.

The first patient, 30 years old, also presented low titre antibody against FVIII (low titre at the time of the operation); the second patient, 42 years old, was HCV and HIV coinfected, treated by HAART for HIV. Replacement therapy with plasma-derived FVIII concentrates was used in both surgical operations without hemorrhagic complications, for an average of 8 days.

After five-year follow-up, both cases presented stable improvement of ROM, no intra-articular bleedings were reported and there was good quality of life. Unfortunately, the patient HCV/HIV coinfecion died six months ago of severe liver disease.

Although the number of data in literature is limited, we think that such a surgery may be considered as the gold standard in severe ankle hemophilic arthropathy after failure of other conservative therapies.

Key words: ankle prosthesis, hemophilia

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CLINICAL, RADIOLOGIC AND MAGNETIC RESONANCE FINDINGS FOLLOWING \( \text{\textsuperscript{32}P} \) SYNOVIORTHESIS IN HEMOPHILIA

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Introduction: Diagnostic imaging is used to assess hemophilic arthropathy. Magnetic resonance imaging is a more sensitive tool in delineation of early changes within hemophilic joints compared with conventional radiographs. It has the advantages of visualization of articular cartilage and synovium.

Aim: We performed radiologic and MR evaluation of the hemophilic joints undergoing \( \text{\textsuperscript{32}P} \) radiosynoviorthesis for recurrent hemorrhrosis. Possible correlations between alterations in bleeding frequency and radiologic and MRI findings were looked for.

Material and Methods: Between 2002 and 2006 we performed 66 procedures on 53 patients. Eight joints were excluded. The mean age of patients at the time of injection was 15.9 years (range: 6 to 28 years). Radiographic as well as MR imaging studies were performed before treatment and during follow-up. Arnold-Hilgartner and Pettersson scales were applied for radiologic scoring of the plain films. Denver and Soler scoring systems were used for MRI assessment of treated joints.

Results: Joint destruction progressed as demonstrated by Arnold-Hilgartner radiologic \((P= 0.03)\), Soler \((P= 0.005)\) and Denver \((P= 0.014)\) MRI scoring scales despite the significant decrease in bleeding rate \((P< 0.0001)\). Cartilage erosion progressed significantly after treatment \((P= 0.014)\). Synovial hyperplasia severity decreased following \( \text{\textsuperscript{32}P} \) radiosynovectomy \((P= 0.03)\).

Conclusion: Joint degeneration and cartilage erosion continues despite reduction in bleeding rate following synoviorthesis. Radiosynovectomy using \( \text{\textsuperscript{32}P} \) isotope effectively reduces the severity of synovial hyperplasia examined by MRI. Patients with a better response to treatment in terms of reduction in hemorrhosis frequency may not necessarily have a higher regression of synovial hyperplasia on MR images.

Key words: Hemophilia, radiosynovectomy, clinical, magnetic resonance imaging, radiology

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**MUSCULOSKELETAL STATUS OF THE CANADIAN HEMOPHILIA PROPHYLAXIS STUDY COHORT AFTER 10 YEARS**

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Background: Standard prophylaxis is effective but costly. We have been studying a tailored prophylaxis regimen since 1997. Objective: To describe the musculoskeletal status of 51 boys with severe hemophilia A treated with tailored prophylaxis. Methods: Boys with hemophilia A (<2% factor) and normal joints were enrolled between the ages of 1 and 2.5 years. They were initially treated with once-weekly factor infusions; the frequency was escalated in a step-wise fashion if unacceptable bleeding occurred. During the first 5 years, study physiotherapists examined subjects every 3 months—and subsequently every 6 months—using a modified Colorado Child Physical Examination scale. Physiotherapists were centrally trained. The Childhood Health Assessment Questionnaire (CHAQ) was administered at each study visit. Results: Mean age at study entry was 19 months (range 12–20); mean follow-up is 54 months (range 1–102). Average number of joint bleeds/year is 0.9. Median joint score excluding axial deformity and swelling (possible range 0–134) is 0–0.5 by age group (inter-quartile range 0–4). 16/51 (31%) of the boys developed a target joint defined as 3 bleeds in a joint in a 3-month period. Seven of sixteen boys with a target joint showed persistent scores >0 on the physiotherapy exam. Median CHAQ score (possible range 0–3) is 0 for all age levels. For the different age levels the range of median scores for pain were 0.45–2.26, for illness 0.83–2.55 and for well-being 0.1–1.05, as measured on a 10 cm visual analogue scale.

Conclusion: Canadian boys treated with a tailored prophylaxis regimen have minimal joint damage and physical disability.

**Key words:** musculoskeletal, prophylaxis

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**PRIMARY KNEE ARTHROPLASTY USING RECOMBINANT FACTOR VIIA (RFVIIA) AS FIRST-LINE THERAPY IN HEMOPHILIA PATIENTS WITH HIGH RESPONDING INHIBITORS**

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Haemophilia Centres from Germany², Italy², France², Spain³, and UK⁴

Clinical report forms have been developed with a clinical research organization to collect data on primary knee arthroplasties (KA) performed with rFVIIa as first-line therapy. To date, 27 KAs (13 right, 14 left) have been reported in 25 patients (21 severe HA, 3 severe HB, 1 mild HA) with an average age of 37 years (range: 17–70) from 12 European hemophilia centres. Prior to KA, inhibitor titres were 0–400 BU (median: 5 BU); in 2 patients titre was <1 BU, in 12 it was 1 to 5 BU, and in 12 cases > 5 BU. rFVIIa was used as bolus injections (BI) only in 12 cases or as continuous injection after BI in 15 cases. Antifibrinolytics were used in 24 cases. Red blood cell transfusion (RBC) was required in 15 cases (median: 4 units (U) RBC; range: 1–11 U). More than 4 U RBC (7–11 U RBC) was required in 6 patients including a bilateral KA. Five bleeding complications were observed in the post-operative period; in 1 patient, high dose FVIII rescue treatment was used. Median follow-up since KA is 51 months (7–129 months). Global assessment was excellent or good in 23 cases, fair in 2 cases and worse in 2 cases (1 KA infection requiring KA revision; 1 arthrodesis for a post-traumatic fracture above KA). Collection of additional cases from Europe is required to obtain a global view of KAs performed with rFVIIa in inhibitor patients and will allow the comparison of primary KA in inhibitor patients versus non-inhibitor patients as well as of the two treatment regimens used.

All participating physicians and centres to the EUREKA data collection and the CIC-INSERM-Rouen University hospital are gratefully acknowledged for their contributions.
ASSESSMENT OF PHYSICAL PERFORMANCE IN ADULT HEMOPHILIA PATIENTS: DEVELOPMENT OF A SUBJECTIVE MEASURE (HEP-TEST-Q)

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Introduction: Recommendation of sport activities in hemophilia has not always been taken for granted. Although today sport activities are considered beneficial, their importance as an integral element in hemophilia treatment has not yet been widely recognized. In the Hemophilia and Exercise Project (HEP) physical performance was evaluated objectively (orthopedic joint score, EMG) and subjectively with the newly developed performance-specific questionnaire (HEP-Test-Q).

Objectives: Development and validation of an instrument for the subjective evaluation of physical performance in adults with hemophilia. Methods: Development of HEP-Test-Q consisted of a pilot and field testing phase. Item pooling was based on the modular training program. The preliminary HEP-Test-Q was pilot-tested for feasibility and preliminary psychometric characteristics in 23 German adult hemophilics attending the HEP sport camp. The revised HEP-Test-Q consisting of 26 items pertaining to 5 dimensions (mobility, strength and coordination, endurance, body perception, general questions) was administered to 33 patients during field testing and psychometrically analyzed in terms of reliability and validity. Results: Feasibility testing revealed that mean completion time for HEP-Test-Q was 13 minutes, it was well accepted by patients and they estimated it as related to physical activities. Psychometric testing showed excellent characteristics for reliability and validity. Participants reported good mobility, but were mainly impaired in strength and coordination and endurance. Relevance to hemophilia care: Subjective evaluation of physical performance can be measured by HEP-Test-Q, a short psychometrically sound questionnaire, which might be combined with objective assessments in order to reveal aspects, which cannot be measured objectively such as body perception.

Key words: hemophilia, physical performance, subjective assessment

HEMOPHILIC INTRAOSSEOUS PSEUDOTUMOUR OF THE TALUS IN CHILDREN

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Hemophilic intraosseous pseudotumour is a rare complication of hemophilia consisting of an encapsulated, hemorrhagic fluid mass occurring after repetitive bleedings into the bones. Progressive expansion may lead to deformity or pathologic fracture. Femur, pelvis, tibia and small bones of the hand are most frequently implicated. Plain radiography, CT and MRI scans are useful in determining the location and extent of the lesion. The management of hemophilic pseudotumour aims at preserving function and includes conservative methods (immobilization, substitution therapy), extirpation, and irradiation. We report three cases of hemophilic pseudotumours in a very rare location (talus) in children. Case1: A 12-year-old boy with severe Hemophilia A and bilateral ankle arthropathy underwent routine radiographic examination. Bilateral flattening of articular surface of the talus was revealed. CT and MRI scan demonstrated bilateral ankle arthropathy and a cystic lesion with characteristics of intraosseous pseudotumour in the right talus. Surgical curettage of the lesion and bone grafting were performed. The diagnosis was confirmed by the histological findings. One year post op complete healing of the lesion was confirmed with new CT scan. Cases 2 and 3: Two boys with severe hemophilia A, 12 and 13 years old respectively, underwent MRI examination of their ankles because of recurrent bleedings. MRI and CT scans revealed, apart from findings of hemophilic arthropathy in examined joints, extensive hemorrhagic masses at the centre of right and left talus respectively, with no cortical thickening or fracture. The children are ongoing conservative treatment, for one and three years respectively, without any complication.

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