Physiotherapy management in haemophilia

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Background and practical guidelines

Series: Haemophilia care and treatment

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Content

Point-of care ultrasound is of value in the evaluation of acute haemarthrosis, and is effective in identifying early synovial and cartilage changes.

As in low-income countries clotting factor concentrate resources are restrained, rehabilitation, and especially physiotherapy, should play an important role in Twinning programmes.

Compression should never be applied to a muscle bleed where compartment syndrome is suspected or present.

Foreword

The predominant manifestations of haemophilia are musculoskeletal related to bleeding into joints and muscle. Even though such bleeding has reduced significantly in those patients who receive regular replacement therapy (prophylaxis) with clotting factor concentrates (CFC), more than half of these patients and nearly all other patients in the world who do not receive prophylaxis, develop some or significant musculoskeletal dysfunction by their adulthood. Physical medicine and rehabilitation (PMR) forms the mainstay of the management of these complications and a very critical component of the comprehensive care approach. The goal is indeed twofold – first, prevent musculoskeletal damage in children as they grow up with the best possible CFC replacement regimen and second, use these modalities to treat those who have developed these complications as a result of inadequate control of bleeding.

Applying different techniques of PMR in the care of people with haemophilia (PWH) involves a range of processes which include assessment of the damage and their functional implications and therapy to not only improve muscle strength and range of motion but also overall musculoskeletal function to allow full participation in social and vocational activities. An understanding of the scope of comprehensive care, the pathogenesis of these changes in the joints and muscles and their functional impact are critical to designing good and effective interventions. There are a limited number of centres in the world that have a high level of expertise in this area of

care for PWH with personnel trained in all aspects of physical and rehabilitative management along with orthopaedic surgical interventions.

The Van Creveldkliniek at the University Medical Centre in Utrecht, the Netherlands is among the best in the world in this field. It is therefore most appropriate that this group has taken the effort to create this textbook on different aspects of physical management of musculoskeletal complications in haemophilia. The multidisciplinary team at Utrecht along with several other colleagues from around the world have put together this very significant collection of information that would be extremely useful for all those involved with care of PWH with musculoskeletal complications anywhere in the world. A section on assessment of outcomes also provides an overview of this rapidly evolving field in haemophilia care.

The editors, Eveline Mauser and Piet de Kleijn, have decades of experience in care of PWH work not only at their own centre but also with people around the world. Through their own work over a long time, they have seen minimal treatment evolve to very effective prophylaxis and the role of physical management at all these stages. There could not be a better group to put together such a textbook.

Alok Srivastava
Christian Medical College,
Vellore, India.

Preface

Of all the inherited bleeding disorders, haemophilia is the disease that probably best reflects the unique overlap and interaction existing between blood coagulation and musculoskeletal diseases. The complete clotting factor VIII or IX deficiency typically affecting severe haemophilia results in spontaneous bleeding complications that primarily affect joints and muscles and can result in major physical disability.

Treating, and ideally preventing, these intra-articular and intramuscular bleeding episodes require replacement therapy initiated and monitored by haematologists. Besides these substitutive therapies for blood coagulation defects, appropriate haemophilia management and assessment require great expertise equally covering both haemostasis and musculoskeletal assessment. This is why a joint and combined management of haemophilia by both haematologists and physiotherapists, all of whom possess genuine interest and complementary expertise in haemophilia, is so crucial for effective care.

Physiotherapists specialised in haemophilia undoubtedly play a crucial role in haemophilia care, providing key contributions to standardised and expert joint assessment in both children and adults, conducting physiotherapy sessions in patients with established arthropathy and rehabilitation programmes following surgery or major bleeds, conservative care like orthoses. They also educate patients and parents regarding prevention, recognition and

non-haematological physical treatment of bleeding episodes, provide advice about physical activities, lifestyle changes and sport practice, contribute to research, and work in close collaboration with orthopaedic surgeons so as to identify ideal candidates for surgical interventions. Haemophilia-specialised physiotherapists are also increasingly involved with the haematologist in defining the appropriate personalised replacement therapy for each patient considering his joint status and its changes over time as well as his lifestyle and physical activities. They play a key role in designing and providing care to both child and adult haemophilia sufferers, thus fulfilling a unique role in the transition phases from childhood into adulthood via adolescence. By assessing and following the joint status regularly throughout life, the haemophilia physiotherapist provides valuable outcome data that are increasingly needed for sustainable haemophilia care.

Given these numerous advantages in a combined haemophilia-physiotherapy approach, all efforts and initiatives to attract, educate, and foster physiotherapists in the haemophilia care setting should be highly encouraged. One of these recent successful initiatives has been the creation of a committee of physiotherapists by the European Association of Haemophilia and Allied Disorders (EAHAD) and the launch of several projects to create a new platform of European collaboration and networking.

This book, to which all physiotherapists committee members of EAHAD and many other experts contributed, represents a first and promising achievement of this new collaboration as well as a unique tool to promote the major role of physiotherapy in haemophilia care.

Professor Cedric Hermans
EAHAD President, 2016-2018

Introduction

This book is the result of close co-operation between physiotherapists and physicians, active in a multidisciplinary haemophilia treatment centre. The medical treatment of choice is infusion with clotting factor concentrates, ideally administered as prophylaxis to prevent bleeding. As haemophilia is a haematological condition with musculoskeletal manifestations physiotherapy, rehabilitation and orthopaedic surgery are essential in comprehensive haemophilia care.

In many haemophilia comprehensive care centres in the world, both low and high income countries, even basic physiotherapy is not implemented yet. And in centres where physiotherapy is implemented, guidelines and protocols often do not exist. This goes for acute situations like intra-articular and intramuscular bleedings, as well as for chronic situations like synovitis and haemophilic arthropathy.

The aim of this book is to provide basic and practical knowledge in various situations for physiotherapists, but also for all other members of the comprehensive care team. At the end scientific proof – if available – and most relevant literature is added. Therefore this book can be read as a regular book, but for special clinical situations each chapter can be consulted as a separate entity as well. Furthermore it might be a basis for future development of guidelines and protocols which in the end could and should be implemented in various haemophilia centres and countries worldwide.

HAEMOPHILIA

Haemophilia A and B are both hereditary bleeding disorders caused by a mutation at a recessive allele on the X-chromosome. Haemophilia A is characterised by a deficiency in factor VIII, and haemophilia B by a deficiency in factor IX. Haemophilia A and B are clinically identical. Because of the sex linkage it occurs almost exclusively in males. However female carriers may have decreased factor VIII or IX levels too. Deficiency of factor VIII or IX may result in joint and muscle bleeds, prolonged bleeding after injuries, tooth extractions, or surgery and renewed bleeding after initial bleeding has stopped. The severity of haemophilia is related to the amount of clotting factor in the blood. About 40% of people with haemophilia have less than one percent of the normal amount and suffer from severe haemophilia. Both age of diagnosis and frequency of bleeding episodes are related to the remaining clotting factor activity.

Severe haemophilia often becomes clinically apparent in the first years of life as soon as the child starts to move around. Haemorrhages occur in synovial joints, particular weight baring joints like knees and ankles, even after minor trauma, causing pain and functional limitations. Muscle bleeds may be life-threatening and may result in contractures or pseudotumours. Significant and recurrent bleeding in joints can cause contractures, muscle atrophy, synovitis and cartilage damage and finally crippling and painful haemophilic arthropathy. This degenerative process can begin at an early age in several joints, especially when clotting factor concentrates are not readily available for either on-demand treatment or prophylactic administration.

A small increase in the clotting factor concentration, up to two percent of normal, results in a decrease of symptoms. Persons with moderate haemophilia seldom have spontaneous bleeding but bleed after minor trauma mostly in joints. Persons with mild haemophilia do not have spontaneous bleeding however without treatment they do have prolonged or delayed bleeding after trauma and surgery which may, when not adequately treated, become life-threatening. In mild haemophilia untreated musculoskeletal bleeding may result in contractures and arthropathy, mostly only one joint is affected.

Some patients develop inhibitors in response to replacement therapy with clotting factor concentrates. Inhibitor patients cannot be

treated adequately with prophylaxis and suffer more often from recurrent bleeding and arthropathy.

THE ROLE OF PHYSIOTHERAPY

In all age categories and in various situations physiotherapy is essential in haemophilia care. Normal motor development is the ultimate goal of preventive exercise. Pain can be an important issue at all ages, and may be differentiated in both acute or chronic situations. A better understanding of the basics of pain helps our patients to develop coping strategies. The same understanding of posture and gait, both typical haemophilia related items, is the only way towards adequate advice and treatment plans. Sports play an important role in the lives of children and adults, but merely in high-income countries where quality of life and life expectancy approaches that of the general population. In acute situations the RICE protocol may be helpful, however evidence is not completely clear. Furthermore, an active training programme to regain complete functional recovery after a bleed is not always part of comprehensive care – even in established haemophilia treatment centres – nor its measurable goals. The editors of this book have the opinion that, although not scientifically proven, this intervention might prevent recurrent bleeding.

Worldwide it is impossible to totally prevent chronic synovitis and haemophilic arthropathy in all persons with haemophilia. In these situations physiotherapy is part of a rehabilitation programme, set up to maintain physical functions and activities, and in the end the most optimal participation. If a conservative programme does not guarantee the aforementioned physical (and social) capabilities, orthopaedic intervention might be required. Any intervention always has to be followed by a rehabilitation programme.

The editors emphasise that the approach of physiotherapy on a more functional basis can well be used in situations where there is no or limited clotting factor, or where patients live (too) far from their haemophilia centre to effectuate regular physiotherapy. In developed countries it seems an effective way to fight the non-compliance, if personal and more functional milestones are included. We hope that this book will help to improve the level of care and quality of life of all persons with haemophilia.

ACKNOWLEDGEMENT

The editors thank the authors for their contributions. We are honoured that Alok Srivastava, former member of the World Federation of Hemophilia (WFH) executive committee contributed a foreword and Cedric Hermans, chair of the European Association of Haemophilia and Allied Disorders (EAHAD), was willing to write the preface of this book.

We thank Sean de Jong for correcting the manuscript.

We hope that our aim, improvement of the basic knowledge of physiotherapy in the rehabilitation of persons with haemophilia, will be achieved, and that physiotherapy will become an integrated part of care in all haemophilia (comprehensive) care centres for the benefit of the quality of life of persons with haemophilia.

Utrecht, January 2017
Eveline Mauser-Bunschoten & Piet de Kleijn

PART I

Comprehensive care

EVELINE MAUSER-BUNSCHOTEN AND ALOK SRIVASTAVA

CHAPTER I

Why comprehensive care? WHF principles and guidelines

WHY COMPREHENSIVE CARE?

Haemophilia is an x-linked disorder that typically affects males, while females are carriers. It is a rare disease whose diagnosis and management is complex. It is a haematological disorder with predominantly musculoskeletal manifestations. Optimal care of persons with haemophilia, especially those with severe haemophilia, requires more than the treatment and prevention of acute bleeding with clotting factor concentrates. As haemorrhages or muscle bleeds may cause joint damage and contractures, rehabilitation is part of care. Besides prophylaxis with clotting factor concentrates, normal motor development decreases the risk of bleedings and improves optimal recovery after each bleeding. Haemophilia, therefore, also has an impact on quality of life.

While nurses are often the first contact and educate patients and parents about haemophilia and teach them how to do (self)infusion and home care, support from other members of the team such as physiotherapists, occupational therapists and psychosocial workers may be of great help in developing coping strategies. In this setting physical and psychosocial health and quality of life are promoted in the best way while morbidity and mortality are decreased.

SETTING

Persons with haemophilia should ideally be managed in a comprehensive care centre where a sufficient number of persons with se-

MEDICAL DIRECTOR	paediatric and/or adult haematologist, or a physician with interest and expertise in clinical haemostasis
NURSE COORDINATOR	a nurse with specific training and expertise in the management of patients with bleeding disorders
MUSCULOSKELETAL EXPERT(S)	physiotherapist, occupational therapist, physiatrist, orthopaedist, rheumatologist
PSYCHOSOCIAL EXPERT	social worker, psychologist

Table. Core team members of a comprehensive care centre

vere haemophilia is treated, and which is staffed by multidisciplinary core team members (Srivastava et al., 2013; Colvin et al., 2008; Evatt et al., 2006)

Depending on the needs of the haemophilia population and situation in a particular country other specialists could be added to the core team. For example a dentist, geneticist, hepatologist or infectious disease specialist.

COMPREHENSIVE CARE TEAM REQUIREMENTS

Members of a core team should have expertise and experience in treating various aspects of bleeding disorders and should be accessible to patients 24 hours a day, seven days a week. As all bleeds should be treated promptly to prevent deterioration and disability in the long term, appropriate stock of clotting factor concentrates for treatment of haemophilia A and B, either plasma-derived or recombinant, as well as other appropriate haemostatic agents such as desmopressin (DDAVP) should be available in a treatment centre. And if

clotting factor concentrates are not available, access to safe blood components such as fresh frozen plasma (FFP) and cryoprecipitate could be an option, though this should not be encouraged given its safety challenges.

Part of comprehensive care is to support family members. This may include identifying strategies to help cope with risks and problems of everyday living, particularly with management of bleeding, changes associated with different stages of the patient's growth and development (especially adolescence and aging), issues regarding schooling and employment. The risk of having another affected child and the options available can be discussed by a physician specialised in haemophilia or by a geneticist.

COMPREHENSIVE CARE PROGRAMME

Patients should be seen regularly by all core team members. Those with severe haemophilia must be evaluated at least yearly (children every six months) for a complete assessment (haematological, musculoskeletal, psychosocial). Furthermore a comprehensive management plan should be developed with the patient and communicated to all treaters and care facilities. This plan should contain information on type and severity of the disease, product and treatment schedules for prophylaxis and management of bleeds and in case of trauma or medical intervention.

Haemophilia should ideally be managed in a comprehensive care centre staffed by a multidisciplinary core team where a sufficient number of persons with severe haemophilia is treated.

The treatment centre also initiates and supervises home therapy. During yearly check-up data are collected on sites of bleeds and surgical procedures, treatment given, and assessment of long-term outcome, particularly with reference to musculoskeletal function. It provides education to patients and family members (parents, spouse, children, etc.), other healthcare workers, schools, and the workplace to ensure that the needs of the person with haemophilia are met. A centre should conduct basic and clinical research to improve the understanding of this condition and its management.

MONITORING OUTCOME OF TREATMENT

Regular standardised assessment allows longitudinal assessment over time of individual patients, and can discern the development of new problems in their early stages so that treatment plans can be modified and psychosocial deterioration, dysfunction and poor coping can be prevented.

During yearly check-up, patients should be evaluated for the following:

- Venous access related issues
- Haemostasis related issues (bleed record)
- Use of products for replacement therapy and the response to them
- Development of inhibitors
- Transfusion-transmitted infections such as HIV, HCV, and HBV infections
- Musculoskeletal status: impairment and function through clinical assessment of joints and muscles and radiological evaluation
- Overall psychosocial status with respect to participation in activities related to self, family, and society
- Pain and cause of pain (bleeding, venous access, arthropathy, surgery) and its management
- Need for adaptations
- Dental care
- Genetic counselling
- Sexuality
- General health

CONCLUSION

Comprehensive care is essential and indeed critical for optimal management of persons with haemophilia and should be established and supported from the available resources at all large haemophilia treatment centres.

PIET DE KLEIJN

CHAPTER 2

Comprehensive care in a haemophilia treatment centre

A • The role of the physiotherapist

INTRODUCTION

According to the World Federation of Hemophilia physiotherapists should be involved from the time of diagnosis and start of treatment of persons with haemophilia and their families, and this should continue throughout their lifespan (Srivastava et al., 2013). In reality, only in a few haemophilia treatment centres a physiotherapist is involved in daily care, and often not even in an optimal way. How is this possible in a very costly disease like haemophilia? Optimal care not only consists of regular check-ups, with use of valid instruments, but should always include appropriate functional care in acute situations, in close co-operation with a haematologist and other team members.

Recently in the Netherlands a questionnaire among physiotherapists – members of a Dutch haemophilia comprehensive care team – clearly showed that in daily practice they were often not available for, or included in, regular haemophilia care. They found it important to improve this and started to arrange the set up in their own centre, but only after approval of the Dutch Haemophilia Treaters Society (NVHB). Only if "standards" are accepted (chapter 4) formal extension of the comprehensive care team can be a effectuated, and the actual implementation of physiotherapy started. Fortunately a new quality of care control system, effectuated by the professionals (medical doctors) of the Dutch haemophilia treatment centres, recently opened opportunities to implement physiotherapy in all

Dutch haemophilia treatment centres, and thus involve physiotherapists more adequate in daily care (de Kleijn et al., 2016).

GENERAL TASKS OF THE PHYSIOTHERAPIST

We realise that worldwide the (organisational) structure of haemophilia treatment centres differs enormously. We here provide the most regular tasks, and underline that item 2 and 3 are most essential in any smaller centre:

1 General health precautions
2 Functional recovery after acute musculoskeletal bleedings
3 Maintaining physical activities and participation in chronic conditions
4 Pre- and post-operative coaching and rehabilitation
5 Others

Ad 1. A practical way of precautions is purchase of proper equipment, as crutches, and instruct both the child with haemophilia and his parents to use these in an adequate way. To minimise bleeding risk at a young age, physical activity should be discussed freely. A normal neuromuscular development is aimed at, but practical focus is often on muscle strengthening, coordination, general fitness, body weight, and self-esteem (chapter 7).

Ad 2. Musculoskeletal bleedings require an up-to-date RICE protocol (chapter 9). Appropriate rehabilitation must be an active part of the management of an acute joint bleed. It is generally accepted that functional recovery after cessation of intramuscular bleeds is essential (de Kleijn et al., 2004). Optimal functional recovery after every bleed could well prevent recurrent bleeding and starts as soon as pain subsides and swelling diminishes. It should be ideal if patients and parents at home know how to decide the right moment to start rehabilitation based on physical examination (chapter 3). To assure physical activities, it is intensified gradually until joint function, proprioception, muscle strength and length and activity levels are restored. Always, the level of activities present prior to the last bleeding, needs to be achieved, including leisure activities and sports.

Ad 3. Maintaining bodily functions, activities and participation in chronic conditions, such as haemophilic arthropathy, chronic synovitis and muscle contractures (chapter 6). Intervention aims at

maintaining joint function, relieving pain, and thus stabilising daily activities and participation. Detailed joint assessment not only serves as a tool to guide job-related activities, leisure and sports, but also to secure an adequate follow-up. Treatment options depend, besides the country and type of haemophilia treatment centre, on the condition and impact on the patient's lifestyle and functional abilities, sometimes supported by secondary prophylaxis with clotting factor concentrates.

Ad 4. Single (or multiple) joint procedures are followed by intensive rehabilitation, aiming at optimal functional recovery. Most hospitals use their own protocol (chapter 10d), which mainly covers clinical rehabilitation. The advantage for persons with haemophilia visiting a comprehensive haemophilia treatment centre, is personal guidance during the entire process of rehabilitation, conducted by a physiotherapist familiar with haemophilia.

Ad 5. In a larger (e.g. national, or regional) haemophilia treatment centre physiotherapists can have additional tasks, like survival, ski- and sports camps and educational family meetings. Participating in workshops in low-income countries can be a task too, and is often supported by the World Federation of Hemophilia. A well-known example is the Twinning Programme (chapter 16c).

These 5 basic tasks are, in more established haemophilia treatment centres, completed with monitoring of patients, often from a young age onwards, during their whole life-span. Physical outcome is one of the most important parameters of the medical treatment, but it is still under debate how frequently this has to be assessed. In older patients performing an annual complete physical examination might be too frequent and focus could be on specific joints instead (Kuijlaars, 2016) whereas in children with inhibitors not one but two times a year might be more efficient to monitor the effect of frequent bleedings in joint and muscles.

INVOLVEMENT OF PHYSIOTHERAPY

How likely is it that physiotherapy is effective in haemophilia care? Or cost-effective? In which stages of life – childhood, adolescence and adulthood – will patients encounter physical consequences of the disease? Children with haemophilia and their families are ide-

ally coached before, during and after acute bleeds from a very early age onwards (chapter 3). In the Netherlands (early) diagnosis of an acute bleed, and evaluative measures are only optimally implemented when co-operation with a first-line physiotherapists network is present. These physiotherapists should be included into a network of a haemophilia treatment centre (or national network) and should get feedback from such a centre, at any time.

Although tailored prophylaxis in the Netherlands may seem ideal, stopping prophylaxis by youngsters has also been described (van Dijk et al., 2005). During puberty and adolescence, guidance by a physiotherapist well-known to the person with haemophilia, is essential. Adolescent and middle-aged, or older persons with haemophilia consult a haematologist for yearly check-up, however the first intake in acute situations in many haemophilia treatment centres is not performed by a physiotherapist, but by a nurse or haematologist. We cannot expect that these are trained to thoroughly assess the musculoskeletal system.

Assessment in co-operation with a physiotherapist has two main advantages (figure 1). Firstly, an expert on the musculoskeletal system guarantees better differentiation between a flare-up of haemophilic arthropathy and an acute bleed (chapter 12). A clear diagnosis leads to the most adequate treatment and may save expensive clotting factor concentrates in case of a flare-up of haemophilic arthropathy. The second advantage is that in both situations, acute bleeding as well as in haemophilic arthropathy, an adequate physiotherapeutic treatment plan can be prepared and started. This is, in The Netherlands, effectuated in a first-line setting. The patient will be assessed by a local physiotherapist, who can always rely on (back-up) an experienced physiotherapist or medical doctor of the haemophilia treatment centre. Unfortunately in some centres referral to physiotherapy is effected via the physiatrist (figure 1). Especially in acute situations, i.e. an intra-articular or intramuscular bleed, this causes an unacceptable delay.

When in case of haemophilic arthropathy conservative treatment like pain medication, physiotherapy, orthopaedic devices and adaptations, is insufficient, orthopaedic surgery might be indicated. Optimal rehabilitation under the supervision of a physiotherapist is indicated after each single orthopaedic intervention as well as after multiple joint procedures (de Kleijn et al., 2011). Contact between

the (rehab)specialist from the haemophilia centre and first-line professionals (physiotherapist and/or occupational therapist) guarantees optimal care. The Van Creveldkliniek showed multiple joint procedures to be cost-effective (Schild et al., 2009). We should realise that these complicated procedures will only be possible when optimal postoperative rehabilitation is secured.

CONCLUSION

The role of the physiotherapist is important in all life stages of persons with haemophilia. But that role is also dependent on local possibilities (de Kleijn et al., 2012), number of professionals in a haemophilia comprehensive care team and co-operation with the leading haematologist. In this chapter basic roles are mentioned, which are more or less applicable in all situations. Unfortunately, the quality and level of physiotherapy itself varies in different parts of the world.

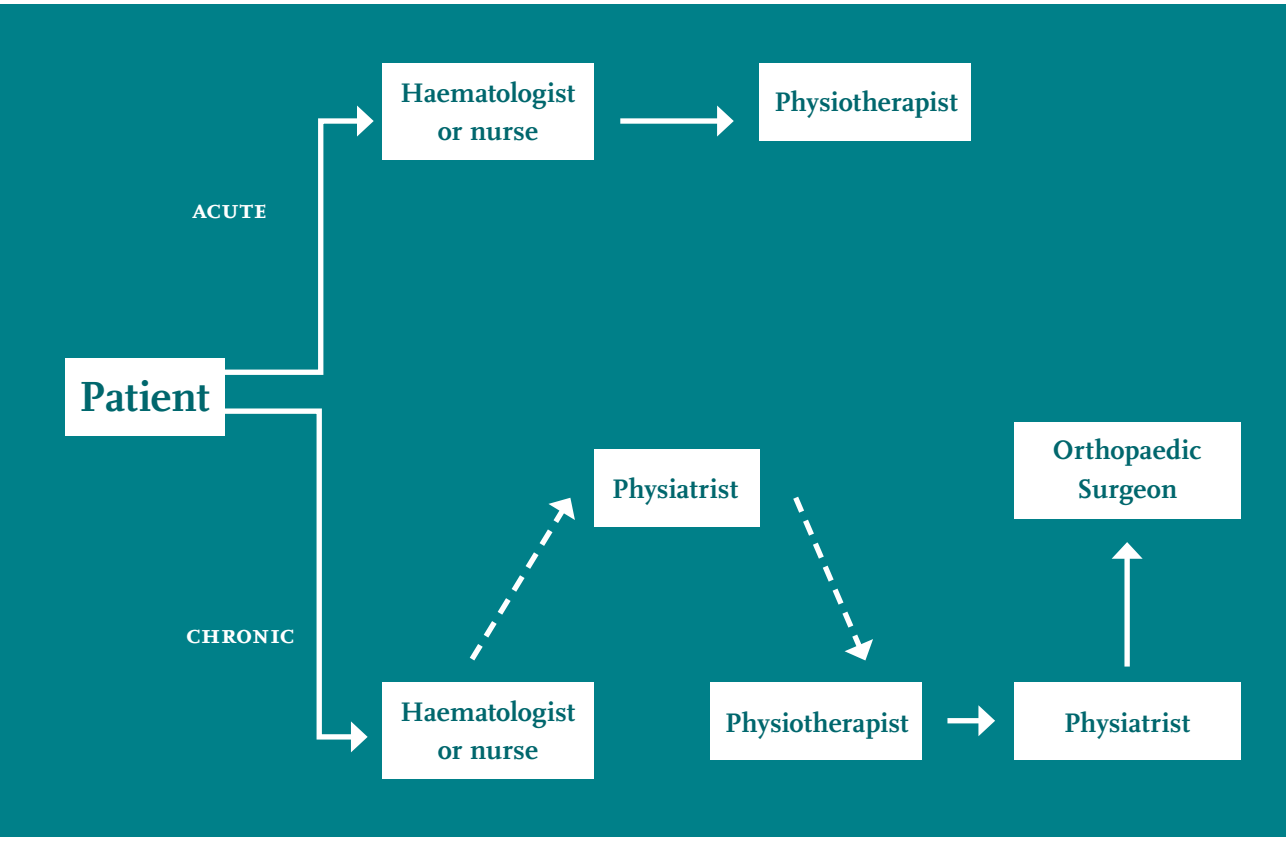


Figure 1. The role of physiotherapy in a haemophilia treatment centre

CASPER VAN KOPPENHAGEN

CHAPTER 2

Comprehensive care in a haemophilia treatment centre

B · The role of the rehabilitation specialist

INTRODUCTION

A specialist in physical medicine and rehabilitation (PMR), also known as physiatrist or rehabilitation physician, or physical and rehabilitation medicine specialist (PRM) outside the United States, is a branch of medicine that aims to enhance and restore functional ability and quality of life to those with physical impairments or disabilities.

This specialist might function as chief practitioner, as co-practitioner or as a consultant involved in all levels of rehabilitation; works mainly in hospitals and rehabilitation centres; co-operates with other medical specialists, paramedics, orthopaedic technicians and psychosocial workers in a multidisciplinary team, suggests treatment goals, develops a treatment plan in consultation with the patient; determines the composition of the management team and manages the team. In rehabilitation medicine special treatment techniques are available, such as virtual reality, sensor technologies, injection techniques, (functional) electrostimulation and robotics. Also, specific expertise within the orthesiology, prosthetics and adjustments (provisions) is used. Regular assessment makes it possible to adjust the interim goal of treatment and/or treatment plan.

DIAGNOSTICS, PROGNOSIS AND HAEMOPHILIA

The rehabilitation specialist uses his diagnostic knowledge and skills of disorders affecting mobility and cognition. He deploys his

specific expertise in biomechanics and movement control mechanisms using specific diagnostic capabilities, such as instrumental movement analysis, electromyography, diagnostic x-ray, blood tests, etc..

The rehabilitation specialist uses his knowledge of the relationship of the impairments and disabilities and problems of social participation, in order to compose a functional prognosis. He also uses his knowledge of the natural history and the expected effect of applying treatments.

A rehabilitation specialist might play an important role in lifetime medical follow-up for persons with haemophilia. While other medical specialists focus on the treatment of diseases or disorders, a rehabilitation specialist focuses in particular on eliminating, reducing or, if possible, avoiding the consequences of the haemophilia. It is not only the function of the body (e.g. muscles or joints), but also the impact of a disease on activity (e.g. walking and daily life activities) and participation (e.g. work or relationships). In a complex disorder like haemophilia with a great impact on the musculoskeletal system, the role of lifelong follow-up is focused on prevention of progressive disability in order to maintain mobility, autonomy and participation.

CONCLUSION

In daily practice the rehabilitation specialist uses instruments and terminology that fit within the International Classification of Functioning, Disability and Health (ICF) model. Within the ICF model human functioning, and the factors affecting it, is approached from the interaction between the different aspects of health and environmental and personal factors. The ICF covers the whole patient and his environment.

The rehabilitation specialist can function as a consultant, as co-practitioner and as chief practitioner, and is involved in all levels of rehabilitation. Through his knowledge and understanding of all the possibilities for specific target groups, he can play a key role in triage, indexing, reference and treatment, according to the principles of stepped care. That is, the rehabilitation specialist provides patients primarily the most effective and efficient form of treatment (or advice) which is possible given the nature and seriousness of the problem.

CHAPTER 2

Comprehensive care in a haemophilia treatment centre

C · The role of the haemophilia nurse

INTRODUCTION

In order to provide high quality care, it is essential for specialist haemophilia professionals to effectively co-operate with each other. Fundamental here is the mutual understanding of each profession's expertise and skills and how these might best be employed to the benefit of persons with haemophilia. Nurses play important roles in health promotion, disease prevention and maintaining health and wellbeing. The haemophilia nurses in most centres perform triage of bleeds and consult the physician only in a later stage. Thus, in most cases the nurse is the first person who the patient meets when entering the haemophilia centre.

ROLE OF THE HAEMOPHILIA NURSE

The haemophilia nurse has the main responsibility for preparation and administration of medication, venepuncture peripheral, and by a central venous access device, providing education and telephone consultation, coordination of (multidisciplinary) care and assist with (clinical) trials (Schrijvers et al., 2014).

The nurse is supposed to, like all other professionals involved in comprehensive care, follow-up patients throughout their lifespan. Each patient has different needs during different phases of his life. For example, in children, education of the parents is one of the most critical issues to avoid needle phobia. Once these children become adolescents, nurses can start negotiating with them directly and

develop a strong relationship, which often lasts for many years. Here the haemophilia nurse plays an important role in acquiring and maintaining self-management skills for the intravenous prophylactic home treatment (Khair et al., 2013). In older patients, it is important to be respectful of their knowledge and experience, but at the same time nurses have to bring their knowledge up to date. All of the above have created a need for highly skilled and specialised nurses to deal with the complexity of haemophilia care (Schrijvers et al., 2014; Colvin et al., 2008).

CURRICULUM

Recently, a curriculum of haemophilia nursing care was developed to achieve agreement on the knowledge and skills acquisition nurses need to have to work in haemophilia (EAHAD Nurses committee, Harrington et al., 2016).

Haemophilia nurses need to have (or acquire) knowledge on:

1. Applied biological science – physiology and presentation and diagnosis of bleeding disorders
2. Treatment and management of bleeding disorders – bleeding, treatment and management, delivery mode, venous access, life stages and complications
3. Genetic practice – Inheritance, family history, knowledge of genetic testing
4. Care management of carriers
5. The impact of a bleeding disorder – psychosocial implications and supportive strategies
6. Evidence based and applied research – awareness, knowledge of and evaluation of evidence for practice
7. Developing specialist role – continuing education, coordinating and facilitating care pathways, inter-professional collaboration

Nurses play important roles in health promotion, disease prevention and maintaining health and wellbeing.

CONCLUSION

It is obvious that in any haemophilia comprehensive care team worldwide the nurse is a key person. In their function they have on the one hand to deal directly with the haematologists and medical staff (e.g. when a patient presents in the centre with an acute bleed), but on the other hand they have, as part of the non-medical comprehensive team, their very own tasks. Worldwide the nursing is a key to the provision of optimal haemophilia care, both as coordination of multidisciplinary care and through the specialist haemophilia nursing contribution.

The outcomes of the aforementioned curriculum are desired at a specialist level; high levels of clinical skills, competence and autonomous decision making, including advanced practice, are needed. This is the challenge of improving the equity of haemophilia care across all regions.

Along with other haemophilia professions, nursing continues to evolve and develop its knowledge base and evidenced clinical competence in order to best respond to the changing needs of people living with haemophilia.

Over the next decade the key challenge for all haemophilia professionals is to address the inequity of haemophilia care across the regions and help all gain access to effective care. This will require more advanced advocacy and empowering skills along with stronger inter-professional organisation.

Besides the physical impact, the personal coping needs attention, i.e. the way a person can handle his disease.

RUUD BOS

CHAPTER 2

Comprehensive care in a haemophilia treatment centre

D · The role of the social worker

INTRODUCTION

The impact of haemophilia is far more than only physical. It is a lifelong disease with consequences for the patient himself, his family, and other persons in his personal context. This personal context may vary per person. (gym)Teachers at primary school and secondary school are often involved for a longer period of time. More variable is the involvement of neighbours, relatives, sports trainers and coaches, but also of persons responsible during activities like scouting. Although in many high income countries the life expectancy is the same as that of their healthy peers, the impact of complications of haemophilia may be serious and long lasting. It is, besides the physical impact, the personal coping that needs attention, i.e. the way a person can handle his disease. The social worker is the professional in the comprehensive care team who addresses these problems and finds solutions in which the patient himself and his parents are actively involved.

THE ROLE OF THE SOCIAL WORKER

Psychosocial counselling is addressed to prevent, reduce, or eliminate those factors which are disturbing adequate lifestyle and thus effective haemophilia treatment. Psychosocial care includes advice, guidance, support, and practical help to parents and child, and can offer mediation to external bodies like school, sports, leisure activities and so on. When professional contact starts at a very young age,

in general the effect of guidance by a social worker has a greater and better impact on the life of an adolescent and adult with haemophilia.

One of the tasks of a social worker is to organise contacts, not only between families with young children with haemophilia, but also during later stages in life. Examples are co-operating with the Dutch Haemophilia Patient Society and sports and education camps, like sailing, survival and skiing camps for haemophilia.

Psychosocial care focuses on:

- Practical circumstances/conditions of home therapy to carry out the directives
- Adherence and coping of parents and child
- Ability and burden of parents and child
- Lifestyle of child and family
- Choice of sports and hobbies: education and provide guidelines on how to act in case of a bleeding, events, emergency (chapter 3)
- School education, including information on clotting factor supply in school, and protocol(s) or guidelines on how to act in case of bleeding events or other emergency

CONCLUSION

The earlier and longer a professional ''bond of trust'' exists between the social worker familiar with haemophilia, and a patient and his family, the more effective they can act. This is beneficial for the quality of life of both patient and his family. Contacts need to be structural, and not only in urgent situations. The psychosocial support of children in our centre takes place during a so-called "structural children's carrousel" and adults during regular out-patient clinics. If follow-up contacts are needed, this can be effectuated. Even home visits for parental guidance, individual support and individual coaching are options as well as creating awareness during for example school visits.

More information can be found on the site of the World Federation of Hemophilia: http://www.wfh.org/en/resources/wfh-treatment-guidelines

KATHELIJN FISCHER, PIET DE KLEIJN AND
EVELINE MAUSER-BUNSCHOTEN

CHAPTER 3

Family integrated and comprehensive care model

INTRODUCTION

Comprehensive haemophilia care promotes physical and psychosocial health and quality of life while decreasing morbidity and mortality in persons with haemophilia (chapter 1). Prophylaxis with clotting factor concentrates is the optimal treatment, and early or primary prophylaxis continued throughout life enables any person with haemophilia an almost normal life. However, precautious input of the different professionals of the comprehensive care team is not yet implemented in haemophilia treatment centres at all. Especially in acute situations, children and their families react "ad hoc" and do not follow a standardised multidisciplinary protocol. Aspects of such a protocol could include:

- Inspection of a joint suspected of bleeding
- Decision making regarding management
- Optimal recovery after a bleed, including use of functional milestones
- Decisions who to involve in this process

In case an intra-articular or intramuscular bleed is treated with clotting factor concentrate only, recovery may be incomplete. This might result in unnecessary long-term physical complications. Treatment other than clotting factor replacement is not officially implemented yet, which may cause recurrent bleeding and musculoskeletal complications in time. Rather than referral to a rehabilitation specialist

or orthopaedic surgeon, immediately starting a training programme under the supervision of an experienced physiotherapist, should be the first choice. If this is implemented adequately, including guidelines and protocols, this approach could prevent late complications of both joint or muscle bleed.

CLINICAL RELEVANCE AND ROLE OF THE NURSE AND SOCIAL WORKER IN HIGH-INCOME COUNTRIES

To prevent bleeding, the optimal treatment is prophylaxis, ideally started after the first joint bleed (Fischer et al., 2016; Fischer et al., 2002). The paediatrician is responsible for prescription, but monitoring of clotting factor consumption is performed by both doctor and nurse (chapter 2c). The nurse is responsible for instruction of home-treatment, which is mostly started by the parents at a young age (Schrijvers et al., 2012). From start of self-infusion until adolescence the nurse supports optimal compliance and adherence to prophylaxis. Parents and caregivers play an important role in the development and self-management of their child with haemophilia. They bear a great responsibility, but often lack sufficient knowledge and skills of all aspects of haemophilia and its management. Obtaining self-management skills takes the whole adolescence (Khair et al., 2015).

The social worker of the comprehensive care team has a major role in helping families to cope with the impact of a lifetime disease on personal and social development. Focusing on acceptance of haemophilia is a key aspect of successfully integrating haemophilia treatment into everyday life (Schrijvers et al., 2015).

CLINICAL RELEVANCE AND ROLE OF THE PHYSIOTHERAPIST IN HIGH-INCOME COUNTRIES

Besides prophylaxis with clotting factor concentrates an adequate physiotherapy protocol should be part of treatment. Such a protocol includes 4 phases:

1 Health instruction
2 Recognition of onset and cessation of a bleed
3 Functional recovery after a bleed has stopped
4 Evaluation

AD 1. HEALTH INSTRUCTION

Prevention in general focuses on a normal motor development including the attitude of the parents, with special attention to the importance of physical activity. Do they offer their child(ren) enough possibilities to be physically active in a safe environment?

Questions like participating in gymnastic classes at (primary) school, for example shortly after a bleeding, or which activities can or cannot be performed, and does the (gym) teacher know the boy has haemophilia? Does he know what to do and do the other schoolteachers know what to do in case of a bleeding? The role of the social worker is to support acceptation, and translation of the consequences towards daily participation at school, during gymnastic lessons, leisure activities, and sports (chapter 2d). All items mentioned include the evaluation of potential medical consequences.

Instructions on aids (such as cold packs, crutches and a sling), and their use are provided. Does the family have adequate aids at home in case of a bleed? As bleeds occur in ankles, knees and elbows, this implicates that the child should have a minimal set of aids at home: a pair of crutches, a sling and four cold packs, as well as an instruction how and how long to apply all of these. Nowadays this can be done by means of an app.

AD 2. RECOGNITION OF ONSET AND CESSATION OF A BLEED

– Acute bleed, recognition and acting.

For ankles, knees and elbows separately, instruction should be given on aspects and function in both the normal situation, and at the time of an acute bleed. In young patients the non-bleeding contralateral joint or side can (almost) always be used as a control. If not, take this into consideration during baseline instructions. In case of a bleed: start with clotting factor! Secondly, relative rest (local or general) is paramount: this includes local rest with the use of aids and/or general rest with adjustments of daily activities and the agenda.

– Did the bleed stop?

The same characteristics to recognise a bleed will be used to determine whether the bleed has stopped. Baseline knowledge will be used to discuss recognition of a bleed in general, but in such a way that the parents are more capable to determine when it did stop. The child has to recognise this too. He has to be encouraged to think about it, and thus take responsibility. When in doubt, families

should contact the haemophilia specialist.
– *Actions to be taken.*
In case of an acute bleed, start with RICE protocol, although this is (partly) still under discussion (chapter 9).

AD 3. FUNCTIONAL RECOVERY AFTER THE BLEED HAS STOPPED

Functional recovery after bleeding has stopped, will be explained step by step to parents and patient. During each step we recognise "Activities" (functional milestones) and "Exercise". The basic idea is that every new milestone is "tailored", and thus fits in the regular daily activities of that person.

From the point of view of the international classification of functioning a person with haemophilia tries to reach any new (next) activity, which fits in his natural behaviour. This should be guided by lack of increase in either warmth or swelling. The following sequence of steps can be distinguished: rest in bed, change position in bed, from lying to sitting, from bed to chair, functional goals inside the house, increase these goals, restart activities of daily life/school/work, and regain level of before the last bleed, inclusive leisure activities and sports.

Key is that exercises specific on body level must be performed, in order to continue more functional exercise, mostly on activity level. For example: after a major knee bleed, first active stabilisation is needed before starting to sit on the edge of the bed, just to control the leg and prevent rebleeding. Importantly, exercise on knee extension is needed before one can proceed from standing to walking, and weight-bearing. Or after a Psoas muscle bleed: start standing when tiptoeing is possible, start walking when standing in an upright position is easy to perform. Both steps require exercises on hip extension, which should always be combined with Psoas muscle inhibition by means of stimulating the antagonist muscles, i.e. abdominal and gluteal muscles.

AD 4. EVALUATION

Evaluation always starts with parents and other persons in the direct environment of the child with haemophilia, like grandparents, gym teacher and neighbours. Ask them to document in which sequence (step by step) it was done and stimulate the child to participate. Conclude which actions by patient and others were adequate,

detect less adequate measures and try to change them.

During evaluation in the haemophilia centre, the paediatrician or physiotherapist discusses with the child and his family what they concluded. If necessary the paediatrician refers the child to other disciplines if things were not adequately done, for example when a local physiotherapist was not ''found'', or when sports activities were restarted too quickly or too late.

CLINICAL RELEVANCE AND ROLE OF THE PHYSIOTHERAPIST IN LOW-INCOME COUNTRIES

Unlike in the Netherlands, where physiotherapists are available in every village, town or neighbourhood, persons with haemophilia in developing countries visit their haemophilia centre both for assessment and physiotherapy. Especially in big cities and metropolitan areas, distances and traffic jams limit access to treatment, disturbing adequate physiotherapy management after a bleeding. In remote areas, where patients have to travel a day or longer in order to reach their haemophilia centre, the advice in case of a moderate bleed could rather be to stay at home and get rest, ice and pain medication. In those situations physiotherapy has to rely on functional exercise, and patients are coached to exercise the physical activities they normally do in their daily lives.

EVIDENCE

Several studies have been performed on home exercise programmes for persons with haemophilia. Hill et al. (2010) describe a home exercise programme in which balance exercises, strength exercises and a walking schedule were performed by 12 patients for 5-7 days a week for 4 months. During this period the patients met with the physiotherapist twice for modification of the exercises. A diary on performed exercises, bleeding frequency, and pain was completed. The exercise programme did not cause any increase in pain or joint and muscle bleeds. No participant reported that the joint bleeds that did occur, were considered a result of exercise. Secondly, the walking component was most regularly performed compared to the isolated exercises. In other words, patients are most likely to do functional integrated exercises rather than isolated non-functional exercises.

Goto et al. (2014) conducted a randomized controlled trial in which 32 patients performed strength exercises, stretching exercis-

es and balance training for 8 weeks. Significant improvements were seen for strength of knee extension, range of motion of the knee and ankle and exercise adherence. Again, there was no change in pain or bleeding frequency during this intervention, which shows that a home programme is safe as long as the patients are instructed carefully and are willing to follow these instructions. In other words the patient becomes physically healthier (improved joint health, muscle strength and balance) and as a result can enjoy a higher quality of life through increased social inclusion and self-esteem.

Self-monitoring (diary/self-assessment) during a home exercise programme is very important. It not only leads to an increase in exercise adherence and self-efficacy, but also reassures the patient that there is no increase in bleeding frequency through physical activities when performed carefully. Besides self-monitoring, patients are also more likely to be compliant and adherent with their health management plan if they have been proactively involved in the decision-making process. Involvement promotes participation in the therapy programme, and thereby enhances the outcome. This can contribute to the empowerment of patient and family members, which is essential for continuation of their active participation, long-term independence and quality of life. Kang et al. (2012) studied the effect of a 5 week self-help group for mothers of a child with haemophilia with professional guidance. The mother's self-efficacy, knowledge of haemophilia, parenting stress, depression and quality of life were improved significantly compared to the control group, which only received education materials. This in turn improves the parent-child relationship and the child's development and functioning.

CONCLUSION

In high-income countries prophylactic treatment is the standard. Currently, there is no published information on preventive (precautious) efforts of a comprehensive care team. To develop a first version of such an approach, including the involvement of young boys and their families, provides an important step in future efforts to optimise comprehensive care.

PAUL MCLAUGHLIN

CHAPTER 4

Standards of practice

INTRODUCTION

A team from Oxford in the early 1960's identified that the musculoskeletal side effects of bleeding required a multi-disciplinary approach to haemophilia care. They were one of the first in the world to implement comprehensive care, with physiotherapy being stated as an integral part of it (Biggs and McFarlane, 1966).

The World Federation of Hemophilia (WFH) guidelines (Srivastava et al., 2013) name physiotherapy as one of the key components of comprehensive haemophilia care, although no further detail is given on what physiotherapy provision should consist of. The NHS England service specification for Haemophilia (2013) recommends that this physiotherapy access should be regular and be carried out by an experienced physiotherapist. Both Canada (2007) and the Nordic countries (2015) have produced more detailed guidance on what should be expected of a physiotherapy service in haemophilia which as well as "assessment and treatment" include the educational and preventative role that physiotherapists may have.

DEVELOPMENT OF UK PHYSIOTHERAPY STANDARDS

As a way of supporting physiotherapists in haemophilia care in the UK, the Haemophilia Chartered Physiotherapists Association (HCPA) was formed in 1990 (Bladen et al., 2016), with an initial remit to "promote the interchange of ideas about the management of patients with congenital bleeding disorders". Within a few short years

the group had gained support from the professional body, the Chartered Society of Physiotherapy (CSP), and the UK Haemophilia Society, to develop standards of care for physiotherapy in haemophilia (Standards for Haemophilia, Chartered Society of Physiotherapy, 1996).They were designed to be used in conjunction with, and as a complement to, the CSP's own Standards of Physiotherapy Practice – a set of professional standards that physiotherapists in the UK must adhere to in order to practice in the UK. They were not meant to replace clinical judgement but to assist in the therapeutic management of patients. They had 5 sections (totalling 12 standards):

- Provision of the service
- Musculoskeletal assessment
- Physiotherapy management
- Provision of information to patient/carer and other relevant agencies
- Annual reviews and documentation

They also suggested what continuing professional development should consist of for clinicians in the field, in order to progress and develop more specific knowledge in haemophilia management, which included the recommendation for attending conferences, as well as local HCPA meetings.

These standards were updated in 2002 (Haemophilia Chartered Physiotherapists Association Standards of Care, Chartered Society of Physiotherapy, revised 2002) and again in 2012 (Service Provision of Physiotherapy for Children and Adults with haemophilia & other inherited bleeding disorders – UK Standards of Care, February 2012). The latest version had standards for both adult and paediatric physiotherapy. They are:

- *Physiotherapy provision within the comprehensive care setting*
  Detailing knowledge, training and dedicated service time
- *Referral and triage*
  Detailing how patients can access physiotherapy and suggested time frames
- *Physiotherapy clinical management*
  Assessment, clinical review and use of outcome measures
- *Regular multi-disciplinary review*
  Function of multi-disciplinary team review, regularity of assessment, use of suggested outcome measures, sharing of information and recording

- *Education*
  The physiotherapist as an educator of patients, peers, team members, schools and workplaces
- *Transition (paediatric only)*
  Role in transition, information sharing and preparation of the patient for transfer to adult care

In early 2017 the UK standards will be reviewed and updated again. The aim is also to present these documents to be endorsed by the United Kingdom Haemophilia Centre Doctor Organisation (UKHCDO) as a commitment to ongoing clinical excellence, and for the standards to be published online within the Haemnet forum (www.haemnet.com). The HCPA acknowledge some aspects of the standards may be viewed as inspirational in nature, with regular attainment of them in day to day clinical practice being difficult. Nevertheless, such standards remain justified to strive towards developing a quality service provision.

DEVELOPMENT OF LOCAL PHYSIOTHERAPY STANDARDS

The autonomy of practice and professional regulations laid down by the professional bodies of UK physiotherapists, is reflected in the construct of these standards. However, it remains that there is no uniform model for the provision of physiotherapy in haemophilia, and that input can vary considerably between haemophilia centres. This is further magnified when considered across Europe, where type of training, roles and responsibilities for the profession of physiotherapy impact upon how haemophilia care may be delivered. However, if such guidance is lacking in other countries, how might similar approaches be made to consider developing a similar document?

The World Confederation for Physical Therapy (WCPT 2011) describes physiotherapy as both, an academic and vocational discipline. Further:

- Physiotherapy should be based on specific knowledge, academic education and autonomous professional responsibility
- Physiotherapists work with people to identify and maximise their ability to move and function
- Physiotherapy provides services to individuals and populations to develop, maintain, restore and enhance health and prevent disease through their lifespan

- Physiotherapy has a key role in enabling people to maximise their quality of life and movement potential within spheres of promotion, prevention, treatment/intervention, habilitation and rehabilitation (physical, psychological, emotional and social well-being)
- Physiotherapy involves the interaction between physiotherapist, patients/clients, other health professionals, families, care givers and communities

The European arm of the WCPT (ER-WCPT) is an organisation of professional physiotherapy associations across 38 countries, which in 2015 listed a strategic plan to present realistic projections of how physiotherapy in Europe can and should develop. As well as promoting the role of physiotherapy and encouraging collaboration, it focuses on how physiotherapy can:

- Demonstrate its engagement with person-centred care
- Demonstrate its innovation and leadership
- Demonstrate and celebrate its wide scope
- Develop its scope of practice
- Articulate and promote its distinctive contribution in meeting patient and population needs
- Demonstrate its clinical and cost-effectiveness, value and benefit

CONCLUSION

Consideration of the above, alongside the WFH guidelines for haemophilia, local haemophilia societies, country specific documents on professional guidelines, and resources such as the WFH physiotherapy curriculum may provide sufficient information on which to base such locally agreed standards. The newly formed physiotherapy committee of EAHAD may provide a forum in which to discuss and develop such standards, to help drive forward the ER-WCPT vision of collaboration across Europe (www.EAHAD.org).

PART 2

Musculoskeletal consequences of haemophilia

LIZE VAN VULPEN

CHAPTER 5

Pathogenesis of haemophilic arthropathy

JOINT BLEEDS

Large peripheral joints (ankles, knees and elbows) are vulnerable to bleeding because of mechanical loading, as this exposes the highly vascularised synovial tissue to the risk of traumatic vessel damage. The importance of loading is stressed by the fact that the first joint bleed in severe haemophilia often occurs when children start walking (and/or running), at a median age of 1.8 years (van Dijk et al., 2005).

Besides the mechanical properties, the coagulation balance within the joint differs from other tissues, contributing to the risk of bleeding. Even in the absence of haemophilia, the coagulation cascade in the joint is impaired compared to other tissues. Expression of tissue factor, the spark initiating the cascade, is relatively low, whereas the activity of some inhibitory factors is increased. Moreover, intra-articular clot lysis is enhanced, therewith decreasing clot stability and further increasing the risk of an ongoing bleeding (Brinkmann et al., 1994).

SYNOVIAL CHANGES

Upon bleeding, a combined cascade of inflammatory and degenerative processes is induced. An important factor is haemoglobin-derived iron. During each intra-articular bleeding iron is released from haemoglobin, the oxygen-binding protein within erythrocytes. This iron is removed by the synovium, which lines the joint cavity:

a thin membrane responsible for removing waste material from the joint cavity and for producing synovial fluid. In case of a severe, ongoing or repeated bleeding, the capacity of the synovium is exceeded causing iron depositions in the form of haemosiderin. The presence of iron evokes an inflammatory response. Although the inflammatory synovial changes are mild, the synovial production of pro-inflammatory mediators, including interleukin-1 (IL-1), IL-6 and tumour necrosis factor (TNF), approaches that of rheumatoid synovium (Valentino et al., 2007). Moreover iron induces genes involved in cell proliferation leading to hyperplasia. This thickening of the synovium in combination with increased metabolism upon inflammation requires an enhanced oxygen supply. In an effort to produce adequate blood flow, vessel formation is stimulated. A rich network of capillaries develops underneath the hypertrophied synovium, but these vessels have an abnormal vascular architecture, increasing the susceptibility to recurrent bleeding (Acharya et al., 2011). In combination with the increased vulnerability to mechanical trauma due to the thickening of the synovial tissue, a vicious cycle may be initiated, leading to chronic synovitis. The time to recover completely from the previous bleeding is too short, inducing a self-perpetuating cycle of haemarthrosis-synovitis-haemarthrosis. This cycle can only be abrogated by fully preventing recurrent bleeding. When three or more bleeds occur in the same joint within a six month period, this is called a "target joint". About 25% of the patients with severe haemophilia develops a target joint (Mulder et al., 2004). Ultimately, the number of bleeds will subside due to fibrotic changes in the synovium.

CARTILAGE

Cartilage changes result from both direct and indirect blood-induced damage. The indirect effects are a result of the above-mentioned synovial hypertrophy and inflammation. The hypertrophied synovium can directly invade the cartilage at the periphery of inflamed joints. Moreover, the inflamed synovial tissue releases cartilage-destructive pro-inflammatory cytokines and cartilage matrix degrading proteases, resulting in long-lasting damage comparable with osteoarthritis (Lafeber et al., 2008).

Direct effects of blood on cartilage result from iron and pro-inflammatory cytokines. Iron is derived from spontaneous lysis of the erythrocytes as well as from erythrocyte-phagocytosis by mono-

cytes/macrophages. These cells are therewith activated causing the release of pro-inflammatory cytokines like IL-1, IL-6 and TNF. These cytokines by itself can induce extracellular matrix degradation via proteases. Moreover, these cytokines activate chondrocytes to increase hydrogen peroxide production, which in combination with iron leads to oxidative stress. Highly toxic hydroxyl radicals are formed leading to chondrocyte apoptosis. Chondrocytes are responsible for the production and maintenance of the extracellular matrix. Apoptosis results in long-lasting impaired matrix turnover. This direct effect of blood is most pronounced on immature articular cartilage, but also is seen on mature and even impaired cartilage (van Vulpen et al., 2016). As such, it is important not only to prevent intra-articular bleedings in children but also in adult patients, even when intra-articular deterioration already exists.

BONE

Although it is clear that blood has devastating effects on bone, leading to subchondral cyst formation, epiphyseal enlargement and osteoporosis, the pathogenic mechanisms underlying these changes are not well understood. Persons with haemophilia are susceptible to the development of osteoporosis as they frequently have predisposing factors: reduced weight-bearing activity, arthropathy, muscle atrophy, a lower body mass index, presence of an inhibitor, and the influence of blood-borne virus infections and its treatment (Gerstner et al., 2009).

Also an intra-articular bleeding itself might induce an imbalance in bone turnover. In a haemophilia mouse model, deformation and loss of trabecular bone are demonstrated already within 2 weeks after a single massive haemarthrosis. In synovium of persons with severe haemophilic arthropathy, a shift towards bone resorption is found in an important molecular pathway involved in bone turnover. These changes all might contribute to disorganised bone remodelling causing the observed malformations, cysts and osteoporosis.

CONCLUSION

It appears that the pathogenesis of haemophilic arthropathy is a multifactorial event, dictated by degenerative and inflammatory processes elicited by the combination of iron and inflammation.

CAESAR HADDAD AND ADLY SABBOUR

CHAPTER 6

Aetiology of intramuscular bleeding and consequences

INTRODUCTION

Muscle bleeds are the second most common complication in haemophilia. In severe haemophilia they represent 10 to 15 % of all bleedings. In general muscle bleeds are more difficult to treat than intra-articular bleeds. Insufficient treatment may result in contractures, limiting the musculoskeletal system, but its complications can be more serious and even become life-threatening. Massive blood loss, compression to nerves and blood vessels, may result in direct and long-term harmful – even life-threatening – complications. If resorption is not complete, pseudotumours may be formed.

FUNCTIONS AND CLASSIFICATIONS OF THE MUSCULAR SYSTEM

The human muscular system plays a vital role in maintaining the posture and movement of the body and its functionality. Muscles are composed of contractile cells called muscle fibres, and involved in all movements. Most of our muscles are "voluntary", controlled by the human will, and almost always attached to bony surfaces. Their contraction results in all kinds of movement in different parts of the skeleton.

Muscle functions are:

- *Ensuring posture and stability*

Skeletal muscles have a role in the static control of posture and the alignment of joints ; they guarantee an upright posture.

- *Providing movement*
  Skeletal muscles are responsible for all voluntary movements of human body parts. They provide force by active contraction and are the motors of the body, converting energy into mechanical action.
- *Provide important proprioceptive input to the central nervous system*
  This is needed to be sure that activities are performed in a more or less ''automatic'' way, so that for instance ''double tasking'' of human beings is possible.
- *Production of warmth*
  As a result of a high metabolic rate, muscles produce a great amount of heat, important to maintain a constant body temperature.

Muscles can be classified in different ways, we provide the classification according to their functional characteristics. This implies that muscles have either a more stabilising or a more mobilising character. To reach muscle balance, muscles with primarily stabilising characteristics demonstrate greater tonic recruitment, i.e. the ability to sustain relatively low-force contractions for long periods of time. Muscles with mainly mobilising characteristics demonstrate greater phasic recruitment, i.e. the ability to generate relatively high forces, albeit briefly (Beeton et al., 2012).

CAUSES OF A MUSCLE BLEED

As a spontaneous muscle bleed is very rare, the general thought is that intramuscular bleeding is due to micro-traumata. We distinguish:

Overexertion

Overusing muscle groups may cause an overstress of muscle tissues, resulting in micro-fibre damage and thus bleeding. Persons with haemophilia may have less muscle strength (atrophy) because of previous joint bleeds and consequent inactivity. As a result even low-impact movement can cause a haemorrhagic episode. This occurs mostly as a result of fatigue, overuse, or improper use leading to muscle strain.

Overstretching

When muscles are not stretched often, they will be relatively short and the related joints become less mobile, resulting in a decrease in range of motion. Putting the muscle under stress and stretching also may result in fibre damage risking intramuscular bleeding.

Direct muscle injury

A sudden trauma, a fall, twist, or blow to the body leading muscle fibres to tear may result in a bleed.

Intramuscular injection

Vaccination without clotting factor replacement may cause an intramuscular bleed.

GENERAL SIGNS OF A MUSCLE BLEED

There is a time gap between the onset of an intramuscular bleed and the first clinical signs, which is clearly different from an intra-articular bleed (Beyer et al., 2010). Muscles can bleed for a long time without any symptoms, depending on the exact location and type of muscle. Muscle bleeds should be treated with clotting factor concentrate as soon as the first sign(s) occur, to prevent muscle damage and minimise the indirect consequences for surrounding tissues. In time muscle damage may cause fibrotic scar tissues and flexion deformities, resulting in a crippling, walking pattern.

Symptoms of a muscle bleed are:

Pain

Pain in the affected muscle can be difficult to detect in muscles located in deeper segments, for example hip rotators and abductors.

Limited Motion

The patient puts his affected part in a position of comfort. Stretching passively or contracting the muscle actively is difficult and or impossible when the bleeding proceeds.

Swelling

The muscle is tense and tight, the swelling can be enormous.

Warmth

The muscle feels warmer than surrounding areas. Again, in deeper located muscles, such as the Iliopsoas muscle, this cannot be determined by manual testing.

ADDITIONAL DIAGNOSTICS AND START OF PHYSIOTHERAPY

Ultrasound has shown to be useful in identifying the location and size of muscle haematomas and the relationship with adjacent anatomic structures (Querol et al., 2011). The rate of resorption of haematomas can be visualised by repeated ultrasound imaging and can thus be used to guide rehabilitation and programmed return to activities, in order to reduce the risk of recurrent bleeding. Visualising the haematoma may also enhance patient's compliance regarding rest, rehabilitation and return to physical activities.

As it is impossible to discuss all different intramuscular bleeds, we provide the basic concept to start. The three examples that are

provided are chosen for the reason that they are common, have a high recurrence rate or complications which determine the (functional) outcome. In general, during a bleed the muscle is not really shorter, as we see when there is a contracture, but it is being protected

ILIOPSOAS MUSCLE BLEED

The Iliopsoas muscle is a typical postural muscle important for standing, walking and running and co-operates closely with the Iliacus muscle. A bleeding in the Iliopsoas muscle may be caused by overloading or overstretching, climbing big steps of stairs or sexual intercourse which puts a lot of tension on the muscle. Especially youngsters between the age of 10 and 20 years are vulnerable. It is a very serious bleed and may end up with severe complications if not treated properly. Recovery may take a long time. In literature up to 42 % of recurrence is described (Beijer et al., 2010). Because this postural, ''soft'' muscle can contain a large amount of blood it may compress the Femoral nerve resulting in function loss of the Quadriceps muscle. The femoral nerve passes the Iliopsoas muscle and innervates, besides the Quadriceps, also the Pectineus, and Sartorius muscles.

CLINICAL SIGNS OF AN ILIOPSOAS MUSCLE BLEED

- Pain in rest: groin and/or lower back
- Pain when straightening the leg, lying prone or standing in upright position
- Inability to fully straighten the hip
- Typical posture: hyper lumbar lordosis and resting hip position in flexion
- If the bleeding persists, it can specifically lead to decreased sensibility in the anterior and internal part of the thigh

The pain from an Iiopsoas muscle bleed on the right side may be confused with appendicitis or other abdominal diseases. There may even be a positive Blumberg's sign which is indicative of appendicitis.

CALF MUSCLE BLEED (TRICEPS SURAE)

This bi-articular muscle, located in the posterior part of the lower extremity ends up in the Achilles tendon. Its role is to provide plantar flexion during walking, to stabilise the ankle complex during

locomotion, and to empower jumping. A bleed into the proximal part of the Calf muscle often results in an inability to take full steps and a tendency to toe walking. This bleed is often caused by a sudden muscular contraction during sports, running, or jumping or direct injury .

CLINICAL SIGNS OF A CALF MUSCLE BLEED

- Pain and swelling
- Pain is aggravated upon activation
- Pain when stretching the muscle
- Tenderness and swelling in the lower leg
- Limited range of motion in the ankle, combined with lack of maximal extension in the knee
- Unable to stand on flat feet
- Unable to walk properly, certainly with some pace

FOREARM MUSCLE BLEED

Forearm muscles, involved in the movements of the wrist, are divided into two compartments: flexors and extensors. There are 8 muscles in the anterior forearm and 12 in the posterior forearm. Increased pressure in the anterior compartment of the forearm, for example in case of a bleed near the Brachial artery, may interrupt normal blood flow to the compartment and result in ischaemic damage to the deep flexors, causing muscle scarring and flexion deformity of the wrist and fingers, known as Volkmann's contracture. This is defined as a permanent flexion contracture of the hand at the wrist, resulting in a claw-like deformity of the hand and fingers. Causes of a forearm muscle bleed are sudden stress, too much or intense tension on the muscle for a long time as in participating certain sports (for example tennis, bowling, baseball) or playing musical instruments that strain the forearm (horn, piano). The clinical signs of a forearm muscle bleed are inability (and pain) of finger extension especially in combination with dorsiflexion of the wrist. The function of the entire upper extremity is minimal, from a functional point of view.

DEALING WITH MUSCLE BLEEDS

Recovery after a severe muscle bleed usually takes a long time, because it is difficult to fully stabilise the muscle and prevent it from moving. Phases of the healing process are:

- *Acute inflammation*. Phase immediately after onset of the bleed. It may last for around 5 days after the bleed has stopped. In this stage the patient is at risk to develop a rebleeding.
- *Repair and regeneration stage*. This starts when the inflammation phase ends and lasts around 6 weeks. There is an increased fibroblast activity, resulting in increased connective tissue strength and formation of adhesion. The muscles and connective tissues are not yet at full strength and the patient remains at risk of recurrent bleeding.
- *Remodelling stage*. This stage may last up to 6 months. In the remodelling stage muscle strength training to challenge its abilities can be started. Without complications, an exercise programme is designed. The training should begin gently and slowly increase. Stressing the muscles and connective tissues stimulates growth and improves functionality. Lack of training results in weak tissues that are vulnerable to rebleeding.

THERAPY

MEDICAL TREATMENT

Prompt infusion of sufficient amounts of clotting factor concentrates. In case of severe life-threatening bleeds complete clotting factor correction is required. Exact dose, infusion frequency and duration depend on the severity and location of the bleeding and the availability of clotting factor concentrate (for guidelines see www.wfh.org).

REST

In case of a bleed in the lower extremities: crutches or keep the patient off his feet! In case of an arm bleed: restrict arm movement using a sling. Depending on the severity of the bleeding complete bed rest may be indicated.

MONITORING

The patient should be monitored for neurovascular compressions. The arm or leg can be temporarily supported in a splint or half cast, but only after bleeding has stopped. If the splint can be adjusted it is preferable to modify it over time to gently stretch the muscle back to its normal length.

COMPRESSION

Any type of compression (bandages, strap) is strictly NOT recommended during a muscle bleed because it can increase the intramuscular pressure and compress passing nerves.

ICE

Ice/cold packs can be applied for 10-15 minutes every 2 to 3 hours to relieve pain, reduce inflammation. As it becomes easier to move and use the muscle partly, oedema will decrease more easily. Do not apply ice in direct contact with the skin; for deeper muscles, as the Iliopsoas muscle, ice is not indicated.

ELEVATION

Elevation of the injured area with the use of a pillow to help reduce the swelling.

Cave: do not take painkillers containing NSAIDS, do not put the muscle into hot water, do not apply hot packs to the bleeding area.

EXERCISE

Once the bleeding has stopped, and the muscle is no longer tense and painful, the patient can begin to use the muscle in the pain-free range, it is best to start with light isometric muscle contractions. At this stage the patient should not push himself "through" the pain and avoid stretching the muscle as this may cause a rebleed. Crutches to support these movements are required. It is important to train the antagonist muscle too to prevent a contracture of the affected muscle. Intensifying the exercises depends on the clinical situation

	CLINICAL PRESENTATION	AIMS OF PHYSIOTHERAPY	POSSIBLE PHYSIOTHERAPY STRATEGIES
ACUTE MUSCLE BLEED	• Pain on palpation • Pain on stretching muscle • Limitation on movement • Bruising may be evident • Neural compression	• Relieve pain • Reduce swelling • Restore function • Prevent recurrence programme	• Rest • Ice • Elevation • Electrotherapy • Graded exercise • Appropriate stretching • Advice and education

Table. Aims and strategy in muscle bleeds (Kim, 1993)

Picture 1a. Patient walking with a flexed hip after a Psoas bleed

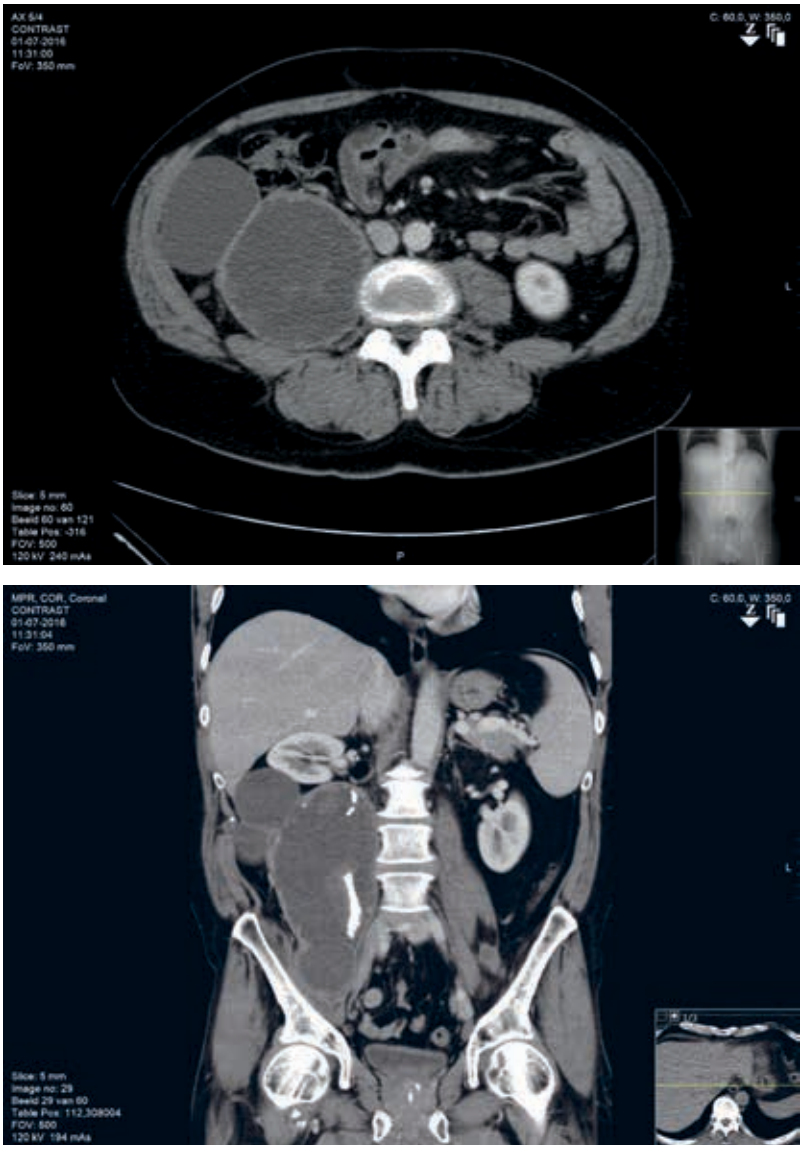
Picture 1b. Training hip extension during stance phase to prevent contracture and improve gait

and pain. Once pain-free range of motion and muscle flexibility have been achieved, resistance exercises can be started to increase muscle strength. Start with very light weights, slightly increasing the number of repetitions and adding weight. Proprioceptive exercises are indicated once full weight-bearing and range of motion are achieved. They are important to regain the equilibrium in order to prevent recurrent bleeding (picture 1a and 1b).

COMPLICATIONS OF MUSCLE BLEEDS

CONTRACTURES

Contractures are mostly seen as an equinus deformity of the ankle, or at the knee or elbow in the form of a flexion deformity (Atkins et al., 1987).The cause is fibrosis following intramuscular haematoma, which may be complicated by a peripheral nerve palsy causing muscle imbalance.



Picture 2. Pseudotumor of the Iliopsoasmuscle

PSEUDOTUMOUR

A pseudotumour is a progressive cystic swelling involving the muscle. It is a rare but serious complication. The majority of pseudotumours are seen in the long bones. Repeated and unresolved haematomas lead to encapsulation and calcification, with progressive enlargement of the mass and subsequent erosion of the adjacent bone. The most frequently affected muscles are Psoas, Iliac, Quadriceps, and the Soleus of the Triceps surae muscle. Ultrasound and

CT scan are indicated to support the diagnosis and determine the size of the bleeding and the involvement of vital parts (picture 2).

COMPARTMENT SYNDROME

Compartment syndrome is an increased pressure due to bleeding within one of the body's compartments which contains muscles and nerves. Early recognition of significant bleeding with swelling in an extremity compartment (e.g. forearm, wrist, or calf muscle) is essential. Clotting factor correction should be adjusted to this situation. A bleed that is treated in an early phase stops before pulse and nerve function are impaired. In case pain emerges increasing to a maximum and the distal part of the extremity becomes paler and cooler than the opposite corresponding distal extremity, extreme caution is required and even surgical intervention (fasciotomy) might be indicated.

In case an intra-articular or intramuscular bleed is treated with clotting factor concentrate only, recovery may be incomplete resulting in long-term physical complications.

WYPKE DE BOER AND JANJAAP VAN DER NET

CHAPTER 7

Normal motor development and haemophilia

INTRODUCTION

Child development takes place in several domains that strongly influence each other, amongst others physical, social, cognitive, behaviour and speech development. In this chapter we will focus on motor development and physical activity.

Bleeding risk in children with haemophilia is heavily dependent on the treatment protocol that is available in a specific country. If on demand treatment is the leading protocol, bleeds will occur and damage may develop in the tissues that have been exposed to the bleed. Consequently this may result in musculoskeletal impairments or cognitive and motor-planning disorders in cases where the bleed was intracranial. The result of all this is that the prognosis

of joint health, functional capabilities and physical activity level of developing children may differ substantially per region in the world.

If during development (e.g. motor, physical or cognitive development) bleeds occur one may observe adaptation behaviour. A child may change his behaviour temporarily to adapt to the physical impairments. Finally behaviour becomes compensatory to regain the functionality that has been lost.

Case 1

A toddler 2 years of age developed an ankle bleed, consequently he stopped walking and chose to get around "bottom shuffling". This is an adaptation strategy.

Case 2

A teenager developed a contracture in the right elbow after repetitive bleeds. As a tennis player he consequently developed left-handedness when playing tennis. This is a compensatory strategy.

MOTOR DEVELOPMENT

Typical motor development is characterised by a variation of movements, within the child as well as between children. The diversity increases with age and is related to differences in motor experience. Certain "motor milestones" are prominent, e.g. standing or walking independently, but these milestones are not fixed time points on every child's calendar. One child may walk independently at the age of 10 months, while another child might not be able to achieve this until he is 18 months old. When children acquire new motor milestones, the execution will usually be "uncoordinated" at first. As the child repeats the movement more frequently, he develops a fluent, coordinated and automated motor skill. For an optimal motor development, a healthy musculoskeletal system is important, as well as a healthy neuro-motor system. Non-walking and lack of motor variation are alarm signals, which should lead to an examination of the musculoskeletal system as well as the neuro-motor system by a (paediatric-) physiotherapist.

The development of children with haemophilia in the Netherlands, as in most countries with a similar prophylaxis regime, is comparable to their healthy peers. They have got similar motor skills, daily life activities, aerobic capacity and muscle strength. The majority has a normal range of motion.

In every developmental stage the child may be at risk for a bleed, especially when a child learns a new motor skill. Several of the main risk factors will be discussed below. Motor development is motor learning by "trial and error". As parents with a child with haemophilia are tempted to (over) protect their child, this may obstruct these children to explore and gain motor experiences.

Parents should be notified about the importance of physical play to allow motor learning for a normal motor and cognitive development by their (paediatric-) physiotherapist. The fact that a physically fit child will be better protected against bleeds because of his motor skills, needs to be addressed. The parents should be informed on how to find a balance between letting the child explore his world and protecting the child.

In the first 6 months of life bleeds are relatively rare. If bleeds do occur, it is frequently the result of an unexpected movement of the child while handling it during grooming. The moment a child starts to crawl and walk the risk of a bleed increases, especially bumping the head, or falling on the head increases the risk of (intra-) cranial bleeds. In general the same protective measures apply as in any other child, like putting up "stair-gates" and covering up (sharp) edges on furniture.

The toddler, at the age of 1-4 years, brings an extra challenge. The child becomes increasingly active, climbs on furniture, starts running and jumping and learns how to ride a tricycle (or bicycle). The child often does not see any danger. He is seeking autonomy, he wants to do and discover everything by himself. He imitates behaviour of others and this can lead to increased risks. In this time in his life the use of prophylaxis should be started, when available. This will likely reduce the risk and number of bleeds. A child should get the opportunity to develop himself within safe boundaries. Parents and caretakers should be aware that continuously slowing a child down or warning him to be careful, can make the child apprehen-

sive. This may undermine his development of self-confidence. In this stage the same safety precautions apply as with any toddler. While learning how to ride a bicycle a helmet is advised as a safety precaution, as may elbow and knee protectors.

A 4-6-year-old child becomes increasingly independent. He goes to school and is able to perform most activities of daily life independently. The fact that he is very active in climbing, running, riding bicycle and interactive play makes him especially prone to joint bleeds. However, learning to swim is a safe activity for children with haemophilia at this age. And swimming is generally regarded as a safe leisure time or sport activity further in life.

In a 6-12 year-old the developmental focus is on agility, strength, speed and social encounter. Playground activities, active leisure and sports are demanding these physical skills, especially since they are group activities. The frequency in muscle and joint bleeds may increase as the child becomes more involved in these activities. Social as well as physical development plays an important role in further development. Parents and children may start to seek the best (sport) activity and ask for counselling. The (paediatric-) physiotherapist is the designated professional to advise in the choice for a sport, together with the (paediatric-) haematologist. In literature there is a difference of opinion on what is, or is not, a risky sport for children with haemophilia. In general caution is advised in high-impact sports and contact-sports, like soccer, which are often combined. Depending on the prophylaxis regime available in the country or region the child lives in, a choice should be made. To see if a sport is suitable for a child, aspects of the sport itself, as well as child factors are considered. These are for example, age, severity of the haemophilia, interest, motivation and physical capacities of the child. It is a personal deliberation. Pros and cons of certain sports are to be discussed. To see if the chosen sport is still suitable for that particular child, one will need to evaluate regularly.

In puberty, age 12-17 years, a child becomes taller, his weight increases and his body proportions are changing. During a growth spurt there is a difference in growth speed between different tissues. Bones grow faster than muscles and tendons. Particularly peri-articular muscle mass may relatively decrease in this phase. This can

lead to temporarily decreased (dynamic) stability in a joint.

The body of a teenager feels and moves differently, it is less flexible and therefore more prone to accidents and bleeding risks (both in muscles and joints). The body is more vulnerable to overuse and sports-related trauma, e.g. in this phase there is more risk of a Psoas muscle bleed, or knee and ankle bleeds, especially in competitive soccer, but also to non-bleed related injuries, such as tendonitis and bursitis ("overuse" injuries). As these may give symptoms very similar to musculoskeletal bleeds, it is important that the child and his health providers are alert and provide good monitoring.

Besides physical changes, changes in behaviour (more risk seeking, less compliance with treatment and medical advice and experimenting) and psychosocial behaviour (relationships and independence) play a major role in an increased bleeding risk.

Teenagers in general do not except "no" for an answer, they push their limits and most of them are unaware of the risks they take and consequently of potential joint damage later in life. Considering the fact that they have often been on prophylaxis all their life, they usually do not assess the risk correctly in not consequently taking prophylaxis. It is important to educate them on relevant (joint) health issues such as taking their prophylaxis in time, to use joint protection, to follow warm-up and cool-down regimes during sport events, all to prevent musculoskeletal injuries.

MUSCULOSKELETAL PERFORMANCE AND EXERCISE

As from the age of 6 years typically bone mineral density (BMD), muscle strength, flexibility, speed and agility increase, and this continues well beyond the adolescent age. BMD, muscle strength and flexibility classically are trained by "physiological loading" of the musculoskeletal system. Speed and agility are trained through repetition and increased complexity of the activity.

Early life is also characterised by a development of the exercise system (cardio-respiratory and musculoskeletal system), reaching its final capacity around the age of 27. Young children have a relatively well-developed anaerobic system, this enables playing with short bouts of activities. With increasing age, the aerobe-capacity develops and becomes more prevalent. Daily training of the exercise system is a prerequisite for this growth and development. Therefore many countries provide guidelines for the daily and weekly amount of healthy exercise for children (and adults). Besides monitoring

motor development, it is also important to monitor cardio-respiratory fitness.

PREVENTION

Prevention starts with the fine-tuning of the use of prophylaxis, if available, to the moment of physical activities and playing sports. Optimum timing would be a few hours before the activity. Depending on the severity of the haemophilia, the individual half-life of the clotting factor concentrate used and the training intensity, the paediatric haematologist will suggest a prophylactic scheme.

Physical activity such as sports are important for any child, but even more so for a child with haemophilia. Besides participating and the general effects on health and quality of life, the effect of playing sports is beneficial to, amongst other things, motor development, health related fitness, endurance, muscle strength and coordination. Proprioception is of great importance for the control and timing of movements. It demands substantial training efforts to increase skills and agility. In sports there are often unexpected explosive movements. It is very important that children have been taught a correct technique to execute a movement correctly. This has a preventative effect on bleeds. Proper warm-up and cool-down practices have shown to be effective to prevent sports-related injuries in healthy children and it is advocated for children with haemophilia as well (chapter 15).

Inactive children with little movement experience are more prone to a bleed compared to active children. Most (sports-related) injuries are caused by contact, mostly with other players or material. Fatigue can lead to injuries because of decreasing coordination and anticipation. It is of great importance to find the optimal balance between stimulating playing sports on one hand and preventing unnecessary bleeds on the other hand.

During playing sports proper guidance is important. The coach or trainer needs to be well informed about the haemophilia and its potential problems. Possibly the child will need to be coached or trained prior to starting a sport, to be able to meet certain requirements. Besides good technique, protective sports gear (including good shoes) is essential.

Obesity and overweight are more prevalent in children with haemophilia compared to their healthy peers. This might have a negative

influence on joint health and the quality of life. Mechanical overuse due to overweight may lead to higher risk of joint bleeds and early arthropathy.

It is expected that overweight may be related to decreased physical activity and poor nutritional habits, as is the case in healthy children. Overprotection in children with haemophilia also may lead to decreased physical activity. These two factors might be the explanation for the fact that overweight in children with haemophilia has shown to be more prevalent. Health education in children with haemophilia should also include prevention of overweight and obesity.

TREATMENT AFTER PHYSICAL ACTIVITY-RELATED INJURIES IN YOUNG CHILDREN

Recognising a muscle or joint bleed in young children can be difficult. Parents might notice their child starts to cry when changing clothes or diapering, the child may be limited in its movements and fixate his arm or leg, or show a "limp" during ambulation. An older child may complain about pain or a tingling sensation around a joint.

In case of a (joint) bleed keeping children immobilised is a challenge, especially younger children. They tend to bear weight on their injured limb prematurely. They do not understand the necessity of (temporary) non-weight bearing until pain and swelling has subsided for (total) recovery and prevention of a potential recurrent bleed and/or joint damage. Defining a day programme for these children that provides enough non-weight bearing time to be therapeutic, is a challenge for both, parents and therapists. Temporary absence from physical education and sports participation are part of the recovery programme.

Learning how to use crutches usually starts around the age of 8 years. Before that time a wheelchair is used. Bicycles without pedals can be used to be ambulant and non-weight bearing at the same time (picture 1). The use of a sling or another movement restriction in case of elbow bleeds could help to speed up recovery.

After the first phase of recovery in which limited joint and muscle use is allowed, one should start soon with exercise therapy to optimise full recovery and to prevent negative effects of joint immobilisation and temporary rest, such as muscle atrophy, loss of endurance and joint stiffness.

Picture 1. Bicycle without pedals can be used to be ambulant and non-weight bearing at the same time.

CONCLUSION

In the life of a growing child with haemophilia, besides availability of prophylaxis, factors like motor development, participating in sports and knowledge of muscle and joint bleeds have an impact on their functioning in daily life and therefore on quality of life.

In puberty, less compliance with treatment and medical advice, experimenting, and psychosocial behaviour play an important role in increasing the bleeding risk.

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CHAPTER 8

Acute bleed, physiotherapy protocol and use of ultrasound

MANAGEMENT OF ACUTE HAEMARTHROSIS AND HAEMATOMA

Repeated spontaneous and traumatic musculoskeletal bleeding is the predominant clinical feature of haemophilia. Bleeding in persons with severe haemophilia can occur spontaneously without any obvious cause or trauma and account for 60 % of all bleeding episodes. In countries where prophylaxis is common place, the ankle joint is the most common site of joint bleed, whereas, the knee joint is more common when access to prophylaxis is not routine treatment. The underlying cause of the dominance in ankle joint bleeding is not known, however improved quality of life and participation in higher impact sports and activities associated with greater compressive loading and shear joint forces at the ankle joint may be contributing factors (Buzzard et al., 1995).

An acute haemarthrosis is characterised as a painful, swollen, flexed joint with minimal joint movement due to the increased volumes of intra-articular blood. Furthermore, if the knee or ankle is involved, weight bearing is restricted.

Full recovery from a haemarthrosis may take 2-6 weeks and during this period, joint range of motion is restricted, use of the muscles of the affected limb reduced, and subacute haemarthrosis may occur prior to complete recovery.

When a joint bleed occurs, the most important treatment is immediate factor replacement. The goal of physiotherapy in the initial acute phase is to decrease pain and swelling, support wound healing and maintain haemostasis, and is currently based on the concept of immediate (P)RICE regime (Zourikian et al., 2011). With regards to acute muscle haematomas, all therapies that impede the haemostatic process, such as massages and source of warmth, are contraindicated.

The RICE regime is described in detail in chapter 9. The "rest" imposed to a joint can be viewed in the light of immobilisation and/or non-weight-bearing. When haemostasis is impaired, synovial tissue may be predisposed to rebleeding during the fragile, wound healing phases of angiogenesis and fibroblast proliferation (Hoffman, 2005).

In the past, bed rest and prolonged joint immobilisation were advocated after a haemarthrosis, leading to concomitant complications, such as muscle atrophy and contractures. Currently, it is advocated that joints should be rested in a functional non-weight-bearing position for the first 48–72 hours following a bleed to prevent further haemorrhage. The use of crutches (or pushchair/wheelchair for young children) is recommended for lower limb joint bleeds and a support sling for upper limb joint bleeds. Externally applied compression helps to limit joint swelling by increasing external pressure and limiting joint capsule distension and therefore leading to a halt in bleeding by achieving tamponade sooner (Charalambides et al., 2005). Elevation is also an effective method to reduce swelling due to haemarthrosis. Positioning of the swollen area above the level of the heart helps by reducing tissue capillary hydrostatic pressure and using gravity to help with fluid return.

After the short immobilisation period, conservative, early, gentle mobilisation can be performed once haemostasis is achieved and the volume of blood within the joint begins to decrease. At no stage whilst the joint is still swollen, should it be passively forced to increase range of motion. As regards to the load that can be applied to a lower limb joint during the acute phase, an animal study (Hakobyan et al., 2005) indicated that forced loading of a joint with intra-articular blood results in more cartilage matrix damage when compared without forced loading. Thus, it may be beneficial to avoid weight bearing of a joint with intra-articular blood (Acharya et al., 2012). A balance should be established between rest, early mobilisa-

tion, and weight bearing to prevent unwanted complications associated with immobilisation, while minimising rebleeding, synovitis, and cartilage damage.

OVERVIEW OF PHYSIOTHERAPY MANAGEMENT FOR HAEMARTHROSES

ACUTE

- **Rest, Ice, Elevation**
- **Minimise loading / weight-bearing**
- **Education to prevent rebleeding**

SUB-ACUTE

- **Gentle and gradual mobilisation and active range of motion exercises**
- **Isometric muscle strengthening**

REHABILITATION TO RETURN TO PRE-BLEED STATUS AND PREVENT TARGET JOINT DEVELOPMENT

- **Progression of mobilisation and range of motion exercises**
- **Concentric muscle strengthening**
- **Consider hydrotherapy and functional exercise**
- **Assessment and treatment of biomechanical and muscle function**
- **Education, advice and guidance to prevent re-bleeding / target joint development and return to sports and physical activities**

As the haemarthrosis resolves, a specific muscle strengthening programme is advocated, beginning with isometric contractions, followed by concentric exercises. Aggressive passive stretching should be avoided. Following a muscle haematoma, low-intensity stretching exercises should be started within the limits of pain in order to distend the maturing scar at a phase where it is still plastic (Sorensen et al., 2012). Hydrotherapy is particularly recommended for patients with multiple joint arthropathy, for whom land-based functional stretching and strengthening is difficult (Blamey et al., 2010). An assessment of global biomechanical and muscle function together with posture is important in order to identify possible predis-

posing factors, as well as prevent compensation strategies. The decision to conclude the rehabilitation can be based on the ability to move, stretch and control the relevant limb to pre-bleed levels and the pain-free use of the joint or limb. In some cases where simple movements of daily living have induced the haemarthrosis or haematoma, it is important to continue rehabilitation beyond pre-bleed levels to improve functional movement patterns. Determining the possible cause of joint bleeding along with education and strategies to prevent rebleeding and development of a target joint is an important part of the rehabilitative process. In children, this may involve multiple sources of information and resources involving parents and teachers.

USE OF POINT-OF-CARE ULTRASOUND

Determining whether a painful joint is bleeding and detecting early signs of joint damage are two current challenges in haemophilia management. There is increasing interest in utilising point-of-care ultrasound to evaluate joints and muscles. A point-of-care ultrasound approach is usually optimised by adopting a focused, decision-making strategy to answer specific clinical questions, or identify relevant biomarkers, without the need for detailed, radiological assessment (Martinoli et al., 2016). Point-of-care ultrasound is not comparable with a comprehensive ultrasound examination performed by imaging specialists, but rather supports a more time-efficient, straightforward, real-time approach to critical clinical issues that may affect patient management.

A review of the use of ultrasound in haemophilia concluded that point-of care ultrasound is of value in acute haemarthrosis, as it can be used to objectively identify the presence of blood in the joints, measure its size, pinpoint its location, assess its evolution and confirm its complete disappearance (Querol et al., 2012). A study utilised ultrasound to assess joint bleeding in adults with haemophilia and demonstrated that two-thirds of acutely painful joints were not haemarthroses (Kidder et al., 2015). In those painful joints without signs of haemarthrosis, findings of synovitis, tendinitis, enthesitis, bursitis and fat pad inflammation were found.

Ultrasound imaging has been shown to be effective in identifying early synovial and cartilage changes as part of the patient's routine outpatient clinic appointment. The recently developed Haemophilia Early Arthropathy Detection with Ultrasound Score (HEAD-US) has

been shown to be repeatable in identifying synovial and cartilage changes in haemophilic joints (Martinoli et al., 2013). The HEAD-US protocol has been developed for non-imaging specialists, as a fast to perform technique, capable of screening six joints (the elbows, knees and ankles) in a single examination. The HEAD-US system has also been designed to recognise certain biomarkers reflecting disease activity and osteochondral damage. It is proposed that in daily practice, the HEAD-US system would find its place as a supplement to physical examination assessment tools, such as the Haemophilia Joint Health Score (HJHS), in order to provide more objective assessment of findings and increase sensitivity in detecting joint abnormalities. In a recent study, Altisent and colleagues (2016) compared the HJHS, HEAD-US scores and bleeding frequencies of joints in 25 patients aged 4–19 years with severe haemophilia A, and found ultrasound examination, but not clinical examinations were related to bleeding frequency. Interestingly signs of blood induced joint damage on ultrasound were found in almost twenty percent of joints with a normal clinical evaluation, and the absence of joint damage was found in twelve percent of joints with abnormalities on clinical evaluation. In a similar study comparing the same outcomes from 6 elbows, 20 knees and 38 ankles of 32 children with haemophilia aged 4–16 years, Foppen et al. (2016) noted ultrasound showed abnormalities in ten percent of joints with reported bleeds, and discrepancies between clinical function and ultrasound assessment in six percent of joints.

CONCLUSION

Point-of-care ultrasound is emerging as an important modality as a supplement to physical examination assessment tools, such as the HJHS, in order to provide more objective assessment of findings and increase sensitivity in detecting musculoskeletal bleeding together with joint abnormalities, and therefore may in future facilitate a personalised approach to haemophilia care. Furthermore, it has the potential to enhance patient education and knowledge, as well as compliance with treatment interventions.

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CHAPTER 9

The use of RICE in haemarthrosis

INTRODUCTION

The concept of Rest-Ice-Compression-Elevation (RICE) was introduced in the first aid and sports medicine fields in the 1970s as a treatment for acute injury, and transferred into the adjunct management of haemarthrosis in persons with haemophilia, aside from clotting factor concentrate infusion. Recommendations for RICE are widely evident in articles, pamphlets, books and websites across haemophilia organisations around the world. However, there has not been a discussion of the risks or benefits, or evidence that this method of adjunct treatment is relevant in haemophilia. There are no evidence-supported guidelines for the application of RICE in haemophilia. An intra-articular bleeding in a person with haemophilia is not the same as injury from a soft tissue trauma, sprain or even intra-articular bleeding in a person without haemophilia. It is not logical that we could use an identical strategy to treat a patient with a coagulation disorder. There are specific, unique processes, that are present in haemarthrosis, along with the coagulation defect, such as swelling, inflammation, and blood induced joint damage, that can occur and must be considered when offering interventions.

In this chapter, we will review each part of RICE and provide information, evidence and suggestions for application in haemophilia.

REST

The main goals of rest are minimising direct blood-induced joint damage and inflammation, protecting the joint from continued bleeding or early rebleeding, and promoting healing. However, there are both benefits and risks with rest, so it is critical to evaluate each situation and determine how best to advise rest parameters (chapter 14).

The presence of blood within the joint space leads to damage (Jansen et al., 2008). Weight-bearing on a joint that contains intra-articular blood can cause additional damage to the cartilage, especially young cartilage. It is unclear how long it takes to remove the blood from the joint space, but estimates are around 2 weeks. Rest will influence the healing process and inflammation. Each joint bleed is a type of wound within the synovial membrane. In order for a wound to heal, it must go through a well-defined process, including four overlapping phases (Buckwalter et al., 1999; Guyton et al., 2000; Hoffman et al., 2010):

- Haemostasis (immediately at injury)
- Inflammation (within minutes - 7 days)
- Proliferation/repair (2 days - 3 weeks)
- Remodelling/resolution (weeks/months)

In the case of haemarthrosis and rest, emphasis is placed on the first 2 phases which may last for 2 weeks or even more if repeated bleeds occur in the same joint. Hoffman (2010) demonstrated impaired wound healing in haemophilia B mice. Increased angiogenesis (new vessel formation) in the synovium occurs in the proliferative phase and may add to continued bleeding and rebleeding. In response, perhaps the advice for rest should extend until 2 weeks or more, to protect the fragile vessels from re-bleeding. Hoffman also showed that a single dose of clotting factor concentrate was not sufficient to support complete wound healing. The animals needed 7 days of dosing to complete wound healing. This underscores the possibility only one dose may not be sufficient to support wound healing and that all four phases may be prolonged in haemophilia, especially if treatment with adequate clotting factor concentrate is not possible, for whatever reason.

Blood also causes both, direct and indirect negative effects to the synovial membrane and cartilage, including a robust inflammatory response within the joint space and the synovium (chapter 5). Even after the blood has been resorbed, haemosiderin continues to cause

inflammation. Other inflammatory markers can remain in the synovial fluid for weeks following a bleed. Too much loading/weight-bearing during periods of any inflammation is not conducive to healing (Buckwalter et al., 1999) and can cause more damage by delaying or preventing the repair phase, thus further prolonging healing. Controlled loading, however, can offer a positive effect on healing when applied at the right time, during the proliferation/remodelling phases, where it can accelerate restoration of the tissues.

PRACTICAL APPLICATION OF REST

Rest can be used right away, as first aid for a bleeding joint. This can protect the joint from excessive movement and weight-bearing, and potentially more bleeding from mechanical pinching of swollen tissues, protect the cartilage from weight-bearing in the presence of blood. Rest also helps to manage pain and hold the joint in a comfortable position while infusing clotting factor concentrate or during transport to the clinic for assessment.

When prescribing rest for your patient consider the following:

1.Where is the location of the haemarthrosis?

If a weight-bearing joint, determine the length of time to recommend non-weight bearing. There are 2 main reasons not to allow weight-bearing within the first 2 weeks or more. During the inflammatory phase there is a risk of rebleeding because of the fragile vessels forming through angiogenesis. There is also the potential for more cartilage damage as blood has not yet been cleared from the joint. Even as the blood resorbs, haemosiderin induced inflammation is still present and a danger to the cartilage.

2.How to rest?

Rest can include the use of supports, splints, braces, or assistive devices. For weight-bearing joint bleeds choose an assistive device/mobility aid that is right for your patient, and takes into account any other target areas. A wheelchair (or a stroller for young children) may be the safest option if there is multiple joint involvement or if the child is too young for other devices.

3.Plan to follow up

Rest is a temporary recommendation. There can be severe consequences to the musculoskeletal system with too much rest, the misuse of splints and braces or with prolonged non-weight bearing status. Schedule the patient for reassessment and regular follow-up after the initial period of rest is completed. When the time is right,

loading the healing tissues can be accomplished through active or passive ROM, isometric muscle contraction and progressive weight-bearing (Buckwalter et al., 1999). This may commence approximately around weeks 2-3, or later if there has been prolonged healing or rebleeding.

ICE

Ice is said to reduce bleeding, pain, and swelling and is commonly applied in the clinic, recommended as first aid, and in the home situation as a treatment for haemarthrosis. However, these recommendations are not all evidence-based.

When an ice pack is used for 15-30 minutes over the joints, even the deep, intra-articular space undergoes significant cooling in addition to the obvious cooling of skin surface. Therefore, the superficial synovial membrane that is closer to the skin surface, is also cooled. Since joint bleed originates in the synovial membrane, cooling the vessels within this structure can impair coagulation and haemostasis (Forsyth et al., 2012).

Haemostasis and coagulation are biochemical processes that occur most effectively at body temperature. Cooling impairs these processes in both, humans and in animal models in the non-haemophilia population. There is no reason to think that this effect is different in persons with haemophilia. Cooling causes the following negative effects: prolonged bleeding time, prolonged coagulation time, prolonged clotting time, impaired clot firmness, decreased platelet aggregation, size and adhesion, decreased coagulation enzyme activity and decreased factor VIII and IX activity. Therefore, it would be counterintuitive to recommend an intervention that has the potential to interfere with haemostasis and coagulation.

The sole benefit for using ice in haemarthrosis would be for temporary pain relief. However, in order to reduce nerve conduction velocity to cause the analgesia effect, cooling must be achieved in the same range that interferes with coagulation and haemostasis. The other stated benefits, such as reduced bleeding and swelling, are not supported by evidence. Research showed no potential of ice to stop bleeding. Although vasoconstriction may occur, bleeding times are still prolonged. In fact, this local vasoconstriction at the bleeding synovial membrane may even hinder the infused factor from getting to the affected area. In addition, whereas immediate ice application may be effective in reducing interstitial oedema for-

mation from soft tissue, it will not affect the type of swelling caused by a joint bleed. The swelling in haemarthrosis is simply a distension of the joint capsule as the intra-articular space fills with blood.

PRACTICAL APPLICATION OF ICE

Ice may **not** be appropriate right away, as first aid for a bleeding joint, unless the sole benefit of ice for temporary pain relief is determined by the clinician to outweigh the potential risks.

When prescribing ice for your patient consider the following:

1.What is the goal for using ice?

If it is pain relief, then yes, cooling the joint can achieve a reduced nerve conduction velocity and a temporary analgesic effect. Determine if the benefit of this application outweighs the risk in a patient. If your goal is to reduce joint swelling or bleeding, there is no evidence that ice can achieve either of these goals.

2.Are there other pain relief methods available?

Determine if other suitable methods are available to manage pain that do not carry a potential risk to further impair coagulation and haemostasis.

3.How to ice?

Crushed ice in a plastic bag, applied with a wet towel layer, applied for 15-30 minutes will be sufficient to lower the temperature enough to reduce pain. However, this is the same temperature range that impairs coagulation and haemostasis, so the potential risk for prolonged bleeding is present.

4.Plan to follow up

If advising ice, thoroughly educate on the proper use and application. Many patients will keep ice on for longer than recommended, and some may also add a compressive wrap to secure the ice bag which can further amplify the cooling and compromise the skin. Schedule the patient for reassessment and regular follow-up as needed.

COMPRESSION

Compression using an elastic bandage or sleeve adds external pressure to the joint that is swelling from haemarthrosis. The goal is to achieve tamponade sooner, slowing bleeding from the lesioned synovial capillaries, limit joint capsule distensibility, and reduce joint swelling (Forsyth et al., 2012). When applied properly, compression carries little risk. It should be noted that compression should never

be applied to a muscle bleed where compartment syndrome is suspected or present.

In clinical practice cooling and compression are combined. However, there is little evidence to support that cooling adds any additional benefit in the reduction of swelling and bleeding versus using compression alone (Forsyth et al., 2012). A qualitative survey in 9 persons with haemophilia using a cold compressive device (CryoCuff®) following acute haemarthrosis, showed a favourable subjective response (D'Young et al., 2008). However, the study did not have a control group using room temperature instead of cold water, nor a control group receiving only a standard RICE protocol, to help differentiate between effects of compression vs. cold, vs. CryoCuff® itself. In two randomised studies in the general population (Dervin et al., 1998; Edwards et al., 1996). CryoCuff® was applied immediately following arthroscopic anterior cruciate ligament reconstruction – using room temperature water in CryoCuff® vs. ice-water filled CryoCuff®. Both studies (n=78 and n=71 respectively) did not find any significant differences in length of hospitalisation, (haemovac) blood loss, oral or intravenous analgesic use, subjective pain measured by visual analogue pain scores, or knee range of motion upon discharge.

In non-haemophilia patients following total knee replacement benefits of compression without ice were shown to be: reduced postoperative swelling, bleeding, and length of hospital stay, improved recovery and increased range of flexion at discharge. A firm bandaging reduced intra-articular pressure so that tamponade occurred sooner. Instead of the normal of 52–62 mm Hg, tamponade occurred at 28-32mm Hg with the use of compression (Forsyth et al., 2012).

PRACTICAL APPLICATION OF COMPRESSION

Compression is appropriate right away, as first aid for a bleeding joint. It is likely to help manage pain as well, if applied prior to the joint capsule being severely distended. However, often compression is not applied quickly enough and can be very painful when applied to an already swollen joint.

When considering a prescription of compression consider the following:

1.Apply compression at the very first indication of bleeding

Often, persons with haemophilia experience a sensation or "aura" as a preliminary symptom before a joint bleed is evident. To gain

maximal benefit, compression should be applied at this time. Once the capsule distends, and joint has begun to swell, it may be more painful to add compression.

2.How to compress?

Elastic bandages should be applied to the affected joint, wrapping from distal to proximal, overlapping half the width of the bandage, each time the bandage is wrapped, on an angle, diagonally across the joint. Ensure never to wrap circumferentially as this could compromise circulation. Always take care with the amount of pressure being applied. If the bandage is too loose, no benefits will be realised. If the bandage is too tight, the neurovascular compromise can occur distal to the wrap, causing paraesthesia and reduced circulation to that area. It is possible to teach patients and caregivers proper wrapping techniques.

3.Plan to follow up

When advising compression, thoroughly educate on the proper technique and how to monitor if the compression is too tight. Patients may need time and practice with their physiotherapist during a regular, non-acute visit to adequately acquire this skill.

ELEVATION

Elevation is the simplest of all four components and done properly it carries minimal risk. For elevation to be effective, the bleeding joint is positioned above the level of the patient's heart. The goal of elevation is to reduce hydrostatic pressure in the capillaries at the site of bleeding and to use the properties of gravity to assist in fluid return.

After total knee surgery a 25% reduction in blood loss was documented in non-haemophilic patients who were supine positioned, with leg elevated 35° at the hip with the knee extended (Forsyth et al., 2012).

PRACTICAL APPLICATION OF ELEVATION

Elevation is appropriate right away, as first aid for a bleeding joint and can be easily combined with rest and compression.

When considering a prescription of elevation for your patient consider the following:

1.Use elevation at the very first indication of bleeding

Often persons with haemophilia experience a sensation or "aura" as they are getting a joint bleed. To gain maximal benefit, add eleva-

tion to compression and rest at these first signs of bleeding.

2.How to elevate?

Ensure that the body part being elevated is above the level of the patient's heart. This often necessitates a supine or semi-reclined position and the use of blankets, pillows or bolsters. Take care to properly support the posterior surface of limbs, especially at the hinge joints so that the knee or elbow are not forced into a fully extended or hyper extended position.

3.Plan to follow up

When advising elevation, thoroughly educate on the proper and supportive positioning technique.

COMBINATION OF RICE

It is obvious that each of the interventions mentioned above can be combined. For instance, ice can address pain, however in order to address swelling you may combine rest, compression and elevation. Also take this opportunity to provide the patient with exercises or advice to address other target areas which have no acute bleeding, so he may complete a home programme on these areas while being immobile during rest or elevation or an ice application.

Case 1

Tomas, 12-year-old, severe haemophilia A, injured his right ankle while at school. He is waiting for his parents to infuse him with factor VIII. Which elements of RICE are appropriate at this time and how should they be applied?

DISCUSSION: Rest/Compression/Elevation: It would be appropriate for Tomas to rest comfortably in a semi-reclined position. Pillows and blankets can be used to support the posterior right leg in an elevated position, ensuring that the right ankle is positioned at a level above the heart. If a compression bandage is available, trained staff (or Tomas, if he has been trained) should properly apply the bandage to the ankle as he rests in this position. Ice is not recommended for pain management since other pharmaceutical and non-pharmaceutical management techniques may be considered. For example, the school nurse may administer acetaminophen (paracetamol) or perhaps have Tomas rest in a quiet room while listening to his favourite music.

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CHAPTER 10

Chronic sequels

A • Chronic synovitis

INTRODUCTION

Chronic synovitis is a common complication in haemophilia, often seen after (recurrent) haemarthrosis that causes changes in the synovial membrane (chapter 5). Each intra- articular bleeding results in a release of iron from haemoglobin, which is removed by the synovium. In case of a severe or repeated bleed, the capacity of the synovium is exceeded, causing iron depositions in the form of haemosiderin evoking an inflammatory response. Chronic synovitis can be prevented by prevention of (repetitive) joint bleeds. To this end adequate prophylaxis, started at a young age immediately after the first joint bleed, is indicated (Fischer et al., 2002). In case of a breakthrough bleed, extra doses of factor VIII or IX are required to stop the bleeding in an early phase. This will minimise the amount of blood in the joint and thus prevent synovial tissue damage and synovitis. In countries with restrained resources prophylaxis is hardly given, and sometimes adequate treatment for bleedings is lacking. In this situation recurrent haemarthrosis causing chronic synovitis is a common complication (picture 1).

FROM SYNOVITIS TO CHRONIC SYNOVITIS

In haemophilia care the term chronic synovitis is generally used for a synovitis existing for 3 months or longer. It is difficult not to mix up terms like synovitis, chronic haemarthrosis and chronic synovitis with ''target joints''. A target joint is defined by the fact that these

Picture 1. Chronic synovitis and muscle atrophy as a result of recurrent untreated joint bleeds (courtesy of Kathy Mulder)

joints have 3 or more bleeds within a 6-month period of time (Mulder et al., 2004). The time to recover completely from the previous bleed is too short, inducing a self-perpetuating cycle of haemarthrosis-synovitis-haemarthrosis. This cycle can only be abrogated by fully preventing recurrent bleeding. Besides the medical prevention of chronic synovitis, the functional recovery after each bleed contributes to prevention, but is, unfortunately, not yet evidence-based. After every intra-articular bleed primarily the joint, but secondarily the structures around the joint, the whole extremity, and the total body of the person with haemophilia are physically disturbed. Some consequences are visible (swelling), palpable (warmth), or measurable (pain, range of motion), but others are not. Besides loss of strength (not preferred to measure in acute situations) and instability (this should not be tested in acute situations), proprioception is disturbed. Persons with haemophilia are often completely unaware of this, and in many cases professionals do not include specific exercises into their recovery (rehabilitation) programme.

CLINICAL FEATURES OF CHRONIC SYNOVITIS

Finally, chronic synovitis presents as a painless swelling, palpable as a soft tissue firmness of the joint, with more or less instability,

and atrophy of the surrounding muscles which is also a result of recurrent bleeding. In general range of motion is not very limited. Joint swelling in combination with muscle weakness make the joint contribute to the continued vicious circle of haemarthrosis-synovitis-haemarthrosis. Synovitis can easily be distinguished from haemarthrosis. Haemarthrosis is characterized by a painful swelling, the joint is maintained in a position of comfort (typically in flexion), and at palpation the swelling is more fluid.

MEDICAL THERAPY FOR CHRONIC SYNOVITIS

To stop chronic synovitis we prescribe daily prophylaxis with 10 IU/kg factor VIII or 20 IU/kg factor IX for 10 weeks to prevent recurrent bleeding, in combination with an anti-inflammatory drug like celecoxib. Celecoxib is a cyclo-oxygenase 2 (COX-2) inhibitor which has an anti-inflammatory, anti-angiogenic and analgesic property without affecting platelet function in the manner of traditional non-steroidal anti-inflammatory drugs. Rattray et al. (2006) studied the effect of celecoxib in 8 persons with haemophilia suffering from chronic synovitis. Patients were treated twice daily with 200 mg celecoxib for 30 days. He found a positive effect in 7 patients. No serious side effects were seen, especially no cardiovascular events. In some cases, when celecoxib is not effective, ibuprofen in combination with an antacid is prescribed. However there are no publications supporting evidence of this strategy.

REHABILITATION DURING CHRONIC SYNOVITIS

Daily infusion of clotting factor concentrates should always be combined with physiotherapy. The goal of treatment is to deactivate the synovium as quickly as possible and preserve joint function (Roosendaal et al., 1995)

EVALUATION OF CONSERVATIVE THERAPY

Conservative therapy is rarely completely successful. Complete success is characterised by:

- Disappearance of swelling
- Absence of recurrent bleeding in the affected joint
- Optimal muscle strength
- Acceptable stability of the joint (no sudden events)
- Decrease of synovial hypertrophy as monitored by ultrasound or MRI

PHYSIOTHERAPY PROGRAMME

WEEK 1-4

- **Ice application on inflamed joint as frequent as possible, i.e. multiple times per day. An advantage of applying cold packs is that the persons rests in the meantime**
- **Joint stability training in a non-weight bearing situation.**
- **Instruction on controlled home exercises for adjustment of activities of daily living**

OPTIONAL

In case of serious swelling, ROM restriction of > 10° and pronounced joint instability:

- **Weight bearing should be reduced to partial weight bearing with the use of elbow crutches**
- **Bandaging of joint or elastic joint protector. In serious cases, and young children a splint can be used (chapter 14)**
- **Use of sling (elbow joint)**

WEEK 5-10

In case of persistent joint swelling:

- **Application of interferential currents and/or pulsed ultra-short wave**
- **Continue exercise programme as described for week 1-4**

In case joint function has improved:

- **Increase weight bearing**
- **Intensify joint stability training also in a weight-bearing situation**

When daily prophylaxis in combination with physiotherapy is completely successful, prophylaxis can be tapered or stopped and rehabilitation changed into a more coaching process with functional goals. As always, pain *and* swelling are determining factors to evaluate progress.

If only partial success is obtained, an extension of the conservative programme with 4 weeks is suggested. Evaluation should always be multidisciplinary: the haematologist or paediatrician together with both, rehabilitation specialist and physiotherapist.

SYNOVIORTHESIS (MEDICAL SYNOVECTOMY)

In case of partial success, after 4 weeks extension of the conservative treatment or when synovitis persists, there is an indication for more invasive therapeutic options. Prophylaxis can be tapered or stopped, but the rehabilitation programme should be continued.

The indication for a synoviorthesis is chronic haemophilic synovitis associated with recurrent haemarthroses, unresponsive to haematological treatment (Rodriguez-Merchan et al., 2001). It aims to diminish the amount of synovial hypertrophy and to stabilise the synovial membrane. Synoviorthesis should be performed as soon as possible to minimise the degree of cartilage damage. Before starting an intervention, diagnosis of synovitis should be (re)confirmed radiologically by MRI or ultrasound.

There are two types of synoviorthesis: chemical and radiation synoviorthesis. Chemical synoviorthesis with intra-articular injections of rifampicin is mostly used in countries with restrained resources, and can be given weekly with a maximum of 5-10 injections. Radiation synovectomy is more efficacious. The current recommendation is to use Yttrium^{90} for the knees and Rhenium^{186} for elbows and ankles, maximal 3 times with at least a 3 month interval (Rodriguez-Merchan et al., 2016). In general 75-80% of patients have a long-term positive outcome (Molho et al., 1999). An injection for synoviorthesis may be complicated by an inflammatory reaction. Rest and celecoxib are indicated to control these symptoms.

Only in case consecutive synoviortheses fail, there is an indication for a surgical arthroscopic synovectomy. Open synovectomy is only performed in case of an enormous formation of synovial tissue requiring radical removal which cannot be achieved with arthroscopic techniques. Postoperative a surgical synovectomy requires more intensive rehabilitation than a synoviorthesis.

POST- SYNOVIORTHESIS REHABILITATION

Unfortunately, patients are often not referred for physiotherapy after radiation synovectomy (de Kleijn et al., 2006). However, structures involved in the functionality of a joint, stability, muscle strength and proprioception, will still be disturbed and require rehabilitation. Post synovectomy, if successful, the vicious circle is broken resulting in less bleeding. This new situation makes a more intensive training programme possible. Physiotherapy following (medical) synovectomy is basically the same as for acute and chron-

ic synovitis, and can in general be started 48-72 hours after the intervention. Training consists of active unassisted exercises, and to improve muscle strength and trophism, light exercises of resistance that are gradually stepped up (Querol et al., 2001). After a training session ice should be applied for 20-30 minutes. Activities of daily life and weight bearing can be increased gradually in compliance with the physiotherapist's instructions. Physical rehabilitation continues until complete anatomical and functional recovery is achieved. Coordination and proprioceptive stimulation complement the exercises to recover original muscle strength and functionality.

PSYCHOLOGICAL ASPECTS OF TREATMENT OF CHRONIC SYNOVITIS

To increase the compliance with conservative treatment, it is of great importance that the patient and his family are supported by a psychologist or a social worker. Psychosocial support should focus on motivation of the patient and discuss the effect of this intensive programme on social and personal aspects. This could be part of a home exercise family support programme. When a patient is motivated to follow the regimen results will be better. Functional milestones to guide and develop such a programme are needed, always in close co-operation with the person with haemophilia.

CONCLUSION

Chronic synovitis is the result of recurrent haemarthroses and is often seen in countries with limited access to clotting factor concentrates. Good motor development may help to prevent bleeding. Furthermore, clotting factor, anti-inflammatory drugs and (in some cases), synovectomy are indicated. Besides medical treatment physical rehabilitation is essential and should be continued until complete anatomical and functional recovery is achieved.

Besides medical prevention of chronic synovitis, functional recovery after each bleed contributes to prevention.

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CHAPTER 10

Chronic sequels

B • Haemophilic arthropathy and exercise

CLINICAL FEATURES OF CHRONIC ARTHROPATHY

People with haemophilic arthropathy in multiple joints tend to develop a typical posture consisting of flexion contractures at the elbow(s), hip(s) and knee(s), and equines at the ankle(s) (Lobet et al., 2014). Depending on the degree of elbow contracture, the shoulders may be carried in extension. If these deformities are primarily localised to one side of the body, there may also be pelvic obliquity and scoliosis.

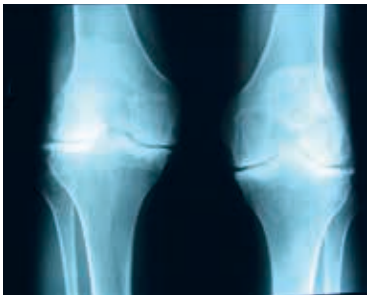
These postural changes begin in response to the typical position of comfort that each joint assumes during haemarthrosis, and are perpetuated if the ensuing muscular imbalances are not addressed after each bleed. Intramuscular bleeds, such as into the Gastrocnemius, Hamstrings, or Iliopsoas muscle, also contribute to this altered posture, especially if muscle length is not restored after bleeding stops. If a person develops arthropathy in only one or two joints, these postural adaptations may not be as marked. However, each affected joint will go through a similar series of clinical and radiologic changes (picture 1).

Table 1 shows many of the changes that occur as arthropathy progresses. The progression through these stages is not necessarily as simple as this table suggests, and some features from each of the three stages may be present simultaneously within the same joint.

	EARLY CHANGES	INTERMEDIATE CHANGES	LATE CHANGES
X-RAY/MRI CHANGES			
		• Joint space narrowing • Subchondral cysts • Osteopenia • Osteophytes	• Joint space is very narrowed and incongruent with erosions • Osteoporosis • Osteophytes • Angular deformities • Subluxation of joint
	Enlarged epiphysis – begins in childhood, does not change after skeletal maturity		
CLINICAL FINDINGS			
Crepitus	• Palpable with movement	• Palpable +/- audible	• Painful audible coarse (grinding)
Range of motion	• Joint range of motion maintained	• Some loss of joint motion; joint feels stiff afterinactivity, improves with movement	• Limited joint motion* • Fixed contracture
Joint stability	• Joint is stable with ligamentous testing • Dynamic stability may be decreased (proprioception)	• Joint may feel unstable with ligamentous testing	• Functional instability, giving way while motion still exists • May be stable if ankylosed >>>

Table 1. (Kilcoyne et al. 2006, Jelbert et al. 2009)
* Joint may be fibrosed/ankylosed, or subluxed

	EARLY CHANGES	INTERMEDIATE CHANGES	LATE CHANGES
>>>			
Heat/swelling	• Slightly warm and swollen especially after some active synovitis		• Joint is scarred and fibrotic: no swelling palpable
Pain	• Some discomfort after activity or weight bearing	• With motion or weight-bearing if ROM is still present If no motion present, there may be little/no pain in joint	• Pain with weight-bearing and movement
Muscle bulk	• Some muscle wasting	• Muscle wasting	• Severe muscle atrophy
Muscle length	• Some muscular tightness limiting full range of motion	• Loss of muscle length; may be difficult to distinguish from joint contracture	• Loss of muscle length affecting adjacent joints
FUNCTION AND PARTICIPATION	• Relatively intact: able to do most regular activities without modification	• Altered ability to do functional activities and participate due to pain, decreased tolerance/endurance	• Severe restrictions in role functioning and participation Will require physical assistance/devices/ environmental modifications etc.



Picture 1. x-rays knees of 32-year-old male with severe haemophilia A with haemophilic arthropathy.

THERAPEUTIC EXERCISE

Therapeutic exercise, that is, a physical activity that is planned, structured, repetitive, and purposive. However, many types of "physical activity" can be enjoyable for people with arthropathy and achieve many of the same fitness goals. In people who have developed arthropathy due to degenerative or inflammation-mediated processes (e.g. osteoarthritis and rheumatoid arthritis), the clinical manifestations of arthropathy would be treated with various forms of therapeutic exercise in addition to medical management. There are very few high-quality studies that have investigated the use of exercise for people with haemophilia: a recent Cochrane review (Strike et al., 2016) found only 8 randomised controlled studies, which included 233 subjects. However, 120 of the subjects were children, and the severity of arthropathy was not specified in any of the studies. Nevertheless, these studies, several other review articles (Gomis et al., 2009; Negrier et al., 2013; Schäfer et al., 2016) and several less rigorous studies support the use of therapeutic exercise for people with haemophilia.

When prescribing exercises for this population, the primary consideration must be "Do not cause new bleeding". This is especially true in settings where availability of clotting factor is limited.

GOAL SETTING AND TYPES OF EXERCISE

The (types of) therapeutic exercises that are chosen depend on the goals of treatment, which can be related to parts 1 and 2 of the World Health Organization International Classification of Functioning Disability and Health (ICF) either sequentially or concurrently.

Part 1 of the ICF deals with impairments of Body Structures and Function. The main "Body Structures" impaired by haemophilic arthropathy are the joints; however, impairments of muscle structure and neurological structures can be present too. "Body Functions" affected by haemophilia include joint mobility, muscle length, power, coordination, and proprioception. Therapeutic exercises can address each of these. Part 2 of the ICF deals with Participation: that is ambulation/mobility, self-care, domestic life, education and occupation, recreation and leisure, and others. Haemophilic arthropathy can severely impact each one of these domains.

In the past, and this is still present in some parts of the world, many exercise interventions were designed to address complications at the body structure and function level. Many older patients

with haemophilia can give examples of when they did not perceive these to be useful or effective because "they didn't work". Many of the chronic sequelae, such as fixed contracture, cannot be improved with exercise alone, so a different approach was needed.

Patients (with any disorder or condition) rarely present to an exercise professional and say "I am lacking range of motion" or "I have insufficient muscle power". They usually describe a functional concern: "I can't walk as far as I used to", "I can't get up from a chair", "I can't hold my new grandchild" etc.. These functional limitations can be influenced by an exercise programme. Therefore, it is critically important to discuss these participation issues with the patient when designing an exercise programme.

Case study

A 45-year-old male with severe haemophilia has fixed flexion contractures at both elbows and both hips. His knees each move from 15 to 30 degrees of flexion and show posterior subluxation of the tibiae. One ankle was fused surgically, the other ankylosed. He expresses concern that his walking tolerance and balance have deteriorated following a recent hospitalisation. He attends a weekly exercise programme, consisting of exercise in the hydrotherapy pool, strengthening exercises with light weights, and light recreational activity (badminton). At the end of the 8 week programme he tells his physiotherapist "Well, my knees don't bend any better than they used to, but now I feel so light- like I am walking on air. I have more energy, and I don't worry so much about falling because I know I can catch myself."

To facilitate discussion and patient-specific goal setting, but also to demonstrate progress and value to the patient (and to those paying for the exercise sessions) the use of a function-based assessment tool, such as the Haemophilia Activities List (HAL) can be very helpful. Once the patient's main functional concerns are identified, assessment of body structure and function can identify relevant impairments. Exercises can be chosen, as part of a *comprehensive* management plan, to develop or enhance the neuromuscular skills required to perform the activity.

TYPES OF EXERCISES

JOINT MOBILITY

If there is adequate muscle control, active range of motion exercises can be done against gravity. If there is significant weakness, active-assisted exercise, active exercise in positions with gravity neutralised, or active exercise in water (aquatic exercise or hydrotherapy) may be preferable. Exercises should begin within a comfortable range, and are only increased to the ends of range as comfort allows: difficulty achieving "normal" range of motion may be due to soft tissue fibrosis, or due to mechanical obstruction from altered joint surfaces. Therefore, passive exercises (i.e. externally applied forces) are **not** usually recommended for persons with haemophilia. Firstly, there is the risk of causing (new) bleeding if tissue capacity is exceeded. Secondly, it is unlikely to improve range of motion when the articular surface is not intact and the capsule is fibrotic.

MUSCLES

Muscle function can be altered by:

- Bleeding and fibrosis within the muscle itself
- Bleeding and/or arthropathy in an adjacent joint
- Nerve compression which is sometimes seen with bleeding into deep muscle compartments.

Muscles can be classified as a. mobilisers or b. stabilisers (Sahrmann et al., 2002). These two groups contain different muscle fibre types, and respond differently to injury.

a. Stabiliser muscles tend to be deeper and close to the joints. They work for extended periods of time, at relatively low loads, to provide stability to the trunk and limbs. The stabiliser muscles react to injury by becoming weak and inactive.
b. Mobiliser muscles are usually more superficial, and may cross more than one joint. They are capable of generating large forces but fatigue quickly. When they are injured, they react by developing protective muscle spasm and may become overactive, tight and shortened if the adjacent stabiliser muscles are weak. The resulting muscle imbalance may limit joint motion and alter the axis of movement at the adjacent joints.

MUSCLE LENGTH

Exercises to improve muscle length must proceed carefully and be progressed slowly to minimise the risk of causing a new bleed into the muscle or stressing a joint with altered mechanics. **Active** stretches, using the antagonist muscle and with the amount of force controlled by the patient, are preferable because they use the muscles in a functional and natural way. Ballistic (bouncing) movements are not recommended. Passive stretches are not generally recommended: they may cause tearing of muscle fibres and bleeding! However, if necessary, such as if the antagonist is paralysed and active stretching is not possible, they may be used with caution. Careful attention must be paid by the therapist to tissue tension and by the patient to sensations of discomfort. Techniques to promote relaxation of the tight muscle, such as use of heat, massage, or gentle rhythmical shaking of the limb may help prepare the muscle for active stretching exercises.

MUSCLE STRENGTH

Exercises to improve strength must proceed carefully and be progressed slowly in small increments. Exercising to the point of muscle fatigue or pain is not useful. If the patient experiences pain, either during or after exercising, he is likely to interpret this as symptoms of bleeding and he will be reluctant to continue the programme.

Exercises should be chosen that allow the patient to use each muscle the way it is most often used in its own functional situation: is it a stabiliser or mobiliser? Does it need to work eccentrically or concentrically? Is it used in weight-bearing or non-weight-bearing positions? In which part of the range of movement does it need to work? Does it need to generate large amounts of force? Does it need to be able to repeat the same contraction for longer periods of time?

Stabilisers and mobilisers require different approaches: As previously mentioned, stabilisers become weak and inactive with injury or disuse. The first goal is to ensure that the patient can isolate and activate the correct muscle without overly involving adjacent mobilisers. Biofeedback, for example via surface EMG or palpation of the muscle belly, can be useful in the early stages of retraining. Further training is designed to build endurance at low loads.

Mobilisers may be overactive after injury, or may try to compensate for weak stabilisers. They may need retraining to contract only

when they need to, but still be able to generate force for specific tasks for short periods, sometimes against resistance.

Regardless of muscle type, if there is significant weakness, it may be necessary to begin in a position where gravity is neutralised or the level arm is shortened; alternatively, assistance to move into inner range, followed by active eccentric control back to outer range, can be used until there is adequate active concentric control against gravity. Isometric exercise is often recommended for people with haemophilia "to protect the joint". However, isometric exercise is not particularly functional.

Isotonic exercises, in functional positions, are preferred and sometimes the simplest exercises are quite adequate. Using exercise apparatus may be too difficult for someone with arthropathy. Selecting practical, functional exercises, using body weight as resistance (as tolerated) will allow the person to achieve success with his programme. If the patient understands how the exercise may make the activities of his daily life easier, he is more likely to understand the importance of practice and repetition.

COORDINATION

As neuromuscular control and confidence improve, slow deliberate contractions can proceed to faster movements possibly using resistance, and through larger arcs of motion. Again, this depends on the functional requirements of the patient: for example, requirements for a teen who wishes to continue to play sports will be different from a senior whose goal is to cross the street safely.

PROPRIOCEPTION

Proprioception is the sense of position and movement of the limbs and body in space and the process that allows the body to react to changes in joint position. Sensory receptors in the joint capsules and ligaments signal the brain to send messages to the muscles to contract and prevent the joint from injury. Proprioception can be impaired in persons with haemophilia due to a few reasons. First, the receptors can be damaged when the capsule is stretched during bleeds. Second: muscle bleeds or disuse weakness may mean that muscles are not able to respond quickly or strongly enough in response to the signals. Third: joint surface incongruence may produce structural instability or sudden pain when the muscles are contracted causing the joint to "give way". Finally, proprioception also declines with age, even in healthy individuals.

Failure to restore proprioception means that joints may not be able to respond quickly enough to new stresses, and will be re-injured easily. Proprioceptive exercises should progress from simple (stable surface, eyes open) to more complex. Proprioception requirements will vary according to the patient's activities (e.g. walking on pavement vs walking on ice and snow). Most of the literature about proprioception describes training for the lower limbs (e.g. ankle, knee in sports) but the upper limb must also be included to ensure that the elbow can react quickly when challenged (e.g. when using crutches).

AQUATIC EXERCISE

For people with arthropathy, exercises in water may be more comfortable and better tolerated than dry-land exercises (picture 2). Aquatic therapy can be used to promote all of the above goals. The warmth of the water promotes relaxation and easier movement.

Picture 2. Aquatic exercise: training coordination and muscle strength

Buoyancy can assist limb movements when muscles are weak. Water depth relative to the person's height can be adjusted to relieve or promote weight bearing. Speed of movement can be altered to change resistance and force required. Addition of turbulence can challenge balance reactions (Vallejo et al., 2010).

EXERCISES AND PATIENTS WITH INHIBITORS

Inhibitors (circulating antibodies to clotting factor VIII or IX) represent a significant challenge to patients and their care teams. Medical management to control bleeding is less effective, extremely expensive and not always available. Bleeding cannot be prevented with prophylaxis in most cases. Whenever a bleed occurs it cannot easily be controlled, therefore there is great reluctance to allow participation in activities which could increase the risk of bleeding, including therapeutic exercise. It is the opinion of these authors that people with inhibitors can safely participate in therapeutic exercises as long as the exercises are gentle, cause no pain during the exercise, and are progressed very slowly in terms of speed, repetitions and resistance. People with inhibitors need to be able to walk, perform self-care and participate in their social roles just like everyone else. Therapeutic exercise may be a necessity to allow participation in daily life activities.

CLINICAL PEARLS

Scientific evidence to guide exercise prescription is lacking. The following comments represent clinical opinions gathered over the authors' combined clinical experience of over 50 years.

How many repetitions?

This depends on the patient. The individual and the therapist must listen carefully to the signals from the body- discomfort usually means that this is enough for this session!

The number of repetitions will also depend on which type of muscle is being exercised. The stabiliser muscles need to be able to work over and over for long periods. They should be trained with low resistance but many repetitions.

How much exercise is too much?

If there is soreness during an exercise, that is probably too much. If there is soreness after an exercise, (e.g. later the same day, or the next day) it can be difficult to distinguish this soreness from a new bleed without sophisticated diagnostic imagery equipment. It is bet-

ter to start with low loads and few repetitions and assess the response before progressing.

What about the other joints?

Some of the exercises that are designed to help one joint may place too much stress on other joints. For example, using weight-bearing exercises to strengthen a knee may be too difficult if the ankle on the same leg is damaged. Bicycle ergometry or treadmill walking for cardiovascular fitness may be too much stress on ankles and knees.

Factor or no factor?

If factor is readily available and part of the person's usual regime, discuss with the team to use it prior to exercise sessions. Lack of factor prior to exercise is not a contraindication against exercise as long as the precautions discussed throughout this chapter have been observed. If factor is not readily available for treatment of new bleeding, then even more caution should be exercised and progression of exercises must be done very slowly.

Physical activity or "exercise"?

This chapter has discussed therapeutic exercise, that is, a physical activity that is planned, structured, repetitive, and purposive. However, many types of "physical activity" can be enjoyable for people with arthropathy and achieve many of the same fitness goals. Swimming is often suggested as a suitable activity for people with haemophilia because the risk of injury is felt to be small. However, swimming does not promote weight-bearing which is necessary for bone density. Yoga, Tai Chi and dance for people with haemophilia have all been reported in the literature and all promote neuromuscular control and core strength. Pilates and Nordic pole walking have not been studied in persons with haemophilia to date, but do promote strength, postural alignment and endurance.

EXERCISE AS PROPHYLAXIS AGAINST BLEEDING

Discussion regarding the benefits of regular physical activity in the prevention of obesity, osteoporosis, hypertension, cardiovascular disease, diabetes, etc. is beyond the scope of this chapter, but the importance of maintaining a healthy neuromuscular system compatible with the demands of daily living is not.

Exercise that promotes proprioception and balance reactions may be useful in preventing stumbles and falls. Exercises that promote muscle length and joint mobility will help ensure that when stum-

bles do happen, muscles and joints have enough excursion to not be forced beyond their limits. Exercises that promote muscle strength and coordination will ensure that people can react to sudden loss of balance or sudden movement and protect themselves, such as when riding public transport or slipping on ice. Exercises that promote muscular endurance will ensure that muscles are not injured due to fatigue during activities such as shopping. Exercises that allow a person to continue to participate in leisure and recreational activities with his friend and family may contribute to overall well-being.

CONCLUSION

Therapeutic exercise and suitable physical activities are important components of the comprehensive management of people with chronic haemophilic arthropathy.

When prescribing exercises, the primary consideration must be "Do not cause new bleeding". This is especially true in settings where availability of clotting factor is limited.

RUBÉN CUESTA-BARRIUSO

CHAPTER 10

Chronic sequels

C · Haemophilic arthropathy and joint techniques

INTRODUCTION

Joint haemorrhages (haemarthroses) occur in 70-80% of the cases in knees, elbows and ankles. Associated disorders secondary to haemophilic arthropathy include abnormal biomechanics, loss of proprioception and periarticular muscle atrophy, resulting in loss of activities, e.g. gait. Physiotherapy is involved in many stages, but in haemophilic arthropathy joint techniques are not very well recognised, nor effectuated yet.

INVOLVEMENT OF THE JOINT CAPSULE

Progression of haemophilic arthropathy gradually leads to loss of joint mobility. As a result of the limited range of motion, the laxity of the joint capsule decreases proportionally on the side opposite to the limitation. As an example: loss of laxity on the ventral side of the elbow is found in a patient with haemophilic arthropathy of the elbow characterised by a limitation at extension. To improve, or at least maintain joint mobility, clinical studies have been conducted that have specifically addressed the mobility of the joint capsule.

Heijnen and de Kleijn (1999) implemented treatment involving joint traction, but combined with mobilisation techniques, muscle strengthening and stretching, joint stability training, postural and functional (gait) training. Despite the progression of arthropathy, joint mobility was maintained after 5 years with sustained improvements in relation to activities of daily living, walking and pain.

Years later, through a programme implementing joint traction, passive stretching of the Gastrocnemius muscle, and strength and proprioception exercises, the effectiveness of these manual techniques has been demonstrated (Cuesta-Barriuso et al., 2014a) in terms of improving joint pain after treatment and at 6 months follow-up. Similarly, in patients with haemophilic arthropathy of the ankle, joint traction (degree I-II) has proved to be effective by proximal fixation of the joint at a submaximal range of motion without pain, improving mobility and joint pain (Cuesta-Barriuso et al., 2014b).

INVOLVEMENT OF PERIARTICULAR MUSCLES

Loss of muscle strength is typical in haemophilic arthropathy. Although there are numerous articles that have analysed the effectiveness of active exercises (mainly isometrics and counter-resistance) and electrotherapy, further research is needed on the effectiveness of manual therapy in improving strength. Active and passive muscle stretching, in addition to muscle contraction exercises in favour of gravity and counter-resistance, have shown to improve muscle strength of these patients in the short term. Luterek et al. (2008) published a case study of a 44-year-old person with haemophilia, with advanced haemophilic arthropathy of the knee and ankle. After 8 weeks of treatment, using proprioceptive neuromuscular facilitation (PNF) techniques, an improvement in mobility and joint pain was observed. Although this treatment obviously has no haemophilia-specific contraindications, clinical studies need to be conducted to prove its effectiveness in a larger cohort.

INVOLVEMENT OF THE FASCIAL SYSTEM

The degenerative process of joints is one of the underlying causes involving the fascial system. Typical limitations of haemophilic arthropathy favour the loss of elasticity, of flexibility, and start a process of pathological cross-linking of collagen fibres. The role of the fascial system and its direct relationship with certain processes of pain and loss of mobility affecting the locomotor system are, today, one of the most interesting topics of discussion in the field of manual therapies. The fascia is a form of connective tissue and also a colloidal structure. Colloid means a set of solid particles floating in a liquid medium and are moreover flexible. Functions pertaining to the fascial system include: coating, protection, suspension, adaptation to mechanical forces, postural integrity, transmission of mo-

tion, compartmentalisation, ensuring vascularisation and innervation.

One study (Meroño-Gallut, 2016) proposes a fascial therapy protocol for patients with lower limb haemophilic arthropathy, following standards of safety and effectiveness, and whose first results will be published shortly. This therapy involves a physiotherapy technique that does not require aggressive manoeuvres for use in the treatment of haemophilic arthropathy. Its increasingly widespread use in physiotherapy makes fascial therapy a promising technique for the treatment of joint, muscle and fascial restrictions, which are characteristic of haemophilic arthropathy.

CONCLUSION

In contradiction with fear of bleeds caused by techniques directly on joints with haemophilic arthropathy, the benefits from such techniques can be enormous. The typical manifestations of haemophilic arthropathy, combined with this fear, demands proper knowledge of this arthropathy combined with understanding of these patients, especially their lifelong fear of bleeds.

Methodological characteristics of manual therapy interventions used in the treatment of haemophilic arthropathy >>> see next page

In case off loss of muscle strength: active and passive muscle stretching, in addition to muscle contraction exercises in favour of gravity and counter-resistance, to improve muscle strength in the short term.

TECHNIQUES	INTERVENTION	CHARACTERISTICS	DURATION
Joint traction	Superficial thermotherapy	Shallow to 50 cm away from the ankle, using a bulb of 250 W	5 min
	Joint traction, grade I-II	Fixation of distal tibia and fibula with cinch and manual fixation of proximal talus. Patient in supine position and the traction is carried out in the submaximal ranges of dorsal and plantar flexion	15 min
	Proprioception exercises	With unipodal support, with and without visual support, and posterior destabilisation	10 min
	Local cryotherapy	With ice pack and protection between it and the skin	10 min
Muscle strengthening	Proprioceptive Neuromuscular Facilitation		
	Isometric and resisted exercises	In submaximal ranges, of dorsal and plantar flexion	10 min
	Passive muscle stretching (within the limits of mobility)	Through compression muscle, passive muscle stretching and relaxation of muscle	10 min
Myofascial therapy protocol	Superficial sliding anterior part of the leg	The strokes are performed assisted by slight movements of dorsiflexion and plantar flexion by the patient	2 min

>>>

TECHNIQUES	INTERVENTION	CHARACTERISTICS	DURATION
> Myofascial therapy protocol	Superficial sliding anterior part of the thigh		2 min
	Superficial sliding popliteal fascia	Movements applied to the popliteal region. Repeat the manoeuvre 3 times	2 min
	Superficial sliding posterior part of the leg	The strokes are performed assisted by slight movements of dorsiflexion and plantar flexion	2 min
	Superficial sliding posterior part of the thigh	1st line on the region of comfort. The 2nd on the outer thigh. 3rd on the inner thigh	2 min
	Superficial sliding side part of the lower limb	The manoeuvre starts at the trochanteric region and ends in the posterior region of the lateral malleolus	2 min
	Ankle joint complex	Overcome between 3 and 5 restriction barriers	4-6 min
	Anterior compartment of the knee	Cross-hand technique applied to the anterior compartment of the knee	4-6 min
	Thoraco-lumbar fascia	Cross-hand technique applied to the thoracolumbar region	4-6 min
	Telescopic manoeuvre	Degravitation and slight traction of the lower limb	5 min

PIET DE KLEIJN

CHAPTER 10

Chronic sequels

D · Physiotherapy protocols following elective orthopaedic surgery

INTRODUCTION

If conservative treatment is not, or only partly, successful orthopaedic surgery is an option, in general to restore or maintain physical functioning in persons with haemophilia. This is even more important if living independently is at stake. As the clinical outcome in haemophilia is mainly determined by intra-articular bleeds in ankles, knees and elbows, it can be expected that those are focus of surgery as well. If more than one joint is affected, not unusual in elderly persons with haemophilia, surgery of more than one joint can be beneficial and cost-effective (Schild et al., 2009). As walking is an essential function, orthopaedic surgery of lower extremities is more frequently performed than upper extremities. Best results will be achieved with ongoing communication, not only between physiotherapist and orthopaedic surgeon, but also with the patient and all other members of the comprehensive care team involved.

ORTHOPAEDIC SURGERY IN HAEMOPHILIA

SYNOVECTOMIES (AND SYNOVIORTHESES)

Synovectomies can stop uncontrolled, repetitive cycles of intra-articular bleeds, which lead to chronic synovitis, subsequent instability, loss of strength and proprioception. Patients often come to the hospital (too) late, merely because alarming symptoms, such as pain and loss of range of motion, are only partly present. In high-income countries, such as the Netherlands, synovectomy is rarely

done, and open synovectomies are no longer performed at all. Also in countries with restrained resources open synovectomy is no longer first choice, but chemical synoviorthesis is. Disadvantage of chemical synoviorthesis is that it is very painful, and has to be repeated to have fair or good results. In high income-countries radiation synoviortheses are first choice (chapter 10a).

Potential candidates for radiation synovectomies are patients presenting with chronic synovitis that is resistant to medical treatment. Functional recovery after these interventions is very important (de Kleijn et al., 2006), and has to be carried out by a physiotherapist familiar with these long-lasting rehabilitation programmes, during which slow progress is made and patience is the key.

TOTAL KNEE AND TOTAL HIP ARTHROPLASTIES

As the knee is one of the three most affected joints in haemophilia, it is evident that total knee arthroplasty is performed frequently. To a lesser extent this goes for total hip arthroplasty. Patient guidance both pre- and postoperative by a physiotherapist is needed in patients without haemophilia, but even more for those with haemophilia. Main differences between haemophilia and other patients are:

- Pain perception
- Regaining active range of motion
- Starting mobilisation
- Duration of hospitalisation
- Medical treatment, namely continuous infusion with clotting factor

The post-surgery mobilisation protocol may vary per hospital and adaptations for rare disease as haemophilia do not exist.

MULTIPLE JOINT PROCEDURES

Due to recurrent joint bleeds during their youth, elderly persons with haemophilia suffer from haemophilic arthropathy in up to five joints from adolescence onwards. Single orthopaedic procedures decrease pain and restore function in one joint only, often not resulting in a satisfying level of activities and participation. During the 1990s, the Israel National Hemophilia Centre demonstrated that multiple joint procedures could be carried out in a safe manner, and they aimed at restoring optimal function of one complete lower extremity (Horoszowski et al., 1996). Multiple joint procedures have

been carried out in the University Medical Centre Utrecht, the Netherlands, since 1995 and were defined as any combination of total knee, total hip arthroplasty and/or ankle arthrodesis. During the in-hospital rehabilitation 11 subgroups could be distinguished. So far the description of these groups is the only available information to disentangle a complex and physically very demanding period, in this population (de Kleijn et al., 2016).

In our centre ankle arthrodesis is the first choice in case of severe haemophilic ankle arthropathy, whereas in other countries the choice is total ankle replacement. Both strategies have been reported to be successful.

CONCLUSION

Locations of orthopaedic surgery and typical difficulties in rehabilitation have been highlighted, but briefly. This is of importance because postoperative rehabilitation protocols, both in-hospital, and after discharge, do not exist for rare diseases such as haemophilia. Multiple joint procedures are a fair option for this population, both functionally and financially. Surgery of the ankle, especially the choice between arthrodesis and replacement still depends on location and professionals.

Functional recovery after orthopaedic interventions is very important, and has to be carried out by a physiotherapist familiar with these long-lasting rehabilitation programmes.

PAUL MCLAUGHLIN

CHAPTER II

Pain and haemophilia

"The fact that there are so many words to describe the experience of pain lends support to the concept that the word "pain" is a label which represents a myriad of different experiences, and refutes the traditional concept that pain is a single modality which carries one or two qualities."

MELZACK AND TOGENSON 1971

INTRODUCTION

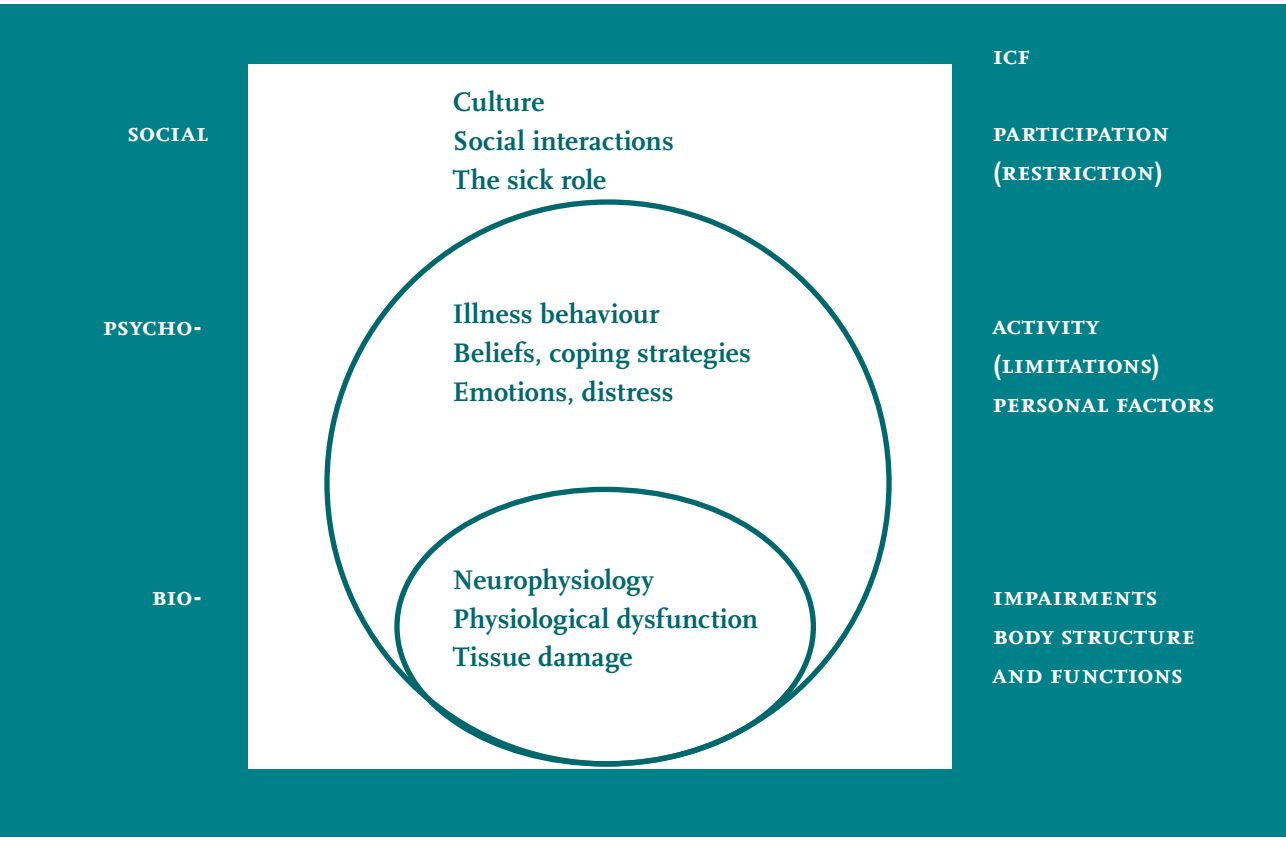
The word pain derives from the Greek *"poena"* meaning punishment, with the word for patient *"patior"* meaning to endure suffering or pain. Early experiences of pain were associated with a punishment from God. But in the 1600's René Descartes was one of the first to propose that pain was associated with the machinery of the human body, with disturbances of nerves travelling to the brain, opening a valve and releasing a warning signal for the body. Advances in medicine and understanding of brain function permitted the development of the pain gate theory by Melzack and Wall (1965). As our knowledge progresses, so too does our understanding of the brain and its ability for neuroplasticity. Current pain theory acknowledges that the brain is a very changeable neuro-immune organ and plays a major role on how we individually construct pain (www.noijam.com).

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Merskey et al., 1994). This definition recognises the emotional and contextual elements of pain as well as the physical effects, and how ultimately all affect the individual perception of nociception or the noxious stimulation.

APPROACH TO MANAGEMENT

The medical model of care is not appropriate for the management of pain. Pain is pain and people are individual, and so a biopsychosocial approach sees the whole person within their world and acknowledges their role within that world. Figure 1 illustrates how the varying aspects of pain experienced by an individual may fit within this model and that of the ICF.

Figure 1. Biopsychosocial approach and the ICF



BIOLOGY OF PAIN

In a normal joint innervation Hiltons Law applies, that is, the nerve supplying the muscles extending directly across and acting at a given joint also innervates the joint. Myelinated axons innervate Ruffini endings (stretch and slow), laminated articular corpuscles (rapid movement and vibration) and the structures resembling Golgi tendon organs. The joint capsule, made of bundles of white collagen, encloses the joint. It is perforated by vessels and nerves and is lined by a synovial membrane. The synovial membrane covers non-articular regions where movement occurs. There are no end organs or simple endings in the synovial membrane, thereby rendering it relatively insensitive to nociception production. Nociceptors are found throughout the joint, in capsule, ligaments menisci and subchondral bone.

NOCICEPTORS

The nociceptor is a highly specialised nerve ending, which responds only to noxious stimuli, and is the body's first line of defence. It communicates information accurately to the CNS at the level of the dorsal horn. It is highly modifiable in response to injury of its axon and when it is exposed to inflammation. This plasticity is integral to its "noxious" generating functions. The two main types are the thinly myelinated, rapidly conducting Aδ fibres and the unmyelinated, slowly conducting c-fibres (Woolf et al., 2007).

Acute inflammation results in these endings being exposed to inflammatory mediators such as neuropeptides, prostanoids and cytokines. This reduces the activation threshold and increases responsiveness. They change then from being exclusively noxious detectors to also then detecting innocuous stimuli. These low intensity stimuli gain access to the nociceptive pathway to the brain, thereby contributing to the pain response. This process is known as *peripheral sensitisation* (Julius et al., 2001).

If a joint remains chronically painful, a slightly different process is at work. Chronic nociception may be as a result of residual inflammation that is depolarising the nerve ending, or it may be that the nerve threshold has actually been reduced so that a usually normal input e.g. temperature or movement, activates the nociceptor. Any axon potential not at the peripheral terminal (the axon or the cell body) may result in ectopic firing, that is, signalling being stimulated through the nerve without input from the periphery. This

increased activity to the dorsal horn means increased excitability of neuronal membranes, known as *central sensitisation* (Woolf et al., 1999).

JOINT PAIN AND NOCICEPTION

With noxious stimulus, the firing rate of joint nociceptors increases. Inflammation fires off the silent nociceptors which are present in all joints and are normally in a quiet state. Synovitis reduces the activation threshold of large diameter c-fibres. The newer blood vessels present in an active synovitis also have free nerve ends, which are susceptible to increased firing rate. Joint swelling stresses the receptors in the capsule. If there is loss of capsular elasticity from disease, stress on the free nerve end fibres within the thickened collagen fibres is increased. The joint is now hyper-responsive to previously normal movement, thereby permitting these receptors to fire off. Activation of the silent nociceptors means they may fire spontaneously, contributing to the phenomenon of resting joint pain (McDougall et al., 2006).

NO BRAIN NO PAIN

Multiple regions of the brain are involved in processing of noxious stimuli and other competing inputs to permit the pain output. They include the motor and pre-motor cortex, basal ganglia, cerebellum, insular, limbic system, amygdala, anterior cingulate cortex (ACC), hypothalamus, per-aqueductal grey (PAG) matter and the locus cereleus. There is no one pain region in the brain, and how many and to what extent each of these regions are involved in the processing of input perceived to be painful is unique to the individual involved (Tracey et al., 2007).

Cortical re-organisation (known as plasticity) has been observed after injury and after stimulation such as rehabilitation. With chronic pain, changes have been seen in an altered representation of the affected body part in the thalamus and cortex, as well as some decreases in the grey matter in the cingulate cortex (May, 2008), perhaps best illustrated by the phenomenon of phantom limb pain.

PSYCHOLOGICAL IMPLICATIONS OF PAIN

How an individual is feeling at the time of acute injury or with pain of a more chronic nature, can directly influence how that pain is mediated and processed, ultimately affecting the coping strategy and outcome.

The evaluative context of noxious stimuli actually affects the pain response it evokes. Anticipation of pain shows activity in the ACC and the PAG as well as increasing activity in the thalamus, insula and prefrontal cortex. This can serve to increase the response to the noxious stimuli (i.e. making it feel worse) or help prepare an individual for what is to come giving more control over the situation (Moseley et al., 2003). Those with fear of pain may provide more attentional bias towards pain related information, whereas those with anxiety about impending pain show a heightened response to pain and it lowers CNS performance, known as NOCEBO (Arntz et al., 2004). Pain is perceived as less when an individual is distracted from it, with a corresponding increase activity in the PAG, and the use of positive, pleasant emotional input (such as music, pictures or humour) reduce pain perception (Moseley et al., 2007). Stress can be both a positive and negative modulator of pain response. Anxiety induced hyperalgesia is where attention of the individual focuses on pain as the stressor, making the pain output stronger, whereby in stress induced analgesia the attention of the individual is on the environment as a stressor (e.g. in a war zone) (Colloca et al., 2007)

SOCIAL ASPECTS OF PAIN

An individual's response to pain is modulated by his home and social environment, and this starts from childhood. Parental response to a child's pain or injury has a direct effect on the pain behaviour displayed by the child. Parents who display more solicitous behaviour (reinforcing, attending to) may actually increase the sick role in the child, increase functional disability and increase pain severity (Chamber et al., 2002). High pain intensity in a child is often associated with increased distress by the parent, with those who catastrophise about a child's pain report more parenting stress, anxiety and depression (Goubert et al., 2008).

Pain behaviour displayed by the individual can be augmented by the caregiver at home. It can promote disuse and deconditioning in the individual complaining and living with pain, with the sick role becoming embedded in the behaviour of the individual. But those partners who are perceived to have an accurate perception of their partner's pain show less negative behaviour, are less stressed, and provide more emotional support (Martire et al., 2006).

THE IATROGENIC EFFECT OF PAIN

The effect on an individual with pain of each intervention with a medical professional should not be underestimated. Clinicians interacting with individuals in pain should be aware not to convey their own beliefs about that individual and their pain. Over-investigation or over-treatment may add to the burden of presentation as can inappropriate prescription of medication (Kouyanou et al., 1997). Taking the medical route within a consultation to avoid experiencing a patient's unhelpful hostility or emotional response, may actually add to the iatrogenic harm by the provision of unhelpful advice or information (Kenny, 2004).

THE INDIVIDUAL PAIN RESPONSE

The peripheral input from the nociceptors to the CNS is only one part of the pain experience. The underlying chemical and structural brain effects such as maladaptive plasticity and neurodegeneration, mood (anxiety, depression) combined with the context that the brain attributes to the experience (pain beliefs, placebo) and the cognitive set active at that time (attention/distraction, catastrophising, hypervigilance) create an individual pain experience, sometimes referred to as a pain "neurosignature" (Tracey et al., 2007). This is changeable, unique and must be observed within the context of that individual, highlighting the need for the biopsychosocial approach with such individuals.

SO HOW DOES ALL OF THIS FIT IN WITH THE PERSON WITH HAEMOPHILIA WHO IS COMPLAINING OF PAIN?

Studies suggest that 32-50% of people with haemophilia report living with chronic pain (Witkop et al., 2012), with one study also identifying 20% of children reporting mostly joint pain whilst attending treatment centres for clinical review (Rambod et al., 2016). Pain is a common symptom reported in both, acute haemarthrosis and haemophilic arthropathy, with factor replacement commonly used by persons with haemophilia to treat both, acute and chronic pain (Witkop et al., 2012). Persistent pain is most commonly described as aching, throbbing and nagging, with a wide variety of approaches described by persons with haemophilia to try and manage their pain (Witkop et al., 2012). However, even with these data, adequate assessment and management strategies for pain (acute and chronic) remain lacking in haemophilia care.

This chapter does not aim to provide detailed description of management strategies for pain. But instead will attempt to clarify an approach of assessment within a biopsychosocial framework that may inform how clinicians may start to manage pain in their haemophilia population.

There is absolutely no doubt that persons with haemophilia have many reasons to report pain, both acute and chronic. Acute joint bleed leads to swelling, joint pressure and inflammatory response, coupled with the fear and anxiety that such a bleed may impact upon life at work, school or in the family home. Synovitis brings with it new blood vessels and therefore more new free nerve ends. Chronic joint changes may promote arthrofibrosis and capsular thickening, exposed chondral bone and patient anxiety and worry about their mobility and ability to work or participate in their local social circles.

So how might clinicians begin to assess the problem of pain in their patients? One approach is that from www.bodyinmind.org. It is a methodical approach that aims to include and address all domains mentioned above:

1 What is the modifier/maintainer of this individual's pain?
   - Mechanical stimuli/ inflammation
   - Depression/fear/anxiety or joy/peace/distractions/faith
2 What are the features of the pain they present with?
   - Localised peripheral or segmental or non-localised
3 What is the location of the driving input to the pain response?
   - Local tissue injury and nerve terminals through to spinal cord/ midbrain/ forebrain
4 What type of pain is it?
   - Nociceptive/ peripheral neuropathic/ centrally driven
5 What output is being displayed as a result of this pain response?
   - Muscle spasm/ weakness
   - Multiple area sensitivity/ allodynia/ pressure hypersensitivity
   - Mechanical/ heat provoked pain
   - Pain behaviours, high disability, unpredictable pain episodes
6 What medications could/should be used and will they be effective?
   - Oral analgesics
   - Neuropathic pain medications
   - Central acting – e.g. opioids
7 How should the clinician "test" this pain?
   - Physical assessment – modifying stressors such as mechanical

irritation or neural tissue mechanical sensitisation testing
- Patient reported assessment – pain questionnaires

This type of assessment approach allows the individual time to talk and be listened to, as well as providing an opportunity for the clinician to listen, reassure, educate and manage expectation. It helps identify what the individual believes may help them and thereby begin to formulate an agreed intervention plan. Effectively managing expectation has been shown to promote physiological response, increase motivation, change their understating of the problem and mediates anxiety (Flood et al., 1993), and it should be the approach of the entire clinical team.

CONCLUSION

Pain is a problem in haemophilia, but it is unclear what kind of problem it is. The pain reported by many persons with haemophilia is poorly managed and this may be because in part it is poorly defined and categorised. As clinicians, we need to have up to date knowledge of modern pain science, and how this applies to our patient group. A biopsychosocial approach is imperative, taking into account the biological, social and psychological effects of living with haemophilia, and how living with pain modulates each of these factors. We must be mindful of our language when communicating with individuals in pain, for example, are we aiming to "treat" or "manage" pain. Effective assessments and interventions need to be investigated so as to further improve care. And the individual with pain must be involved at every stage so as to understand, learn and take control of their life with pain and haemophilia.

MEREL TIMMER

CHAPTER 12

Differentiating between acute haemarthroses and flare-ups of haemophilic arthropathy

INTRODUCTION

Elderly patients with haemophilia and younger patients without the benefit of replacement therapy suffer from both haemarthroses and haemophilic arthropathy. Currently, the diagnosis of a haemarthrosis is made based upon clinical presentation. No standard diagnostic criteria are available. However, in a recent publication it was reported that one-third of the painful episodes was diagnosed correctly (Ceponis et al., 2013). Early and accurate diagnosis is crucial in order to offer appropriate treatment. Clotting factor replacement therapy is a costly treatment, which makes differentiating haemarthroses from non-bleeding complaints even more important. Adequate differentiation is therefore not only in the best interest of the patient but can also decrease health care costs.

DIFFERENTIATION BETWEEN HAEMARTHROSES AND FLARE-UPS OF ARTHROPATHY BASED ON CLINICAL PRESENTATION

Signs and symptoms associated with a starting haemarthrosis are a feeling of fullness, stiffness and/or tingling sensation in the joint. These symptoms are in the literature also referred to as an aura. If untreated, increasing pain, swelling, warmth, limitation in range of motion (ROM), redness, tenderness, a shiny skin, a tense feeling, inability to load the joint, muscle spasm and a fixed flexed position will follow. Many of these signs and symptoms are also associated with (flare-ups of) haemophilic arthropathy (Timmer et al., 2015).

Differences and overlap between signs and symptoms associated with haemarthroses and signs and symptoms associated with (flare-ups of) haemophilic arthropathy are illustrated in figure 1.

In addition to the overlap in symptoms between haemarthrosis and flare-ups of haemophilic arthropathy, differentiating based on signs and symptoms is complicated by the following factors: Firstly, advanced haemophilic arthropathy is characterised by a fibrotic capsule, which limits swelling (Arnold et al., 1977). A haemarthrosis can therefore be present in an arthropathic joint without any swelling on clinical presentation. Secondly, in the acute phase existing flexion contractures make limitations in range of motion difficult to assess. Baseline measurements of range of motion are necessary in order to assess limitation in ROM caused by a haemarthrosis. Lastly, patients use the same words to describe chronic pain and acute pain (Choiniere et al., 1987) and 38% of patients use clotting factor for chronic pain (Witkop et al., 2011). This implies that differentiating based on type of pain is difficult.

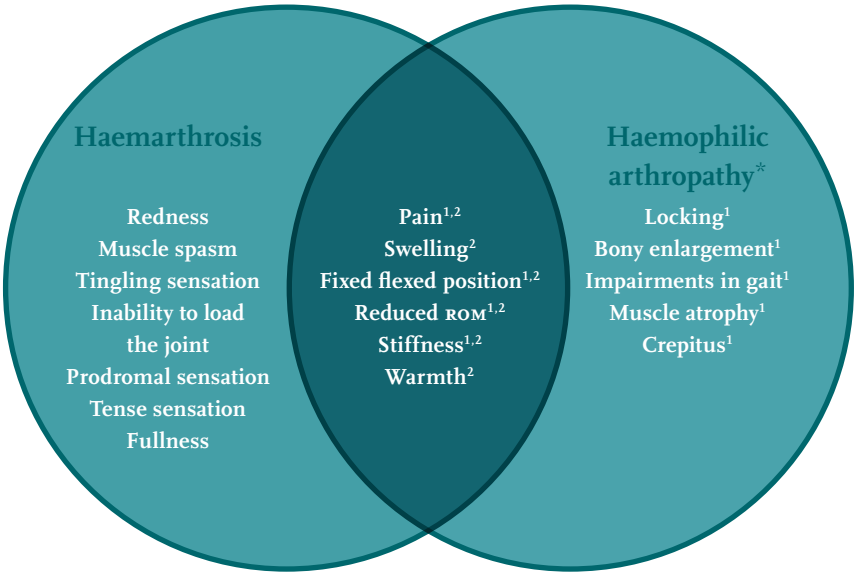


Figure 1. Overlap in symptoms between haemarthrosis and haemophilic arthropathy (Timmer et al., 2015)

* Including symptoms derived from literature on symptoms of osteoarthritis

1 Symptoms associated with chronic complaints of haemophilic arthropathy

2 Symptoms associated with flare-ups of haemophilic arthropathy

DIFFERENTIATION BETWEEN HAEMARTHROSES AND ARTHROPATHY PAIN USING ADDITIONAL TECHNIQUES

Joint aspiration is the preferred technique to identify haemarthroses in patients without a blood clotting disorder. However, in persons with haemophilia the use of aspiration as a diagnostic tool is questionable because of the need for replacement therapy with clotting factor concentrates to reduce the risk of provoking a bleeding. Additionally, narrowing of the joint space and fibrosis of the joint capsule in haemophilic arthropathy will make it technically more difficult to aspirate an arthropathic joint. MRI is considered the most accurate tool to assess soft tissue changes associated with haemophilic arthropathy (Doria et al., 2010). However, little is known about the possibility to differentiate between blood and a non-bloody effusion with MRI. Moreover, practical and logistic difficulties make this tool less preferable. Persons with haemophilia with recurrent bleeding episodes usually self-administer clotting factor and hospital transfer to make a diagnosis is therefore not feasible. Ultrasound seems a promising tool for this purpose (Melchiorre et al., 2011), but requires extensive training and knowledge of the musculoskeletal system (chapter 8). Furthermore, similar logistic disadvantages are present as with MRI.

INITIAL PROPOSAL FOR A DIAGNOSTIC CRITERIA SET

The use of a diagnostic criteria set, which preferably can be performed by patients themselves, could be a helpful tool to enable them to make a more adequate decision in an acute situation. Such a tool would also be applicable in areas with limited resources, where clotting factor must be used even more wisely. An initial proposal for items to include in a diagnostic criteria set was made by Timmer et al. (2016). The most important items are: course, cause, joint history, type of pain and limitation in ROM. The full overview of items is shown in table 1 (page 118). More research is necessary to validate the use of these criteria by means of a reference standard.

CONCLUSION

Differentiating based on clinical presentation is currently preferred. A diagnostic criteria set is proposed, however validation of these criteria is needed. Furthermore, ultrasound might be an option for patients living near a haemophilia treatment centre and have easy access to it.

	ITEM	JOINT BLEED	FLARE-UP HA
1	Course	Prodromal sensation/"aura" and gradually increasing complaints	Alternating course: stiffness after a period of inactivity, which decreases with movement, but increases after prolonged activity
2	Cause	Trauma or sudden onset	Overuse of the joint
3	Joint history	Young age, known unaffected joint (x-ray), no bleeding history of the joint	Known arthropathy of the joint (x-ray) or history of recurrent bleeding in the joint
4	Type of pain	Diffuse (entire joint) and pressing	Local and stabbing
5	Limitation in ROM	More pronounced	Less pronounced
6	Swelling	Increases quickly	No swelling
7	Loading the joint	Inability to load the joint	Loading the joint possible, but painful
8	Effect clotting factor	Complaints decrease after clotting factor	No effect
9	Duration (pain, swelling, limitations ROM)	Persisting	Decreasing after 1-1,5 hours
10	Rotation of the joint	Rotation limited	Rotation not limited
11	Traction	Painful	Pain relieving

>>>

ITEM	JOINT BLEED	FLARE-UP HA
12 Absolute rest	No influence on complaints	Alleviates pain
13 Locking	No locking	Possibly
14 Warmth	Possibly	No warmth
15 Judgement patient	Patient indicates joint bleed	Patient indicates no joint bleed
16 Haematoma / redness	Possibly	No redness or haematoma
17 Palpation of swelling	Painful	Not painful

Item 1 is considered the most important item, higher numbers indicate less important items
HA = haemophilic arthropathy

Table 1. Items patients and professionals use to differentiate between a joint bleed and a flare-up of haemophilic arthropathy (Timmer et al., 2015)

Adequate differentiation between haemophilic arthropathy and a joint bleed is not only in the best interest of the patient but can also decrease health care costs.

SÉBASTIEN LOBET, JOANNE POSTMA-ROWDEN
AND PIET DE KLEIJN

CHAPTER 13

Gait

INTRODUCTION

Gait is the most important way for people to move. As such it is crucial to functionality and thus participation. Persons with haemophilic arthropathy are characterised by their typical posture (chapter 10b) and gait alterations. According to the International Classification of Functioning, Disability, and Health (ICF) (WHO 2001) (www.who.int/classifications/icf), musculoskeletal alterations in haemophilia may stem from structural and functional abnormalities, which have traditionally been evaluated radiologically or clinically. Radiological scores strictly focus on the structural aspects of impairment, whereas clinical scores address both the structural and functional features of impairment. There are two main options to describe gait patterns: visualisation and technical (instrumented) gait analysis.

Recently an interest in the biomechanical status of haemophilic joints has emerged. Due to the rapidity of movement, simple direct observation of gait is rarely sufficient to give any insight into the pattern of limb movement, or to determine the biomechanical causes of an abnormal human gait. In instrumented gait analysis, physics and mathematics are applied to unravel the biomechanics of a pathological human gait and pinpoint which joint or muscle system is responsible for the functional deficit. In contrast to radiological and clinical examinations performed in a supine position, the uniqueness of instrumented gait analysis is that it assesses the

patient during the act of walking, under weight-bearing conditions. This is of utmost importance, as pain induced by weight-bearing activities significantly influences the functional performance of arthropathic joints.

The aim of this chapter is to give some practical starting points, explanations of parameters used and evidence available in gait assessment.

CLINICAL FEATURES OF GAIT

Gait may be characterised by a cyclical movement and periods of loading (stance phase) and unloading (swing phase) of the lower limbs. By convention, the gait cycle equals one stride and contains a sequence of events that usually begins with floor contact (0%) with one foot, and ends with the next contact of the same foot (100%), which corresponds to the initial contact of the next cycle (figure 1). Therefore, one stride is made up of two steps. In a normal symmetrical gait, the stance phase typically accounts for 60% of the gait cycle, while the swing phase represents the remaining 40%. There is some overlap between the stance phases of the right and left gait cycle. The period during which both feet are in contact with the ground is called the double support (contact) phase, which lasts for about 10% of the gait cycle and occurs twice during each cycle. These functional measurements, which provide valuable clinical information about the patient's movement patterns, include cadence, step length, and the percentage of stance phase and swing phase duration.

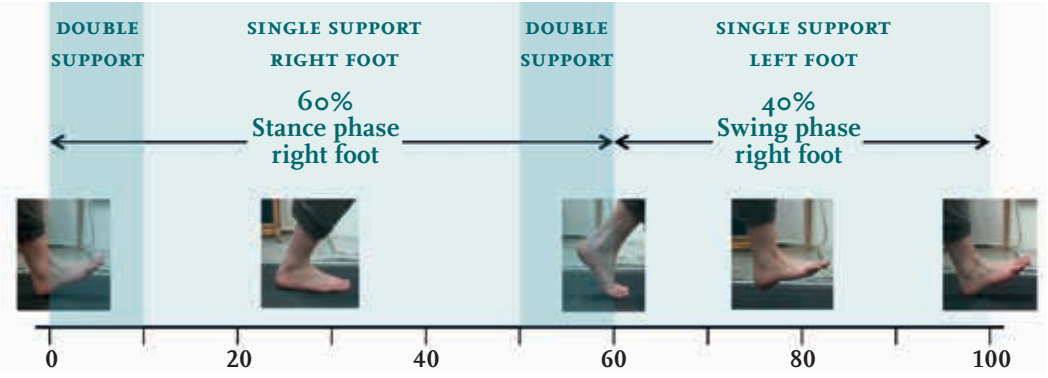


Figure 1. A complete gait cycle is defined as the movement from one foot strike to the successive foot strike on the same side (right foot on these pictures).

From a functional point of view we have to realise that gait is not the only thing to assess, but is a part of a series of movements: from a sitting (or lying) position → get up, stand on two feet and balance → start walking. And vice versa when going back to rest. Besides this, to walk there are certain requirements which depend on the purpose of walking, such as:

- Is speed necessary (e.g. goals at work)
- Are besides speed other skills needed (e.g. sports)
- Is the surface smooth or uneven
- Going uphill or downhill
- Are there different tasks at the same time (multitasking)
- Are direct surroundings busy (e.g. in street during shopping)
- Is a person carrying things (small or large) in his hands

In this chapter only gait on smooth surfaces wearing shoes is discussed. Besides this, age differences do exist. Ostrosky et al. (1994) compared walking between men and women aged 20-40 years and 60-80 years. Less knee extension and shorter stride length were significant, and these might influence other gait characteristics too.

VISUALISATION

Assessment by physiotherapists includes observation of a walking pattern. When an exercise programme is started, walking (exercise) should be part of it. An example is changing from natural trunk rotation towards a more lateral movement (body sway), which is found to be inconsistent within subjects. Another example is stride length, however this varies with age. For younger subjects it averages from 151-170 cm, and in older people from 135 -153 cm (Ostrosky et al., 1994). It is often impossible to objectify this during regular assessments in a traditional setup, where there is no room to perform tests like a Figure 8, or to visualise walking patterns from anterior, posterior and laterally, let alone to include all this in a functional exercise. However it might be effective, as shown by the example in chapter 16c, where we focussed on body and legs, but in practice the ankle, especially when wearing shoes, is even harder to inspect visually.

In order to properly follow up a patient's walking pattern over time, the Nijmegen Gait Analysis might be a good tool (table 1). It makes use of questions along with a complete explanation of terms

	QUESTION	SIDE	STANCE PHASE			SWINGING PHASE		PRIORITY
			EARLY	MID	LATE	EARLY	LATE	
General	Stance phase shortened?	Left - right	yes/no					yes/no
Trunk	Anterior to the hips?					yes/no		yes/no
	Posterior to the hips?					yes/no		yes/no
	Lateroflexion visible?	Left - right	yes/no					yes/no
	Too little armsway?	Left - right				yes/no		yes/no
Pelvis	Too much back rotation?	Left - right			yes/no			yes/no
Hip	Too little extension?	Left - right			yes/no			yes/no
Knee	Too little extension?	Left - right					yes/no	yes/no
	Flexion movement absent?	Left - right	yes/no					yes/no
	Too little flexion?	Left - right	yes/no					yes/no
	Too little extension?	Left - right		yes/no				yes/no
Ankle	Too little plantar flexion?	Left - right			yes/no			yes/no

Table 1. Nijmegen Gait Analysis list (modified), Bunnekreef et al., 2005)

used. It is an observational and visualising tool. Although reliability, validity and sensitivity of this tool have not been established, it can be a useful clinical tool.

During walking, stance and swinging phases are differentiated. The item is scored only if it is clearly visible. The same goes for the position of the trunk, normally above or just anterior to the hips. This item is only scored if the trunk is evidently anterior (or posterior) to the hips. For the other items we refer to Van Brunnekreef et al. (2005) who concluded that structured visual gait observation by use of a gait analysis form is found to be only moderately reliable and that clinical experience appears to increase the reliability of visual gait analysis.

INSTRUMENTED GAIT ANALYSIS

In instrumented gait analysis, the patient is asked to walk on a treadmill or a walkway equipped with force sensors that measure the ground reaction forces (GRF) under the patient's feet, while the patient is filmed by infrared cameras that track and record the trajectories of reflective markers positioned on the skin to define body segments. This video-based motion analysis system measures the three dimensional kinematics of locomotion. From the marker's positions the 3D trajectory of each marker in time and space is calculated, which allows to calculate the joint angles and range of motion (ROM) between two adjacent segments in a particular anatomical plane (e.g. the knee ROM is defined by the angle between the thigh and leg segments).

From the GRF we can also obtain kinetic values, such as the moments of force and power generated or absorbed at the major joint muscles although this is not performed routinely in all gait labs (Lobet et al., 2013a).

GAIT IN PERSONS WITH HAEMOPHILIA WITH MULTIPLE ARTHROPATHIES

The goals of achieving an optimal gait are not only to decrease the stress on the muscles and joints, but more importantly, to decrease the energy required to move from place to place (Waters, 1999). In patients with gait abnormalities after neurologic or orthopaedic disorders walking may consume two to three times more energy compared to healthy individuals. Energy expenditure is measured

indirectly, based on the rate of oxygen consumption using an ergospirometer and the net metabolic cost (the energy consumed by the muscles per unit of distance) can be calculated as the net oxygen consumption over walking speed.

People will tend to naturally walk with an economical style, a sinusoidal pattern of the head in space, allowing a smooth and efficient progression of the body's centre of mass (COM), in order to minimise energy expenditure. In walking, the COM which is located approximately 10 cm lower than the navel near the top of the hip joints, is lifted up and down during the stride. The pathway of the COM is therefore a smooth, regular sinusoidal curve that moves with an average rise and fall of about 3-4 cm. This vertical movement of the COM enables individuals to save energy, as gravitational potential energy is passively transformed into kinetic energy and back again (Cavagna et al., 2002). The pelvis, hips, knees and ankles play a major role in decreasing the vertical displacement of the COM by smoothing its trajectory and are therefore crucial in economic walking (Massaad et al., 2007).

Few studies have assessed the changes produced by arthropathies of the lower limbs on gait. Lobet et al. (2013b) investigated the kinematics, metabolic cost and efficiency of walking in 31 persons with haemophilia with multiple arthropathies compared with healthy subjects walking at the same speed. In theory, in persons with haemophilia, with loss of ROM of the knee and ankle, the strategy of vertical COM displacement reduction is compromised, leading indirectly to an increase of metabolic cost. This theory was confirmed, metabolic cost was dramatically increased in haemophilia, and highly correlated to a loss in joint ROM at ankles, knees and hips level. For instance, in case of isolated ankle artropathy, the increase in metabolic cost was proportional to ankle dysfunction: the less ankle power was generated, the more metabolic energy was consumed and efficiency of walking was more impaired (Lobet et al., 2012a). The disruption to the normal walking process by an orthopaedic disorder in haemophilia appears to generate mechanical and metabolic changes that follow a continuum linked to the progressive loss of mobility in the joints.

In persons with haemophilia, compensations in order to increase the dynamic stability may elicit a substantial and meaningful metabolic energy demand. Stiffening the body through co-contractions could be one of these strategies. As these co-contractions from an-

tagonist muscles do not produce any movement, they consume a lot of metabolic energy without any apparent work produced. Part of the muscular work may also be used to overcome internal friction and viscosity in the ligaments, muscles, or joints in order to deform the body segments. This is supposed to be greater in haemophilia as joint stiffness and muscle fibrosis are common complications of arthropathy (Lobet et al., 2008).

IS INSTRUMENTED GAIT ANALYSIS A SUITABLE TOOL TO ASSESS THE FOLLOW-UP OF JOINT STATUS AND EFFICACY OF HAEMOPHILIA TREATMENT IN CLINICAL STUDIES?

In light of these methodological and fundamental investigations, instrumented gait analysis appears to be a powerful tool to quantitatively characterise the locomotor functions of patients with gait disturbances, including haemophilia. Gait analysis can also be used in clinical trials to objectively quantify the effects of a conservative orthopaedic treatment in haemophilia.

Foot deformities are common in persons with haemophilic ankle arthropathy and often responsible for discomfort when walking or standing for long periods. Foot orthoses will likely make a substantial difference in terms of comfort and function. Lobet et al. (2012b) experimentally investigated the effects of custom-made orthopaedic insoles and shoes in persons with ankle arthropathy, with special attention to pain and gait. They suggested that orthoses may have beneficial effects, as they provide significant pain relief and comfort improvement, with minimal side effects, with only limited impact on gait pattern. Increases in ankle moment and knee flexion in the stance phase, also suggested that patients with orthopaedic shoes experienced improved weight acceptance, probably due to improved comfort and reduced ankle pain.

Recent work evaluating joint status and functional impairments associated with lower limb haemophilic arthropathy, using specialised laboratory equipment to study biomarkers of human motor performance, has shown that, when young pre-adolescent boys with haemophilia with a history of ankle joint bleeding are compared to age and size matched typically developing peers, lower limb muscle strength and size is reduced in boys with haemophilia (Stephenson et al., 2012).

CONCLUSIONS

Instrumented gait analysis can highlight the effect of an orthopaedic disorder in haemophilia during walking which can be a useful tool for clinicians.

Gait and gait analysis seem of utmost importance, since activities and participation of persons with haemophilia rely strongly on these skills and on functional adaptations. It is however, difficult to objectify without structured circumstances such as a gait lab. Besides there is a complete lack of reliability, only a few parameters can be observed during one session.

The Hemophilia Joint Health Score(HJHS) (Hillard et al., 2006) extended the original WFH score (Gilbert et al., 1993) of persons with haemophilia towards activity level. However in the HJHS gait can only be scored as normal or abnormal. To develop this part of the instrument more towards a discriminative, but also sensitive way of measuring, stair walking, running and skipping were added. Developments of the HJHS, especially for the use in elderly persons with haemophilia, are still in progress. In near future more aspects of gait have to be studied and incorporated, based on knowledge of experienced physiotherapists (clinical relevance), but also on proper research (effects).

Instrumented gait analysis can highlight the effect of an orthopaedic disorder in haemophilia during walking which can be a useful tool for clinicians.

MELANIE BLADEN

CHAPTER 14

Inhibitors in children: functional consequences

INTRODUCTION

An inhibitor is an antibody against factor VIII or IX that stops factor replacement from working. They bind to the injected clotting factor VIII or IX and prevent haemostasis. Overall 30% of persons with severe and 9% with mild and moderate haemophilia A may develop an antibody against factor VIII (Hashemi et al., 2015). Only 3% of people with haemophilia B develop an inhibitor against factor IX.

Risk factors for the development of an inhibitor are:

- Haemophilia severity
- Previous positive family history of inhibitors
- Ethnicity
- Number of exposure days to clotting factor
- Intensive treatment at a young age
- Gene mutation causing haemophilia

Inhibitors typically occur within the first 50 exposure days to factor concentrate and mostly within the first 20 days, meaning that inhibitors are more common in children with severe haemophilia and in older persons with mild or moderate haemophilia. The inability to prevent or stop a bleed results in frequent and severe bleeds. Inhibitor patients have worse joint scores, more functional limitations and a lower quality of life (Bladen et al., 2013). The long-term outcome for patients with inhibitors is not known, but the mortality rates for inhibitors are twice as high compared to non-inhibitor pa-

tients (Darby et al., 2007). These patients require additional medical support, of which the physiotherapist plays an important role. Frequent reviews and timely appropriate rehabilitation are essential to bleed prevention and management.

MEDICAL MANAGEMENT

Inhibitor management consists of prevention and control of bleeds as well as eradication of the inhibitor. Unfortunately prophylaxis with bypassing agents is not as effective as standard replacement therapies for non-inhibitor patients. However, prophylaxis with activated prothrombin complex concentrate and recombinant factor VIIa may reduce bleeding frequency, maintain or improve joint scores and quality of life (Leissinger et al., 2011; Konkle et al., 2007). This therapy is extremely expensive and due to the short half-life of these products, patients remain at a higher risk to bleeding and should always be treated with care.

Immune tolerance therapy with regular infusions of factor VIII aims to eradicate the inhibitor. 80% of patients will become tolerant and normal prophylaxis and therapy with factor will be possible again (Hay et al., 2012). Normally immune tolerance therapy is started as soon as an inhibitor is detected and continued until normal factor recovery and half-life are obtained.

PHYSIOTHERAPY MANAGEMENT

There is limited literature to support evidence-based guidelines on the physiotherapeutic management of patients with inhibitors.

Table 1. Consensus of opinion based on the literature (Forsyth et al., 2012)

IMMOBILISATION	REHABILITATION
Is used to promote healing	Progress slowly (cautious)
May reduce the risk of rebleeding	Tailored to the individual
In position of comfort	Monitor closely
Until pain resolves	Age appropriate
Adjust position as function allows	Should begin when pain subsides
Short-term use	If increased pain, swelling or limitation of active movement – reinstate resting the affected limb

Most publications are based on anecdotal, clinical experience or expert opinions and all lack the how, when and why (table 1) (Forsyth et al., 2012)?

Listed below are the common characteristics of patients with inhibitors, which may be important for physiotherapists to know. These patients:

- Are seen in the centre more frequently
- Have more frequent and severe bleeds
- Often need immobilisation with splints to prevent recurrent bleeding (especially smaller children)
- Rebleed more frequently
- May have unusual muscle bleeds (especially mild haemophilia patients with an inhibitor)
- Have an altered pain threshold
- May require more intensive rehabilitation after a bleed
- May have a recovery that is slower in pace
- Have weaker muscles, poor joint function and altered proprioception
- Often require physiotherapy local to home as well as in the haemophilia centre
- Require closer links with school due to school absence

IMMOBILISATION/REST AFTER ACUTE INJURY AND ITS EFFECTS

Current literature on acute soft tissue injury advocates a period of rest, avoiding replication of the injury forces in the acute phase. The rationale for rest post injury is to minimise bleeding and to prevent re-rupture at the site of injury (Bleakley et al., 2011). There is no evidence on the optimal timing, frequency on how to progress loading after a period of rest/immobilisation. Splints or braces may be used in the acute phase. Bleakley's guideline warned that prolonged immobility may affect wound healing and may increase loss of motion and contracture formation due to a decrease in glycosaminoglycans formation and water content of the matrix. This causes a dysfunction of normal gliding between collagen fibrils and an increase in the cross-linking between existing collagen fibres and new collagen, as well as proliferation of fatty tissue. Together these parts of the process then mature as scar tissue and this ultimately limits joint motion and may lead to joint contractures.

Immobilisation has multiple implications for the musculoskeletal system:

- Reduction in sarcomeres
- Reduction in protein synthesis after fewer than 7 days in cast immobilisation
- Reduction in cross-sectional area of muscle after fewer than 10 days
- Degree of atrophy dependent on muscle function
- Muscle function is length-dependent and the degree of atrophy is related to the muscle.

Muscle loss occurs after 5 days of immobilisation in patients without haemophilia (Wall, 2014). Muscle atrophy following bleeds in haemophilia is not unusual and, in patients with inhibitors, increased episodes of immobilisation are likely to lead to more muscle atrophy.

WHY DO WE IMMOBILISE MORE IN INHIBITOR PATIENTS THAN NON-INHIBITOR PATIENTS?

There is no evidence available in the haemophilia literature to suggest that current physiotherapy management is to immobilise patients with inhibitors more than non-inhibitors. However, what is known is that clot kinetics are abnormal in patients with inhibitors. Patients with severe haemophilia still retain clot-forming ability from the un-measurable circulating factor VIII, whilst patients with inhibitors have a true zero factor VIII function. This means that the time required to form a clot after infusion of bypassing agents is prolonged and deranged, therefore we can presume that the quality

There is no evidence to suggest that current physiotherapy management is to immobilise patients with inhibitors more than non-inhibitors.

and strength of clot formation may be less than adequate.

In vivo studies in haemophilia B mice found that cutaneous wounds healed more slowly in the haemophilia mice than in mice without haemophilia (Hoffman et al., 2010). There are no articles to support the use of immobilisation in children with inhibitors although, in reality, children may find it more difficult to rest or taper their activity; once they start feeling better, they tend to return to their pre-bleed activity status, often causing a rebleed.

REHABILITATION AFTER ACUTE INJURY

Healing of a muscle haematoma can take up to 30 days, depending on the degree of tissue injury that precedes it, which is longer than for joint bleeds.

The balance between immobilisation, rest and rehabilitation is difficult and is dependent on knowledge of normal healing times and clinical assessment. It is however advocated that the transition from immobilisation to tissue loading necessitates a structured approach that considers the affected limb and the range of movement. Rehabilitation needs to be progressive considering the affected structures, the range of movement required, repetitions and the speed at which they are performed (Bleakley et al., 2011).

HOW SHOULD WE PROGRESS REHABILITATION IN PATIENTS WITH INHIBITORS?

Sorenson et al. (2012) presented a combined perspective from physician and physiotherapist in the form of recommendations for both non-inhibitor and inhibitor patients in muscle haematoma management as shown in table 2.

All these phases may be difficult to adhere to with children, where stage of development (age), behaviour, parental support and cognitive ability affect rehabilitation. The ability to perform repeated muscle exercises can be challenging in children, particularly very young children. Such exercises are an important part of rehabilitation and must be progressed slowly and individualised, balancing the need for immobilisation and activity.

CONCLUSION

Patients with inhibitors suffer from recurrent severe joint and muscle bleeds, which are often slow to resolve. Even when a bleed has

PHASE 1 CONTROL OF HAEMORRHAGE	PHASE 2 RESTORATION RANGE OF MOVEMENT AND STRENGTH	PHASE 3 FUNCTIONAL REHABILITATION AND STRENGTH
PRICE Immobilisation in position of comfort Splinting may be used in children	In children complete rest may be initially advocated ROM Auto-assisted/active ROM within pain-free range Progressive stretching programme-as pain allows Strengthening isometric to isotonic / concentric to eccentric Progressing to hydrotherapy, gym and stability / proprioception exercise programmes Adjuncts used for complete bleed resolution Manual therapy / electrotherapy/ therapeutic heat	Maintenance programme of stretches, strengthening and stability exercises Progressive functional exercises- activity specific to the individual (This may be as simple as sit to stand activities or incorporate plyometric exercise) Exercises / interventions to address any biomechanical insufficiencies which may have caused the bleeding episode or resulted from it

Table 2. Phases of rehabilitation in inhibitor patients (Sorenson et al., 2012)

Case history

We report on an 18-month-old boy with severe haemophilia A and a high titre inhibitor. He is on daily prophylaxis with recombinant factor VIIa (rVIIa). He lives with his mum, dad and older brother. He sustained a right knee bleed, for which he was initially treated with 2 hourly rVIIa, tranexamic acid, rest and ice. For the pain he received paracetamol. He was cast in a soft cast splint to immobilise his knee. However, even after 2 weeks, the knee remained warm, painful and swollen despite maximising haemostatic agents. As there was uncertainty as to whether there had been any trauma, an x-ray was performed. No fracture was identified. He was sent home in a bi-valved splint and the parents were advised to leave the splint on for the majority of the day and take it off during bathing. However, the parents kept the splint in place for 1 week without removal. On assessment post-splint he had a fixed flexion contracture, was unable to weight bear and had no quadriceps muscle activity, but his knee was no longer hot or painful. He received daily physiotherapy for 3 months to address his flexion contracture. Physiotherapy consisted of hydrotherapy, stretches, standing frame, sit-on trike, night splints and functional play-based activities. Initially good progress was made, but improvements in ROM began to plateau and it was at this point that an appointment was made with the rheumatologist for a stretch and cast under sedation. Seven months after intensive rehabilitation, range of motion was near normal, he was able to run, but still had with some residual decrease in muscle strength on assessment (table 3).

stopped, wound healing is impaired compared to non-inhibitor patients. Due to recurrent bleeding such patients may have muscle contractures, muscle atrophy and altered proprioception.

RECOMMENDATION:

Patients with inhibitors remain at a higher risk of experiencing bleeding episodes and should always be treated with care due to the short half-life of the treatment products. To optimise physiotherapy,

	POST 2 WEEKS SPLINTING	PRE STRETCH AND CAST (5 MONTHS)	1 MONTH POST STRETCH	7 MONTH POST STRETCH
KNEE EXT/ FLEX	-65/90	-45/125	-10 (-5) / 120	-10 (0) / 147
QUADRICEPS	None	Filckers	Grade 3 partial ROM	Grade 3 available range
SWELLING	Yes, no bony landmarks (warm)	None (bony overgrowth)	None	None (symmetrical)
GAIT	No	PWB on tip toe (independent)	Intermittent flat toe / tip toe	Flat foot / lacking dorsiflexion
FUNCTION	Standing assisted / crawling / NWB	Running /kicking / squatting asymmetry	Run / stairs / soft surfaces	Run / gallop/ squat symmetry/ half kneel to stand.

Table 3. Progress in rehabilitation in patient from case study

treatment should occur as soon as treatment has been administered.

Immobilisation may be used more in inhibitor patients than in non-inhibitor patients due to their abnormal clot kinetics and delayed wound healing. The age of the individual may also contribute to the need to immobilise a joint. The balance of establishing haemostasis and minimising muscle atrophy is individualised and based on clinical improvements. Tissue loading is essential to soft tissue rehabilitation and as such immobilisation needs to be kept to a minimum. The lack of evidence on how to manage patients with inhibitors means we must rely heavily on empirical observations and clinical expertise. This in turn highlights the need for very regular clinical follow-up and review in such individual cases.

Rehabilitation of inhibitor patients should be individualised with progress implemented slowly, balancing the need for immobilisation and activity.

AXEL SEUSER AND LILY HEIJNEN

CHAPTER 15

Sports and haemophilia

INTRODUCTION

Physical activity or exercises are not sports! Physical exercises help to improve athletic abilities like endurance, flexibility, strength and coordination. This training is necessary to improve the outcome in sports. Sports follow rules and sport specific motor patterns with an individual mixture of the above named skills. Thus reflecting the needs of the performed sport. To perform the individual sport safely one should be able to fulfil the sport specific physical needs.

All published data about sports, exercise and physical activity indicate the positive impact it has on persons with haemophilia. It may lead to lower impact of haemarthrosis, increased range of motion, higher quality of life, less pain and optimal improvement of overall physical condition (Negrier et al., 2013). Regular physical activities prevent overweight and obesity. This adds to reducing bleeding frequency (Negrier et al., 2013) and may result in reduced factor usage. Children with severe haemophilia and good joint health can be as active as their healthy peers and report good scores on quality of life (Broderick et al., 2010).

Unfortunately all those activities (sports, exercise and physical activities) are often studied together. This is why we do not know the real impact of specific sports on haemophilia. But from the existing data we may conclude that there is more benefit in sports and physical activity than risks. As a matter of fact all persons with haemophilia are unique and we need to follow an individual approach to

find suitable sports or exercise programmes. In this chapter we will focus on the best choice with maximised safety for sports in haemophilia.

SAFE SPORTS FOR PERSONS WITH HAEMOPHILIA

HAEMATOLOGICAL BASICS

The most important issue is a good compliance both to physical activity and factor replacement. The person with haemophilia has to understand all the positive and negative implications of performing sports. Gonzales et al. (2008) showed that there is a higher daily mean time engagement in light, moderate and moderate/vigorous physical activity in adolescent persons with haemophilia than in healthy controls. He also underscored the important fact that haemophilia A patients who experienced at least one bleeding episode during the previous year, spend more time engaged in vigorous activities than those who had not experienced a bleeding episode. This illustrates the impact of acceleration on the joint mechanics during vigorous activities that might lead to a higher incidence of synovial impingement. If clotting factor concentrate is available, prophylaxis could be adjusted to sports activities. In situations of limited or no factor resources it is still beneficial for persons with haemophilia to participate in sports and physical activities appropriate to their individual circumstances. In this situation the potential risk of injury from any activity should be carefully considered.

As we do not have any literature comparing bleeding frequency in persons with haemophilia with and without inhibitors performing sports, the same goes for inhibitor patients. Our advice is to carefully monitor patients and physiotherapy or exercise programmes and avoid high-risk sports and suggest swimming, biking or walking (Heijnen, 2008).

CLINICAL AND ORTHOPAEDIC EXAMINATION

The basis for all decisions concerning sports in persons with haemophilia is a thorough clinical orthopaedic examination. This should not only include testing for range of motion, but also a detailed manual examination of the complete locomotive system. Using a score like the Haemophilia Health Joint Score (HJHS) does not suffice for the individual information we need. We advise a joint specific assessment with an examination of the condition of periarticular structures like tendons, ligaments and the articular capsule

of the ankle, knee, hip, and elbow joint. Muscle strength and coordination are always a part of clinical examination as explained below.

In 273 children with haemophilia (A n=216 [70% <1%; 80% on prophylaxis], B n=47 and Von Willebrand disease (n=10)) we found that, although 90% did not complain of acute pain before the assessment, the subsequent physical examination revealed so-called silent symptoms. These are unexplained pains on pressure that were verified upon detailed physical examination of tendons, ligaments and joint capsule. Of all the children with haemophilia A 82.6% had subclinical muscular-skeletal abnormalities. Most findings were associated with the knee and the ankle joint. The healthy control group had significantly less silent symptoms. In another study, using thermography as a diagnostic tool those tender points matched with hot spots, indicating that these tender points are correlated to low grade inflammation due to overloading (Seuser et al., 2013).

LOSS OF MUSCLE CONTRACTION PATTERN

There is evidence for a negative input of disturbed muscle contraction patterns in the biomechanical and orthopaedic literature. In an EMG study in San Jose (Costa Rica) (Seuser et al., 2011) a severe loss of muscle contraction patterns in the muscles of the lower extremities in 51 persons with haemophilia was found (mean age 16.5 years). Diminished muscle strength and changed coordination patterns are intimately associated with cartilage disease (Nigg et al., 2006). Even intra-articular saline in the knee causing capsular distension gives reflex inhibition of the Quadriceps muscle contraction.

3 DIMENSIONAL MOTION ANALYSIS

We advise 3 dimensional motion analysis because most children with haemophilia in our population (Seuser et al., 2009) and that of Lobet (Lobet et al., 2007) present functional disturbances in 3D motion analyses (chapter 13).

GENERAL PERSONAL PREPARATIONS

Persons with haemophilia should be encouraged to regularly participate in sports appropriate to their individual circumstances and age. Sport should be encouraged from as young an age as practical

to help to establish a positive attitude, and develop a lifelong habit of participation.

Before starting sports they should work with their haemophilia treatment centre. Evaluation for joint and muscle function (including balance, coordination, flexibility, muscle strength and endurance and synovitis) should be performed. In general sports with low impact are preferable. The impact of some sports can be reduced for example by playing on sand or using a lighter ball (badminton, volleyball). They should be aware that the non-impact aspects of sport such as running, turning, throwing, swinging a racket etcetera, can involve joint hyperextension and rotation stresses that may lead to bleeding due to synovial impingement (Negrier et al., 2013).

Activities of interest should be identified and realistic goals set based on capability, previous experiences, severity of haemophilia and clotting factor resources.

TIPS AND TRICKS

- Engage in active warm up and perform gentle stretching movements to maintain a normal range of flexibility. Gentle stretching can also be part of cooling down after activity.
- Use the proper equipment and wear any necessary protective equipment.
- Make sure the whole team is aware of the rules of the sport.
- Let children participate with peers of their neuro-muscular skeletal developmental age.
- If you are in doubt about a sport performance, contact a coach.
- If an individual is unfit for a desired sport, physiotherapy can be initiated to try to relieve any physical deficiencies preventing participation.
- The physiotherapist, physiatrist or orthopaedist can advise on the adaptions or modifications to sports that are needed to safely participate.
- If there are abnormalities of ankle and feet appropriate shoes and the use of inlays can reduce the clinical manifestation of joint bleeds in a cost-effective manner.
- If possible gait analysis and superficial kinetic EMG should be performed.
- Patients in low-income countries with access to sports and exercise programmes should be checked and treated for chronic synovitis, muscle atrophy, inflammation and pain prior to participation (Negrier et al., 2013).

- Age or arthropathy should not be seen as a barrier to sports particularly for low impact activity such as swimming and cycling (with a helmet and if there are safe cycle paths or quiet roads).
- Consider providing written advice regarding prevention in treatment of bleeds for the school coaches or parents of children with haemophilia.
- Physical activity as a preparation to perform sports should also be initiated for elderly patients.

SAFEST SPORT?

Sports injury statistics in literature vary so much that they are not useful for individual advice. So we have to rely on experience of professionals and persons with haemophilia and common sense.

EXACTLY DEFINE THE RIGHT SPORTS FOR THE PERSONAL STATE OF FITNESS

Before a particular sport can be recommended to a patient, minimum requirements of fitness and athletic skills must be met. Test balance and coordination, torso strength, aerobic endurance, flexibility and body fat. After testing the individual fitness, it is compared to the basic needs of the desired sports. If the demands of the sports are fulfilled the patient can perform the sport. If the demands are not achieved the individual fitness can be improved by the right exercise and training programme. By doing so the patient can broaden the range of sports available.

SPORT SCIENTIFIC CONSIDERATIONS

EVIDENCE

The topic sports and haemophilia is underrepresented in high-level scientific studies. The Oxford-level of evidence is as low as level 4 or 5 representing mostly the authors experiences with this subject (Negrier et al., 2013). The existing studies mainly focus on outcome, determining the individual performances of persons with haemophilia in different kinds of sports in comparison with a healthy control group. Some studies focus on the individual skills of patients necessary for performing sports. Those are endurance, strength, flexibility and coordination. We find positive correlations for physical activity and sports reported in a lot of papers. But on the other

hand a lot of papers do not distinguish between physical activity and sports (Negrier et al., 2013).

ENDURANCE AND CARDIOVASCULAR FITNESS

Appropriate endurance activities suitable for children and adolescents with haemophilia can be started at a young age. Endurance workouts must remain attractive, progressive and individualised. Physical activity should be performed two to five times a week for 30 to 120 minutes each to provide measurable health benefits.

FLEXIBILITY AND MUSCLE STRENGTHENING

Flexibility of the major muscle groups should be improved or maintained by stretching exercises. The focus for strength training should be predominantly on the abdominal and back muscles and the muscles of the lower extremities, especially the Gluteus Maximus, Gluteus Medius, Vastus Medialis, Peroneal and Tibialis Anterior muscles. It can be safe and effective if light weights and correct techniques are used. Slow movements and small joint excursions are necessary in the beginning. In general training of strength should not be started before the age of ten years. From approximately ten to fourteen years an overall and variable muscle strengthening programme is recommended with a very slow increase in weight. Care should be taken not to overload the spine. Over 15 years this strength training may be stepped up progressively, if desired when physical and skeletal maturity is reached. Intense strength training can be hazardous for patients with joint problems (Negrier et al., 2013).

COORDINATION AND BALANCE

Balance and coordination training can help to improve proprioception helping to avoid common everyday incidents such as bruises and is essential to enable young persons with haemophilia to reduce the risk of trauma. It can start as early as possible using the milestones of motor skills and perform age-related exercises (Gonzalez et al., 2011). It should be possible to perform all the components without pain and the programme needs to be modified as appropriate based on regular reassessments of patient status and fitness.

SCHOOL SPORTS IN GERMANY

AN EXAMPLE

Since 2002 the "Fit for Life" campaign has been running regularly in German haemophilia treatment centres. The results of these tests are the basis for the "Fit for Life" school sports counselling (Joeres et al., 2012). Additionally collected data are age, height, weight, severity of illness and type of treatment. Patients run through standardised fitness tests for flexibility, coordination, strength, and endurance, as well as a body composition analysis. This is the basis for the school sports counselling, done by a sports teacher. At the end of the counselling every student gets an individual and age-related selection of exercises. All exercises are characterised as suitable (green), suitable with restriction (yellow) or not suitable (red). By individualising the movement tasks to the ability of the students with haemophilia, they can be active with a diminished risk of injury during selected parts of the curriculum, even in otherwise risky sports. As a result there is a participation in the sport lessons, and no longer a sitting on the side-lines. In this way the aim of including students with haemophilia into sports lessons with other students can be achieved without losing the attractiveness of sports for the rest of the class. Very important is the fact that with an active student with haemophilia in the sports lesson, the teacher has the chance to fulfil school law, and give a real mark for the student, without just looking for a theoretical performance, or using the performance as a referee to give a sports mark. Such a "true" sports mark is of high psychological importance for the student, because it adds a stronger feeling of participation than only a theoretical mark in school sports.

CONCLUSION

Sports can be fun and physically and psychosocially beneficial for persons with haemophilia if chosen with some care.

Exercises are a way to improve physical health and prepare persons with haemophilia for sports and activities.

In the absence of sufficient clotting factor resources or presence of inhibitors the potential risk of injury from any activity should be carefully considered.

MERLYN TILAK, ARUN PAUL AND JUDY DAVID

CHAPTER 16

Physiotherapy in countries with limited resources

A • A single case study on fixed flexion deformity

INTRODUCTION

Joint contractures are common in countries with limited access to clotting factor in persons with severe haemophilia – occurrence is reported between 50% and 95%. Recurrent haemarthrosis in knee causes increased intra-articular pressure followed by adoption of mild flexion of the joint, a position of least tension in the joint capsule. This later worsens by further haemarthrosis and muscle wasting resulting in fixed flexion deformity of the knee (Fernandez-Palazzi et al., 1999) due to increased intra-articular pressure and distension of joint capsule. Joint distension causes reflex inhibition of the Quadriceps muscle. With the knee held in flexion, the knee flexors overcome the weakened knee extensors, pulling the tibia into posterior subluxation (translation) in respect to the femoral condyles (Rodriques-Merchan et al., 2008). This progressive posterior traction causes a shortening and tightening of the posterior knee capsule. When the fixed flexion deformity is established, the abnormal position of the joint seems to cause an increased number of intra-articular bleeding episodes. These contractures impact independent mobility and normal biomechanics of the body eventually leading to severe disability.

COMPREHENSIVE CARE

At the Christian Medical College, Vellore, India fixed flexion deformities of the knee in persons with haemophilia have been exten-

sively managed by conservative methods and it includes graded physiotherapy comprising of manual mobilisation of the knee joint, joint traction, electrical stimulation and strengthening of Quadriceps muscles for a few weeks until there is no further increase in range of motion. This is followed by serial casting and casting under anaesthesia. The graded physiotherapy and serial casting which are done are not supported by prophylactic clotting factor infusion. If fixed flexion deformity is not corrected completely with all these conservative methods, surgical correction is done.

Case

A 10-year-old boy, severe haemophilia A, studying grade 5, presented with difficulty to straighten his left knee and inability to walk for 8 months. In March 2011, he had sustained an injury to his left knee while playing. After this the joint became a target joint and he developed bleeding episodes (around 12 bleeds in 8 months) even with minimal activities e.g. an abnormal position while sleeping, and trying to move or weight bear on this joint for assisted mobility. The acute bleeding was managed at different occasions with a combination of Fresh Frozen Plasma, cryoprecipitate, and clotting factor concentrates, as an episodic management for the bleeds that he had in these 8 months. He had taken just one session of physiotherapy from a local physiotherapist from May to September 2011, with only minimal improvement in his range of motion. On the day of assessment on the 6th of December 2011 the knee range of motion (ROM) was 50 degrees short of full extension and his flexion range was 105 degrees. The muscle power of the left Quadriceps muscle was just a flicker (1/5). He had an equinus gait with pain when asked to walk. His HJHS score using the HJHS version 1.0 was 25 and the left knee joint score was 19.

FIRST PHASE

Fixed flexion deformity correction involved graded physiotherapy for one session per day. During this time, gentle manual mobilisation was done for the knee joint, both tibiofemoral and patellofemoral joint were mobilised. Quadriceps setting exercises, assisted by electrical stimula-

tion was started. It was followed by intermittent traction to the knee joint for 15 minutes in supine position. Patient was advised to lie prone for 20 minutes every night. Use of a knee brace with a posterior towel roll reinforcement at the Calf muscle was started to reduce the subluxation at the tibia as well as night bracing was taught. This was continued as long as tolerated by the patient. In addition, exercises for strengthening other limbs were included into the program. There were no bleeds during these sessions, and patient was not supported by prophylactic clotting factor infusion for therapy. A minimum of 5 degrees per week was expected. After 3 weeks of graded physiotherapy the ROM improved to 40 degrees short of full extension. There was a total of 10 degrees improvement in extension and 5 degrees improvement in flexion. His total range was 40 – 110 degrees (from extension to flexion).

SECOND PHASE

Since there was no further improvement with physiotherapy, serial casting was effectuated by his physiatrist. At the end of one week the cast was removed to explore and to mobilise into flexion and the next cast was applied on the same day. He underwent four periods of serial casting. For each cast there was a small window cut in the cast for stimulating the Quadriceps to prevent atrophy of the muscle. There was 10 degrees improvement in extension ROM. His total range at the end of 4 serial casting was 30 to 75 degrees (extension to flexion). He was allowed to walk with a walker within the house and to ambulate on a wheel chair outside the house.

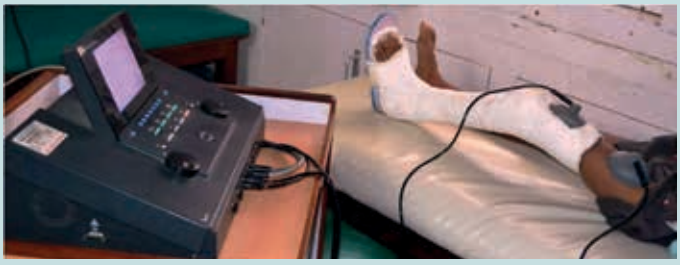
THIRD PHASE

The knee was then mobilised under general anaesthesia and a cast was applied by the physiatrist. Painkillers were administered and the cast was kept for 1-2 weeks. After casting under anaesthesia (CUA) his extension range was 25 degrees with a flexion of 40 degrees. After removal of the cast physiotherapy was restarted for Quadriceps strengthening and knee mobilisation for approximately 2 weeks. At the end of this session his extension range was 15 degrees short of extension and the flexion range was 60 degrees. During this entire

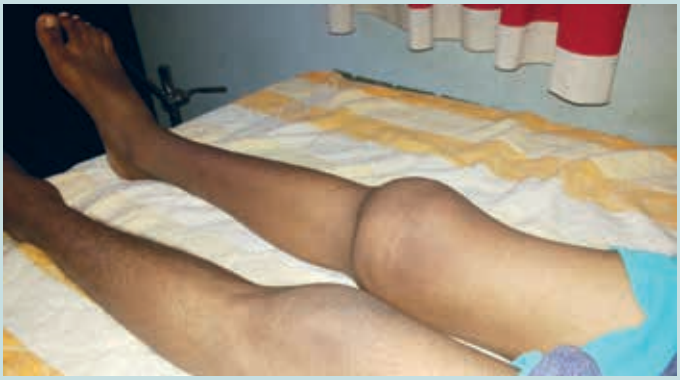
correction programme the patient developed only one bleed post CUA during therapy, which was managed with clotting factor concentrate. He was ambulated with a unilateral elbow crutch and left knee brace and was discharged from therapy and advised to continue the night bracing and follow the knee exercises at home. At discharge his knee range was 15 degrees short of full extension with 60 degrees of flexion. His HJHS score was 24 and his left knee joint score was 18.

FOURTH PHASE

During his follow-up visit a month later his range was 10 degrees short of extension and 40 degrees of flexion. After 1 week of physiotherapy his range improved to 5 – 45 degrees and he was again advised to continue the exercises at home. 5 years later with continued exercises his range is 5 – 125 and his muscle power is good (5/5), which was a significant improvement due to continued exercises at home and he is now ambulant without any assistive device or walking aids.



Cast in maximal extended position with possibility for electrical stimulation



Almost complete extension

EVELINE MAUSER-BUNSCHOTEN AND PUDJO WIDJAJANTO

CHAPTER 16

Physiotherapy in countries with limited resources

B · (Im)possibilities of comprehensive care

INTRODUCTION

In low-income countries care is different from high-income countries due to limited resources. But organisation of care can be problematic too. Distances are often long and infrastructure is poor or lacking completely. Even when there is public transport, people lack money to go to the hospital. People are treated in local hospitals, where there are no knowledge and laboratory facilities to diagnose and treat diseases like haemophilia.

And when patients are treated in a haemophilia centre stock of clotting factors is limited, and bleedings are treated with low doses of clotting factor concentrate. Prophylaxis is very uncommon. Parents consult a medical doctor in a hospital when their child has a visible bleed like epistaxis or severe bruises. Joint bleeds are not always recognised as problematic, which is the reason that clotting factor is mostly given for severe joint bleeds only. Paediatricians (and haematologists) are not aware that normal motor development, functional recovery after every bleed, as well as additional measures are of utmost importance to keep a patient physically functioning and help to prevent recurrent bleeding. It improves participating in a society where social support is scarce, and has a positive effect on quality of life. Due to lack of adequate treatment many patients suffer from synovitis, have functional limitations or are disabled.

WHAT ARE THE POSSIBILITIES?

- Implementation of comprehensive care centres with dedicated team members that coach local medical posts or hospitals how to treat haemophilia.
- Continuous education of medical and paramedical staff.
- Involvement of patients and parents to improve awareness. This can be effectuated during annual or regular patient group meetings, and more individually based during yearly check-up.
- Coaching of a patient or his parents by a physical therapist and a haemophilia nurse of the haemophilia treatment centre: What to do in case of a joint and muscle bleed, besides administration of clotting factor.
- Improvement of diagnostics. Availability of laboratory assays i.e. reagents and educate technicians.

WHAT ARE THE IMPOSSIBILITIES?

- Physicians are not aware of the value of comprehensive care and thus not interested.
- Financial compensation is not always sufficient to keep team members motivated.
- Education of paramedical members like nurse and physical therapist may not be sufficient to support people with haemophilia.
- Due to long distances and lack of money it may be a challenge to involve patients and parents in yearly patient contact meetings and educational sessions.
- Reagents are expensive, many hospitals lack trained technicians. Even when assays are possible patients cannot afford blood tests.

WHAT CAN WE DO?

Haemophilia care in emerging centres is not always well developed. Established centres can help emerging centres to improve haemophilia care by setting up a comprehensive care team and increase awareness, and in this way improve quality of life of people with haemophilia. In our experience the Twinning programme of the WFH is an adequate set-up to improve the quality of basic care in haemophilia treatment centres in developing countries. As clotting factor is not or insufficiently available, emphasis on the facilities that are available, such as (basic) physiotherapy, should be integrated more.

PIET DE KLEIJN AND EVELINE MAUSER-BUNSCHOTEN

CHAPTER 16

Physiotherapy in countries with limited resources

C • Twinning and the use of functional milestones: a case study

INTRODUCTION

The World Federation of Hemophilia recognises two kinds of Twinning programmes: between haemophilia treatment centres and between national member organisations. This chapter describes developments to improve haemophilia care in emerging countries through a formal, two-way partnership between two haemophilia treatment centres for a period of four years (http://www.wfh.org/en/twins). During this period, and often beyond, twinned organisations share information, exchange expertise, experience, skills, and resources. In each Twinning programme established centres help to improve diagnosis and medical care for people with haemophilia in emerging centres. The Van Creveldkliniek, the Netherlands, has been involved in this programme for more than 15 years.

In the emerging centres clotting factor concentrate resources are restrained, and only very few patients are treated in a prophylactic way. Thus, many patients suffer from recurrent joint bleeds, and as distances are long, people are poor and infrastructure is lacking, they often only go for treatment in case of a severe bleed. After a bleed has stopped, there is no follow-up and no active rehabilitation programme. Therefore optimal functional recovery is almost never achieved, and patients suffer from crippling contractures and (multiple) arthropathic joints, unfortunately already at a young age. For this reason rehabilitation, and especially physiotherapy, should play an important role in Twinning programmes. It has a recognised

position in the Twinning programmes established by the Van Creveldkliniek.

During presentations, bedside teaching and outpatient clinics we increase the awareness of the role of adequate rehabilitation and teach physiatrists and physiotherapists the principles of good communication, and basics of comprehensive care, in order to implement basic physiotherapy. This is always based on functional goals and performed purely in an active way, in order to prevent recurrent bleeding. If necessary aids (for example crutches) are bought and an individual training programme, for the duration of one year!, is designed. Both, patients and parents, need to co-operate closely, because one year is a long period. By using personal functional goals non-compliance seems less problematic, as illustrated by the case below.

FREQUENCY OF PHYSIOTHERAPY AND END OF TREATMENT

During our visits, children with haemophilia are assessed. Often they are not able to stand properly or to walk, making it a priority to discuss different treatment strategies. For this purpose we present parts of the general guidelines of the Royal Dutch Society of Physiotherapy (KNGF). Its general statement is that duration of a total sequence of sessions and its frequency strongly depend on:

- The ''request for help''
- Possibilities for the patient (ICF – external factors)
- Effects of treatment

The treatment focusses on the most important problem in an individual patient that is related to the request for help. This implies that intervention by a physiotherapist focusses on improving physical functioning and participating in society in a most individual way. Only three publications on the evidence of length of treatment sessions were found. There are indications that after a bleed improving activities to a level of daily functioning, may take as long as four weeks. To play sports safely may require a minimum of eight weeks extra. In this phase, a low treatment frequency of once a week may be sufficient (Royal Dutch Society of Physiotherapy). This implies that patients have to exercise at home, following balanced instructions, guided and coached from a distance. Weekly coaching is merely a check if during the previous week certain goals were achieved, or just partly, or not at all. Based on these findings the programme for the next period will be proposed. Safety of patients should be guaranteed at all times.

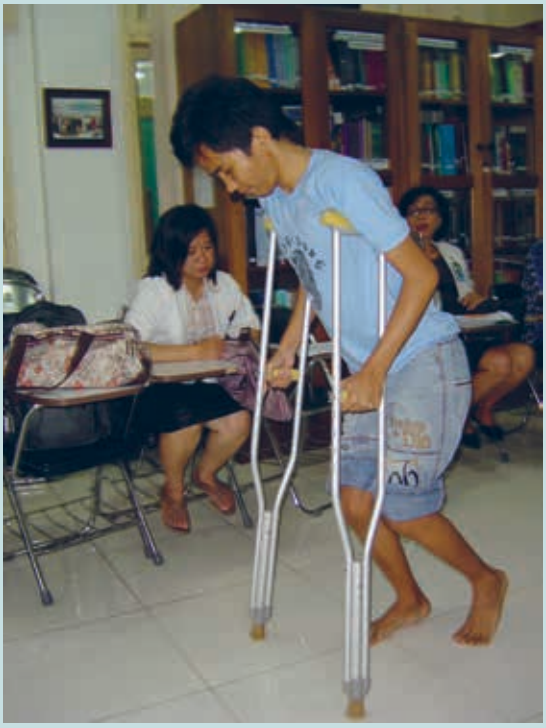
Case Mario

We first met Mario in the year 2010, during our initiating visit of the WFH Twinning with the Estella clinic, Dr Kandou Hospital, Manado (Sulawesi), Indonesia. He was transported to the hospital by family. He could sit upright, but was not able to stand. Even measuring his weight was performed sitting on his grandfather's back, weighed together, and after that grandfather alone. The difference in weight was Mario's weight. To move forward he crawled on the ground using both arms and both legs.

Picture 1. The first time we met Mario

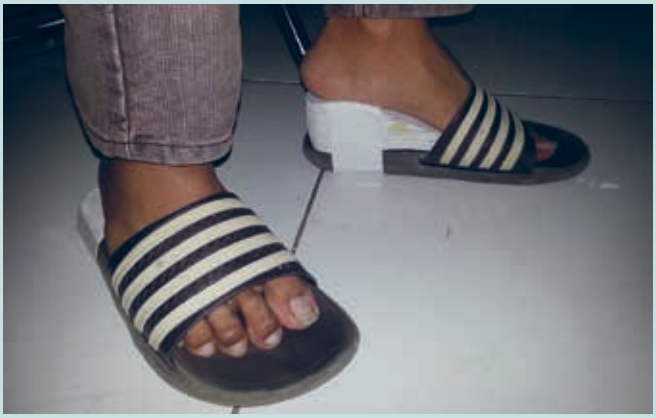
Picture 2. 2010 Mario crawling

After a first assessment a rehabilitation plan was made, tailored to Mario's main wish: to walk independently. During the first visit he was asked to exercise on a regular basis, but within pain limits, to stand for short periods, and walk tiny distances, always supported by axillary crutches. The main advantage of axillary crutches, above forearm crutches, is that one can stand and walk in an almost sitting position.



Picture 3. 2011 Mario able to walk on crutches in an almost sitting position

After one year (2011) the crutches had to be made longer in order to improve the posture, and mainly to force his knees to partially bear his weight in a more extended position. It took months to achieve this, and after a few months a second lengthening of his crutches was effectuated by a nurse, so that he could really adopt a more upright position.
The next year (2012) Mario was able to walk without any aids, and even walked the stairs. His right leg was dominant, the left foot had no heel contact. This is needed because it activates knee extension. So a heel raise was made by Dr Joudy Gessal, rehabilitation specialist, and his team.
The pictures tell us that he is more independent, and he has strong ideas how to raise his own income.



Picture 4. Heal raise

Picture 5. Mario with heal raise

In 2013 and 2014 we visited Mario at home, together with the staff of the Dr Kandou haemophilia treatment centre.
In 2013 he lived in the back part of the house of his family, and was able to produce some local candy: custard powder in a special folded banana leaf, topped with palm sugar. Then it is melted by means of steam. Outside Mario drives a scooter.
In 2014 his business went well, in case of a bleed he went to the hospital on his scooter. We bought, with help of an

Picture 6. 2014 Mario making cookies

anonymous donation, three extra steam pots. On market days he starts at three in the morning, making this pastry and to sell it to the market tradesmen. With three extra pots he enlarged his capacity and increased his income.
Every Twinning ends after a maximum of 4 years, but we heard from the staff of Dr Kandou hospital that Mario got married on the 14th of February 2015, and this year his wife gave birth to a son. Mario gave his permission to use all pictures taken of him during his whole "process".

ACHIEVEMENT OF MARIO AND THE USE OF THE ICF

Mario started to gain more extension in both knees, and muscle strength, which are needed to stand and walk with crutches. Gaining range of motion and strength are purely ''Body level'' (chapter 17). Walking without crutches enlarging his functioning is ''Activity level". His final goals were on ''Participation level'': a normal life, including earning his own income and having his own family. During our last visit Mario mentally supported other patients, as a "role" model with a very strong will to survive.

PART 3

Outcome

KATHELIJN FISCHER AND PIET DE KLEIJN

CHAPTER 17

Outcome measurement and International Classification of Functioning in haemophilia care and research

INTRODUCTION

The International Classification of Functioning, Disability and Health (ICF) is a framework of the World Health Organization (WHO) for measuring health at individual and population level (figure 1). Since 2001 it is the international standard (WHO, 2001a), as a classification of health and health-related domains. As the functioning and disability of an individual occurs in a context, ICF also includes a list of environmental factors. It focusses on impact of disease on all aspects of life, including the impact of the environment and other contextual factors. This creates a basis and framework in which all conditions can be compared using a common metric. In haemophilia the main environmental impact is the access to medical treatment (i.e. clotting factor concentrate), and strongly related to the country of residence. Another factor is the size of a country and number and locations of haemophilia treatment centres. This determines the distance persons with haemophilia, and their families, have to travel, in particular in acute situations, but also for scheduled treatment and check-up control visits.

BASIC MODEL

The "Evaluation of the non-bleeding joint" as advised in the early 1980s by the World Federation of Hemophilia (Gilbert, 1993) originates from a period that the focus of health care practitioners was on pathologies and impairments. Impairment parameters like mus-

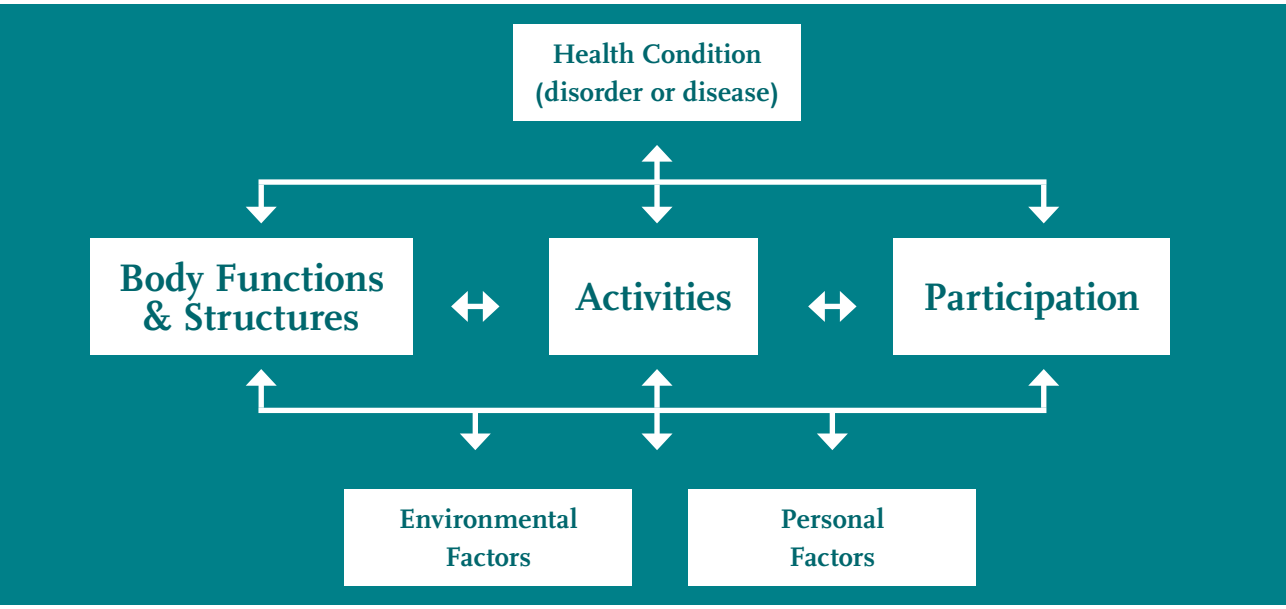


Figure 1. Interactions between components of the International Classification of Functioning (WHO, 2001b).

cle strength and range of motion merely reflect the function of organs and organ systems. For example, muscle strength and range of motion only reflect musculoskeletal function, but do not necessarily reflect a person's perception of his capacity to live a successful life. However fundamentally this model was created to describe the consequences of any disease (or disorder), totally independent of that disease. In this sense it complements the International Classification of Disease, which now has its 12th edition since 1893. Over the years the more negative terms as impairment and handicap, were replaced by activities and participation (Thuriaux, 1995).

PRACTICAL USE

The use of the ICF in rehabilitation medicine has been explored by Stucki et al. (2003, 2004). He stated that the success of the ICF will depend on its compatibility with measures used in rehabilitation and on the improvement of its practicability. From their starting point that rehabilitation is merely multi- and interdisciplinary management of a person's functioning and health, existing patient file forms were adapted to include categories of body structure/ function, activity and participation, environmental and personal factors. In addition, the form was divided into two parts: patient's and

healthcare professional's perspective. In a formal workshop the comprehensiveness was tested, and no missing domains were detected for indicator conditions stroke, back pain and osteoporosis. Unfortunately the ICF in its original form is not practical or feasible. It takes more than an hour to describe a person's functioning and health using the original version. Even the checklist (12 pages) takes more than half an hour.

The next step was to detect core sets of outcome parameters including only specific domains to be assessed. In haemophilia care and research, the core sets are almost reaching the phase of definition. The variation within this particular population makes this very difficult, because it should cover children and adults, medical treatment and non-medical treatment, developing versus developed countries, complicated and uncomplicated patients, surgery versus haemophilic arthropathy, arthropathy and chronic synovitis and so on.

Case

A 45-year-old man with severe haemophilia A and invalidating haemophilic arthropathy of both knees, both ankles and one elbow presented at the rehabilitation specialist. He questioned whether "Some support" for the knee could possibly improve mobility. He had not been able to continue his job (partly field work, local inspections of large buildings), and is on sick-leave.

During the intake it seemed that he stopped using painkillers, because he had the idea that medication was not good for his body and mind. Secondly he seemed depressed, stopped his leisure activities (coaching his son's tennis team) and became more passive. Instead of braces a strict pain schedule was prescribed. Concomitantly, the social worker coached, stimulated, and suggested him to contact his employer to change his work from field work to a more managing function.

After several weeks, he was seen again. He told that less pain occurred in both knees and that he increased his activities. He resumed coaching his son's tennis team and his work, but in a more coordinating function.

CONCLUSION

The model of the International Classification of Functioning can be a great help in both our daily care, and in haemophilia research, but it has its limitations. The most frequently seen omission is that the three main levels (bodily functioning, activities and participation) do not merely present a sequence of limitations, but interact with each other.

The model strongly advises, and this is effectuated in haemophilia care, that consideration of personal factors (e.g. depression) should be included into the total package of care. This model also shows that changing environmental factors can be part of a total treatment plan developed by the haemophilia comprehensive care team.

Muscle strength and range of motion only reflect musculoskeletal function, but do not necessarily reflect a person's perception of his capacity to live a successful life.

PAMELA HILLIARD AND AGNE JUODYTE

CHAPTER 18

The Haemophilia Joint Health Score

INTRODUCTION

The development of outcome measures for assessing the musculoskeletal health in persons with haemophilia dates back to the early 1980s with the development of the World Federation of Hemophilia (WFH) Orthopaedic Score. This score, although widely used in clinical studies did not have established measurement properties (reliability, validity and sensitivity to change) and did not appear to detect early joint changes. Particularly in studies of children treated with prophylaxis, a more sensitive scoring instrument was required. This led to the development of the Haemophilia Joint Health Score (HJHS) (www.ipsg.ca/working-groups/physical-therapy/info/hjhs) by the Physiotherapy Expert Working Group of the International Prophylaxis Study Group (IPSG), established in 2001. The international group of physiotherapists and physicians agreed to amalgamate existing scores and developed one instrument initially for children ages 4-18 years that could be used worldwide for research or clinical purposes such as comparing different prophylactic regimens with clotting factor concentrates, and tracking progression of joint changes over time. The HJHS is a clinical measure of joint structure and function using the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization.

INITIAL DEVELOPMENT

The HJHS, version 1 inter-and intra-rater reliability, tested in Toronto, Canada in 2003 was excellent (Hilliard et al., 2006). In a subsequent 2 year, multicentre validation study (2005-2007) the HJHS demonstrated excellent construct validity, and higher sensitivity for mild joint arthropathy than the WFH Orthopaedic Score (Feldman et al., 2011). Changes were made to the HJHS to reduce or change items that were redundant or poorly endorsed.

The current version is 2.1 and consists of 8 impairment items: swelling, duration of swelling, muscle atrophy, crepitus, flexion loss, extension loss, joint pain on motion and muscle strength measured on the 6 key index joints in haemophilia: elbows, knees and ankles. The maximum score for each joint is 20, with 0 being the best score. In addition, there is a global gait score (maximum 4) based on observing 4 gait skills (walking, stairs, running and hopping on 1 leg). A detailed instruction manual was developed in order to improve the assessor's reliability in both examining and scoring each item. An instructional video was also produced and can be downloaded and viewed in whole or in part. The work sheets (used to record examination findings), score sheet, instruction manual and video have been methodically translated into French, Spanish, German, Portuguese, Chinese (Mandarin) and Thai to date and are all available on the IPSG website at www.ipsg.ca.

SPECIFIC EXAMPLES

A few specific details relating to four items of the HJHS (swelling, flexion and extension loss and muscle strength) (picture 1) that evaluators have reported finding more challenging to assess and score will be highlighted here. Full details are available on the website listed above.

SWELLING

Visually examine and palpate the joints in both a flexed and extended position, comparing the left and right sides. Observe and feel the bony contours and the "hollows" or "valleys" around the bones. If swelling is visible, does it feel soft and puffy, spongy or boggy, or firm and tense? Are the bony contours partly or fully obscured? Is there bony deformity but no visible or palpable swelling? The latter should not be scored as swelling. A score of 1 is given if one area of the joint appears puffy and feels relatively soft on palpa-

Picture 1. Flexion loss and extension loss

tion. A score of 2 is recorded if swelling is visible and palpable (more spongy or boggy in consistency) in more than one area of the joint (e.g. suprapatellar and in the medial aspect of the knee). The bony contours are usually partly obscured. A score of 3 is given if the swelling obscures much of the bony contours and is tense or firm on palpation.

Each joint is measured with a goniometer (picture 2) (preferably with one degree gradations) and the measurements are recorded on the work sheet. Calculate the difference between the two sides and use the scoring chart labelled "Normal Contralateral Side" (on the work sheets, score sheets and in the manual). Since some persons with haemophilia may not have an unaffected side to compare to, normative tables (derived from a large US Range of Motion study) are provided in the manual. There is a separate scoring chart labelled "Normative Range Tables". It is very important for accuracy and reliability that each measurement is compared to both the contralateral side and to the age-related normative values. Examples are provided in the HJHS manual Addendum section. This may seem confusing at first, but becomes easier with practice. The two tables are used in an attempt to maintain sensitivity as well as specificity.

Picture 2. Use of goniometer

MUSCLE STRENGTH

Each identified muscle group should be strength tested and given a numerical score using Daniel & Worthingham's five point grading scale and is recorded on the raw data worksheet (picture 3). Since the patient's effort on the first test may be lessened due to not completely understanding the instructions or the last test due to fatigue or boredom, it is recommended that each test be repeated 3 times and that the best effort be recorded. Since all joints move in more than one direction, the direction that is given the weakest grade is used to determine the strength score. Ankle plantar-flexor strength is tested in standing if the person is able to actively clear his heel off the floor when asked to perform a heel raise. For a score of zero, four to five good heel raises must be performed.

If the assessor feels that any of the examination items could result in joint bleeding or injury to the patient, he or she would use his or her professional judgement in administering each examination item. If an item cannot be evaluated, it is recorded on the score sheet as NE (Non-Evaluable).

FURTHER DEVELOPMENT

The HJHS has subsequently been used in a number of studies in children and young adults with haemophilia. Following a four day "Train the Trainer" workshop involving physiotherapists and physiatrists in China in 2009, a reliability study (mirroring the original reliability study design) was conducted. This study also yielded excellent inter-and intra-rater reliability results (Sun et al., 2014).

Fischer and de Kleijn studied HJHS (version 1) validity in 22 and inter-observer reliability in 12 adolescents and young adults (ages 14-30 years). They found moderate to good concurrent validity and strong inter-observer reliability and concluded that the HJHS can be used to evaluate teenagers and young adults with limited joint arthropathy (Fischer et al., 2013).

Two systematic review articles of outcome measures have included the HJHS, highlighting its strengths and gaps for clinical and

Picture 3. Measuring muscle strength

research purposes (Stephensen et al., 2014; Fischer et al., 2016). Recognised strengths of the HJHS included its acceptable construct validity, internal consistency and repeatability. It is also able to distinguish between different prophylactic regimens in young adults with severe haemophilia, between severe and non-severe haemophilia in children and is responsive to changes following physiotherapy treatment. The need for experience in joint evaluation and training in the use of the tool, limited ability to discriminate changes in physical function and the need for further study in adults and those with more advanced joint arthropathy were recognised as current weaknesses or gaps.

FUTURE DEVELOPMENTS

Currently, a multicentre study of the convergent and discriminant construct validity of the HJHS version 2.1 in adults with mild, moderate or severe haemophilia (through the age spectrum) is being conducted in order to address some of the identified gaps. Concurrently, age-matched non-haemophilic adults will also be examined using the HJHS. Further studies will help to identify the numerical HJHS score that may signify a clinically significant difference and need for intervention.

The role of the physiotherapist is important in all life stages of persons with haemophilia.

Cartilage changes result from both direct and indirect blood-induced damage.

In case of rehabilitation after a muscle bleed it is important to train the antagonist muscle too to prevent a contracture of the affected muscle.

Contractures impact independent mobility and normal biomechanics of the body eventually leading to severe disability.

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