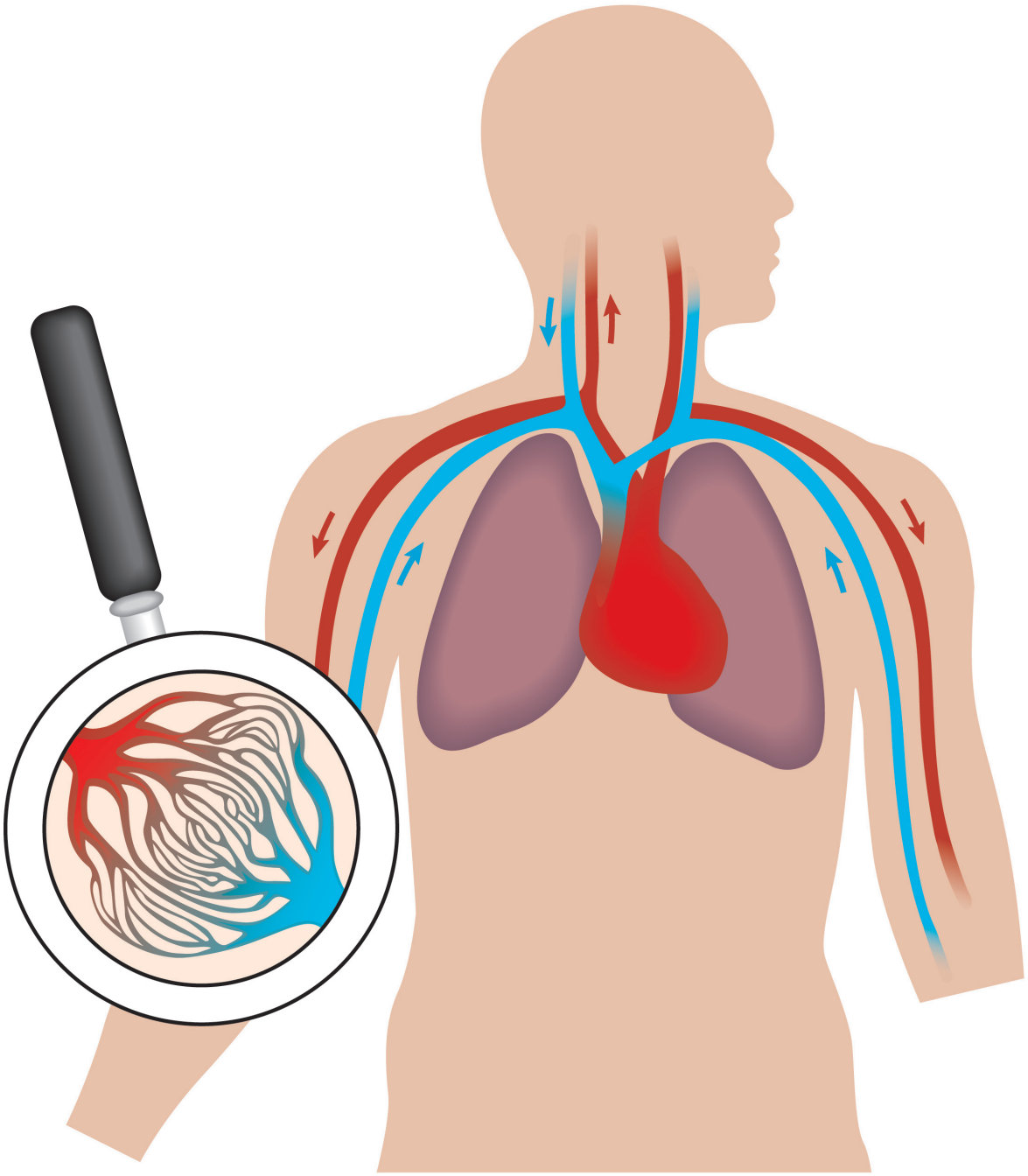
Hemophilia in Pictures

Educator's Guide



World Federation of Hemophilia

Published by the World Federation of Hemophilia

This publication is available as a PDF file on the World Federation of Hemophilia's website at **www.wfh.org**. Additional copies are also available from the WFH at:

World Federation of Hemophilia
1425 René Lévesque Boulevard West, Suite 1010
Montréal, Québec H3G 1T7
CANADA
Tel. : (514) 875-7944
Fax : (514) 875-8916
E-mail: wfh@wfh.org
Internet: **www.wfh.org**

The *Hemophilia in Pictures Educator's Guide* is intended to provide general information on the treatment and management of hemophilia. The World Federation of Hemophilia does not endorse particular treatment products or manufacturers; any reference to a product name is not an endorsement by the WFH. The World Federation of Hemophilia does not engage in the practice of medicine and under no circumstances recommends particular treatment for specific individuals.

Acknowledgements

The *Hemophilia in Pictures Educator's Guide* was developed by WFH volunteers from around the world. Much appreciation goes to the guide's contributors: Lara Oyesiku, Els Haan, Cathy Turner, Frederica Cassis, David Page, Kathy Mulder, as well as to the WFH Nurses Committee and the Inhibitors Working Group for reviewing it. These professionals volunteered their time and expertise to provide a practical guide for educators using *Hemophilia in Pictures*.

Table of Contents

Introduction: Teaching about Hemophilia

Basic Principles and Approaches to Patient Education

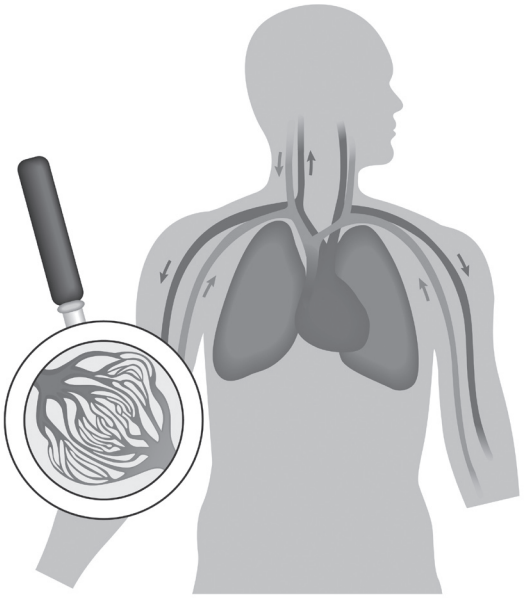
Patient education contributes significantly to one's total physical, intellectual, and emotional development. Healthcare professionals must have comprehensive knowledge of their area of expertise (nursing, physical therapy, counselling, etc.) so that they can effectively share information and resources with their patients.

Hemophilia care is a team endeavour. As educators teach people with hemophilia how to take care of their medical and emotional needs, and how to understand, accept, and live with a chronic condition, it is important to remember that people with hemophilia have much to teach as well.

Through their stories and experiences, people with hemophilia can teach educators what it is like to live with the disorder, thus informing them of ways they can better help. Educators, for their part, can teach people with hemophilia about their disorder and the impact it will have on their lives. Patients need guidance and training on how to self-infuse, treat bleeds with first aid and/or replacement factor, control pain with appropriate analgesics, exercise to improve and maintain mobility, learn to accept the chronic condition, and go on to lead productive lives at home, work, and play. Families, friends, and co-workers can learn about the disorder from both people with hemophilia and educators so that they can provide support and understanding when needed.

Through a collaborative learning process, educators teach, talk, listen, and learn, enabling them to share their expertise and knowledge more effectively with both patients and other healthcare professionals.

To find out more about how people learn best, look for resources on learning styles, principles of adult learning versus child learning, and the theory and practice of patient education. You can start with the patient education titles listed in the references at the end of this guide.



How to Use *Hemophilia in Pictures* as a Teaching Tool

The purpose of *Hemophilia in Pictures* is to provide basic knowledge about hemophilia through pictures and easy-to-understand information.

This educator's guide has a dual purpose:

- To give healthcare professionals key information to help them explain hemophilia to patients, including management and complications associated with the disorder.
- To give learners (patients or healthcare professionals undergoing basic hemophilia training) main points about care and treatment and expand their knowledge and understanding of hemophilia.

Goals for educators

- Like any disease, hemophilia is only one aspect of a person's health. Deal with the person holistically—medically, emotionally, and intellectually.
- Get to know the patient. Find out how much he knows about hemophilia. Ask about his experiences living with a chronic condition.
- Provide information in a logical, step-by-step way. Do not overwhelm patients with too much or overly technical information.
- Encourage patients, their friends, families, and co-workers to educate other people about the disorder. For example: "When I get hurt and start bleeding, it takes longer for the bleeding to stop. This delay in the way my blood clots is because something is missing in my blood. Bleeding can sometimes give me health problems that make it hard to work or play games."
- Educate people with hemophilia about the importance of taking the condition seriously and knowing basic elements of self-care. It is important that a person with hemophilia be able to:
  - Quickly detect instances of bleeding;
  - Know when and how to treat a bleed, when to self-infuse, and when to go to the treatment centre or emergency room for treatment;
  - Use first aid procedures such as rest, ice, compression, and elevation;
  - Achieve a healthy balance of rest and exercise.
- Teach parents the importance of letting their children experience their bodies as a source of pleasure and not just pain, such as by encouraging them to take part in appropriate games and sports and to use exercise and physical therapy to strengthen their bodies.
- Reassure families that support is available from other family members, physicians, nurses, hemophilia treatment centre personnel, social workers, physical therapists, support groups, national and regional associations, and the World Federation of Hemophilia.
- Explain the multidisciplinary nature of hemophilia care. The ability to be empathetic and to advocate with other healthcare professionals on behalf of patients and their families is very important.

Goals for people with hemophilia

- With time, you will learn how your hemophilia affects you. You will know what causes a bleed, how to prevent or treat a bleed, and what types of activities to avoid.

- You have your own personal experience and story to share. Your family and your healthcare team are there to help you, work with you, teach you, and be with you on your journey of learning to live with hemophilia.
- As the patient, you have rights and responsibilities:
  - You have a right to ask for the best care you can get.
  - You have a responsibility to take an active part in the learning process, learn more about your hemophilia, and share your experiences so that your family and the multidisciplinary team can support you.

Teaching Tips for Patient Education

Whether you are educating patients at a hemophilia treatment centre, or teaching family members or caregivers how to care for people with hemophilia, these tips can come in handy.

Preparing to teach

- Set a general goal and specific objectives for each session no matter how short the session is. It will help you stay focused and keep the learners on topic. This will improve their ability to retain new information.

  Example: By the end of the session, learners will be able to:
  - Explain how blood moves around the body.
  - Demonstrate with dominoes how bleeding starts and stops.
  - Demonstrate with dominoes why people with hemophilia sometimes bleed longer than other people.
- Make the session "learner-centred" instead of "teacher-centred." Avoid doing all the talking and ensure that learners are able to fully participate by asking questions, telling you what they already know about the topic, doing activities that will help them absorb new information, and then reviewing it.
- Create a teaching kit so all of your lesson plans and teaching aids are kept together.

Learners will remember:	
10% of what they read	50% of what they see and hear
26% of what they hear	70% of what they say
30% of what they see	90% of what they say as they do something

Teaching effectively

- Hand out printed materials.
- Use simple language.
- Speak slowly.
- Read instructions out loud.
- Write out instructions.
- Be careful not to overwhelm learners with too much information and check for understanding.

- Give examples to help explain difficult words and concepts.
- Use medical terms consistently rather than alternating between two terms that mean the same, such as "hypertension" and "high blood pressure."
- Ask patients how they will follow instructions at home.
- Ask if the patient would like a family member to join the discussion.
- Ask the patient to repeat information. ("Teach back")
- Underline key points in patient information handouts.
- Ask office staff to review instructions with patient.
- Draw pictures.
- Use models to explain.
- Follow up to check understanding and compliance.

Asking open-ended questions

Asking strategic questions is the best way to identify a patient's needs, abilities, health beliefs, and level of understanding. Avoid asking questions that can be answered with "Yes" or "No" such as "Do you understand?" Instead, ask open-ended questions that reveal understanding such as the ones listed below. Be sure to give learners time to think and respond.

Examples:

- What questions do you have?
- When you think of _____ (hemophilia, exercise, etc.), what image or word do you think of?
- What does this page tell you about _____ (subject)?
- What does this illustration tell you to do?
- What problems do you think you might have in starting an exercise program?
- What will be your family's biggest challenge with _____.
- What would you do if _____?
- What changes would you like to make first? (Give the learner a list of recommended actions to choose from.)
- If you _____ (take this medication, do physical therapy, etc.), what are you afraid might happen?
- What do you think causes _____ (hemophilia, pain, etc.)?
- Why is _____ important you? (beliefs related to health, exercise, eating habits, etc.)
- How much of this _____ (medication/exercise) do you need to _____ (take/do) every day?
- On a scale of 1 to 10, how sure are you that you can do this? (A specific action, such as self-infusion or a physical therapy exercise. If answer is 7 or less, ask the learner to revise the goal to ensure success.)

General tips for educators

- Once the patient has received his diagnosis, help him and his family take the time to absorb the facts. Encourage feelings to be expressed openly. Reassure the family, where possible, that there are psychologists and social workers at hemophilia treatment centres who will support them through the process. If not, many centres will have access to emergency psychosocial support through hospital departments or community organizations.
- Advise the patient that while there are similarities in the experiences of people with conditions such as hemophilia, each person will experience unique emotions. Provide ample opportunity for patients to tell their stories. Treat each family member as unique and resist the temptation to impose preconceived ideas of how they "should be feeling."
- Help the patient and his family learn as much about the disorder as they can. Discuss it in simple terms. This will take time but ultimately will facilitate their acceptance of hemophilia and their understanding of when to seek appropriate medical or psychological treatment.
- Help parents find the balance between encouraging their children with hemophilia to actively participate in life and ensuring that they do not take unnecessary risks. Encourage parents to be aware of when they may be too overprotective.
- Encourage parents to stimulate good body coordination and reflexes in their toddlers through activities for balance, hand-eye coordination, etc. This will encourage movement and play, and help the child with hemophilia develop self-confidence and body awareness early on and under supervision.
- Prepare the child with hemophilia to have to deal with emotions such as fear of needles, pain, and anger earlier than other kids would have to. Help parents deal with their own emotions about hemophilia and develop strategies to create a calm atmosphere for themselves and for their child.
- Encourage a proactive approach to managing related issues such as dental or surgical procedures. Parents need to explain any nessesary procedures to their child carefully, in easy-to-understand terms. They must be open and truthful about pain, complications, etc.
- Remind parents that children with hemophilia mostly have the same needs and same cognitive development as children without hemophilia. Help parents keep in mind that certain behaviours (e.g. tantrums) are ordinary in child development and are not in any way due to hemophilia.
- Help families recognize "burnout," to know when stressors have become overwhelming, and to know when and where to seek help. Encourage them to join a hemophilia organization or a support group, to access information, share knowledge, network, and reduce stress.
- Remind the family that understanding the impact of hemophilia is a gradual learning process. Assure them that there is a lot of support available from professional psychosocial staff and hemophilia organizations. Provide them with clear and concise contact details to give a real sense of support following the initial meetings.
- Try to improve the patient's and family's health behaviours by incorporating, not changing, their existing cultural beliefs and values unless they are actually harmful.

Developing and Using Teaching Tools

Teaching aids such as transparencies, videos, audiotapes, and booklets can help learners meet an educational objective. You do not need to buy a lot of expensive, professionally made aids, though. Simple magazines, books, toys, and other objects lying around your house or treatment centre can be adapted at virtually no cost.

Visual aids—especially ones showing sequences and cause and effect—can be valuable tools in patient education. For example, the illustrations on pages 18 and 19 of *Hemophilia in Pictures* can be used as storyboards or cartoon strips to get a teaching point across. You can also ask the patient to put the story in order and retell it (after covering up the numbers on the frames).

General guidelines

- Use aids to enhance communication with patients, not replace it.
- Consider whether the aid is suitable for the patient and the situation. Will it improve progress toward a relevant learning objective?
- With teenagers and adults, explain why you are using the teaching aid. Does it contain additional information relevant to the patient? Will it be useful to review key points of a discussion?
- Accompany the aid with verbal instructions rather than simply sending it home with learners to read on their own.
- Point out sections of particular importance and cues to perform skills demonstrated.
- Demonstrate how the patient can review the information at home.

Teaching toddlers and children

- Find cartoons and pictures from books or magazines, or draw your own simple illustrations, and glue or paste them onto cardboard or pieces of wood to form flash cards.
- Make photocopies of the illustrations and captions in *Hemophilia in Pictures*. Personalize the captions using the child's name, etc. Cut out the captions so that a child who reads can match the caption to the picture.
- Make black and white photocopies of relevant pages in *Hemophilia in Pictures* and invite children to colour in particular areas of the illustration as you discuss them. Then ask the child to tell you what they can remember about the coloured areas.
- Use the illustrations or develop flashcards on different aspects of hemophilia to engage the child. Have the child tell the story as you go through the flashcards. The goal is to personalize the flashcards to the child's experience.
- Use picture books that you already have at home or from a local library. Adapt the characters from those books and retell the stories, relating them to the child's hemophilia.
- Try to find simple images that convey complex ideas. For example, draw simple images of a plug and water to show the idea of platelets and clots not forming. Or, depict blood as a pool of water with little fish to symbolize different cells in action before and after infusion. Give the missing factor a name that the toddler will remember. Use anything that will be a good reference point for the toddler and make your explanation and his understanding easier.
- Develop flashcards showing first aid procedures. The child will eventually learn what steps need to be taken. Then, if bleeding occurs when he is on his own, he will know what to do and in what order.

- Use simple drawings, flashcards, dolls, puppets, etc. to "rehearse" hospital visits, injections, and other potentially frightening situations so that the child has an idea of what to expect. De-mystify the process using simple language he can understand. Answer questions honestly.
- Describe what he will see, hear, smell and feel during a new medical procedure and have very young children point to their eyes, ears, nose, and hands as you speak about the corresponding sense.
- Use a wide range of learning tools and age-appropriate language. Work with many different educational tools. Be creative. Use images, drawings, cartoons, and games for both adults and children. Get learners to repeat what they have learned back to the instructor, to make sure that the message is getting across.
- For review, you can switch roles so that the child is the teacher and you are the student. Give him a prop that will help him feel like the teacher, such as a white coat or clipboard.

Teaching teens

- Use the images in *Hemophilia in Pictures* as points for discussion. The illustrations are valuable as tools in patient education.
- Expand on the illustrations by describing relevant problem situations and asking the teen to choose the best solution. Find out the reasons for his choice and discuss other effective solutions.
- Test the teen's understanding and retention of the material by using the review quiz at the end of each chapter in *Hemophilia in Pictures*, after you have read each section together.
- Remember that the adolescent years can bring rebellion and a desire to test limits. Address these issues honestly and directly.

Review Activities

To help learners of any age remember what they learned in each section of *Hemophilia in Pictures* or other educational materials, do a written or verbal quiz such as the one in the appendix on page 41. If you have the time, consider giving the quiz in an interactive way (see the examples described below) or adapt a game that children in your area already know.

The four-part review quiz in this guide is designed to test knowledge and retention. You can use the questions page by page as you work through *Hemophilia in Pictures* or test learning at the end of each section: Parts 1, 2, 3, and 4.

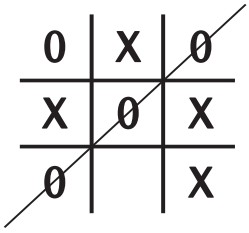
Question Pockets

Make a board with 11 pockets. Write "ANSWERS" on one pocket and number the other pockets from 1-10. (You can use envelopes as pockets on a large sheet of cardboard.) For each section of *Hemophilia in Pictures*, write up to 10 questions and their answers on separate cards so that you have up to 20 cards in total. Mix up the question cards and place one in each pocket. Give the answer cards to the learner(s). Ask them to put each answer card in the pocket with the matching question. Demonstrate how to do this. Do not help them with their decisions unless they are really unsure of themselves. When they are finished, check each pocket. If the answer does not match the question, give it back to the learner(s) so they can match it to another question as you check each pocket. Repeat this activity to reinforce the information but ask learner(s) to do it more quickly or do it as a race between two teams.

- **Non-Readers:** For learners who do not read, photocopy pictures from *Hemophilia in Pictures* and put one in each pocket. Ask them to choose a pocket, and pull out the picture. You can ask them a question about it or they can ask each other questions and try to answer them.
- **Waiting Room Activity:** When not using the question pockets in a session, put it in the waiting room so that patients and families can test themselves. (Put a folded sheet with the correct responses in the "ANSWERS" pocket.)

Tic-Tac-Toe

On a flipchart or piece of paper, draw a grid. Divide into two teams. (In an individual session, you are one team and the learner is the other.) Decide which team will be represented by an "X" and which one will be "O." Tell them that the goal is to get three of their team's symbols in a row vertically, horizontally or diagonally. (See illustration.)



Ask Team 1 a question and give them 30 seconds to answer. If correct, one of their team members puts an X in a square of their choice. If incorrect, Team 2 answers the question. If Team 2 is correct, they put an O in a square of their choice. If neither team is correct, elicit the correct answer by giving hints but do not put a symbol on the grid. Move on to the next question.

- **Tip:** The answers to the questions can be "True or False" or you can provide them with multiple choice questions (for example, give them three possible answers and have the learner(s) try to choose the correct one).

Categorizing Race

Put the name of a different category or topic on about three containers, such as paper bags or boxes. For each category, make up about 5 cards with one picture or key word on each. Mix them up and give them to the learner(s). Ask them to put them in the correct category as quickly as possible. This can be done as a race in two teams by asking players to pick one card at a time and run or walk quickly to the correct container at the far end of the room. At the end, ask each team to choose a category and use the cards or pictures to present or demonstrate the information to the other team.

Examples of categories:

- Things you need for self infusion
- How to treat a bleed with first aid
- Things you can do to stay healthy
- Basic information about hemophilia

Using the Educator's Guide with the illustrated *Hemophilia in Pictures*

The *Hemophilia in Pictures Educator's Guide* was developed as a resource for educators using the WFH illustrated publication, *Hemophilia in Pictures*. References to illustrations in the original *Hemophilia in Pictures* are indicated by the 💧 symbol.

Example:
What are some common signs of hemophilia? (💧 page 8)

💧 = *Hemophilia in Pictures*

Words in **bold** found throughout the *Hemophilia in Pictures Educator's Guide* are defined in the glossary on pages 44-49.

Part 1: Introduction to Hemophilia

It is important that families affected with hemophilia understand how the condition is inherited, what its effects are, and the treatment options availble in their country. Health-care professionals also need to be aware of family experiences of hemophilia in order to provide appropriate care.

Blood Coagulation Process

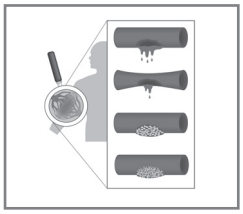
Hemophilia is a bleeding disorder, so it is important to understand the blood system.

How does blood move around the body? (page 1)

The heart pumps blood around the body. Blood moves through the body in tubes called **arteries, veins**, and **capillaries**. Some are large (arteries and veins) and some are small (capillaries).

How does bleeding start and stop? (page 2)

Bleeding starts when a capillary is injured and blood leaks out. The capillary tightens up to help slow the bleeding. Then blood cells, called **platelets**, make a plug to patch the hole. Next, many **clotting factors** found in **plasma** work together to form a **clot** over the plug. This makes the plug stronger and stops the bleeding.



Why do people with hemophilia sometimes bleed longer than other people? (page 3)

In hemophilia, a clotting factor is missing, or the level of that factor is low. This makes it difficult for the blood to form a clot, so bleeding continues longer than usual, not faster. Since there are many clotting factors in plasma, each factor is named with a Roman numeral (i.e., factor VII, VIII, IX, etc.).

Is all hemophilia the same? (page 4)

There are two different types of hemophilia. People with low levels of factor VIII have **hemophilia A**, and people with low levels of factor IX have **hemophilia B**.

Each type of hemophilia can be mild, moderate, or severe, depending on the amount of clotting factor that is missing from the person's blood.

MILD HEMOPHILIA 5% - 30% of normal clotting factor activity	• Might bleed for a long time after surgery or a very bad injury • Might never have a bleeding problem • Do not bleed often • Do not bleed unless injured
MODERATE HEMOPHILIA 1% - 5% of normal clotting factor activity	• Might bleed for a long time after surgery, a bad injury, or dental work • Might bleed about once a month • Rarely bleed for no clear reason
SEVERE HEMOPHILIA Less than 1% of normal clotting factor activity	• Bleed often into the muscles or joints • Might bleed one or two times per week • Might bleed for no clear reason

How is hemophilia diagnosed?

Hemophilia is diagnosed through **coagulation testing** to determine the amount of factor VIII or IX in one's blood. A deficiency of factor VIII is known as hemophilia A, while a deficiency of factor IX is known as hemophilia B. The prevalence of hemophilia A and B in the general population is 1 in 10,000 and 1 in 50,000, respectively.

Coagulation testing can indicate whether one might be a carrier. Lower than normal levels of factor can be an indication of a likely carrier, however, carriers may also have normal levels. The only reliable way to identify a carrier is by DNA testing.

It is important to rule out other bleeding disorders such as factor X or XI deficiency or von Willebrand disease. It is important to take a personal history along with the family history.

Inheritance Patterns and Diagnosis

A person born with hemophilia will have it for life. It is essential that people with hemophilia be aware of the disorder's inheritance pattern and reproductive options, such as prenatal diagnosis, selective abortion, and new reproductive technologies, so that they can make an informed decision about having children.

How is hemophilia inherited? (page 6)

Hemophilia is a sex-linked **recessive** bleeding disorder that is usually passed on through a parent's **genes**, specifically the X **chromosome**. Women are born with two X chromosomes, whereas men are born with one X and one Y chromosome. A woman who has one normal X chromosome and one defective X chromosome is considered a **carrier** even if she does not have any symptoms of hemophilia herself, because the normal X chromosome compensates for the defective gene. She may pass on this hemophilia gene to her children; there is a 50 per cent chance with each pregnancy that any son she has will have hemophilia or not and a 50 per cent chance that any daughter she has will be a carrier like herself or not. When the father has hemophilia and the mother is not a carrier, the disorder is not passed on to sons, but all daughters will necessarily carry the hemophilia gene (obligate carriers).

Figure 1:
Inheritance of hemophilia
Female carrier

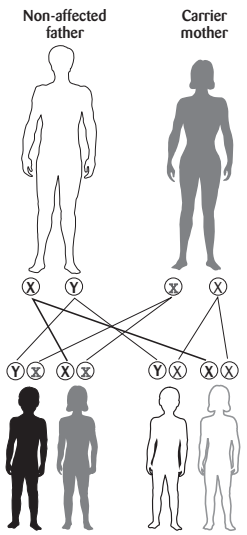
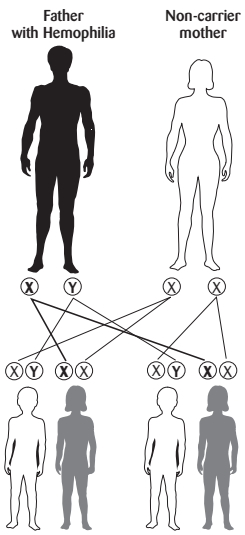


Figure 2:
Inheritance of hemophilia
Male with hemophilia



Genetic Counselling and Reproductive Options

Healthcare professionals need to be aware of family experiences of hemophilia in order to offer appropriate **genetic counselling**. It is important that families understand how the condition is inherited, what its effects are, and the treatment options available in their country.

What is genetic counselling?

Genetic counselling is the process of helping couples evaluate and understand their likelihood of passing on certain genetic diseases or disorders, and offering options. A genetic counsellor will:

- Evaluate family history and medical records;
- Determine if genetic testing is needed;
- Evaluate test results;
- Help prospective parents understand the implications so that they may reach an informed decision on how to proceed.

As part of genetic counselling, couples need to examine their perceptions and feelings about hemophilia, which will have a major impact on their decision whether to have children. Some couples may choose to go ahead with a pregnancy, especially if they are fully informed of up-to-date treatment options in their country, should their child be born with hemophilia.

What are some of the options available to couples affected with hemophilia?

Following genetic counselling, couples affected with hemophilia may consider a number of options:

- Natural conception with the possibility of having a boy with hemophilia or a carrier daughter
- Natural conception with prenatal diagnosis
- Assisted conception using donor eggs
- Assisted conception using **pre-implantation genetic diagnosis** (PGD)
- Washed sperm (for HIV **serodiscordant** couples)
- Fostering or adoption

Natural conception with the possibility of having a boy with hemophilia or a carrier daughter

Some couples affected with hemophilia may choose natural conception with the possibility of having a boy with hemophilia or a carrier daughter. In countries where advanced, quality care with safe clotting **factor concentrates** is available, hemophilia can be seen as a manageable disease. As a result, some couples accept the risk of a child being born with hemophilia and many forego prenatal testing.

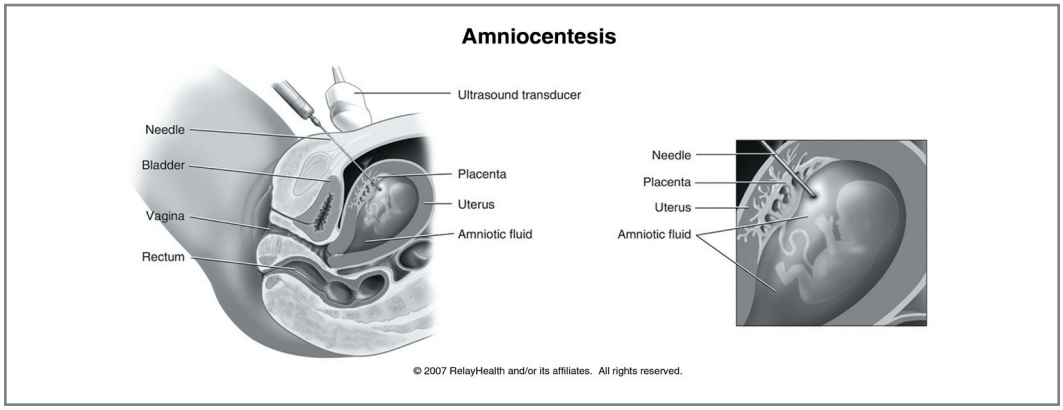
Natural conception with prenatal diagnosis

Couples affected with hemophilia can undergo prenatal diagnosis to determine if the fetus has hemophilia. Some centres only offer this procedure if the couple's choice is to terminate the pregnancy if the fetus is found to have hemophilia. Couples are referred to a fetal care centre for specialized information and counselling prior to making a final decision about testing. It is important that these couples understand that they may conceive a son with hemophilia or a carrier daughter. The decision to terminate a pregnancy is an extremely difficult one. For many people, termination of pregnancy may not be acceptable

for religious, ethical, or cultural reasons. The prenatal diagnosis tests and procedures are described below.

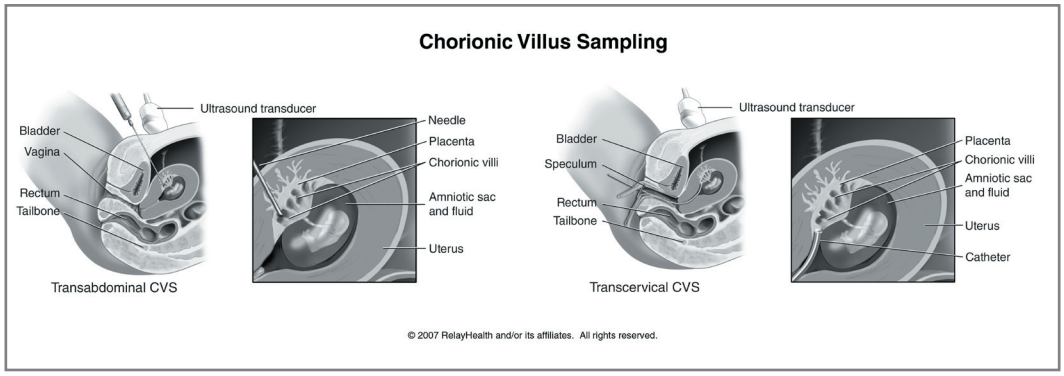
Amniocentesis: A small amount of **amniotic fluid** is removed, usually between the 15th and 18th week of pregnancy, using a fine needle inserted into the uterus either **trans-abdominally**, or **trans-vaginally**. The route used is determined by the position of the fetus. Both routes are carried out under ultrasound guidance.

Amniotic fluid contains cells shed from the fetus that can be analysed to determine the sex of the fetus and to detect certain genetic conditions, such as hemophilia. There is an associated miscarriage risk of one per cent above background risk based on gestational age (one per cent risk in addition to the usual risk based on the number of weeks pregnant).



Chorionic villus sampling (CVS): Under local anesthesia and ultrasound guidance, a fine needle is passed trans-abdominally or trans-vaginally to take a sample of chorionic villi cells from the placenta. Since the baby and placenta originate from the same cell, the chromosomes present in the placental cells are the same as those of the baby.

CVS is performed between 10-12 of weeks of **gestation** and carries a higher risk than amniocentesis. This is because the background risk of miscarriage is higher the earlier the gestational age. There is an associated rate of miscarriage of one per cent above background risk based on gestational age. CVS is the method of choice to obtain fetal cells for diagnostic purposes in hemophilia.



Sexing of the fetus: This can be performed by one of two methods: fetal sex typing from maternal plasma or ultrasound scan.

- **Fetal sex typing from maternal plasma:** A blood sample is taken from the mother between 7-11 weeks of gestation (optimal time is 8 weeks of gestation), from which the sex of the fetus can be determined from the fetal cells that are circulating in the mother's blood.

  This procedure is currently only carried out in specialist units. It has the benefit of identifying the sex of the fetus in the first trimester of pregnancy. This provides the ability to determine fetal sex by 10 of weeks gestation and identify the possibility of X-linked disorders such as hemophilia without the need for CVS, an invasive procedure.
- **Ultrasound scan:** The sex of a fetus can be detected by ultrasound from around the 11th week of gestation.

  The ultrasound method is not available for fetal sexing until the second trimester, by which time it would be too late to offer CVS if indicated. While fetal sex typing from maternal plasma has a good accuracy rate, it is not 100 per cent and it is good practice to confirm the sex of the fetus by ultrasound scan when possible.

Assisted conception

A number of procedures are available to assist conception. In preparation, couples undergo fertility tests, a medical examination, and surgical review. The female undergoes a vaginal ultrasound to assess **pelvic morphology** and a **hystosalpingogram**. For the male, a semen analysis is carried out to assess the volume and number of sperm and their **motility**. Options in assisted conception include:

- **In vitro fertilization with donor eggs:** If the female is a carrier, donated eggs are considered an option for couples who would not wish to have a child with hemophilia or a prenatal diagnosis leading to possible termination of affected pregnancy. After a medical exam, blood screening, and counselling, the donor eggs are collected and fertilized using sperm retrieved from the partner on the same day. Usually two of the resulting **embryos** (but this number may vary in some countries) are implanted in the carrier, who is given hormone medication to create a suitable environment for the embryos. Donor eggs are more readily available in some countries than others.
- **Pre-implantation genetic diagnosis (PGD):** Pre-implantation embryos are produced using conventional in vitro fertilization methods. Female embryos are identified through PGD and are implanted in the uterus. However, this technique is still experimental and not yet available in most countries.
- **PGD with specific diagnosis for hemophilia:** When the exact genetic mutation has been determined in the parent, it may be possible to diagnose hemophilia in the embryo using a specialized **polymerase chain reaction (PCR) technique**. This technique offers couples the chance to have unaffected male or female embryos transferred into the prospective mother.

What are the psychological effects related to reproductive therapies?

Couples embarking on these new reproductive choices face challenging ethical dilemmas. Counselling is an integral part of the treatment. Many patients often have unrealistic expectations of reproductive therapies, therefore it is important to convey that they are embarking on a very stressful and experimental treatment program.

Most couples who have a baby following a successful course of reproductive treatment have made more than one attempt. The psychological implications of reproductive therapies

are well documented. Infertility is associated with stress and anxiety, especially when it involves in vitro fertilization. Risk of genetic disease is associated with stress, depression, and anxiety. Some find reproductive therapy so stressful that they choose not to repeat the experience.

Having hemophilia can have far-reaching effects on the individual as well as on close family members. This can be further complicated in the case of HIV serodiscordant couples, where the man has hemophilia and is affected with HIV and his partner is **seronegative** (does not have HIV), and they want to have children.

What reproductive options are there for couples affected by hemophilia and HIV?

There has been significant improvement in the treatment of HIV in many countries. Many people with HIV have low or non-detectable levels of the HIV virus in their blood and are consequently enjoying a good quality of life. Therefore, they may wish to consider having a family.

Studies have shown that unprotected vaginal intercourse between an infected male and an unaffected female carries a 3-6 in 1,000 chance of viral transmission. For some serodiscordant couples, where the man is affected with both hemophilia and HIV while his partner is seronegative, this may not be a risk they are willing to take and they may prefer to pursue assisted conception techniques as their first option.

Some in vitro fertilization units have facilities that offer treatment to HIV serodiscordant couples. Assisted conception techniques, such as sperm washing, intracytoplasmic sperm injection (ICSI), and the use of donor sperm offer these couples a risk-reduced or risk-free opportunity to have a child without infecting their partners.

- **Sperm washing:** This procedure is based on the assumption that HIV infective material is carried primarily in semen and not within sperm itself. The semen is separated from the sperm by **density gradient** and **centrifugation.**

  The sperm is tested for the HIV virus and, if negative, is **inseminated** into the female during the ovulation phase of her menstrual cycle. This method may be considered if all fertility investigations are within normal parameters.
- I**ntracytoplasmic sperm injection (ICSC):** This technique, in which a single sperm is injected directly into an egg in a glass tube, is used when the sperm is found to have poor motility and/or poor ability to penetrate the egg. In serodiscordant couples, ICSC reduces the risk of HIV transmission, not only because it is done outside the body, but also because it guarantees fertilization with fewer attempts to conceive.
- **Use of donor sperm:** Donor sperm comes from someone other than the male partner. There are options for sperm donation locally and regionally in many countries. Some couples seeking sperm donations travel to other countries where the laws regarding anonymity are less strict than in their own. Donors are screened for viruses and given genetic counselling. Their sperm is then frozen and quarantined. After 180 days, the donation is screened again and, if clear, is thawed and prepared for insemination.
- **Fostering or adoption:** Some couples choose to adopt or foster a child to avoid passing on a genetic defect to future generations. Genetic counsellors, physicians, fostering or adoption agencies, and hemophilia organizations can provide more information on the local processes involved.

Review Quiz

Part 1: Introduction to Hemophilia

1. Blood moves through the body in tubes. The large ones are called _____ and _____. The smaller tubes are called _____.

2. Bleeding occurs when a _____ is injured and blood leaks out. The _____ tightens up to help slow the bleeding. The blood cells, called _____ make a plug to patch the hole.

3. When one clotting factor is missing, or the level of that factor is low, bleeding continues (longer/ faster) _____ than usual.

4. Is all hemophilia the same? (yes / no)

5. Is hemophilia contagious? (yes / no)

6. Hemophilia is a bleeding disorder that is inherited through a parent's _____, specifically the _____ chromosome.

7. X and Y chromosomes determine a person's sex. A male is born with _____ and _____ chromosomes. A female is born with two _____ chromosomes.

8. A man with hemophilia passes the hemophilia gene to all of his (daughters / sons).

9. When a carrier has a baby, her chances of passing on the gene are: (one in two / one in four / always).

** Please see the Appendix for answers.*

Part 2: Assessing and Managing Bleeds

Common Signs of Hemophilia

What are some common signs of hemophilia? (page 8)

With hemophilia, bleeding can happen anywhere inside or outside the body as a result of injury or trauma. People with hemophilia bruise easily, and bleed for a longer time after getting cut, having a tooth removed, having surgery, or after injury. Sometimes bruising is noticed and no cause can be remembered. This is called **spontaneous bleeding** but it is likely the result of an injury too small to be consciously recognized. Babies bruise easily when they start to become mobile, such as sitting up, crawling, and walking. They also bleed longer than usual after an injury, especially to the mouth and tongue. As children grow, spontaneous bleeding becomes more common, affecting the joints and muscles.

Assessing Joint and Muscle Bleeds

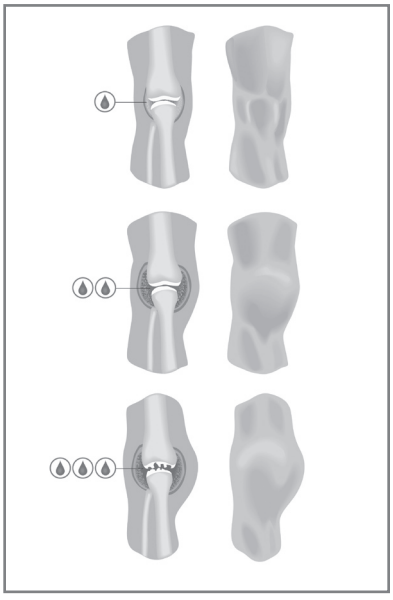
Bleeding inside joints and muscles poses major problems for people with hemophilia.

What causes a joint bleed? (page 9)

The **joint**, the place where two bones meet, is surrounded by a synovial membrane with many small blood vessels. Trauma or even minor injury to the joints can rupture the capillaries in the **synovium** and cause bleeding into the **joint cavity**. Bleeding causes the joint to swell and become painful and hard to move. Joint bleeds first occur in the pre-school years. They predominantly affect the knees, elbows, and ankles but can also happen in toes, shoulders, and hips. Repeated bleeding into the same joint causes **hemophilic arthropathy** and the development of **hemophilic arthritis**.

What happens in a joint bleed? How is it identified? (page 10)

With experience, a person with hemophilia knows when a bleed starts because the joint area is warm to the touch and may feel tingly inside. This feeling often comes on before any visible signs of **hemarthrosis**. It is best to give treatment as soon as possible to lessen joint damage and aid prompt healing.



Patients, healthcare professionals, and caregivers can assess joint bleeds by touch:

- Place the back of your hand about 1 cm away from the skin of the affected area.
- Move your hand back and forth along the limb. Normally, the muscle area should seem slightly warmer than the joint area.
- If there is a joint bleed, the joint area will feel warmer, similar to passing your hand over a candle flame or a light.

It is very important to recognize bleeds as they occur and stop the bleeding as quickly as possible. The more blood that gets into the joint, the harder it is for the bleed to clear up. Sometimes a new bleed starts before the old bleed has been cleared away.

Tip for educators

Have the individual with hemophilia describe their symptoms of joint bleeds and review the list in *Hemophilia in Pictures*, page 10.

Which joint bleeds are most common? (page 11)

The knees, elbows, and ankles bleed more often than the other joints. This is due to a number of factors:

- The knee, elbow, and ankle joints move only in two directions—bending and straightening, like a hinge on a door—whereas hip and shoulder joints can move around in all directions, like a ball in a socket. Joints that can move more freely are not affected as often by bleeds.
- These joints are not surrounded by muscles that can protect them. The knee, elbow, and ankle muscles are attached to the bones above and below the joints. Only the tendons cross over the joints, so the joints are not protected on all sides, whereas hip and shoulder joints are covered by many strong muscles.

Each joint has its own preferred position when it is bleeding. When a joint bleed occurs, the patient automatically tends to move the joint into the position of maximum comfort:

- **Elbow:** Partly flexed, hand towards shoulder. Attempts to straighten the arm are painful and motion will be limited.
- **Knee:** Partly flexed, heel towards the body.
- **Ankle:** Partly extended, resting with the foot and toes pointed down and away from the body.

What are the long-term effects of joint bleeds? (page 12)

The synovial membrane lining the joint becomes irritated from bleeds. It becomes thickened and red. As the synovium thickens, it is easier for it to be pinched and torn, which starts a new bleed. With repeated bleeding in a joint, the synovium becomes chronically inflamed and eventually **hypertrophies**, causing the joint to appear extremely swollen. This is called **chronic synovitis**. Without treatment, persistent chronic synovitis and recurrent joint bleeds can cause irreversible damage to the joint **cartilage** (hemophilic arthropathy), with loss of motion, limb deformity, and pain.

How can joint deterioration be prevented?

It is very important to try to prevent joint deterioration from occurring. Some ways to prevent permanent joint damage are:

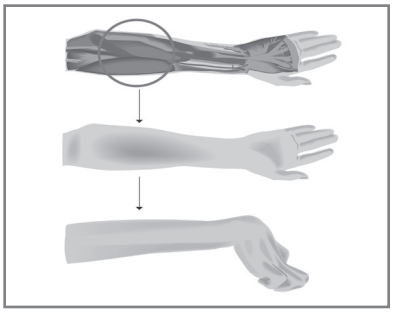
- Treat each bleed as soon as possible
- Rest the joint to give it time to heal
- Do exercises to keep the joints moving, once the bleeding has stopped
- Implement **prophylaxis**

What causes a muscle bleed? (page 13)

Bleeds can happen to muscles anywhere in the body following a direct blow, a sudden stretch or sprain, or an **intramuscular** injection. Bleeding occurs when the capillaries in the muscle are injured. Bleeds often involve a group rather than a single muscle.

What happens in a muscle bleed? How is a muscle bleed identified? (page 14)

The person with hemophilia may recognize the cause or the bleed may be spontaneous, appearing for no clear reason. During the bleed, the muscle feels stiff and painful.



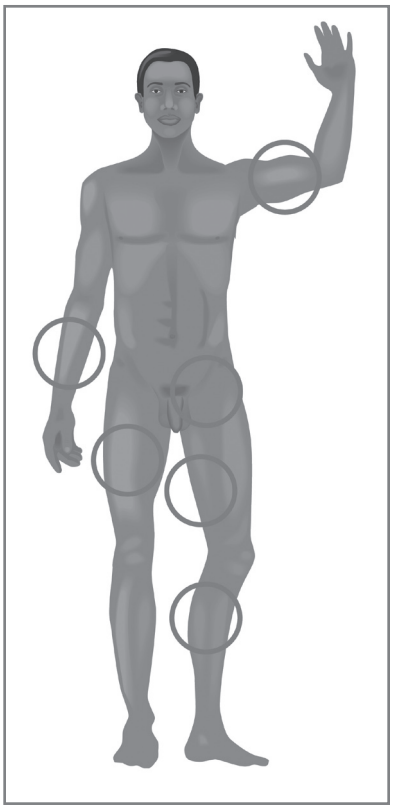
The bleed causes swelling in the muscle that is warm and painful to stretch or touch. Swelling may put pressure on **nerves**, causing tingling and numbness. Patients may feel a "pins and needles" sensation and loss of function.

Early recognition and treatment is important to prevent permanent damage. Patients, healthcare professionals, and caregivers can assess muscle bleeds by touch:

- Assess for warmth by holding the back of your hand about 1 cm away from the skin.
- Move your hand back and forth slowly along the limb. The area of the bleed will seem warmer than the surrounding areas, as if you have passed your hand over a candle or light.
- There may be bruising if the bleed is near the skin. However, bruising will not always be present. Sometimes bruising will only appear one or two days after the bleed starts. In other cases, the bleed is deep inside the muscle and there is no visible bruising.

Which muscle bleeds are most common? (page 15)

The thigh, calf, bicep, forearm, and hip muscles have a greater tendency to bleed. Bleeds in the thigh and forearm muscles may be experienced as tingling or "pins and needles" because pressure on nerves can cut off blood and oxygen supply. Permanent nerve damage, muscle death, and deformities can occur if the bleeding is not treated quickly.



Each muscle has a particular position of maximum comfort when a muscle bleed occurs:

- **Hamstring** (at the back of the thigh): The knee is flexed with the heel toward body.
- **Calf:** The toes point down and the knee is slightly bent.
- **Biceps** (the upper arm): The elbow is flexed with the hand toward shoulder.
- **Forearm** (palm side): The fingers are bent into a fist and the wrist is bent.
- **Forearm** (back of arm): The wrist and hand are extended back and the fingers prefer to stay open.

- **Psoas** (front of hip): The hip is bent with the thigh toward the chest and the back may be arched more than usual.

When a bleed is in the recovery stage, it becomes easier to move the muscles out of their maximum comfort position.

What are the long-term effects of muscle bleeds? (page 16)

Repeated bleeds lead to muscle scarring and weakness. The damaged muscles cease to protect joints, can bleed, and become damaged from abnormal stresses. Untreated muscle bleeds can lead to permanent damage to muscles, nerves, and joints, and deformity that affects how a person sits, stands, and walks.

How can muscle deterioration be prevented?

Rehabilitation following muscle bleeds is very important to prevent long-term problems. Early treatment followed by physical therapy will help maintain good function. After the bleeding has stopped, exercises must be done gently but consistently so that the muscle can stretch and move normally again. Then muscles must be re-strengthened using different exercises. A physical therapist should supervise this rehabilitation process. If possible, begin a scheduled infusion of clotting factors or other treatment as prophylaxis.

Which bleeds are serious or life-threatening? (page 17)

Bleeding within the head or into the nervous system is very serious and can be life-threatening. Symptoms include headache, nausea, vomiting, sleepiness, confusion, clumsiness, weakness, and drowsiness. Throat and neck **hemorrhages** are also very serious bleeds in people with hemophilia.

- **Central nervous system hemorrhage / head trauma:** This is a medical emergency and a major cause of death in hemophilia, especially in children. All significant traumatic head injuries, confirmed or suspected, as well as significant headaches, should be treated as a possible **intracranial bleed**. If any of the symptoms are evident, seek emergency treatment immediately.
- **Throat and neck hemorrhages:** Throat and neck hemorrhages can be accompanied by swelling or difficulty in swallowing or breathing. This is a medical emergency and should be treated immediately, even if assessment is not complete.

Review Quiz

Part 2: Assessing and Managing Bleeds

1. Bleeding or bruising that occurs with no known cause is called _____ bleeding.

2. The place where two bones meet is called a _____.

3. The ends of bones are covered with a smooth surface called the _____.

4. Bones are partly held together by a joint capsule. This joint capsule has a lining called the _____.

5. Two signs of a possible joint bleed are _____ _____.

6. The three most common joint bleeds happen in the _____, the_____, and the _____.

7. Two long-term effects of joint bleeds are _____ _____.

8. Some of the signs of a muscle bleed include _____ _____.

9. Most muscle bleeds happen in the _____, the _____, and the _____.

10. The psoas muscles are located at _____.

11. Bleeds in the _____ and _____ are serious and can be life-threatening.

** Please see the Appendix for answers.*

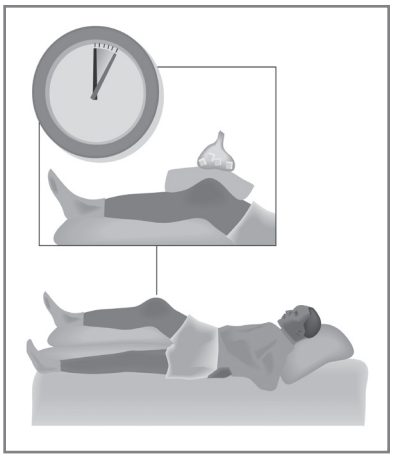
Part 3: Treatment of Bleeds

Managing Joint and Muscle Bleeds

Treatment, management, and prevention of bleeds are key to improving health and quality of life for people with hemophilia. Simple measures applied as soon as a bleed is recognized can help stop a bleed more quickly and prevent long-term damage.

How can bleeds be treated with first aid? (page 20)

Even patients who have access to replacement factor should use first aid measures while they are waiting for their infusion to be prepared. RICE (rest, ice and/or immobilization, compression, and elevation) is important management for muscle and joint bleeds.



Rest: It is vital to rest the injured/bleeding part of the body. If the bleed is in a leg, the person should not walk but rather use crutches or a wheelchair. If the bleed is in an arm, the arm can be supported in a sling. However, it is important that patients maintain independence and continue to use the uninjured joints and muscles to prevent weakness.

Ice: Ice causes blood vessels to constrict, slowing down the flow of blood. Ice also helps decrease pain and **muscle spasm.** There are many ways to use ice, but it must always be used correctly:

- **Ice packs:** Crushed ice or small ice cubes can be wrapped in a towel so that no ice touches the skin directly. Wet the towel with water before applying it to the skin so that the area will cool more quickly. Place the ice on top of, not under, the affected area—body weight on part of the ice pack may interfere with circulation. Leave the ice in place for no more than 5-10 minutes, 3-4 times a day. Remove the ice and continue to rest the body part.

  Advantages: Ice packs are inexpensive, usually available in most households, can be shaped easily to the affected body part, and cool the area quickly.
  Disadvantages: Ice packs can be messy and the cold is sometimes not tolerated well by young children.

- **Gel packs:** Following the same instructions as for crushed ice, be sure that the plastic from the gel pack does not touch the skin.

  Advantages: Gel packs are less messy than ice.
  Disadvantages: Some gel packs are not flexible enough to wrap easily around an arm or leg, and some are very heavy. Some do not cool the affected area as quickly as ice.

- **Ice massage:** Massage using an ice cup or Popsicle® is a very effective way to cool a small area quickly. Small paper cups filled with water can be kept in the freezer until needed. Ice is rubbed on the skin in smooth strokes or circles. The area will usually be cooled enough within 5-7 minutes.

  Advantages: Ice massage is inexpensive, easy, quick to apply, and provides rapid cooling.
  Disadvantages: Ice massage requires a freezer, is not good for a large area (e.g. large thigh bleed), is intensely cold, and may not be tolerated well.

- **Tips on Using Ice:** Four stages of sensation may be felt when ice is used: cold, aching, burning, and numbness. Many people take the ice off at the second or third stage, but it is better to try to leave it on until the area goes slightly numb.

  Some cautions about using ice include:

  - Never use ice over a cut or skin that has been scraped.
  - Never leave ice directly on the skin.
  - Be careful if the person has poor sensation or poor circulation in the area (for example, due to a deep muscle bleed causing nerve compression). Check the skin every few minutes for redness.
  - Do not leave ice on too long. If the area becomes too cold, the function of the platelets may be affected, and the blood vessels may begin to dilate (increase in diameter) to bring more blood to the area. This reflex, called **vasodilation or the Huntington response**, brings more warmth to the area and the skin reddens. The reflex time is approximately 10 minutes, but can vary from 7-12 minutes. It is important to remove the ice before the reflex response kicks in, in order to stop the possibility of further bleeding into the affected area. The recommended protocol is 5 minutes on and at least 10 minutes off.

Immobilization: Keeping the joint or muscle from moving fosters healing. A splint or a half-cast can be used to support the joint or muscle and keep it from being re-injured. Immobilization is very helpful for small children who may not understand that they should not walk on a sore leg or use their sore arm; it may also allow patients to carry on with many normal activities while resting the injured part. Immobilization usually requires a healthcare provider to apply the splint or cast, which should only be kept on for the prescribed amount of time. If the injured area is immobilized for too long, the muscles can weaken, putting the person at risk for re-injury.

Compression: Firm support using an elastic stocking (such as Tubigrip®) or an elastic wrap (such as Tensor or Ace bandage) will help minimize swelling. Compression will not take away swelling once it is established, but it will provide some support to the injury and may make it feel more comfortable.

Caution: Do not apply compression if you think the bleed is causing pressure on nerves or blood vessels. Check the colour and temperature of fingers or toes frequently to make sure that circulation is not being cut off.

When using an elastic bandage:

- Always start at the extremity of the limb or body part, wrapping towards the body.
- Overlap the bandage by 1/3, increasing the overlap to 1/2 the bandage width with each turn around the limb.
- Stretch the bandage only slightly as you wrap, and less tightly as you get closer to the body.
- Remove the bandage and re-wrap it often during the day.

Elevation: Raising the injured part above heart level will decrease pressure in the area and help minimize the amount of bleeding and swelling. Maintaining elevation also reminds the patient to continue to rest the limb.

Tips for educators

- Stress the importance of responding quickly to injuries or bleeds.
- Remind families to keep first aid items available: ice, ice packs, gel packs, elastic bandages, etc.

What other treatment may help?

When a joint has had numerous bleeds, it is referred to as a "target joint" and should be targeted for maximum treatment to prevent further deterioration. Doctors may recommend one of the following procedures to stop the synovium from bleeding.

- **Synoviorthesis:** A substance (either a chemical or radioactive isotope) is injected directly into the joint to cause the synovium to make scar tissue, which can not bleed. This procedure is usually quite effective in reducing bleeding if done early.
- **Synovectomy:** Surgical removal of the compromised synovium is performed to prevent future joint flare-ups.

Both these procedures are safe for people with hemophilia and may help prevent more serious joint damage. Some medical professionals recommend synoviorthesis or synovectomy early; that is, as soon as a pattern of repeated bleeding is recognized in a particular joint, and before there is damage to the joint surfaces.

Factor Replacement Products and Delivery Options

How can bleeds be treated with factor replacement therapy? ( page 21)

Hemophilia is treated by replacing missing clotting factor in blood. Clotting factor therapy is used to treat hemophilia A (factor VIII deficiency); hemophilia B (factor IX deficiency); and other clotting factor deficiencies (I, II, V, VII, X, XI, and XIII). The missing factor is injected intravenously; bleeding stops when enough clotting factor reaches the bleed site. It is very important that treatment be given as quickly as possible to prevent long-term damage.

For people with hemophilia, access to blood products is key to the ability to lead a normal, active life. Without factor replacement products, they face a life of chronic pain and increasing disability. However, blood products are not without risk. Blood and blood products may carry infections, such as HIV and hepatitis, which can be transmitted to people who receive contaminated transfusion products.

How safe are these blood products?

Despite steps to keep the blood supply safe, there is still the possibility that blood products may contain infectious substances, especially if they are not treated to remove or inactivate viruses (see "Transfusion-Transmitted Diseases" on page 33). However, following the HIV/AIDS epidemic in the mid-1980s, governments around the world, blood product manufacturers, and hemophilia patient advocacy groups have done much to improve blood product safety. In many countries, potential blood donors are now screened for risk of transmitting viruses. Donated blood is tested for known viruses and discarded if it tests positive. Donations that pass the screening are then treated to kill viruses that potentially remain.

What are the various clotting factor products available?

Clotting factors are available in the following blood products (in order of decreasing concentration):

- Clotting factor concentrates
- Cryoprecipitate
- Plasma
- Whole blood

Clotting factor concentrates are the treatment of choice for hemophilia. They can be manufactured from human blood (called plasma-derived products), or using genetically engineered cells that carry a human factor gene (called **recombinant** products). All commercially prepared plasma-derived factor concentrates are treated to remove or inactivate blood-borne viruses and rank among the lowest-risk therapeutic products in use today.

Cryoprecipitate is derived from the plasma in blood and contains a moderately high concentration of factor VIII clotting factor, but not factor IX. It is effective for joint and muscle bleeds, but does not undergo viral inactivation—therefore, there is a risk of transmission of blood-borne viruses, such as HIV and hepatitis. Consequently, cryoprecipitate should only be used in situations where clotting factor concentrates are not available. Risk of transmission can be minimized by making cryoprecipitate from plasma donated by repeatedly tested, virally negative donors.

Fresh frozen plasma (FFP) is made by removing red blood cells, white blood cells, and platelets from whole blood and then freezing the plasma. Plasma contains factor VIII and IX, as well as other blood proteins, and is used to treat some rare bleeding disorders where factor concentrates are not available. FFP is less effective than cryoprecipitate for the treatment of hemophilia A because its factor VIII concentration is lower. Large volumes of FFP are required to treat hemophilia A—however, this can cause circulatory overload. FFP also presents a risk of transmission of blood-borne viruses. In some countries, however, it is still the only product available for treatment of hemophilia A and B.

Whole blood is not an effective treatment for hemophilia because of the large volume of blood needed to attain sufficient factor levels, which could cause circulatory overload.

In addition, agents such as **desmopressin** and **antifibrinolytic agents** are useful for controlling bleeds.

- Desmopressin (also called DDAVP) can be used to treat or prevent bleeds in people with mild hemophilia A (people with more than 5% of normal factor VIII activity). Desmopressin is a synthetic compound that boosts the levels of factor VIII and von Willebrand factor (vWF), another protein involved in coagulation. A single infusion at a dose of 0.3 mcg/kg body weight can be expected to boost factor VIII levels three- to six-fold. The compound can be used several days in a row—however, after repeated use the stores of factor VIII may become depleted rendering it less effective. DDAVP can be given three ways: intravenously (through a vein) diluted in 50-100 mL of normal saline and infused over 20-30 minutes; subcutaneously (under the skin) using a high-strength formulation of desmopressin (15 mcg/mL); and intranasally (with a nasal spray), with a high-strength formulation containing 150 mcg desmopressin per spray.
- Less concentrated forms of desmopressin, including tablets, are given for other conditions such as diabetes insipidus or enuresis (nighttime bedwetting). These lower concentrations are not effective in hemophilia.

- Antifibrinolytic agents such as **tranexamic acid** and **epsilon aminocaprioic acid (EACA)** can help promote clot stability and are useful **adjunctive therapies**. Antifibrinolytic agents do not prevent joint bleeds, but are useful for controlling mucosal bleeding (oral bleeding, **epistaxis**, **menorrhagia**) and are particularly useful for dental surgery.

How are factor replacement products delivered?

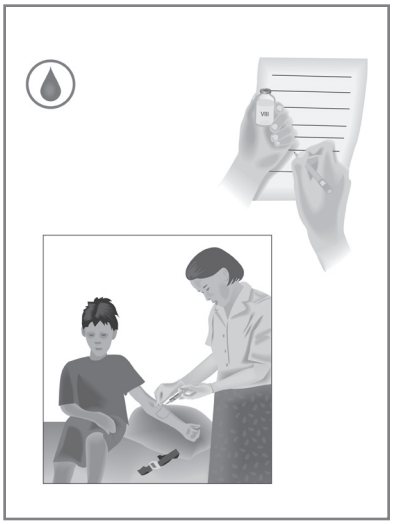
It is very important to treat bleeds quickly to avoid joint damage. Factor replacement therapy is administered either on-demand to treat and stop further bleeding or as prophylaxis to prevent bleeding.

- **On-demand therapy**, also known as episode-based therapy, is the administration of the deficient clotting factor by **infusion**, or another type of treatment, in response to a bleeding episode. The goal of this therapy is to treat and stop bleeding as soon as possible with the aim of preventing long-term damage to joints or muscles.
- Prophylaxis is the scheduled infusion of clotting factors or other treatment, usually one, two, or three times a week, in order to maintain factor levels in the blood high enough to prevent spontaneous bleeding episodes. Prophylaxis has been shown to decrease joint bleeding, help preserve joint function, and improve quality of life. Prophylaxis should be a core component of all hemophilia care programs where sufficient clotting factor is available.
- The goal of prophylaxis in hemophilia care is to maintain **trough factor levels** above one per cent. The majority of the time, one's factor levels will be significantly higher. Prophylaxis has been shown to be beneficial even when factor levels are not maintained above one per cent at all times. Currently, the most commonly suggested protocol for prophylaxis is:
  - Infusion of 25-40 IU/kg of factor VIII three times a week (on alternate days) for hemophilia A;
  - Infusion of 25-40 IU/kg of factor IX twice a week or every third day for hemophilia B.

It is best to give the prophylactic dose first thing in the morning before school or work so that one has high levels of circulating factor when one is active rather than when one is going to bed. However, many different clotting factor replacement protocols are in use, and there is ongoing evaluation to determine optimal prophylactic dosages.

What is home therapy? (page 33)

Self/family infusion of clotting factors at home (and sometimes at school or work), allows immediate access to treatment, and, hence, optimal early treatment. Ideally, home therapy involves clotting factor concentrates or other, safe **lyophilized** products that can be stored in a domestic fridge and reconstituted easily. However, home therapy is also possible with cryoprecipitate, provided the patient has a simple but reliable storage freezer at home.



Self/family infusion must be closely supervised by the comprehensive care centre or hemophilia treatment centre. Proper education and instruction is essential. The infusion technique should be assessed routinely by healthcare professionals at the centre.

Patient education should include how to recognize a bleed and its common complications; dosage calculation; preparation, storage, and administration of clotting factor; aseptic techniques; **venepuncture**; record keeping; and proper storage and disposal of needles and handling of blood spills.

Encouragement, support, and supervision are key to successful self/family infusion. Periodic assessment of techniques, compliance, and educational needs is important. A certification program can be instituted, with periodic re-certification.

Patients or parents should keep bleeding records that include the date and site of bleeding, dosage, and the lot number of the product used, as well as any adverse effects.

Self/family infusion can be started on young children with adequate venous access and by motivated family members who have undergone adequate training. Older children and teenagers can learn self-infusion with family support.

Reliable venous access in small children and adults with hemophilia can sometimes be difficult. In these cases, implantation of a **venous access device (VAD)** may be appropriate.

What is a venous access device (VAD)?

The implantation of venous access devices (VAD) such as a Port-A-Cath® can make infusion much easier. A VAD is a small device that is surgically implanted beneath the skin. It is made up of two parts: a titanium or silicone port with a silicone hub for the needle's entry point, and a silicone tube or catheter, which is connected directly to a vein. The port is visible as a coin-sized bump at the skin's surface and is about a few centimeters in depth.

The VAD should be placed between the clavicle and the nipple in order to reduce the formation of scar tissue. It is important to access the device using a non-coring needle, which causes the least puncture, to avoid making holes in the silicone hub.

When can an implantable device be used?

- To treat bleeding episodes
- To perform prophylactic treatment
- To enable treatment of inhibitors using immune tolerance induction (ITI) therapy (see page 32)
- To take blood samples

What are the advantages?

- Easy venous access at any time for taking blood samples and administering clotting products
- Ease of use for in-patient and out-patient care
- Independence can be maintained when venous access is poor

What are the disadvantages?

- Implantation requires a general anesthetic
- Requires a surgeon with experience in inserting VADs

What are the complications?

- Infections internally and externally around the catheter site
- **Septicemia**
- **Thrombosis**

- **Hematomas** around the VAD
- Erosion of the device through the skin
- Mechanical failures.

How is home treatment with a VAD managed?

- Training in the use of a VAD has to be performed in a specialized hemophilia centre
- Good **aseptic** technique is required
- The patient must be regularly monitored at the hemophilia treatment centre
- The patient's/caregiver's technique for accessing the VAD must be assessed regularly at home and in the centre
- Good hygiene is essential
- A small amount of **heparin** is injected into the catheter after each use, to prevent the development of clots in the system

Complications Related to Hemophilia Treatment

Inhibitor Development

What are inhibitors? (page 23)

Inhibitors are **antibodies** that the body produces to remove foreign proteins (called antigens); in this case, the foreign factor VIII or factor IX proteins in factor concentrates. Because people with hemophilia lack either the factor VIII or factor IX protein in their blood, infused factor VIII or IX are seen as "foreign invaders". To defend itself, the human body produces antibodies, which neutralize the invaders by binding to the infused clotting factor. As a result, the beneficial effects of the infused factor concentrates are decreased and the bleeding problem is not corrected.

People with inhibitors find that their normal treatment does not work. They face uncontrolled bleeding, pain, and joint damage more frequently because treatment with factor concentrates is ineffective. The treatments that do exist are expensive and require a lot of patience, diligence, and persistence to manage.

Inhibitors are a significant concern for people living with hemophilia, and treating them is one of the biggest challenges in hemophilia care today.

Who is at risk of developing an inhibitor?

Inhibitors occur more frequently in patients with severe forms of hemophilia and are rarer in people with moderate or mild hemophilia. The vast majority of patients who develop an inhibitor do so within the first 50-75 **exposure days**, with a maximum risk around the 10th-20th exposure. This means that inhibitors mostly occur in children with severe hemophilia, though they can occur later in life in mild or moderate patients who are not treated as frequently.

Studies of children with severe hemophilia A indicate that about 25-30% develop inhibitors. Inhibitor development in patients with hemophilia B is much lower: about 1-6%. However, it is important to note that hemophilia B patients with inhibitors may experience severe allergic reactions, including **anaphylaxis**, to factor IX concentrates if they continue to receive these products. Because of this danger, it is especially important that treatment for hemophilia B be carried out under direct medical control at a hemophilia treatment centre, particularly during the first 10-20 treatments with factor IX concentrates.

Some of the factors associated with a greater risk of inhibitor development include:

- A history of inhibitors in the family;
- Severe gene defects (defects in which the factor VIII/IX gene is almost completely deleted or subverted in its structure);
- African ancestry;
- Early intensive treatment with high doses of clotting factor (in the first 50 exposure days).

There is evidence that patients who receive early prophylactic treatment have a lower chance of developing an inhibitor.

Unfortunately, less information is available on the risk of developing inhibitors to factor IX due to the low prevalence of this problem in the hemophilia B population.

What are the clinical symptoms of inhibitors?

The presence of an inhibitor does not necessarily change the typical site, frequency, or severity of bleeding.

An inhibitor is suspected when:

- A patient's bleed is not promptly controlled with the usual dose of clotting factor concentrate.
- Treatment seems less and less effective and bleeding becomes more and more difficult to control.

How are inhibitors diagnosed?

Inhibitors are usually diagnosed when patients or family members notice that treatment is becoming less effective than it used to be. They can also be discovered in the course of a routine laboratory check. Inhibitors are a clinical diagnosis that should be confirmed by repeated laboratory assays.

Inhibitors are identified by the Nijmegen method, a test that measures the amount of inhibitors found in plasma. Unfortunately this method requires specific expertise and is not available in all laboratories. For this reason, the diagnosis of inhibitors is sometimes based on the **activated partial thromboplastin time (APTT)** assay. When an inhibitor is present, the prolonged APTT does not fully correct with the addition of normal plasma.

Inhibitor development should be suspected in any patient with hemophilia who does not respond to normal treatment. It is good practice to screen children and newly diagnosed adults for inhibitors at regular intervals between the first and 50th treatment dose. Even after patients have reached their 50th treatment dose, they should be checked at least twice a year until they have reached 150-200 doses, and at least once a year after that. Inhibitor testing should also be repeated before any invasive surgical procedures.

What are low- and high-titer inhibitors?

The amount and, consequently, the strength of an inhibitor is measured in **Bethesda Units** (BU) and referred to as **titer.** The higher the **titer,** the stronger the action of the inhibitor against the coagulation factor. On the basis of the titer, it is possible to distinguish high-titer inhibitors (> 5 BU) and low-titer inhibitors (< 5 BU). It should be noted that this classification, although useful, is not absolute. Some patients may have clinical responses that fall outside of their classification.

Patients with inhibitors can be further classified according to the strength of their **anamnestic response**, an immune system mechanism in which the memory of a previous exposure to foreign substances triggers the formation of new antibodies. Low-responders are people in whom the titer never exceeded 5 BU after exposure to factor concentrates, whereas high-responders are those whose inhibitor titer has exceeded 5 BU at least once in their lifetime.

The strength of the anamnestic response is usually evaluated by re-exposing to factor VIII or factor IX those patients who have a low-titer inhibitor at the time of the initial test.

What are common management strategies?

The management of patients with inhibitors is complex. Ideally, they should be treated in large comprehensive care centres with specialized expertise.

Management of patients with inhibitors includes various approaches:

- **Treatment of acute bleeding episodes:** the choice of first-line therapy is based on the current titer of the inhibitor and on the anamnestic response. **Bypassing agents** (namely activated prothrombin complex concentrates [APCC] and recombinant factor VIIa) are usually used for a current high-titer inhibitor, while for a low-responding inhibitor, factor VIII or factor IX concentrates at higher doses and/or more frequent intervals may be effective. In the case of a life-threatening hemorrhage in a high-responder with a current low titer, factor VIII or factor IX are the preferred treatment options.
- **Conservative strategies:** whether factor concentrates are available or not, it is important to:
  - Rest the limb/area affected by the bleed;
  - Use crutches in the case of a bleed in the leg;
  - Wear a sling when appropriate;
  - Apply ice;
  - Use analgesics and/or muscle relaxants to ease pain or discomfort.
- **Rapid reduction of inhibitor levels through plasmapheresis:** this approach is usually adopted when the inhibitor titer has to be decreased rapidly (e.g. prior to major surgery or in case of severe bleeding not adequately controlled by bypassing agents).
- **Elimination of inhibitors through immune tolerance induction (ITI) therapy:** ITI involves regular administration of clotting factor over several months or years to induce tolerance (see "How does ITI work? on page 32)

The decision-making process on the management of inhibitor patients should take into account the anamnestic response, the current inhibitor titer, and the site and severity of bleeding.

What are the treatment options when the inhibitor persists?

The treatment choice depends on whether the patient is a high- or low-responder, on the current inhibitor titer, the severity of the bleeding episode, and whether or not the patient is planning to undergo ITI.

- **High-dose factor VIII/IX:**

  High-dose factor VIII/IX is the preferred therapy in low-responders. The factor level should be measured right after the infusion to make sure treatment target levels are reached and so that more factor concentrate can be given if needed. Continuous infusion may also be useful.

  If high-dose factor VIII/IX is used in high-responders with a current low-titer inhibitor, it has to be taken into account that the anamnestic response will occur within 5-7 days, and will require a switch to bypassing agents.

- **Bypassing agents:**

  Activated prothrombin complex concentrates (APCC) are plasma-derived products, such as Factor Eight Inhibitor Bypassing Agent (FEIBA®), that contain variable amounts of non-activated and activated vitamin K–dependent coagulation factors such as factor VII, factor IX, and factor X. Frequent dosing (every 8 hours) should be limited to a maximum of 5 consecutive doses, never exceeding the total amount of 200 IU/kg/day due to the risk of thrombosis related to its use.

  Recombinant factor VIIa (rVIIa, NovoSeven®) is a recombinant product that has a very short time of action (2-3 hours). As a consequence, it has to be used frequently (every 2-3 hours) often causing problems with the venous access. Usually it is given in **bolus** injections of 90-120 mcg/kg, but it may be given as a single dose of 270 mcg/kg.

  N.B. Bypassing agents are expensive drugs and may not always be available in every country.

- If the patient plans to undergo ITI and has not yet started, it is preferable not to use factor VIII or APCC to treat bleeding episodes because these products are likely to elicit an increase of the inhibitor titer. In these cases, all bleeds should be treated with rFVIIa, which does not provoke an anamnestic response.
- Tranexamic acid is an antifibrinolytic drug that stops clots from breaking down. It is particularly useful for bleeds that involve the mucous membranes such as nose or mouth bleeds. However, it should not be used in combination with APCCs.

Can inhibitors be eliminated?

In about one-third of patients with factor VIII inhibitors, the inhibitor disappears spontaneously (this is called a transient inhibitor). Among those with persistent inhibitors, 60-80% can be eliminated using ITI (see below). In the remaining 20-40% of cases, ITI fails and inhibitors persist throughout the patient's life.

In patients with hemophilia B, getting rid of FIX inhibitors through exposure to high doses of factor IX concentrate may sometimes be successful in patients who previously suffered allergic reactions or anaphylaxis. However, this must be undertaken very cautiously and is not often successful.

How does ITI work?

With successful ITI, the inhibitor disappears (in pharmacokinetic terms, this is called "in vivo recovery") and the response to factor VIII or factor IX infusion returns to normal (normalization of **half-life**). ITI is based on regular administrations of factor concentrate over at least 9 months. The majority of patients are **tolerized** within twelve months, but more resistant cases can take two years or longer.

Different dosing **regimens** have been used for ITI therapy:

- The Van Creveld regimen uses low doses of factor VIII (25-50 IU/kg) three times a week or every other day.
- The Bonn regimen uses 100 IU/kg doses of factor VIII twice a day.
- A dosage of 100 IU/kg daily of factor VIII has been used widely with success as reported in the International Immune Tolerance Registry (IITR) database.

The optimal regimen remains to be defined. Currently, a prospective international randomized multi-centre study called the Immune Tolerance Induction Study (www.itistudy.com) is trying to determine the comparative cost effectiveness and associated morbidity of non-daily lower-dose regimens. In this study, a high dose of 200 IU/kg/daily is compared with a low dose of 50 IU/kg/three times a week. The results of this study will be crucial to the broader availability of ITI therapy for factor VIII inhibitor patients in both developed and developing countries.

Although high-dose regimens may achieve tolerance rapidly, it is not clear if the overall success rate is better than that obtained with low-dose regimens. Moreover, it is important to consider that high-dose regimens may often require the insertion of a venous access device, which is frequently complicated by infections or thrombosis, while low-dose regimes can commonly be administered using peripheral veins.

What factors influence the outcome of ITI?

The most significant predictors of success are:

- An inhibitor level less than 10 BU (ideally < 5 BU) before starting ITI
- A historical peak titer below 200 BU (ideally < 50 BU)
- A time interval between inhibitor diagnosis and start of ITI of less than 5 years.

Researchers are also looking at whether the concentrate type or the brand of factor concentrate (i.e., intermediate or high-purity factor concentrates or recombinant products) used in ITI can influence success rates. So far, similar success rates have been obtained both with recombinant and plasma-derived products.

Premature withdrawal from ITI, treatment interruptions, or concurrent infections may adversely influence the success of ITI and/or the time it will take to achieve tolerance.

Transfusion-Transmitted Diseases

People treated with blood and blood products risk exposure to blood-borne viruses and contaminants. From the late 1970s to mid-1980s, a large percentage of people with hemophilia became infected with the human immunodeficiency virus (HIV) and hepatitis C (HCV). Since then, however, the development of better viral screening and the introduction of new **viral inactivation** methods (including heat treatment, solvent-detergent cleansing, and other viral reduction steps) have virtually eliminated the risk of transfusion transmission of blood-borne viruses via clotting factor concentrates. No cases of transfusion transmission of HIV or HCV have been reported since the introduction of new treatment processes for clotting factor concentrates.

However, not all viruses and **pathogens** are necessarily eliminated by these purification methods. Certain viruses, such as parvovirus B19 and other potential blood contaminants, are not eliminated even with these inactivation methods. However, viral-inactivated clotting factor concentrates remain among the lowest risk therapeutic products in use today.

It is recommended that people with hemophilia be treated with viral-inactivated blood products to avoid the transmission of HIV and hepatitis.

Hepatitis C

About 15 per cent of people infected with hepatitis C (HCV) recover spontaneously, while 25 per cent will have no symptoms. About 20 per cent of people with chronic HCV ultimately develop **cirrhosis** after about 10 to 20 years. HIV and HCV co-infection increases the risk of cirrhosis, as does co-infection with hepatitis B. Hepatitis infection remains a problem in countries using cryoprecipitate which is not viral inactivated.

How is HCV transmitted?

HCV is transmitted through blood or needlestick injuries. It is rarely transmitted from parent to child. Sexual transmission of HCV is very uncommon.

What treatment is available for HCV?

Chronic hepatitis C can be best treated with a combination of interferon and ribavirin. Treatment usually lasts six to 12 months.

Human immunodeficiency virus (HIV)

Human immunodeficiency virus (HIV) is the virus that causes acquired immune deficiency syndrome (AIDS). Since the introduction of viral-inactivation methods in the mid-1980s, there have been no cases of HIV transmission through clotting factor concentrates. However, HIV can still be transmitted through cryoprecipitate.

How is HIV transmitted?

HIV transmission may occur through contact with blood or body fluids of an HIV-infected individual; through unprotected sex with an infected person; through contaminated needlestick accidents; and from an HIV-positive mother to baby through birth.

What treatment is available for HIV?

Since AIDS was first identified in the early 1980s, there has been much progress in treatment. Where treatment is available, HIV can be managed as a chronic, long-term disease. HIV infection is treated with a combination therapy, called **highly active antiretroviral therapy (HAART)**, which is very effective in controlling HIV infection. HIV drugs can have an effect on the liver, and HIV medications can be used effectively in HIV and HCV co-infected patients with careful monitoring by hepatology and infectious disease physicians.

Variant Creutzfeldt-Jakob disease (vCJD)

Variant Creutzfeldt-Jakob disease (vCJD) is a form of transmissible spongiform encephalopathy (TSE), first identified in the mid-1990s in the U.K. Most cases of vCJD are caused by eating meat from cattle infected with bovine spongiform encephalopathy (BSE), or "mad cow disease." The disease-causing agent, called a prion, destroys the central nervous system and eventually results in death. There is no treatment or cure for vCJD.

Like viruses, prions can be transmitted through donated blood. To date, reported vCJD cases have been caused by the transfusion of red blood cells, not plasma-derived products. There is currently no screening test for vCJD and no method to remove it from blood. The risk of transfusion-associated vCJD is restricted primarily to areas where there have been large epidemics of BSE, in the U.K. and France. Infection risk can be greatly reduced by viral inactivation methods.

Review Quiz

Part 3: Treatment of Bleeds

1. The four elements of first aid treatment for a bleed are _____, _____, _____, and _____.

2. Two clotting factor treatment products are _____ and _____.

3. Infusion is _____.

4. Venepuncture is _____.

5. Infection can be avoided when giving an injection by _____ _____.

6. Antibodies that form in the body to fight off substances it perceives as "foreign" are called _____. In hemophilia, infusion of factor concentrates can provoke the body's defense mechanisms to act against the clotting factor, and the clotting activity suffers.

** Please see the Appendix for answers.*

Part 4: Staying Healthy and Preventing Bleeds

Healthy Lifestyle Habits

Hemophilia is just one aspect of a person's health, and medical treatment is only one part of good health. Other components of good health include exercise and physical activity, regular medical check-ups, and recommended vaccinations.

What Can Be Done to Stay Healthy? (page 25)

Exercise and Physical Activity

Some people with hemophilia avoid exercise because they think it may cause bleeds, but everyone benefits from exercise: regular physical activity is important to the prevention of diseases such as diabetes, heart disease, obesity, osteoporosis, and cancer. For people with hemophilia, regular physical activity can actually help prevent bleeds and joint damage. Exercise is important for building healthy bones and strengthening the muscles that support and protect joints. Exercise can also help reduce stress, anxiety, and depression; build self-esteem and coping skills; and improve performance at school or work.

The WFH publication *Exercises for People with Hemophilia* describes how joints and muscles are affected by hemophilic bleeding and provides suggested exercises for joints and muscles. The exercise progressions aim to counteract the long-term effects of joint and muscle bleeding and the tendency to develop abnormal postures. The exercises are accompanied by illustrations showing how they should be executed.

Participation in regular sports also promotes feelings of well-being and fulfillment, which help counterbalance the loneliness, isolation, or other emotional challenges that can accompany hemophilia. Children of all ages should be encouraged to participate in sports and to learn which activities can result in bleeds. Sometimes, it is possible to facilitate a child's desire to pursue a particular sport by ensuring that appropriate protection (such as helmets and protective padding) is worn or by administering prophylactic factor beforehand.

Sports recommended for people with hemophilia include swimming, table tennis, walking, fishing, dance, badminton, sailing, golf, bowling, billiards, and cycling. The following sports are not recommended for people with severe hemophilia: rugby football, American football, karate, wrestling, motorcycling, judo, hockey, and skateboarding. Patients should talk to their doctor or physiotherapist to determine the sports that are best for them.

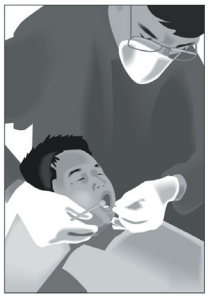
Good Nutrition and Healthy Body Weight

A healthy diet is very important to someone with hemophilia. Along with regular exercise, quality nutrition is key to the maintenance of strong muscles and stable joints. A healthy body weight is important so as not to put extra strain on joints. A nutritious diet is also crucial for those infected with HIV.

Why is dental health important? (page 26)

Good oral hygiene is essential to prevent gingival and periodontal disease. For people with hemophilia, the maintenance of good dental health is very important to reduce the need for dental surgery. Personal dental care should include brushing, flossing, and regular check-ups:

- Teeth should be brushed at least twice daily for plaque control.
- Toothpaste containing fluoride should be used.
- Mouthwashes of triclosan or chlorhexidine can also help reduce plaque.
- Dental floss or interdental brushes help reduce plaque.
- People with hemophilia should see their dentist regularly.



What if medicine or vaccinations are needed? (pages 25 and 29)

Regular medical check-ups, including examination of the joints and muscles, are essential to maintaining good health. Children with hemophilia should have a check-up every six months and adults at least annually.

Individuals with hemophilia should be vaccinated, but vaccination should be administered subcutaneously, not intramuscularly. The following points should be considered:

- Live virus vaccines (such as oral polio vaccine, MMR) should be avoided in those with HIV infection.
- People with hemophilia who have HIV should be given pneumococcal and annual influenza vaccines.
- Immunization to hepatitis B and A is important for all persons with hemophilia and can be given by subcutaneous rather than intramuscular injections.
- Family members handling treatment products should also be vaccinated; however, this is less critical for those using viral-inactivated products.

All medicines should be checked with a hemophilia specialist. Medicine and treatment products must be stored and used according to instructions.

People with hemophilia should not take acetylsalicylic acid (ASA or Aspirin®) in any form to reduce pain. **Nonsteroidal anti-inflammatory drug (NSAIDS)** should not be taken without medical advice.

Why is emotional health important (page 27)

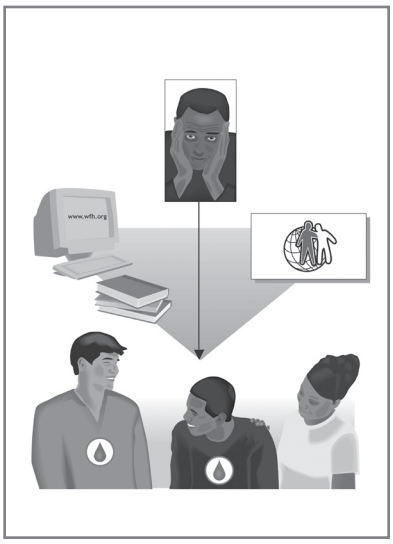
Living with hemophilia causes stress. This stress can affect family members as well as the person with hemophilia.

The word "prophylaxis" in hemophilia treatment has traditionally referred to the regular infusion of factor concentrates to prevent spontaneous bleeding episodes by maintaining the trough factor levels around one to two per cent. From a **psychosocial** perspective, however, prophylaxis refers to a proactive, routine, and preventive approach to the psychological and emotional aspects of living with hemophilia. Hemophilia is not just a physical

condition but has an impact on the psychosocial functioning of both patients and their families. Psychosocial support for patients and their families are an important part of hemophilia care.

Even in countries where factor prophylaxis is available, there can often be delays in obtaining factor concentrates or in getting patients to hemophilia treatment centres. In many emerging countries, factor concentrate is not available, affordable, or accessible.

Where people do not always have easy access to factor replacement products and standard medical treatments, nurses, psychologists, or social workers can provide psychosocial support—consisting of education, information, compassion, and support to help patients through the process of coping with hemophilia. The social worker or psychologist can play a significant role in helping the patient and his family learn about and accept a life-long condition, and enjoy a good quality of life.



In some emerging countries, where access to treatment is severely limited, psychotherapy, physical therapy, and allied health services may be more readily affordable and available. As well, in countries where there is a culture of strong extended family ties and support, there may be additional informal psychosocial support.

Psychosocial support is about detecting, as soon as possible, individual and family difficulties in accepting and coping with the challenges of living with hemophilia. By considering the range of possible emotions, thoughts, and feelings that can occur upon diagnosis or with each new situation that arises, educators, healthcare providers, caregivers, and parents can help the patient accept and learn about his condition. With knowledge comes power, insight, and self-confidence, which ultimately brings the ability to lead a healthy, active, and productive life.

A very important aspect of psychosocial support is to teach the patient that hemophilia is not a "disease" but rather a bleeding disorder. Although the condition is lifelong, it is important to minimize negative physical and psychological effects. All people get ill at some time or another. People with hemophilia will sometimes experience bleeds or episodes of physical pain, but they are not sick all the time. Encourage people with hemophilia to take charge of their own lives, recognize risky behaviours, learn to be responsible, and think of themselves as the same as people without the disorder. Everyone has good and bad days.

Addressing psychological and emotional challenges is a key part of helping people with hemophilia and their families learn how to live with a chronic bleeding disorder. Beyond tips on how to accept certain limitations presented by hemophilia, it is also important to give positive encouragement about how to live happily and productively, where hemophilia is just one aspect of life. Psychosocial support is readily available, accessible, affordable, and easy to supply.

How can parents help?

Parents of children with hemophilia do best when they encourage their children's natural abilities to adapt themselves to the realities of having a chronic disorder. This education process has to extend to siblings, who can often suffer guilt because they don't have the condition, develop fears that they may "catch" it, or harbour resentment that their parents' attention is so often on the sibling with hemophilia.

For both the person with hemophilia and family members, feelings and thoughts may alternate from optimistic and constructive to pessimistic and destructive. This is normal in the gradual process of accepting hemophilia and learning to live a normal and productive life in spite of the disorder. Because hemophilia is a chronic life condition, people with hemophilia must deal with the fact that part of themselves will always be "the patient." Learning how to best integrate hemophilia into daily life will help patients have a proactive attitude towards the condition and enable them to take control of their lives without taking unnecessary risks.

Review Quiz

Part 4: Staying Healthy and Preventing Bleeds

1. Regular _____ and _____ help people with hemophilia stay healthy and can actually help prevent bleeds and joint damage.

2. Some recommended sports for people with hemophilia include _____ _____.

3. Some sports not recommended for people with severe hemophilia include _____ _____.

4. Along with regular exercise, _____ is key to the maintenance of strong muscles and stable joints.

5. Good dental care includes _____, _____ , and _____.

6. Vaccination should be administered _____ , not intramuscularly.

7. People with hemophilia should not take _____ in any form to reduce pain.

8. _____ helps people with hemophilia cope with the challenges of living with hemophilia and enjoy better quality of life.

** Please see the Appendix for answers.*

Appendix

Hemophilia in Pictures Review Quiz

Part 1: Introduction to Hemophilia

1. Blood moves through the body in tubes. The large ones are called _____ and _____. The smaller tubes are called _____.

2. Bleeding occurs when a _____ is injured and blood leaks out. The _____ tightens up to help slow the bleeding. The blood cells, called _____ make a plug to patch the hole.

3. When one clotting factor is missing, or the level of that factor is low, bleeding continues (longer/ faster) _____ than usual.

4. Is all hemophilia the same? (yes / no)

5. Is hemophilia contagious? (yes / no)

6. Hemophilia is a bleeding disorder that is inherited through a parent's _____, specifically the _____ chromosome.

7. X and Y chromosomes determine a person's sex. A male is born with _____ and _____ chromosomes. A female is born with two _____ chromosomes.

8. A man with hemophilia passes the hemophilia gene to all of his (daughters / sons).

9. When a carrier has a baby, her chances of passing on the gene are: (one in two / one in four / always).

Part 2: Assessing and Managing Bleeds

1. Bleeding or bruising that occurs with no known cause is called _____ bleeding.

2. The place where two bones meet is called a _____.

3. The ends of bones are covered with a smooth surface called the _____.

4. Bones are partly held together by a joint capsule. This joint capsule has a lining called the _____.

5. Two signs of a possible joint bleed are _____ _____.

6. The three most common joint bleeds happen in the _____, the_____, and the _____.

7. Two long-term effects of joint bleeds are_____ _____.

8. Some of the signs of a muscle bleed include _____
_____.

9. Most muscle bleeds happen in the _____, the _____, and the _____.

10. The psoas muscles are located at _____.

11. Bleeds in the _____ and _____ are serious and can be life-threatening.

Part 3: Treatment of Bleeds

1. The four elements of first aid treatment for a bleed are _____, _____, _____, and _____.

2. Two clotting factor treatment products are _____ and _____.

3. Infusion is _____.

4. Venepuncture is _____.

5. Infection can be avoided when giving an injection by _____
_____.

6. Antibodies that form in the body to fight off substances it perceives as "foreign" are called _____. In hemophilia, infusion of factor concentrates can provoke the body's defense mechanisms to act against the clotting factor, and the clotting activity suffers.

Part 4: Staying Healthy and Preventing Bleeds

1. Regular _____ and _____ help people with hemophilia stay healthy and can actually help prevent bleeds and joint damage.

2. Some recommended sports for people with hemophilia include _____
_____.

3. Some sports not recommended for people with severe hemophilia include _____
_____.

4. Along with regular exercise, _____ is key to the maintenance of strong muscles and stable joints.

5. Good dental care includes _____, _____ , and _____.

6. Vaccination should be administered _____ , not intramuscularly.

7. People with hemophilia should not take _____ in any form to reduce pain.

8. _____ helps people with hemophilia cope with the challenges of living with hemophilia and enjoy better quality of life.

Answers to Review Quiz

Part 1: About Hemophilia

1) Arteries, veins, capillaries
2) Capillary, capillary, platelets
3) Longer
4) No
5) No
6) Genes, X
7) X and Y, X
8) Daughters
9) One in two (50%)

Part 2: Assessing and Managing Bleeds

1) Spontaneous
2) Joint
3) Cartilage
4) Synovium
5) Joint feels tingly and warm, then swelling
6) Knees, elbows, ankles
7) An irritated (thickened and red) synovial membrane, a chronically inflamed synovium (causing the joint to appear extremely swollen)
8) Stiffness, pain, and swelling in muscle; tingling and numbness in the area of the muscle bleed
9) Thigh, calf, upper arm
10) Front of the hip
11) Head, nervous system

Part 3: Treatment of Bleeds

1) Rest, ice and/or immobilization, compression, elevation
2) Clotting factor concentrates, cryoprecipitate (also plasma, whole blood)
3) The injection into a vein of a treatment product, solution, or drug
4) Putting a needle into a vein
5) Washing of hands, sterile injection practices, proper storage and disposal of needles and handling of blood spills
6) Inhibitors

Part 4: Staying Healthy and Preventing Bleeds

1) Exercise, physical activity
2) Swimming, table tennis, walking, fishing, dance, badminton, sailing, golf, bowling, billiards, cycling
3) Rugby football, American football, karate, wrestling, motorcycling, judo, hockey, skateboarding
4) Quality nutrition
5) Brushing, flossing, regular check-ups
6) Subcutaneously
7) Acetylsalicylic acid (ASA or Aspirin®)
8) Psychosocial support

Glossary

Activated partial thromboplastin time (APTT): A test that measures blood clotting ability. Taken together with a normal prothrombin time, prolonged APPT is the most useful screening test for detecting deficiencies of factors VIII, IX, XI, and XII. It is also the most common method for diagnosing inhibitors.

Activated prothrombin complex concentrates (APCCs): Plasma-derived products, such a FEIBA®, that contain variable amounts of non-activated and activated vitamin K–dependent coagulation factors such as VII, IX, and X.

Adjunctive therapy: Treatment/therapy given together with the primary treatment.

Amniocentesis: Removal of a small amount of fluid in the uterus using a fine needle.

Amniotic fluid: The fluid in the uterus in which the embryo floats.

Anamnestic response: An immune system memory mechanism in which the memory of a previous encounter with foreign substances triggers the formation of antibodies. For example, infusion with clotting factor can bring a rapid increase in inhibitor titer levels.

Anaphylaxis: A severe allergic reaction often resulting in the inability to breathe.

Antibodies: Proteins made by the body to fight off substances it perceives as foreign.

Antifibrinolytic agent: A drug that can help stop the normal breakdown of blood clots and help speed recovery from a bleed. Also called fibrinolytic inhibitors.

Artery: A large tube or blood vessel that carries blood from the heart through the body. The body has several arteries.

Arthropathy: Inflammatory disease affecting the joints.

Aseptic: Uncontaminated; absence of harmful micro-organisms/bacteria.

Assisted conception: Procedures used to help a couple conceive.

Bethesda unit: The amount of inhibitor that neutralizes 50 per cent of one unit of clotting factor during a given incubation period.

Bolus: An infusion procedure in which a concentrated dose of a therapeutic product is given over a short period of time.

Bypassing agent: A special coagulation factor used in patients with antibodies to their usual factor, to overcome the blockage/cessation in the clotting system.

Capillary: Any of the very small tubes or blood vessels that form a network to carry blood through the body. The body has many capillaries.

Carrier: A person who carries a gene that causes a disorder, usually showing no symptoms.

Centrifugation: Rotation in a machine to separate liquids from solids.

Cartilage: The smooth surface covering the ends of the bones in a joint.

Chorionic villi: Tissue in the placenta.

Chorionic villus sampling (CVS): Passing a fine needle through the abdomen or transvaginally to take a sample of chorionic villi cells from the placenta.

Chromosome: A very fine, threadlike strand of proteins and DNA in the centre of human, animal, and plant cells. Two chromosomes (called X and Y) decide a person's sex. Females are born with two X chromosomes (XX = girl). Males are born with one X and one Y chromosome (XY = boy).

Chronic synovitis: Continuous or repeated inflammation of the lining of a joint, causing it to appear very swollen.

Cirrhosis: A chronic liver disease characterized by the formation of scar tissue and the interruption of blood flow.

Clot: A thick lump of blood formed by clotting factors that work together to help stop bleeding.

Clotting factor: Any of the factors in blood plasma that work together to form a clot to help stop bleeding.

Coagulation: The process by which bleeding (hemorrhage) is normally stopped in the body.

Coagulation testing: Testing the blood's ability to clot.

Compression: To apply compression to a bleed means to apply firm pressure or support using an elastic stocking or wrap to help stop the swelling.

Cryoprecipitate: A treatment product made from blood plasma. It contains proteins, such as factor VIII (eight) and von Willebrand factor, but not factor IX (nine). It is infused into a vein over a period of time to treat or prevent bleeds.

Density gradient: A method using liquids of different densities to separate healthy sperm from waste products, such as dead sperm cells and white blood cells.

Desmopressin (DDAVP): A synthetic compound that raises a person's factor VIII (eight) level in blood, but is not a blood product. It can be used to treat mild hemophilia A and some types of von Willebrand disease.

Elevation: In first aid, elevation means to raise the injured part of the body above the level of the heart. This helps stop bleeding and swelling.

Embryo: A fertilized egg during the first eight or 12 weeks of growth in the uterus.

Epistaxis: A nosebleed or hemorrhage from the nose.

Epsilon aminocaprioic acid (EACA): An antifibrinolytic drug that stops clots from dissolving. It stops the activity of the plasmin enzyme, which normally dissolves blood clots.

Exposure days: The number of days a person has been infused with concentrate to treat a bleed.

Factor concentrates: A type of treatment used to replace the missing factor VIII (eight) or IX (nine) by injection into a vein. Factor can be made from human blood plasma and then dried to a powder. This is dissolved in diluent before injection. See recombinant for more information.

Fetal sex typing / sexing of the fetus: Identifying the sex of the embryo by taking a blood sample from the mother or by taking an ultrasound of the uterus.

Fresh frozen plasma (FFP): A type of treatment product made by removing red blood cells, white blood cells, and platelets from whole blood and then freezing the plasma, which contains the clotting factors.

Gene: Genes carry messages about the body's cells. For example, they determine a person's hair and eye colour. Hemophilia is passed on through a person's genes.

Genetic counselling: The process of helping couples evaluate and understand their likelihood of passing on certain genetic diseases or disorders, and offering options.

Gestation: Length of time of growth of an embryo in the uterus from fertilization to delivery/birth.

Half-life: The amount of time it takes for the factor activity level to drop by half after an infusion. Factor VIII (eight) has a half-life of eight to 12 hours. After the first infusion, the half-life of factor IX (nine) increases to 18 to 24 hours for subsequent infusions.

Hemarthrosis: Bleeding into a joint cavity, such as the shoulder, elbow, hip, knee, or ankle.

Hematoma: A localized collection of blood in an organ or tissue, commonly known as a "blood clot."

Hemophilia: A bleeding disorder in which clotting factor VIII (eight) or IX (nine) in a person's blood plasma is missing or is at a low level.

Hemophilia A: A bleeding disorder in which clotting factor VIII (eight) in a person's blood plasma is missing or is at a low level.

Hemophilia B: A bleeding disorder in which clotting factor IX (nine) in a person's blood plasma is missing or is at a low level.

Hemophilic arthropathy: Progressive joint damage caused by bleeding into a joint cavity. Although any joint can be involved, the most frequently affected joints are, in decreasing order, the knees, elbows, ankles, hips, and shoulders.

Hemophilic arthritis: Inflammation of a joint, usually with pain and swelling, due to repeated bleeds. With recurrent bleeds, joint cartilage breaks down and some bone wears away. Sometimes the joint cannot move.

Hemorrhage: A general term for bleeding, either internally or on the surface, with significant blood loss. It may be brought on by injury to blood vessels or by a deficiency of certain necessary blood elements such as factor proteins or platelets.

Heparin: A solution made with the substance heparin, which is found in lung and liver tissue, used to stop blood clotting.

Hepatitis: An inflammation of the liver caused by injury or viral infection through blood product transfusion. The most common strains of the virus are hepatitis A, B, and C.
The introduction of screening and viral inactivation methods has eliminated transmission of hepatitis B and C through clotting factor products. Hepatitis A has been resistant to current viral inactivation methods, however, a vaccine is available. It is recommended that people with hemophilia get vaccines against both hepatitis A and B.

Highly active antiretroviral therapy (HAART): A combination drug therapy that is very effective in controlling HIV infection.

Home therapy: Injection or infusion of a treatment product away from the hospital, usually at home.

Hypertrophy: Increase in size/volume of a tissue or organ produced by enlargement of existing cells.

Hystosalpingogram: An X-ray study to assess the uterine cavity and the patency, or lack of obstruction, of the fallopian tubes.

Immobilization: Preventing movement.

Immune tolerance induction (ITI) therapy: Repeated administration of clotting factor over a few months to induce tolerance.

Infusion: Injection into a vein of a treatment product, solution or drug.

Inhibitor: Antibodies (proteins) made by the body to fight off substances it perceives as foreign that inhibit a clotting factor.

Insemination: Introduction of semen into the vagina by sexual intercourse or by artificial means in the case of assisted conception.

Inter-current infection: An infection that intervenes during the course of another disease process.

Intracranial bleed: Bleeding in the head.

Intracytoplasmic sperm injection (ICSC): A process in which sperm are removed directly from a man's testicles and a single sperm is directly injected into a woman's egg.

Intramuscular: Into a muscle.

In vitro fertilization: Fertilization of an egg outside the womb in a laboratory followed by implantation in the uterus.

Joint: The place where two bones meet.

Joint cavity: The area or sleeve that holds the bones together in a joint.

Lyophilized: The process in which a solid substance is isolated from a solution by freezing the solution and evaporating the ice under vacuum.

Menorrhagia: Excessive bleeding during menstruation.

Mild hemophilia: A disorder caused by factor VIII (eight) or IX (nine) activity of 5-40% of the normal level in blood.

Moderate hemophilia: A disorder caused by factor VIII (eight) or IX (nine) activity of 1-5% of the normal level in blood.

Motility: Spontaneous movement of sperm.

Muscle spasm: Painful tightening of a muscle that a person cannot control.

Nerve: The sensitive, cordlike fibres that pass messages through the body, including pain.

Nonsteroidal anti-inflammatory drug (NSAIDS): A medication, such as ibuprofen, that reduces pain and fever but does not contain steroids.

On-demand therapy: Treatment of bleeds as they occur (rather than treating before a bleed to prevent them from happening).

Pathogens: Organisms that cause infection.

Pelvic morphology: A medical examination to assess the shape and form of the pelvis.

Plasma: Part of the blood that contains fibrin and clotting factors.

Plasmapheresis: A method for collecting plasma from a donor in which a unit of blood is taken from the donor, the plasma is removed from the blood, and the blood cells are returned to the donor. Plasmapheresis allows for a faster donor recovery time than whole blood donation. This means that a donor can give larger volumes of plasma at one time and can give more frequently.

Platelets: Disc-shaped sticky blood cells that make a plug to patch holes in arteries, veins, and capillaries.

Polymerase chain reaction (PCR) technique: A method of amplifying the amount of DNA to a point where it can be manipulated in a laboratory test.

Pre-implantation genetic diagnosis (PGD): A technique pioneered at the Hammersmith Hospital, London, in 1989 that can detect certain inherited diseases in pre-implantation embryos produced using conventional in vitro fertilization methods.

Prophylaxis: In hemophilia, prophylaxis refers to regular infusion of factor concentrates to prevent spontaneous bleeding episodes by maintaining the trough factor levels around one to two per cent.

Psoas muscle: A muscle near the groin (at the front of the hip) that helps move the hip joint and the spine.

Psychosocial: Emotional and psychological.

Recessive: In genetics, a recessive gene is one that will only produce its effects if both copies (one from the mother and one from the father) are identical.

Recombinant: A type of factor concentrate that is manufactured in a laboratory instead of being separated from human blood. Recombinant proteins are copies of certain kinds of proteins found in human blood plasma.

Regime / regimen: A prescribed course of treatment.

Septicemia: A systemic disease caused by the presence of bacteria in the bloodstream, characterized by a systemic inflammatory response and widespread activation of inflammation and coagulation pathways.

Serodiscordant: Being a couple in which one partner has tested positive for HIV and the other has not.

Seronegative: One's blood having tested negative for a particular infection, such as HIV; not having HIV.

Severe hemophilia: A disorder caused by a lack or a very low level of factor VIII (eight) or IX (nine) activity in the blood, usually less than 1% of the normal level.

Sperm washing: A procedure used to separate sperm from semen and remove infective organisms as well as dead sperm cells, white blood cells, and other waste products.

Spontaneous bleeding: Bleeding that happens for no clear reason (not after an injury or surgery).

Synovium: The lining of the joint capsule. It is made of special cells that make a slippery, oily fluid that helps the joint move easily.

Synoviorthesis: A substance (either a chemical or radioactive isotope) being injected directly into the joint to cause the synovium to be ablated. This procedure is usually quite effective in reducing bleeding if done early.

Synovectomy: The excision/removal of the synovial membrane (lining of the joint).

Thromboembolic complications: A risk of blood clots forming in the blood vessels. Blood clots that form in the veins cause deep vein thrombosis. If they occur in the arteries, they can cause cerebral vascular accidents (strokes) and pulmonary embolus (clots in the lungs).

Thrombosis: The formation of a blood clot within a blood vessel (artery or vein).

Titer: The strength of a solution as determined by titration. In medicine it is used to describe the amount of antibodies present in a known volume of serum.

Tolerized: A patient is "tolerized" when the inhibitor to factor VIII or IX has disappeared and does not re-appear with further treatment of factor VIII or IX.

Tranexamic acid: An antifibrinolytic drug that stops clots from dissolving. It stops the activity of the plasmin enzyme, which normally dissolves blood clots.

Trans-abdominally: Through the woman's abdomen under local anesthesia.

Trans-vaginally: Through the vagina.

Trough clotting factor levels: The lowest level the factor reaches before the next infusion.

Variant Creutzfeldt-Jakob disease (vCJD): A form of transmissible spongiform encephalopathy (TSE). The disease destroys the central nervous system and eventually results in death. It is usually caused by eating meat from cattle infected with bovine spongiform encephalopathy (BSE) or "mad cow disease."

Vasodilation / Huntington Response: The increase in diameter of a vein to bring more blood to an area of the body.

Vein: A tube or blood vessel that carries blood through the body to the heart. The body has many veins.

Venepuncture: Putting a needle into a vein. This can be done to take blood or to give an intravenous injection.

Venous access device (VAD): A small device that is surgically placed inside the body so that a needle can be inserted repeatedly with ease for infusions.

Viral inactivation: A process to kill or remove viruses.

References

Costa, J.M., E. Gautier, and A. Benachi. "Genetic analysis of the fetus using maternal blood." *Gynecology Obstetric Fertility* 32 (2004): 646-50.

DiMichele, D.M. *Inhibitors in Hemophilia: A Primer*. Revised Edition. World Federation of Hemophilia, 2004.

Doak, Leonard G., et al. *Pfizer Principles for Clear Health Communication.* 2nd edition. Pfizer.

Falvo, Donna R. *Effective Patient Education: A Guide to Increased Compliance.* 3rd edition. 2004.

Geradts, J., A. Handyside, J. Harper, et al. "ESHRE Pre-implantation Genetic Diagnosis Consortium: data collection 11 May." *Himab Reproduction* 15 (2000): 2673-83.

Kanzer-Lewis, G. *Patient Education: You Can Do It! A Practical Guide to Teaching and Motivating Patients.* American Diabetes Association, 2003.

Kasper, C.K. *Diagnosis and Management of Inhibitors to Factors VIII and IX.* World Federation of Hemophilia, 2004.

Kasper, C.K. *Hereditary Plasma Clotting Factor Disorders and Their Management.* Revised Edition. World Federation of Hemophilia, 2004.

Klug-Redman, B. *The Practice of Patient Education.* 9th edition. Mosby Inc., 2001.

Lavery, S., R. Aurell, C. Turner, et al. "Patients' perspectives of Pre-implantation genetic diagnosis and its psychological impact." Presented at Annual Meeting of European Society of Human Reproduction and Embryology, Bologna, June 2000.

Lavery, S., R. Aurell, C. Turner, D.Taylor, & R. Winston. "An Analysis of the Demand for the Cost of Pre-implantation Genetic Diagnosis in the United Kingdom." *Prenatal Diagnosis* 19 (1999): 1205-8.

Lorig, K., et al. *Patient Education: A Practical Approach.* 3rd edition. Sage Publications, 2001.

Miller, R. *Genetic Counselling for Hemophilia.* World Federation of Hemophilia, 2002.

Oyesiku, J. and C. Turner. "Reproductive choices for couples with haemophilia." Haemophilia 8 (2002): 348-352.

Pertl, B. and D.W. Bianchi. "Fetal DNA in Maternal Plasma: emerging clinical application." *Obstetrics Gynaecology* 98 (2001): 483-90.

Pilu, G. and K. Nicoloides. *Diagnosis of Fetal Abnormalities.* The Parthenon Publishing Group, London, 2003.

Semprini A., P. Levy-Setti, M. Bosso, M. Ravizza, A. Taglioretti, P. Sulpizio, et al. "Insemination of HIV-negative women with processed semen of HIV positive partners." *Lancet* 340 (1992): 1317-9.

Souiss I., J. Harper, A. Handyside, & R. Winston. "Obstetric outcome of pregnancies resulting from embryos biopsied for pre-implantation diagnosis of inherited disease."*Br J Obstetrics Gynaecology* 8 (1996): 784-8.

Wellisch D., A. Hoffman, S. Goldman, J. Hammerstein, K. Klein, & M. Bell "Depression and anxiety symptoms in women at high risk for breast cancer; pilot study of a group intervention." *American Journal of Psychiatry* 156 (1999): 1644-5.

Wilde, J.T. *HIV and HCV Co-infection in Hemophilia.* World Federation of Hemophilia, 2003.

World Federation of Hemophilia. *Guidelines for the Management of Hemophilia*, 2005.

Supported by an unrestricted educational grant from Wyeth

World Federation of Hemophilia

1425 René Lévesque Boulevard West, Suite 1010
Montréal, Québec H3G 1T7
CANADA
Tel.: (514) 875-7944
Fax: (514) 875-8916
E-mail: wfh@wfh.org
Internet: www.wfh.org

WORLD FEDERATION OF
HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA
Treatment for All