All About Carriers
A Guide for Carriers of Hemophilia A and B
The Canadian Hemophilia Society strives to improve the health and quality of life for all people with inherited bleeding disorders and to find a cure.

The CHS consults qualified medical professionals before distributing any medical information. However, the CHS does not practice medicine and in no circumstances recommends particular treatment for specific individuals. Brand names of treatment products are provided for information only. Their inclusion is not an endorsement of a particular product or company. In all cases, it is strongly recommended that individuals consult a hemophilia-treating physician before pursuing any course of treatment.

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The Canadian Hemophilia Society wishes to acknowledge all those who contributed to the development of All About Carriers. We would especially like to thank those women who participated in focus groups and completed the CHS carrier survey. Your words make this publication come alive.

All About Carriers
A Guide for Carriers of Hemophilia A and B
ISBN 978-0-920967-61-4
May, 2007
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# Table of Contents

**ACKNOWLEDGMENTS** ................................................................. I

**PREFACE** .................................................................................. IV

**CHAPTER 1:** An Introduction to Hemophilia ......................... 1

**CHAPTER 2:** Comprehensive Hemophilia Care .................... 21

**CHAPTER 3:** The Inheritance of Hemophilia ......................... 27

**CHAPTER 4:** Symptomatic Carriers ........................................ 35

**CHAPTER 5:** Carrier Testing .................................................. 43

**CHAPTER 6:** Reproductive Issues .......................................... 57

**CHAPTER 7:** Care and Treatment of Carriers......................... 79

**CHAPTER 8:** Complementary and Alternative Medicine ...... 93

**CHAPTER 9:** Carriers’ Quality of Life .................................... 103

**CHAPTER 10:** Taking Control ................................................. 117

**FINAL WORDS** ........................................................................ 123

**FOR MORE INFORMATION** ................................................ 125

**HEMOPHILIA TREATMENT CENTRES** ................................. 125

**GLOSSARY** .............................................................................. 128

**BIBLIOGRAPHY** ....................................................................... 134
Preface

Hemophilia is a bleeding disorder that has been known for thousands of years. While the severe form of the disorder affects almost only males, in recent years problems experienced by females who inherit or “carry” the defective gene are beginning to be recognized by many in the hemophilia community.

Males with clotting factor levels from 5% to 40% of normal were traditionally diagnosed with mild hemophilia; females, however, were designated simply as “carriers” of the gene. This designation was never given to males, though they too “carry” the defective gene. Females could suffer the same problems as males with mild hemophilia—hemorrhaging after surgery or trauma—yet it was not always acknowledged that the bleeding was related to carriers’ low factor levels. Today, the notion of females as potentially having mild hemophilia is becoming more widely accepted. Recent studies have shown that women with clotting factor levels as high as 60% can have abnormal bleeding problems, including but not restricted to gynaecological and obstetrical bleeding.

While the majority of carriers of factor VIII and IX do not suffer from serious bleeding problems, 57% do have gynaecological problems. The problems related to their excessive menstrual bleeding (menorrhagia) can vary from mild to severe. Some carriers haven’t yet made the connection between their own bleeding problems and their carrier status, and so have never spoken with Hemophilia Treatment Centre personnel about these problems.

All About Carriers is written in response to needs expressed in women’s focus groups organized across Canada by the Canadian Hemophilia Society. Detailed surveys were completed by more than 75 carriers of hemophilia A and B. All About Carriers is a collaborative effort written and reviewed by a multi-disciplinary team, including a hematologist, a hemophilia nurse coordinator, a social worker, a psychologist, a genetic counsellor, a naturopathic doctor, carriers and members of families living with hemophilia A and B.

The Canadian Hemophilia Society hopes this book will help girls and women who may have inherited the factor VIII or IX hemophilia gene find answers to their questions. Our goal is to provide the support and information needed to deal with the impact this disorder can have on both their quality of life and their health.
This chapter is intended as a general introduction to hemophilia. It describes:

- who is affected by hemophilia
- the number of people affected
- the symptoms of hemophilia
- the types and severity of hemophilia
- other bleeding disorders
- blood clotting
- the treatments for hemophilia
- the complications of hemophilia
- the life expectancy of people with hemophilia
- the future of hemophilia care.
HEMOPHILIA A AND B

The word hemophilia is derived from two Greek words: haima, meaning blood, and philia, meaning affection.

The blood of a person with hemophilia does not clot normally. He/she does not bleed more profusely or more quickly than other people; however, he/she bleeds for a longer time. Such bleeds are also called hemorrhages.

The blood is lacking a protein that is needed for normal clotting. Some people with hemophilia lack a protein called factor VIII (pronounced factor eight). This is hemophilia A.

Others lack a protein called factor IX (pronounced factor nine). Their disease is called hemophilia B.

Many believe that people with hemophilia bleed a lot from minor cuts. This is a myth. External wounds are usually not serious. Far more important is internal bleeding. This occurs in joints, especially knees, ankles and elbows; and into tissues and muscles. When bleeding occurs in a vital organ, especially the brain, the person’s life is in danger. In women with abnormally low levels of factor VIII or IX, the most common symptom is menorrhagia, heavy and prolonged menstrual bleeding.
THE PEOPLE AFFECTED BY HEMOPHILIA

Hemophilia affects people of all races, colours and ethnic origins around the world.

The most severe forms of hemophilia affect males almost exclusively. In rare cases females can be seriously affected. (See Chapter 3, The Inheritance of Hemophilia). Many women who are carriers of hemophilia, however, have symptoms of mild hemophilia. Health care professionals, and even women themselves, are only now fully recognizing that carriers can have bleeding problems that can affect their quality of life.

As hemophilia is an inherited disorder, children are affected from birth. Severe hemophilia is often diagnosed in the first year of life. It is a lifelong condition. At the moment, there is no way to correct the genetic defect.

THE NUMBER OF PEOPLE AFFECTED

Both hemophilia A and B are rare disorders. Hemophilia A affects 1 in 10,000 males, or about 3,000 Canadians. Hemophilia B is even less common, affecting approximately 1 in 35,000 males, or about 800 Canadians.

The vast majority—90% to 95%—of mothers of people with hemophilia are carriers. The total number of carriers, however, is not known.

Approximately one-third of cases of hemophilia are the result of new genetic mutations. In the other two-thirds, there is a history of hemophilia in the family. (For more information, see Chapter 3, The Inheritance of Hemophilia.)
SYMPTOMS OF HEMOPHILIA

Common symptoms of hemophilia are:

- bleeding into joints (knees, elbows, ankles, shoulders, hips, wrists in descending order of frequency)
- bleeding into soft tissues and muscles (the ileopsoas muscle around the hip, calf, forearm, upper arm, Achilles tendon, buttocks)
- bleeding in the mouth from a cut, bitten tongue or loss of a tooth (especially in children)
- blood in the urine (hematuria)
- surface bruising
- excessive bleeding following trauma or surgery.

These symptoms vary depending on the severity of the disorder.

In girls and women who are carriers of hemophilia A or B, 57% experience heavy, prolonged menstrual bleeding, called menorrhagia. 10% to 20% of carriers can suffer from abnormal bleeding following trauma or surgery. The same numbers experience bleeding after childbirth.
CHAPTER 1 An Introduction to Hemophilia

THE SEVERITY OF HEMOPHILIA

Hemophilia A and B can be divided into three classifications of severity. See Table 1.

<table>
<thead>
<tr>
<th>Classification of Hemophilia</th>
<th>Level of Factor VIII or IX in the Blood*</th>
<th>Percentage of Males with Hemophilia in Each Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>Less than 1% of normal</td>
<td>40% of cases</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 to 5% of normal</td>
<td>20 to 25% of cases</td>
</tr>
<tr>
<td>Mild</td>
<td>5 to 40% of normal</td>
<td>35 to 40% of cases</td>
</tr>
</tbody>
</table>

Table 1

* Clotting factor activity in people without hemophilia ranges anywhere from 50% to 150% of normal. This is measured in units per millilitre (U/mL). For example, a level of 100 U/mL of factor VIII is equivalent to a level which is 100% of normal.

People with severe hemophilia have less than 1% of the normal level of factor VIII or IX in their blood. Without preventive treatment, they can have hemorrhages several times a month. There is often no obvious cause for the bleeding—it just happens. This is called spontaneous bleeding.

People with moderate hemophilia, 1% to 5% of the normal level of factor VIII or IX in their blood, usually bleed less often. Their hemorrhages are frequently the result of minor trauma, such as sports injuries. Some people with moderate hemophilia, however, especially those whose level of factor VIII or IX is 2% or less, can have frequent spontaneous bleeds in the same way as a person with severe hemophilia.
People with mild hemophilia, 5% to 40% of normal levels, have even fewer hemorrhages. They may be aware of their bleeding problem only in the case of surgery, a tooth extraction or a serious injury. The danger for people with mild hemophilia is that, having so few bleeds, they often do not know what to do when one occurs. Delay in seeking medical care can have serious consequences.

Women who are carriers of hemophilia may bleed more heavily than normal during their periods. Recent research has shown that carriers may have increased bleeding problems even if their factor levels are close to normal (in the range of 40% to 60% of normal).

For these reasons carriers of hemophilia also need to be followed at a hemophilia treatment centre.

**OTHER BLEEDING DISORDERS**

Both men and women can suffer from other inherited bleeding disorders. The most common is von Willebrand disease (VWD). The gene responsible for VWD is believed to affect 1 in 100 people to 1 in 1000 people, depending on the population studied. As many as 10% of those carrying the gene, up to 30,000 Canadians, may have bleeding problems. These range from quite mild to severe.

Much rarer are deficiencies in factors I, II, V, VII, X, XI and XIII. These conditions affect fewer than 1000 Canadians.

Platelet function disorders also cause abnormal bleeding. Serious hereditary platelet function disorders are quite rare; however, because the majority of people have very mild symptoms, many cases are not diagnosed.
For more information on these disorders, consult Bleeding Disorders on the Canadian Hemophilia Society Web site at www.hemophilia.ca.

**BLOOD CLOTTING**

Blood is carried throughout the body within a network of blood vessels: arteries, veins and capillaries. When tissues are injured, damage to a blood vessel may result in leakage of blood through holes in the vessel wall. The vessels can break near the surface of the skin, as in a cut. Or they can break deeper inside the body, causing a bruise or an internal hemorrhage.

Clotting, or coagulation, is a complex process that makes it possible to stop injured blood vessels from bleeding. As soon as a blood vessel wall breaks, the proteins that work together to form the clot come together to form a plug at the break. There are several steps involved in forming this plug. **See Figure 1.**

- **Stage 1:** The blood vessels constrict to slow the flow of blood to the injured area. This is called vascular constriction, or vasoconstriction.

- **Stage 2:** Blood platelets, which are very tiny cell fragments, are the first to arrive at the break. Platelets are small cells circulating in the blood. Each platelet is less than 1/10,000 of a centimetre in diameter. There are 150 to 400 billion platelets in a normal litre of blood. The platelets play an important role in stopping bleeding by clumping together, thereby beginning the repair of injured blood vessels. This is called platelet adhesion.

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**Figure 1**
• Stage 3: These platelets then emit chemical signals calling for help from other platelets and from clotting factors, like von Willebrand factor. These spreading platelets release substances that activate other nearby platelets that then clump at the site of injury to form a platelet plug. This is called platelet aggregation.

• Stage 4: The surface of these activated platelets then provides a site for blood clotting to occur. Clotting factors, which are tiny plasma proteins, link to form a chain, called fibrin. The strands of fibrin join together to weave a mesh around the platelets. This prevents the platelets from drifting back into the bloodstream. These proteins (factors I, II, V, VII, VIII, IX, X, XI and XIII) work like dominoes, in a chain reaction. This is called the coagulation cascade. (See Figure 2.)

**Figure 2**

**Clotting Agents**

- Factor XII
- Factor XI
- Factor IX
- Factor VIII
- Factor X
- Prothrombin
- Fibrinogen

**Normal Clotting Sequence**

- Fibrin net and platelet plugs at hole in vessel wall
THE CLOTTING PROBLEM IN HEMOPHILIA

When one of the proteins, for example factor VIII, is absent, or present in lower quantities, the chain reaction is broken. Clotting does not happen, or it happens much more slowly than normal. The platelets at the site of the injury do not mesh into place to form a permanent clot. The clot is “soft” and easily displaced. Without treatment, bleeding can continue for days and sometimes weeks. Re-bleeding often occurs. (See Figure 3.)

Figure 3
TREATMENTS FOR HEMOPHILIA

Current treatments for hemophilia A and B are usually very effective.

Clotting factor therapy

The key treatment for the more severe forms of hemophilia is clotting factor therapy. This therapy involves the intravenous infusion of the clotting factor that is missing in the blood of the person with hemophilia. It is both safe and effective in stopping bleeding. This therapy can even be used in a preventive way—to stop bleeding from happening at all. This is called prophylaxis. With prophylaxis, infusions are given once, twice or three times a week.

Parents learn to administer these infusions themselves, often when their child is still a baby. Once they have mastered the technique, they can provide their child’s care at home, and avoid frequent hospital visits.

Children with hemophilia often learn to administer the infusions themselves. They learn when they’re as young as eight or ten years of age.

For people with mild or moderate hemophilia, clotting factor concentrates may not always be required for bleeding episodes. In many cases, other treatments can be used to reduce or avoid the use of these factor concentrates.
Desmopressin acetate (for factor VIII deficiency)

Desmopressin acetate, also called DDAVP, is a synthetic drug—not a blood product—that is helpful in the majority of patients with mild hemophilia A. DDAVP works indirectly through the release of von Willebrand factor to raise the patient’s factor VIII level.

Desmopressin can be given in different ways:
- intravenously – The drug is injected into a vein.
- subcutaneously – The drug is injected just under the skin.
- intranasally – The drug is taken into the nostrils using an inhaler, in the same way that people with asthma take their medications.

Desmopressin may triple the level of factor VIII in the person’s bloodstream. As a result, a patient with mild hemophilia may raise his factor VIII level high enough to stop further bleeding.

Antifibrinolytics (for both factor VIII and IX deficiency)

Another medication that is helpful is the antifibrinolytic drug, tranexamic acid, also called Cyklokapron® or TA.

This agent acts by strengthening blood clots that form. This prevents the clots from being broken down or dislodged, and bleeding from re-starting. Cyklokapron® is particularly useful in bleeding from the mouth (gums, teeth, tongue), bleeding from the nose (epistaxis) and menorrhagia.
COMPLICATIONS OF HEMOPHILIA

Complications are possible.

Inhibitors

The most serious complication is the development of an inhibitor. In some people with hemophilia, the body’s immune system reacts to the clotting factor concentrate that is infused to stop or prevent a bleed. The factor concentrate is seen as a foreign substance. The body’s immune system fights the invader by producing antibodies, natural chemical substances that circulate in the blood. The antibodies eliminate the infused factor concentrate and thus prevent the medication from doing its job of stopping the bleeding. These antibodies are called inhibitors.

Inhibitors develop in...
- 15% to 35% of people with severe hemophilia A (factor VIII deficiency)
- 1% to 2% of people with mild or moderate hemophilia A
- 1% to 3% of people with severe hemophilia B (factor IX deficiency)
- fewer than 1% of people with mild or moderate hemophilia B.

We now know that a person with hemophilia who has a family member with an inhibitor is more at risk of developing an inhibitor himself. It is also believed that people with certain genetic mutations (usually the most severe) and from certain ethnic groups, notably those of African descent, are at higher risk.
In some cases, inhibitors disappear naturally and clotting factor therapies regain their full effectiveness. In other cases, intensive protocols of factor replacement therapy over many months or even years are used to accustom or tolerize the body to the factor protein and overwhelm the inhibitors. In cases where these therapies are not successful, alternative clotting factor therapies are available; however, they are often less effective than the factor VIII or IX concentrates used for people with no inhibitor.

**Joint Disease**

Many adults with severe hemophilia in Canada have permanent damage in one or more joints. When they were children, treatment was less advanced. Bleeding into joints was less well controlled. Joint disease led to loss of range of motion, muscle atrophy (weakening), pain and limited mobility.

Today, many Canadian children with hemophilia are growing up with normal or nearly normal joints. The use of regular clotting factor therapy, starting at a very early age, to PREVENT bleeding (prophylaxis) has improved their chances of reaching adulthood without serious joint disease.

Damage to the joints is caused by repeated bleeding into the joint cavity. In some cases, joint disease can begin after only one major joint bleed. More often, joint damage is the result of many bleeds over a period of years. For this reason, joint bleeds must be treated immediately to stop bleeding quickly.

Some joints are more likely to be affected by bleeds than others. The joints that bleed most often are the knees, ankles and elbows. These are hinge joints and have little protection from side-to-side stresses.
Joints like the shoulder and the hip are ball-and-socket joints. They are well protected by large muscles, and are designed to move in many directions without being injured.

Research has shown that joint disease can affect people with mild hemophilia. This includes women who are carriers.

**Gynaecological complications**

Women who are carriers of hemophilia and who suffer from symptoms of mild hemophilia can experience gynaecological complications. The most common of these is menorrhagia (excessive menstrual bleeding). See Chapter 4, Symptomatic Carriers.

**Blood-borne infections**

The most serious complications of hemophilia in the 1970s and 1980s were blood-borne infections. Many people with hemophilia in Canada and around the world were infected with HIV (Human Immunodeficiency Virus) and/or hepatitis C during these years. These viruses entered blood products from blood donors who were themselves infected. People with hemophilia received these infections from the plasma, cryoprecipitate and plasma-derived factor concentrates prescribed to control bleeding.

For individuals, families, and the hemophilia community, including members of the comprehensive care teams, these events were catastrophic. The treatment products which promised to make people’s lives almost normal instead brought serious disease and, in all too many cases, death.
This tragedy brought about changes in the way blood products are manufactured.

**Plasma-derived factor concentrates**
Starting in 1985, new blood collection practices and manufacturing processes were developed to make plasma-derived factor concentrates safer.

As a result, there have been no HIV infections from plasma-derived factor concentrates in people with hemophilia in Canada since 1986, and no hepatitis C infections since 1990.

**Recombinant factor concentrates**
Recombinant factor concentrates, made using DNA biotechnology, were developed in the 1990s to treat both hemophilia A and B. Factor VIII and IX concentrates contain almost no human or animal proteins. They are considered extremely safe.

**LIFE EXPECTANCY OF PEOPLE WITH HEMOPHILIA**

Children born with hemophilia today in Canada can look forward to healthy, active lives. Their lifespan is considered to be nearly normal. They are able to work, have children and raise their families.
THE FUTURE OF HEMOPHILIA CARE

It is very important to realize that the current treatments for hemophilia are both very effective and very safe. The progress that has been made in treating this disease over the past 50 years has been dramatic. Nevertheless, scientists continue to search for even better forms of treatment.

New forms of factor VIII and IX proteins

The first area for progress is in new forms of the recombinant clotting factors, proteins made using DNA biotechnology. There are already studies showing that the normal clotting factors can be changed in subtle ways to make the proteins better for hemophilia treatment. This is called clotting factor modification. These modifications can take different forms.

- One example of clotting factor modification is a new factor VIII or IX product with longer activity. In other words, the protein would be better at resisting elimination from the bloodstream. This type of product would circulate in the blood for a longer period and result in a reduction in the frequency of factor VIII or IX infusions for patients on prophylaxis.

- A second example is a form of factor VIII that is less likely to spark a response from the immune system. This new factor VIII would result in a reduced risk of inhibitor development, one of the most serious complications in the treatment of hemophilia.
These and other modifications to the normal clotting proteins will require long study in the research laboratory. The proteins are tested with hemophilic mice and dogs before entering human clinical trials. A longer-lasting factor concentrate may well be on the market within five years.

When thinking of improving clotting factor safety, it is essential to keep in mind the fact that the current recombinant factors are already very, very safe. Recombinant factors have never been known to transmit disease.

**New ways to receive clotting factors**

The clotting factors that are missing from the blood of people with hemophilia are relatively fragile proteins that do not survive for long outside of the bloodstream. This is why current therapy involves direct intravenous injection of the clotting factors into the blood.

However, different ways to administer clotting factors are under investigation. These include the possibility of inhaling the factors in the same way that people with asthma treat themselves with “inhalers.” With this type of delivery, the inhaled protein is absorbed rapidly into the bloodstream from the small blood vessels inside the lungs.

The other possibility that continues to attract attention involves taking the factor by mouth in the form of a tablet or syrup. Here, the problem of getting the factors through the stomach and upper intestine without damage to the clotting activity is a huge challenge.
In summary, although alternative routes to administer clotting factors are still under investigation, it is unlikely that any of these alternatives will reach patients in the near future.

**Gene therapy: A cure for hemophilia?**

Since the first development of gene therapy methods in the early 1990s, hemophilia has been a leading candidate for the application of this new type of treatment because an increase of only 1% to 2% in the level of factor VIII or IX can significantly reduce the risk of bleeding. Successful, long-term gene therapy would cure hemophilia!

The idea behind gene therapy is very simple. In hemophilia, a clotting factor gene is abnormal. The objective of hemophilia gene therapy is to deliver a normal copy of the clotting factor gene to the patient’s cells. In practice, unfortunately, the process is very complicated. The challenge for gene therapy remains in finding the ideal and safe vehicle, or vector, to transfer the gene.

Nevertheless, human clinical trials of hemophilia gene therapy have already been completed in North America. All of these trials were designed to test safety, not effectiveness. The trials were completed without significant side effects. The successful completion of these safety trials tells us that effective gene therapy for hemophilia may well be a reality in the future.

There are growing numbers of hemophilic mice and dogs that have had their bleeding problems successfully treated with gene therapy for periods of several years. The challenge is now to convert these very encouraging “pre-clinical” results to effective use in humans.
Gene therapy will not make the blood of a person with hemophilia completely normal, at least not in the near future. The hope is that the factor levels can be raised from less than 1% to a level between 2% and 5%. In other words, a person with severe hemophilia would then have moderate hemophilia. Infusions of factor concentrates might still be needed for very serious bleeds and surgery.

However, the field of gene therapy is advancing quickly. It is impossible to predict how long it will take before even better therapies are developed. In theory, gene therapy should result in a long-term cure of the disease.

**CONCLUSIONS**

The diagnosis and treatment of hemophilia has benefited enormously from advances in medical science over the past five decades. Now, in the new millennium, with even more rapid progress in the fields of biotechnology and genetics, we can realistically look forward to a long-term cure for hemophilia.

CH A P T E R

Comprehensive Hemophilia Care

This chapter is intended as an introduction to the concept of comprehensive hemophilia care, provided not only to the person with hemophilia, but also to other members of the family, including carriers and potential carriers. It describes:

- the members of the comprehensive care team
- their roles
- the importance of bleeding disorder clinics for women.
emophilia can have an impact on many aspects of family life. Because of this, medical teams take a comprehensive approach to caring for hemophilia. In Canada this began in the 1970s. Comprehensive, in the context of hemophilia care, means complete.

The comprehensive care team is a group of health professionals who work in a Hemophilia Treatment Centre (HTC). They provide the person with hemophilia most, or all, of the health care services needed to live a healthy life. In addition, the comprehensive care team helps family members, including carriers, deal with issues that affect them.

THE MEMBERS OF THE COMPREHENSIVE CARE TEAM

The comprehensive care team usually includes:
- a hematologist (medical director)
- a nurse coordinator
- a physiotherapist
- a social worker
- the patient, carrier or parent/guardian.

The team also works closely with:
- a coagulation laboratory (a lab that does specialized blood clotting tests)
- a hematology laboratory (for all other blood tests)
- a blood bank
- an x-ray department
- a dentist.
Sometimes, the team may also include:
- other hematologists
- a pediatrician
- an orthopedic surgeon
- a gynaecologist / obstetrician
- a rheumatologist
- a genetic counsellor / geneticist
- a psychologist
- a hepatologist (liver specialist)
- an ear/nose/throat specialist.

**THE ROLES OF KEY MEMBERS OF THE COMPREHENSIVE CARE TEAM**

**Medical director**

The medical director is a physician who is an expert on blood clotting or blood diseases. The medical director’s job is to:
- oversee the comprehensive care team
- order diagnostic tests, when necessary
- suggest treatments to control and prevent bleeding
- oversee a person’s health.

**Nurse coordinator**

The nurse coordinator is the key contact in the comprehensive care team. She coordinates care with the other members of the team. In most HTCs, the nurse coordinator is the person who answers telephone calls.
An important part of the nurse coordinator’s job is teaching people about hemophilia. This can include teaching parents or patients themselves how to do intravenous infusions of clotting factor concentrates.

Physiotherapist

The physiotherapist is trained to keep muscles and joints healthy. The physiotherapist can give advice on how to prevent or limit bleeding. She helps patients and their families to:

• understand what a bleed is
• know whether a bleed is serious or not
• learn what to do to regain strength and mobility after each muscle or joint bleed.

The physiotherapist can give advice on how to be active and physically fit.

Social worker

The social worker’s role is to help parents, siblings, people with hemophilia and other family members, including carriers, deal with the impact that hemophilia can have on their lives.

Gynaecologist / obstetrician

This is a doctor who diagnoses and treats disorders affecting the female reproductive organs. A gynaecologist can work with women who are hemophilia carriers and who may have heavy menstrual bleeding. A gynaecologist, in partnership with the hematologist, can find ways to reduce the bleeding and avoid complications.
BLEEDING DISORDER CLINICS FOR WOMEN

In recent years, more and more Hemophilia Treatment Centres in Canada are expanding their services and creating clinics for women with bleeding disorders, including carriers of hemophilia A and B.

These clinics provide expert care, including:
- education
- factor level testing
- carrier testing
- social work services
- genetic counselling
- treatment and prevention of symptoms of bleeding
- specialized services, including the expertise of an obstetrician and/or gynaecologist.

Such clinics are critical for women who are carriers of hemophilia as their care and treatment is different from that provided to those with hemophilia, notably because of the demands of menorrhagia and postpartum bleeding.

For more detailed information on comprehensive care, see All About Hemophilia, Chapter 3, available at Hemophilia Treatment Centres and from the Canadian Hemophilia Society. It can be downloaded at www.hemophilia.ca/en/13.1.php.
The purpose of this chapter is to provide some basic information about genes and genetics, and how hemophilia is inherited. Because genetics can be hard to understand, we suggest carriers talk to the genetic counsellor at a hemophilia treatment centre (HTC). This person has the knowledge and training to answer all questions.

In order to understand hemophilia, a person needs to know about genes and genetics. If there is a history of hemophilia in a family, she will want to know:

- Am I a carrier of hemophilia?
- Am I likely to pass hemophilia on to my child?
- Could my daughter be a carrier of hemophilia?
GENETICS

Genetics is the study of how genes are passed from one generation to the next. Each cell inside the body contains genes. They store, and pass along, information that makes a person unique.

Here’s how they work.

Inside the cell nucleus is a group of structures called chromosomes. Each chromosome is made up of a long chain of a chemical called DNA (deoxyribonucleic acid). The DNA in each chromosome is arranged in thousands of units called genes. There are between 30,000 and 40,000 genes in each cell of the body. Each one of the genes is in charge of telling the body to produce certain proteins. Some genes decide, for example, the colour of the eyes.

Chromosomes come in pairs and every cell contains 23 pairs of chromosomes: one copy of each pair comes from the mother, the other copy comes from the father. Each person has a pair of chromosomes called the sex chromosomes. They decide whether a person is male or female. Women have two X-chromosomes (XX). This is what makes them female. Men have an X-chromosome and a Y-chromosome (XY). This makes them male.

The genes that take care of the production of factor VIII and IX are part of the X-chromosome. They play an important role in how hemophilia is passed from person to person in families.
HEMOPHILIA, A GENETIC DISORDER

Hemophilia is a genetic disorder. This means that it is caused by a change or a mutation in a gene. The mutation causes the gene to not work properly. Like other genetic health problems, hemophilia can be passed from generation to generation.

In about 3 out of 10 cases, however, a boy with hemophilia (or a girl who is a carrier of hemophilia) is born to a family that has no history of the disease. There are three possible explanations for this.

1. It could be that hemophilia was in the family for generations. Because no male showed signs of increased bleeding, no one knew hemophilia was present. The family may have had girls who were hemophilia carriers. But if none of these girls had sons, or none of the sons had hemophilia, and the carriers’ own symptoms went unrecognized, no one knew that hemophilia was being passed on.

2. It could be that the child’s mother received the gene with the mutation at the time she was conceived. The mother is the first person in this family to carry hemophilia. Her daughters may be carriers; her sons may have hemophilia.

3. It could be that the mutation that causes hemophilia happened in the egg from the mother who conceived the child. In such a case, the egg from the mother developed a mutation that was passed on to the child. The mother is not a carrier by analysis of her blood; however, some of her other eggs may also have the mutation. This is called gonadal mosaicism.
A woman’s egg ONLY has X-chromosomes to give to a child. The man’s sperm contains either an X- or a Y-chromosome. Therefore, it is the man’s sperm that determines the sex of a child because he can add either an X-chromosome or a Y-chromosome to the woman’s X-chromosome. In other words:

- If the sperm cell that reaches the egg contains an X-chromosome, the child will be a girl.
- If the sperm cell that reaches the egg contains a Y-chromosome, the child will be a boy.

**GENES DECIDE THE SEX OF CHILDREN**

When a man’s sperm (X or Y) and a woman’s egg (one of two X’s) meet, there are four ways the egg and sperm cells can combine. **Figure 4** shows what can happen.
SEVERE HEMOPHILIA AFFECTS ALMOST ONLY MALES

Here’s why it works this way.

Each human being gets half of his/her chromosomes from each parent. This means that the sex chromosomes inside each cell in the body come from both the mother and father.

The genes that help to produce factors VIII and IX are found on the X-chromosome.

When a gene has a mistake in its structure, it is called a gene with a mutation. The mistake itself is called a mutation. Because a male has only one copy of the X chromosome in each cell, the mutation (or mistake) that causes problems with factor VIII or IX is certain to affect him.

On the other hand, because a female has two X chromosomes, one of those X-chromosomes will be normal. This normal X-chromosome protects a woman from the severe forms of hemophilia, even though some women may have more bleeding than a normal person.

A girl can be born with severe hemophilia if both her X-chromosomes carry the hemophilia gene. This happens only when...

- a woman who carries the hemophilia gene has a girl with a man who has hemophilia
- a woman who is a carrier has a girl with a man who doesn’t have hemophilia and a second new hemophilia mutation happens when the girl is conceived
- a man who has hemophilia has a girl with a woman who is not a carrier and a second new hemophilia mutation happens when the girl is conceived.
There is a fourth way a girl can have severe hemophilia. This happens when the gene with a mutation on the X-chromosome dominates the normal X gene in the production of factor proteins. This is called X-inactivation or lyonization.

These four situations are extremely rare. However, lyonization to varying degrees is fairly common in carriers. (See Chapter 4, Symptomatic Carriers.)

"Our daughter is an obligate carrier of severe hemophilia with low factor levels. She was 11 when we told her the tests showed she has mild hemophilia. She was actually pleased and her reaction was, “Just like Daddy?!" Now, it’s just part of her life and she tells her friends about it.

THE TRANSMISSION OF HEMOPHILIA FROM PARENT TO CHILD

When a man with hemophilia has children with a woman who does not carry the hemophilia gene, none of their sons will have hemophilia. This is because the father passes along his Y-chromosome to his sons. All their daughters, however, will carry the hemophilia gene. This is because the father has passed along his X-chromosome with the gene for hemophilia to them. They are called obligate carriers. See Figure 5.

Figure 5
In the next generation of this family, the daughter who is a carrier of hemophilia is having children with a man who does not have hemophilia. Each time this woman gets pregnant there is the same 1-in-4 chance that one of these results will happen. Each daughter has a 1-in-2 chance of being a carrier. Each son has a 1-in-2 chance of having hemophilia. Figure 6 shows all the possible outcomes.
THE NUMBERS OF PEOPLE WITH HEMOPHILIA

The number of new cases of hemophilia in the world will likely remain constant or increase over the coming years. The reason is this.

Hemophilia is a disease that results from changes to the genetic code for a clotting factor. In many cases it is possible to trace a family history of hemophilia. However, in about one-third of new patients, hemophilia appears to occur in that family for the first time. There is now good evidence to indicate that these cases of hemophilia are due to new changes in the human genetic code. Changes to the genetic code happen in all of us, all of the time. In most instances, the body has ways to detect and repair these changes, but sometimes the new genetic changes remain. Many of these changes go unnoticed, having no effect on the way in which the body looks or works. Very occasionally, however, the genetic change affects a region of code that controls the ways in which certain clotting factors are made. A new case of hemophilia is created!

There is no reason to believe that this new rate of “hemophilia creation” will change in our lifetimes; in fact, the human genetic code has probably been changing at the same rate for millions of years. With new cases of hemophilia appearing at the same rate and people with hemophilia living longer, the total number of people with hemophilia in the population may even increase in the next decades.
C H A P T E R

Symptomatic Carriers

This chapter explains why hemophilia carriers have bleeding problems, why some carriers bleed more than others and what types of bleeding carriers may experience. It provides details on:

• symptoms
• the types of bleeding carriers often encounter, including menorrhagia
• the process of X-inactivation
• the link between menorrhagia and bleeding disorders.
CARRIERS OF HEMOPHILIA CAN BLEED ABNORMALLY

Carriers produce amounts of factor VIII and IX that range anywhere from 5% to 200% of normal. The average is 60%. Although a level of 40% is usually used as the upper limit defining mild hemophilia, research has shown that women with higher factor levels can bleed more than is usually normal. They have symptoms of mild hemophilia and are referred to as symptomatic carriers. Carriers of hemophilia experience more spontaneous and unprovoked hemorrhages than non-carriers. The risk is highest in those with the lowest clotting factor levels.

- They bruise more easily.
- They bleed longer from minor wounds.
- Bleeding from the nose (epistaxis) can be more prolonged.
- They are more likely to suffer joint bleeding.
- Bleeding is more prolonged after tooth extractions, tonsillectomy or other surgery.
- Bleeding can be serious after trauma.
- They have heavier and more prolonged bleeding during their periods (menorrhagia) and are more likely to require an iron supplement or undergo hysterectomy.
- They are more likely to have postpartum bleeding following delivery.

It is estimated that approximately 20% of carriers are symptomatic to some degree. Factor levels in carriers, however, are not necessarily below normal in all cases. While the status of obligate carriers—daughters of men with hemophilia—is a given, their factor levels remain unknown until bioassay tests are carried out.
In the past, factor levels over 30% of normal were considered sufficient to protect against bruising and minor injury. A study of carriers done in the Netherlands in 2006, however, showed that the risk of prolonged bleeding (more than five minutes) from small wounds or following surgery was twice as high in carriers as in non-carriers from the same family. The study also showed that the risk of bleeding occurs not only in girls and women defined as having mild hemophilia with levels from 5% to 40%, but also in females whose clotting factor levels range from 40% to 60%.

Hemophilia “breeds true,” meaning that the same type and severity of hemophilia is passed along in the family; however, clotting factor levels in carriers are independent of the severity of the hemophilia in males, and can vary from person to person. A carrier of a mild form of hemophilia can have the same problems as a carrier of the severe form of the disease. Within a family, factor levels in related carriers can be very different, ranging from very low to normal.

**X-INACTIVATION OR LYONIZATION**

The genes that help to produce factors VIII and IX are found on the X chromosome. The amount of genetic material on one X-chromosome is just the right amount needed for each cell. Males (XY) have only one copy of an X-chromosome in each cell while females (XX) have two. Each cell with 2 X-chromosomes needs to inactivate one of them. Genes on the inactivated chromosome are not available for use. X-chromosome inactivation is a normal and necessary process of development.
The “choice” of which X gets turned off in each cell is thought to be a random process, like flipping a coin. This process is thought to occur near the 8-cell stage of development. So, each embryo flips a coin 8 times, once for each cell, to determine which of the two X-chromosomes in each cell will be inactivated or turned off. An unbalanced ratio of heads to tails (or father’s X turned off to mother’s X turned off) is only a concern if one of those X’s has an altered gene, like hemophilia.

Some carriers inactivate mostly X’s with the abnormal factor VIII protein and have nearly normal factor VIII levels. In other carriers, half the cells produce the normal factor VIII protein, and half produce the abnormal factor VIII protein. Consequently, they have half the normal factor VIII activity. Still other carriers inactivate mostly normal X’s and so have low factor VIII levels and can have symptoms of hemophilia. When this occurs in a carrier, she is known as a symptomatic carrier, and can have mild or, very rarely, moderate or severe hemophilia. It still isn’t known why this happens more often in some families than in others. One hypothesis that’s being studied is the possibility that the choice of which X-chromosome to inactivate may not be random, but is caused by a separate gene or genes that influence the choice of which X-chromosome is inactivated.
TYPES OF BLEEDING

Menorrhagia and metrorrhagia

Heavy, prolonged menstrual bleeding is the most common symptom for women who are carriers of hemophilia A and B.

Some women have heavy bleeding throughout the normal menstrual period. This is called menorrhagia.

Other women bleed throughout the month without stopping. This is called metrorrhagia.

Normally, all women lose a tiny amount of blood at mid-cycle of their period, the moment of ovulation, when the egg is ejected from the ovary. However, carriers can lose a large amount of blood at this time. This can cause abdominal pain (mittelschmerz).

If women lose enough blood over a long period, they suffer from iron deficiency anemia.

Often, because a woman has always bled a lot during her menstrual cycle, and because other women in the family may also be carriers and bleed a lot, she does not realize the menstrual flow is higher than normal. A blood flow assessment chart, in picture form, is available to help women and doctors measure the amount of bleeding. See Figure 7.

Talking about menstrual bleeding is often not comfortable for a young girl. She accepts the increased flow and discomfort, and may or may not discuss it with her mother or friends. It’s simply part of her life.
Menstrual bleeding can be especially heavy at the time of a girl’s first period. This is due to a surge in hormones to provoke her menstrual cycles for the first few times. For this reason, when there is a family history of hemophilia A or B, and even if the girl has not been definitively diagnosed as a carrier, she should be closely followed through puberty. The medical team should include:

- a gynaecologist
- a hematologist with experience in treating bleeding disorders and
- a family physician or pediatrician.

I have to be careful not to book appointments while menstruating because there isn’t enough protection to get me through an hour-long appointment.
Dysmenorrhea and mid-cycle pain

Many women with bleeding disorders have pain during their menstrual period. This is called dysmenorrhea. They can also have pain at mid-cycle of their period, the moment of ovulation.

The cause of this pain is not known. It could be caused by the volume of blood and poorly formed clots in the uterus.

Some women can have a separate condition called endometriosis. With this condition endometrial tissue forms outside the uterus, for example, around the abdomen. When a woman menstruates, endometrial tissue—wherever it is in the body—bleeds. If these women also have a bleeding disorder, the bleeding may be heavy. The blood can irritate the abdominal wall, causing pain.

Other types of bleeding

Women with bleeding disorders appear to be at an increased risk of developing hemorrhagic ovarian cysts. As they grow older, they may be more likely to manifest conditions, which present with bleeding such as fibroids, endometrial hyperplasia and polyps.
THE LINK BETWEEN MENORRHAGIA AND BLEEDING DISORDERS

Research in the late 1990s reported that 1 woman out of 5 who went to see her doctor because of heavy, prolonged bleeding during her period (menorrhagia) actually has a bleeding disorder. This means that menorrhagia caused by bleeding disorders is much more common than doctors thought in the past. In the general population 9% to 14% of women have menorrhagia. But it was found that 57% of women who are carriers of hemophilia A or B suffer from menorrhagia.

Another study indicated that 1 in 4 carriers of hemophilia A or B visited their general practitioners for excessive bleeding during their menstrual periods.

Careful questioning by doctors showed that many of the women with bleeding disorders could report a family history of bleeding problems.

“I paid little attention to my particular symptoms. I didn’t know that they were different from other women because my point of reference for bleeding during menstruation or post-surgery was my mother, who is also a carrier. I did not consider myself a person with mild hemophilia until about five years ago. It was like a light went on. I said to myself, “All of those bleeding-related experiences I had now make sense.”
This chapter presents:

- why, when and where to get tested
- the tests that determine factor levels and carrier status
- some of the psychosocial issues related to testing and diagnosis.
WHY TO TEST

There are two reasons to test a potential carrier:
1. to measure the person’s factor level and, if indicated, take precautions to prevent abnormal bleeding
2. to know the person’s carrier status.

Different tests are used for each of these purposes.
• Factor level testing - Factor level testing, also called a factor assay, is done to determine a person’s level of factor VIII or IX. This can help determine whether she is at greater than normal risk of bleeding. Such a test does not determine beyond all doubt whether or not a person is a carrier.
• Testing for carrier status - This testing is done to determine whether or not a female is a carrier of hemophilia.

What tests are used, and when these tests can be done are discussed below.

WHEN TO TEST

When to test factor levels or carrier status is a controversial subject. The debate centres around whether to test in childhood, specifically before puberty, or to wait until the woman is an adult and can make the decision herself. The issues are different for factor level testing and carrier status testing.
CHAPTER 5 Carrier Testing

Factor level testing

Reasons for testing in childhood
It is important to know the factor level in a potential carrier due to an increased risk for bleeding that she may experience.

With low factor levels, there is increased risk of bleeding after tooth extraction, trauma or surgery such as a tonsillectomy or adenoidectomy, both common childhood operations.

Because of a surge in the hormones involved to provoke menstruation in young girls, there is a tendency for excessive bleeding at the first few menses, sometimes requiring emergency room treatment. This can be a traumatic event for a young girl and she may be frightened by the amount of blood she loses during her first periods. In addition, almost twice as many carriers as non-carriers require medical intervention for nosebleeds.

All of these potential symptoms suggest the wisdom of early testing to learn clotting factor levels. If levels are low, precautions can be taken.

Guidelines developed by the Association of Hemophilia Clinic Directors of Canada (AHCDC) Sub-committee on Women with Bleeding Disorders recommend that a girl from a family with a history of an inherited bleeding disorder be tested before she starts menstruating. This allows the patient and family to prepare for her first and subsequent menstrual periods, which are sometimes heavy and prolonged.

Some gynaecologists suggest “anticipatory gynaecological management” for young girls. Testing could be done at the first
signs of breast development. When possible, investigation should be undertaken before oral contraceptive therapy is begun to control menstrual bleeding.

In addition, if such testing is done, any medical professional who is consulted can be made aware of a carrier’s factor levels. Close collaboration can then be encouraged with the hemophilia treatment team to prevent any medication being prescribed that could affect coagulation or a medical procedure that could cause hemorrhaging.

Reasons for delaying testing until adulthood
If a girl has shown no sign of abnormal bleeding (bruising after childhood injury, bleeding after loss of teeth, etc.) parents may choose to wait before testing factor levels. This will avoid a hospital visit and the pain of the blood test. Parents, however, should assume the girl is a potential carrier and take all necessary precautions in the case of surgery and at the onset of puberty.

Being diagnosed with mild hemophilia may affect access to, or the cost of, insurance.

Carrier status testing

Reasons for testing in childhood
Early testing allows time for the girl to come to terms with the complex nature of being a carrier. The sooner a girl knows about her carrier status or particular health situation, the sooner she can get the information necessary to help her deal with decisions concerning treatment for any type of medical problem, and eventually with issues of conception, pregnancy and childbirth.
Leaving carrier testing until the girl is in a relationship, or until she is ready to conceive or already pregnant, can create unnecessary stress. Genetic testing for carrier status and genetic counselling is best done before pregnancy. Factor levels rise during pregnancy in the case of factor VIII deficiency, and make assay tests unreliable. Genetic studies take time to carry out. The psychological stress and decisions of prenatal diagnosis can be better dealt with if the woman is not suddenly faced with both the announcement of carrier status as well as the decisions for prenatal diagnosis of the foetus.

In a study done in the United Kingdom with 54 women who are carriers, 83% were in favour of testing for carrier status before the age of 16. The median age that these adult carriers had been genetically tested was 24 years. The fact that most adult carriers in the study believe that carriers should be tested at a much younger age than is currently recommended in the UK (over 16 years) has important implications for the delivery of successful genetic counselling.

If the girl is found not to be a carrier, early testing will have eliminated much stress and concern. There have been cases when a young woman, who assumed she carried the hemophilia gene because it was prevalent in her family, planned her life around the possibility of having a child with hemophilia. She then learned that she wasn’t a carrier and had to readjust to this new reality. Early testing could have saved her from this situation.

**Reasons for delaying testing until adulthood**
The World Health Organization as part of its hereditary disease program, the American Society of Human Genetics, the American College of Medical Genetics, and the National Society of Genetic...
Counsellors recommend that, if the medical or psychological benefits from genetic testing will not occur until adulthood, testing should, in general, be deferred until the at-risk female is at an age to understand and make autonomous and informed decisions for herself.

The argument against carrier testing, by DNA analysis, in children is:

- It can harm a child’s self-esteem.
- It can distort the family’s perception of the child.
- It can deprive the girl of the opportunity to make autonomous informed decisions for herself.
- It can adversely affect her capacity to form positive relationships.

Some families tend to delay testing their daughter because they feel the only reason to know about a carrier status is for family planning.

Cultural issues, such as arranged marriages or the possibility of health problems in offspring, may discourage some families from having a daughter tested.

If genetic testing is done in childhood, the girl’s parents are usually the main source of relevant information. If parents misunderstand or don’t remember the test results, the child can be misinformed. Moreover, early testing does not guarantee that parents will inform the child.

In all cases, families should consult their hemophilia treatment team who can help them through the decisional process and with follow-up counselling, if necessary. They will be referred for genetic counselling whose purpose is to provide the carrier and
her parents or partner with adequate information to reach
decisions regarding carrier testing and prenatal diagnosis, and to
provide support throughout the process.

WHAT TESTS ARE DONE

For carriers of hemophilia A and B, the following tests permit
accurate diagnoses:

- Factor VIII assay: This measures the amount of factor VIII
activity in the blood. Having a normal factor range does
not guarantee non-carrier status. Twenty percent of
carriers have a normal level.
- VWF: antigen: This measures the amount of von
Willebrand factor in the blood so as to rule out von
Willebrand disease as the cause of bleeding in hemophilia A.
- Factor IX assay: This measures the amount of factor IX
activity in the blood.
- Genetic studies: These tests determine the exact genetic
mutation and make it easier to provide prenatal diagnosis.
They can identify the mutation in 90% to 99% of cases.

Factor VIII and IX assays

Many elements can affect the results of factor assays. There
seems to be a link between hormones and factor levels. Hormone
levels in carriers with factor VIII may be affected by a number of
factors. Physical and mental stress, recent use of aspirin or other
painkillers, pregnancy, contraceptive pills, breast-feeding, exercise,
recent transfusions or infections may all affect the results of a
factor assay. While it is impossible to avoid all of these influences,
they should be taken into consideration. The time to get tested is
at the time of menstruation when hormone levels are lowest, though this is still controversial. In the case of factor IX carriers however, clotting levels are not affected by hormones and testing can take place at any time.

Before any coagulation investigation, patients should have a complete personal and family history and physical examination, including a gynaecological examination in most cases (not always necessary in adolescents).

**Genetic testing**

There are a number of tests that can be done to determine carrier status. These tests are complex, not available in all centres and, when available, may take many months to have results. Depending on the set of markers found, the accuracy of these studies varies from 90% to 99%. Their results are most predictable if DNA from a family member with hemophilia is available.

Women who are identified as obligate carriers or possible carriers of hemophilia (for example, a woman who has already had a son with hemophilia) are eligible for DNA testing. DNA is the building block of genes and can be extracted from a blood sample. DNA testing for hemophilia is covered by provincial health insurance in local facilities.

**Mutation analysis**

Analysis of the hemophilia genes is done by looking for changes in either the factor VIII or factor IX gene responsible for hemophilia. The laboratory begins the analysis by looking for a
type of mutation known as an inversion in factor VIII. Half of males with severe hemophilia A have an inversion in their factor VIII gene. If this inversion is not found, then the laboratory needs to do further testing which may be more complex and time-consuming. If a specific mutation is found in the person with hemophilia, accurate carrier testing by mutation analysis can be carried out on the mother or other female relatives who may be carriers. When the mutation can be identified (in 90% to 99% of cases), mutation testing is 100% accurate.

DNA linkage studies

If the mutation is not known, DNA linkage studies are the next step. This involves following markers (or normal variations in the DNA) which either are within and/or surround the hemophilia gene. Linkage analysis is not direct testing such as when a mutation is identified; however, it may be able to provide information about carrier status, with a certain degree of probability. DNA samples from other family members, including those with and without hemophilia are necessary. The male with hemophilia has inherited an X-chromosome with a specific “pattern,” which is responsible for hemophilia in this family, with a certain degree of probability. This pattern may provide information about carrier status.

WHERE TO GET TESTS DONE

Hemophilia Treatment Centres are the best choice for comprehensive testing. People at these clinics know that tests often need to be repeated to get an accurate diagnosis. This is because factor level test results can be affected by such elements as a variation in the lab technologist’s technique and even the
A Guide for Carriers of Hemophilia A and B

woman's blood type. (Women with blood type O have naturally lower levels of von Willebrand factor and factor VIII than women with blood types A, B or AB). Many other factors can skew test results. Because of these testing difficulties, many women have been told they have no bleeding disorder when, in fact, they do. Personnel at the HTC are aware of this, and will re-test if a woman continues to have bleeding symptoms. Often, a genetic counsellor or geneticist works very closely with the hemophilia team to provide a multidisciplinary approach to care.

Smaller centres may carry out screening tests including prothrombin time (PT), activated partial thromboplastin time (APTT) and bleeding time, but these tests are not refined enough to detect all bleeding disorders.

Physicians in small centres should refer patients for specialized testing to Hemophilia Treatment Centres. Experts in these centres have the knowledge and experience to do proper testing for carrier status and to deal with the actual treatment of bleeding disorders.

COPING WITH A CARRIER DIAGNOSIS

People cope in individual ways when faced with new, challenging information such as an unexpected diagnosis of being a carrier of a serious chronic illness. This depends on age, their reasons for seeking the testing and their previous experience with the condition. Carriers can receive this diagnosis at a very young age, as adolescents, sometimes because of their own health problems, or as adults after the birth of a child with hemophilia in their immediate or extended family. Potential carriers of hemophilia should be offered qualified assistance in genetic information,
testing, and counselling to help them cope with the psychological and ethical issues related to being a carrier of a genetic disorder.

**Diagnosis as a young girl or adolescent**

Reactions

When a girl finds out that she's a carrier, she experiences a wide range of emotional reactions to her carrier diagnosis.

She may be fearful about the repercussions on future relationships and reproductive options. She may feel a sense of loss that she is not “genetically perfect” and may even fall into a pattern of denial and refuse to acknowledge the diagnosis. Denial is a way of dealing with carrier status. She may feel angry that her body has betrayed her and angry with her parents for passing this gene on to her. Even if a girl has known that she may be or is a carrier, it is in adolescence that the implications will be more fully understood.

A major impact on the attitude of any sibling of a child with hemophilia, such as a sister, is how the parents deal with the condition. Is the child with hemophilia seen primarily as a “hemophiliac,” or as a person with many strengths, who also happens to have a bleeding disorder? If a brother, father, uncle or cousin has had a hard time due to hemophilia, this may affect the girl’s attitude toward the condition.

The young girl could also feel relieved when she receives her diagnosis because there is finally some explanation for her heavy bleeding episodes or her regular bruising and she can now learn how to manage these symptoms. If she has a positive model or a much loved person with hemophilia in her family, the news may
give her a special bond with that person, especially if she herself receives a diagnosis of mild hemophilia, just like him. If, as a parent, a mother has accepted and integrated her own carrier status, then her daughter is much more likely to be able to accept the diagnosis, rather than deny it.

Parents need to be ready to listen and accept their daughter’s emotional concerns and give her the time and support she needs so that she can effectively work through her emotional issues.

**Diagnosis as an adult**

Reactions

In a family with no previous history of hemophilia, the carrier status is usually sought after the diagnosis of a bleeding disorder in a baby or young child. The parents’ response could include shock, disbelief, denial, grief and anger. The parents of the child, one a carrier and one not, may react differently for a period of time. Some women deny the possibility of having a child with hemophilia, even when there is a family history. They can experience the same emotions as those with no known history.

Hearing difficult information often causes parents to experience a state of shock, where little is absorbed following the first few sentences. It has been described as “listening to someone talk underwater.” It is important to keep in mind that adapting to a diagnosis of being a carrier of a bleeding disorder is a process that begins the moment a bleeding disorder is suspected in a child, then continues through discussions with health care professionals, testing, follow-up counselling from a genetic counsellor or family physician, and hopefully, a referral to a Hemophilia Treatment Centre. As the initial shock subsides, the information, which had been given prior to the test, will gradually
filter back into the parents’ consciousness. If nothing else, they’ll remember that there are people who can answer some of their questions and can return to review what they were told.

Support
Parents need time to digest the information and begin to consider the implications for their child and family. They need contacts in the health care system to whom they can return with questions, concerns and fears, and who will reassure them that this is a normal process. Staff at the HTC must be tuned into the parents’ needs, which can range from private time at home to consider their options, through being “information hungry.” Couples, depending on the relationship that they bring to this moment, may need support to understand each other’s point of view, and guidance in not making judgments about each other’s coping style. It is important that follow-up contact be made by the treatment centre for parents of children newly diagnosed with hemophilia to give them another chance to ask questions once the shock has worn off.

Siblings
In a family with no previous history of hemophilia, the affected baby boy may have an older sister, whose potential status as a carrier may be felt by the parents as a second blow, following the son’s diagnosis. Information and support from knowledgeable health care professionals are crucial at this time. The question will arise at some point about testing their daughter. Again, families deal with the issue individually. There are fears for the daughter’s future. If she’s a carrier, will she have symptoms? How will she feel toward her mother for passing on the gene? Will she be a parent of a child with a bleeding disorder and have the same worries her parents have?
The extended family
A person’s decision to progress with carrier identification has implications for the entire family and needs careful thought and negotiations. A positive diagnosis could affect a sister’s choices in finding a partner or in having children, introduce the possibility of hemophilia to sisters who may already be pregnant and influence personal choices about country of residence, marriage, career and desired family size. This could stimulate either approval or disapproval from both the family of origin and the in-laws. Genetic counsellors can provide strategies on how to inform other at-risk female relatives such as sisters, daughters or nieces. Often, and upon request by the family, the social worker in the hemophilia program and the genetic counsellor will meet together with the family member to help facilitate this discussion.

The benefits of knowledge
When women were surveyed about their thoughts and feelings on being a carrier, on having children with hemophilia or daughters who are carriers, they spoke of the benefit of knowledge at every point along the journey; knowledge, which gave, or could have given them strength to understand what was happening and how to manage it. This knowledge can come from the Hemophilia Treatment Centres, genetic counsellors and the Canadian Hemophilia Society at the national and local chapter levels. Others who have been affected by bleeding disorders can serve as mentors on the journey.
This chapter deals with many questions related to reproduction, including:

- family planning
- conception options
- challenges to conception
- prenatal diagnosis of hemophilia
- miscarriages
- pregnancy
- labour and delivery
- postpartum care
- breastfeeding
- care for the newborn with hemophilia
- hysterectomy
- perimenopausal bleeding.
FACTORS THAT CAN AFFECT THE CHOICE TO HAVE A CHILD

Before making any choices, it is important for a carrier and her partner to understand the heredity of the disorder, as well as all the options available for reproduction and prenatal diagnosis.

For some carriers, today's advanced care means that they see hemophilia as a manageable disease. They know that quality care with safe clotting factor concentrates is available in Canada's 25 comprehensive Hemophilia Treatment Centres. As a result, they accept the risk of a child being born with hemophilia. Many forego prenatal testing.

For others, the possibility of passing on a painful disease to a child, and having to live with both the guilt and difficulties, are the deciding factors against pregnancy. Wanting to eliminate the future decision-making stress from a daughter who may be born as a carrier could also be a consideration.

Religious and/or cultural beliefs may limit the choices a woman has. In some instances, personal beliefs or social pressure from others regarding the “obligation” to stop this disease with its financial burden on society weigh heavily on the decision.

Judgments by medical personnel can sometimes have an impact on the decision to conceive a second child. Women have been offered sterilization after the birth of a child with hemophilia, without having asked for it.
Genetic counselling is the process of helping individuals/families to understand and adjust to the medical, psychosocial and familial aspects of the genetic condition. As part of the HTC team, the genetic counsellor or social worker works closely with the clinic team to help the couple come to an informed decision, in a non-judgmental manner, and to adapt to the risk of the genetic condition.

Genetic counselling touches on sensitive issues related to childbearing. Guilt, resentment and blame can be reduced if couples are helped to gain insight into each other's views and wishes in a neutral setting. Genetic counsellors need technical knowledge, skills and clarity of purpose to carry out this task.

**FAMILY PLANNING OPTIONS**

There are several options.

Some people simply accept the possibility of having a child with hemophilia. This choice is often related to the carrier's direct experience of hemophilia in a close relative. The experience of having watched a loved one suffer can affect a woman's decision about having a child with hemophilia. On the other hand, the risk of viral infection through treatment products is virtually zero today, and fears have diminished. Modern comprehensive care means that a child born today can grow up without the complications of joint disease that the older generation had to deal with.
Another option is to adopt children or to become foster parents.

A growing number of couples, and not only those who carry a genetic disease, are opting not to have children. Being childless can have positive repercussions on relationships, and couples may enjoy career benefits and greater financial security.

Finally, there is the possibility of using one of the conception options to eliminate the risk of bearing a child with hemophilia.

Genetic counselling remains an important part of comprehensive hemophilia care. Despite the improved outlook and quality of life with today's factor replacement therapies, genetic bleeding disorders still have an impact, not only on the daily life and psychological health of the affected child, but also on carriers and close family members.

Informed decisions about reproductive options (when there is a risk of hemophilia) require knowledge about inheritance, prenatal diagnosis possibilities and selective termination of pregnancy.
## CONCEPTION OPTIONS

<table>
<thead>
<tr>
<th>Method</th>
<th>Procedure Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In-vitro fertilization (IVF)</strong></td>
<td>Eggs are retrieved from the woman and fertilized in the laboratory with the sperm from the woman’s partner. This is called in-vitro fertilization (IVF). When the embryo is at the 6-8 cell stage, a biopsy is done of a single cell. It takes from 48 to 72 hours to get the results. The goal of this procedure is to select male embryos that do not have hemophilia to be implanted in the woman’s womb. Male embryos may be frozen for future implantation. Couples opposed to termination of pregnancy may choose this option. Some couples also choose to eliminate female embryos that carry the hemophilia gene so that they won’t have to deal with the same reproductive choices. PGD/IVF is expensive and not covered by provincial health insurance. The success rate for a pregnancy with IVF is approximately 30% per cycle, even if the couple has no difficulty conceiving. Couples who are considering PGD/IVF are referred to the appropriate specialists to discuss the procedure in more detail so that they can make an informed decision.</td>
</tr>
<tr>
<td><strong>IVF with egg donation</strong></td>
<td>There is also the possibility of using donor eggs for IVF. In this case, the child would not be at risk of inheriting the hemophilia gene from the mother. This procedure involves finding a fertile woman who is not a carrier of hemophilia who agrees to donate her eggs for an IVF procedure. The embryos are then transferred to the carrier. The success rate is best when the donor is young.</td>
</tr>
<tr>
<td><strong>IVF with sperm donation</strong></td>
<td>This option is also open to men with hemophilia and their wives. The couple may choose to use IVF with donor sperm; this prevents having a daughter who would be an obligate carrier, and would also spare a daughter from having to make decisions about her own reproductive options.</td>
</tr>
<tr>
<td><strong>Gamete intra-fallopian transfer with egg donation (GIFT)</strong></td>
<td>Gametes (the female’s eggs and the male’s sperm) are washed and placed via a catheter directly into the woman’s fallopian tubes. This usually involves a minor surgical procedure for the egg donor (who does not carry the hemophilia gene) with a minor degree of pain that lasts for just a few days. The carrier who has the GIFT procedure can go home the same day. There is a 50% pregnancy rate per retrieval cycle for GIFT.</td>
</tr>
</tbody>
</table>
CHALLENGES TO NATURAL CONCEPTION

One of the problems many carriers have to deal with is heavy and excessive menstrual bleeding (menorrhagia). The psychological impact of menorrhagia, not to mention the physical reality of heavy blood loss, adds an additional challenge to conception. Some women have heavy bleeding at irregular intervals during the menstrual cycle (menometrorrhagia). Mid-cycle ovulation (mittelschmerz) can be extremely painful, and women can also experience pain during their menstrual periods (dysmenorrhea). Menorrhagia can cause anemia, causing the woman to feel fatigued. It’s easy to see that these symptoms are not conducive to an intimate love life! Taking control of gynaecological problems caused by a bleeding disorder is one of the first steps to an improved sex life and higher likelihood of conceiving.

Hormones, conception and “The Pill”

Often the first method to control heavy menstrual bleeding is hormone replacement therapy. The oral contraceptive (OC) pill is a very effective way of managing menorrhagia. For a woman wishing to conceive, however, this therapy is not a suitable treatment option because of its contraceptive effect.

Some women, despite their desire to have children, hesitate to stop their hormone treatment and go back to a life with menorrhagia, anemia, pain and loss of quality of life. If they wish to discontinue the OC, they should do so under a physician’s care so as to deal with possible anovulatory cycles and recurrence of menorrhagia. They need to work closely with their HTC team to discuss alternative treatment options. Effective alternatives to treat menorrhagia are available. (See Chapter 7, the Treatment and Care of Carriers).
**MISCELLANEOUS**

There is no evidence of a higher rate of miscarriage in carriers of hemophilia A and B than in the general population. About 15% to 20% of all pregnancies end in miscarriage. Most of them occur in the first 13 weeks, or first trimester, and are due to the foetus being non-viable; they cannot be prevented. After a miscarriage, a dilation and curettage (D&C) is often carried out. This procedure involves dilating the cervix and gently scraping the tissue from the lining of the uterus. As with any surgical procedure, the hemophilia treatment team must be consulted to ensure proper preparation and follow-up for carriers since this procedure may be associated with bleeding.

**PREGNATAL DIAGNOSIS (PND) OF HEMOPHILIA**

Decision-making process

I was very worried about the safety of blood products after what happened in the past.

Attitudes about hemophilia often depend on personal experience. Some carriers have grown up with a close relative who has complications from the disease. They could belong to a family with inhibitor problems. They might have seen the consequences of HIV or hepatitis C in a loved one. They may have witnessed the pain caused by joint disease. They feel the need for alternatives to having a child with hemophilia. Religion, personal values and culture also play a part in decision-making around prenatal diagnosis and termination of pregnancy. Couples should work closely with the hemophilia treatment team and genetic counsellors throughout the prenatal diagnostic process for both medical and emotional support.
Some couples choose not to have prenatal diagnosis (PND) and simply want a male baby tested at birth. Others, in order to prepare themselves, feel they need to know the hemophilia status, even if they have no intention of terminating the pregnancy.

Other couples are interested in prenatal diagnosis because terminating the pregnancy if the baby has hemophilia—as hard as that decision may be for them—is an option. Precautions must be taken when terminating a pregnancy, as with any surgical procedure, to avoid bleeding complications. The hemophilia treatment team must be involved in preparations and follow-up. Following a termination, counselling should be offered to help couples cope with the emotional strain.

The genetic counselling session should be tailored to support the personal values and beliefs of the family so that the couple feel secure in whatever decision they make. The objective of prenatal diagnosis is to try and provide carriers and their spouses with accurate and current information so they can make an informed decision in a supportive environment. Genetic counsellors protect the couple’s autonomy and confidentiality, and provide support and education. They must be sensitive to the range of values, cultures, religious beliefs and ethnic differences in our society. In this way, individuals or families can make decisions that are in keeping with their value and belief systems.

Medical coverage

Obligate carriers or potential carriers of hemophilia (for example, a case of no family history but a son already born with hemophilia) are eligible for prenatal diagnosis. If available in a laboratory in the province where the family resides, the procedure is covered by provincial health insurance. Otherwise, a special

"It’s not easy every day, but I do not regret having my son and we hope to have another child soon. There will be no prenatal testing done, although I have agreed to find out the sex of the baby just to be on the safe side for delivery.

One thing that really upset me was doctors offering the possibility of prenatal testing with the option of abortion when we hadn’t asked for it.

A Guide for Carriers of Hemophilia A and B
request to the provincial Ministry of Health may need to be made to cover the cost of out-of-province testing.

**Prenatal diagnostic options**

**Ultrasound**

Some couples find out the sex of the baby by ultrasound and then make a decision about invasive testing only if the ultrasound predicts the baby to be a boy. The sex can generally be predicted by ultrasound at 16 weeks gestation. Couples should be informed of the limitations of ultrasound in predicting the sex of the baby. See Figure 8.

![Figure 8](image-url)

![Figure 9](image-url)
I’d like to have known that I was a carrier before my son’s birth so that my husband and I could have been better prepared.

**Chorionic villus sampling (CVS)**

The chorion is a membrane that surrounds the developing foetus. It is located outside of the amniotic membrane. The chorion is a foetal membrane, that is to say, it originates from the same cells as the developing baby. The chorion is covered with finger-like projections called chorionic villi. In early pregnancy, the villi will implant in the uterus at one point to develop into the placenta, and the remainder of the villi disappear. CVS can be carried out after 11 weeks gestation to obtain DNA for analysis. The sample may be taken either by the vaginal or abdominal route, depending on where the placenta is located. See Figure 9.

Vaginal CVS is similar to a pap smear. While an ultrasound is being done on the abdomen to locate the foetus, a speculum is inserted into the vagina. A fine tube is then passed through the cervix and guided to where the placenta is forming. About 10 to 15 milligrams of tissue are aspirated into a syringe. Results can take up to 3 weeks. The abdominal method is similar to amniocentesis. CVS is avoided before 11 weeks because of reports of limb abnormalities occurring when carried out earlier. The miscarriage rate associated with this procedure is approximately 1%. CVS is covered by provincial health insurance.

**Amniocentesis**

Amniocentesis is done after 15.5 weeks. An ultrasound is performed to locate the placenta and to select a pocket of amniotic fluid. A thin needle is then inserted through the abdomen and into the uterus. A small amount of amniotic fluid is removed. This fluid contains cells that the foetus has shed. In some circumstances, the cells need to grow before the DNA from them can be extracted. The risk for complications with the procedure is 0.5%. Test results take 3 to 4 weeks if cells need to be grown before the test can be done. Amniocentesis is covered by provincial health insurance.
CHAPTER 6 Reproductive Issues

The difference between amniocentesis and CVS is that CVS is done much earlier in pregnancy and thus the results are received earlier.

As with any medical procedure in a carrier of hemophilia, precautions must be taken to avoid bleeding complications. Couples should work closely with the hemophilia treatment team, including the obstetrician and genetic counsellors throughout the process for medical and emotional support, including follow-up.

Foetal blood sampling
Foetal blood sampling may be carried out at 18 weeks or more gestation. A sample is taken from the umbilical vein, under ultrasound guidance, through a needle inserted into the abdomen. Blood is taken, and the factor level can be assayed immediately. It is important to ensure that the sample in the tube is truly foetal blood and not maternal. A difficult procedure, the risk of miscarriage is as high as 5%.

Maternal blood test
A new non-invasive method for prenatal diagnosis is at present being developed. In future, a blood sample taken from the mother at 7 to 8 weeks gestation will be tested for foetal blood cells. The foetal male chromosomes will be separated from the mother’s blood and tested for hemophilia. This procedure is still in development.

Potential psychosocial issues at prenatal diagnosis
If a carrier already has a brother or son with hemophilia and the results from prenatal diagnosis show that the baby is a boy and has hemophilia, she may feel ambivalent about stopping a pregnancy, as she dearly loves her son or brother. By stopping a
There is a lot of variation among genetic counsellors across the country in terms of which options they present to which couples, and how they explain the pros and cons. The findings from the carrier survey may open the door to discussions in the profession, which we hope will lead to new national guidelines.

pregnancy when the baby is predicted to have hemophilia, she may feel like she is rejecting her son and/or brother. On the other hand, she may not know whether she can emotionally handle having another child with hemophilia. Her own feelings may conflict with those of her partner.

These are examples of the psychosocial issues that often come up in a genetic counselling session. A genetic counsellor explores these feelings with the couple. This may take more than one counselling session.

In the context of hemophilia, the number of women seeking PND in the developed world seems to be decreasing with the successful use of prophylactic treatment. Prophylactic and on-demand home care has improved the quality of life for young people with hemophilia and their families, allowing most to grow up without severe joint disease or other complications. A study in Sweden showed the main reasons carriers do not use prenatal diagnosis is that they do not consider hemophilia to be a disorder serious enough to justify termination of a pregnancy. Having a child, however, is a personal decision and each woman has the right to choose what’s best for her and her family. Previous personal experience of hemophilia is still the greatest contributing factor affecting decisions.
I would like to have known the dangers and risks of pregnancy and childbirth.

CHAPTER 6 Reproductive Issues

PREGNANCY

Most women with bleeding disorders have few bleeding problems during pregnancy or during childbirth. Factor VIII and von Willebrand factor levels usually increase significantly in pregnancy and this reduces the risk in carriers of hemophilia A. By contrast, factor IX levels do not usually change significantly. Factor levels should be tested in the third trimester of pregnancy when they reach their maximum level, usually between 29 and 35 weeks. If levels are low, this should be borne in mind prior to and before delivery. After delivery, factor levels usually return to baseline levels in 7 to 10 days, but sometimes the drop occurs earlier. Nevertheless, clotting levels should be monitored, especially as the date of delivery approaches. This way, doctors will know whether treatments to prevent bleeding are required and which treatments to consider.

If any invasive diagnostic or therapeutic procedure (for example, amniocentesis) is planned during pregnancy, factor levels should be measured prior to the procedure. A 50% (0.5 U/mL) factor level is generally considered adequate for a surgical procedure or delivery. Desmopressin (DDAVP) is the treatment of choice for preparation for amniocentesis and delivery since it increases factor VWD levels, and consequently factor VIII levels. It is, however, wise to be cautious about the use of desmopressin during pregnancy because it is a vasoconstrictor and can potentially cause uterine contractions with premature labour and, rarely, miscarriage. Once the umbilical cord is clamped, desmopressin can be used if necessary to prevent postpartum hemorrhage in carriers of hemophilia A. It is also reasonable to use desmopressin immediately before a caesarean section. If replacement therapy is required, which is unusual, recombinant factor VIII or IX is the treatment of choice. Plasma-derived
clotting factor concentrates may transmit parvovirus, which has been associated with miscarriage.

A multidisciplinary approach should be taken to managing pregnancy in carriers of hemophilia. Ideally, before the woman becomes pregnant, she and her partner should meet with her hematologist, obstetrician and genetic counsellor to discuss options such as prenatal diagnosis, and treatment during delivery as well as post-natal care. These decisions shouldn’t be left until the woman is in labour.

LABOUR AND DELIVERY

In preparation for delivery, a woman should meet with the medical team, including her hematologist, obstetrician, anaesthetist and pediatrician to discuss possible complications and treatments. This information should be written in the woman’s medical file. She should also have a copy of the recommendations that she can bring to the hospital at the time of delivery in case either her doctor or her medical file is unavailable. While it is preferable to deliver in a hospital where there is access to hemophilia specialists, this may not be possible. If she is not near a hemophilia centre, the local hospital and medical team should be prepared beforehand for the woman’s and for the baby’s possible needs.
CHAPTER 6 Reproductive Issues

There is no reason to plan a caesarean section automatically for a child with hemophilia. In fact, normal vaginal delivery is perfectly acceptable in the absence of other contraindications since the risk of intra-cranial hemorrhage is low. In a study of 120 births of children with hemophilia, only 4 intra-cranial hemorrhages occurred (3%). In the normal population, 1% to 4% of all neonates suffer intra-cranial hemorrhage. Thus, a caesarean section is currently considered to be indicated only if there is an obstetric reason to do so, but in the medical/social context where caesarean sections are being performed for much less serious indications, this question is still being debated.

The sex of the foetus may be determined fairly reliably by an early pregnancy ultrasound, which is helpful to identify male foetuses at risk for hemophilia. In cases where there is a foetus with a confirmed or suspected bleeding disorder, the delivery should be carried out as gently as possible.

In order to prevent bleeding, the following should be avoided in the mother if her factor levels are not clearly normal:

- an epidural (freezing of the lower body by means of a needle in the spine)
- unnecessary episiotomy (cutting of the skin near the vagina to avoid tearing)
- caesarean section, unless the woman has received DDAVP or factor concentrates to bring her factor to safe levels.

The following should be avoided in the foetus whenever possible:

- suction extraction of the baby
- the use of forceps
- scalp electrodes
- foetal scalp blood sampling
- deep intramuscular injections.
ANAESTHESIA

While the risk of hemorrhaging in non-carriers who have an epidural or spinal is extremely low (1 in 150,000 procedures), this risk increases in women with a bleeding disorder, though it cannot be quantified. Epidural and spinal anaesthesia are contraindicated if there is a bleeding disorder. There is, however, no contraindication to regional anaesthesia if coagulation is normalized.

If the need for a caesarean section arises because of a complication, the risks of general anaesthesia and spinal anaesthesia must be discussed with the woman. If regional analgesia/anaesthetics are used, the woman should be observed postpartum to ensure that there are no complications. Women with inherited bleeding disorders can have regional analgesia or anaesthesia provided their coagulation defects have normalised during pregnancy or following factor replacement therapy. Again, these options should be discussed before labour and delivery have started, while the woman is not under duress or in pain.

POSTPARTUM CARE

Factor VIII and von Willebrand factor levels fall off fairly rapidly after delivery. In the event of a postpartum hemorrhage, desmopressin may be used. In case of serious bleeding, factor replacement therapy is considered.

In the general population, the risk of primary postpartum hemorrhage (during the first 24 hours after delivery) is 4% to 5%. This risk is increased to 16% to 22% in women who are hemophilia carriers. The risk of late postpartum hemorrhage is also increased to 11% to 24% in women with bleeding disorders.
CHAPTER 6 Reproductive Issues

compared to less than 1% in the general population. For those women who require factor replacement therapy, it is recommended to keep factor levels at 50% for 3 to 4 days after vaginal delivery, and 4 to 5 days after caesarean section. Women at risk of late postpartum hemorrhage should have their hemoglobin checked before discharge from hospital. Delayed bleeding up to 35 days afterwards is possible, so women should be made aware of this and be seen two weeks postpartum. A telephone follow-up should be done to monitor postpartum bleeding for approximately one to two months.

If postpartum hemorrhage occurs, tranexamic acid and oral contraceptives are the first-line therapy for its management. Prophylactic oral contraceptives may be started immediately after delivery and continued for one month in selected women judged to be at higher risk of bleeding. The use of desmopressin is occasionally required in the post-partum period.

BREASTFEEDING

Breastfeeding increases factor VIII and von Willebrand factor levels. In the cases of VWF and factor VIII, that increase is in response to pregnancy hormones. Women who breastfeed may maintain the high hormone levels they had during pregnancy. This protects them from bleeding in the weeks following delivery.

Neither desmopressin not tranexamic acid pass through breast milk; thus both are safe for the baby.

Women with certain types of bleeding disorders, including factor IX deficiency, can have bleeding problems postpartum whether or not they breast feed. This is because they do not respond to pregnancy hormones.
NEONATE CARE

Bleeding at birth

Bleeding problems in babies at childbirth are often noticed because of abnormal bleeding at the site of blood draws. Babies with hemophilia A (factor VIII deficiency) and hemophilia B (factor IX deficiency) rarely bleed at birth and brain hemorrhage is reported as being rare. Babies with bleeding disorders may have scalp hematomas. Umbilical stump bleeding is characteristic of babies with factor IX deficiency.

Intramuscular injections, surgery and circumcision should be avoided in neonates at risk for severe hemophilia until the diagnosis is excluded. A cord blood sample should be taken at birth to measure the factor level, and the vitamin K normally given to every child after birth should be given by mouth, not by injection. Though brain hemorrhage is rare, a transcranial ultrasound should be done immediately at birth on any baby suspected of a severe bleeding disorder to determine the need for emergency treatment. Recombinant factor VIII or IX is the treatment of choice for any newborn child with hemophilia. The hematologist supervising the case should make arrangements to have it in stock before delivery.

Circumcision

Some parents choose to have their son circumcised for religious or cultural reasons. The decision to circumcise a boy who may have hemophilia should be discussed beforehand with the hematologist and pediatrician. Circumcision of boys with hemophilia should not be considered a minor procedure, and should be performed only when necessary in a baby/child with a bleeding disorder and with adequate precautions. Laboratory tests
should be done to confirm the factor deficiency, level of factor and presence of inhibitors. The World Federation of Hemophilia has published a monograph on circumcision. It can be downloaded from their website at www.wfh.org.

Be Prepared
The most important thing for a woman to remember when she is pregnant is to develop a close working relationship with the medical team members who will be treating her and, as always, to be knowledgeable about her condition and its treatment. She is always her own best advocate. Making decisions beforehand and having a written plan at home and at the hospital for any eventuality will help decrease stress and facilitate childbirth.

HYSTERECTOMY

Despite heavy menstrual bleeding (menorrhagia) that may have been present, in some instances since their early teens, women may go many years, and even reach the age of menopause, without having been diagnosed with a bleeding disorder. Many carriers of hemophilia never make the connection between their own bleeding problems and their carrier status.

When women speak to their gynaecologists about this heavy menstrual bleeding, they are often told that it is a normal thing for women. In families in which all the women bleed heavily, it is seen as “normal.”

There are cases when, once the carrier diagnosis is made, the woman chooses to terminate her menses, no matter what her age, due to the stress and constant fear of bleeding she has been living with for so long. Eliminating the cause of stress and health problems completely is a relief.
Although my bleeding symptoms to this point have been very mild, I am concerned that as I age they will become more problematic.

In response to a questionnaire developed for women with a bleeding disorder in 1998 by D.K. Wysocki, 42% of the respondents had had a hysterectomy. The average rate in the general population varies from 12% to 18%. This response shows a clear difference in the rates for hysterectomy between women with and without a bleeding disorder.

On the other hand, menorrhagia in carriers can be treated successfully, allowing women to retain the ability to conceive and avoid unnecessary hysterectomies.

**PERIMENOPAUSAL BLEEDING**

Menopause is the time in a woman’s life when menstrual periods permanently stop. Perimenopause is a 3- to 10-year period before natural menopause, when hormones are “in transition.” Bleeding can be a special problem at this time.

One of the symptoms of perimenopause is menometrorrhagia (heavy and irregular menstrual periods). Regular periods are the result of a precise hormone balance of estrogen and progesterone that cause ovulation. In perimenopause, hormone levels fluctuate and interfere with ovulation. If ovulation does not occur, the ovary will continue making estrogen, causing the endometrium (lining of the uterus) to keep thickening. This often leads to heavy menstrual bleeding followed by irregular bleeding at other times (menometrorrhagia) and spotting.

Since there are other medical reasons for heavy bleeding, and carriers are at the same risk for these problems as other women, a full medical investigation should be done to eliminate other causes of bleeding.
Treatment options
As in all women, the cause of the abnormal menstrual bleeding needs to be determined before any treatment is offered. If the bleeding is caused by lack of ovulation, hormone replacement therapy (HRT) will usually control the problem. However, if a woman is already using HRT, she may need to discuss other options with her gynaecologist and her hematologist. Other treatment options, including endometrial ablation and hysterectomy, are listed in Chapter 7, Treatment and Care of Carriers.

Now that carriers are beginning to receive effective treatment for their bleeding disorders, including menorrhagia, more women may enter the menopausal age with their reproductive organs intact. They may require other forms of treatment, but won’t necessarily have to undergo major surgery. However, if they do choose this option, they must work closely with their gynaecologist and hematologist to plan the surgery in order to prevent possible post-operative bleeding.
CHAPTER

Care and Treatment of Carriers

This chapter describes:

- the multidisciplinary clinics for women with bleeding disorders that are being created in Canada
- the medical and surgical options available to women to treat their bleeding symptoms.
MULTIDISCIPLINARY WOMEN’S CLINICS

Hemophilia Treatment Centres are now beginning to recognize the importance of having an expert team to deal specifically with problems in women who have an inherited bleeding disorder.

Objectives

Objectives of a multidisciplinary clinic for women are to:

• Improve the quality of life of women with bleeding disorders.
• Create a forum for discussion between physicians, allied health professionals with expertise involved in the care of women.
• Advance knowledge in the care of women with bleeding disorders.
• Provide education for physicians, patients and, ultimately, for the general public.

Specific objectives are to:

• Provide adequate diagnostic workup for women with bleeding problems, and accurately identify underlying gynaecological and hematological diseases.
• Provide adequate therapeutic interventions for bleeding problems; to reassess interventions in a timely fashion.
• Avoid unnecessary surgery.
• Avoid unnecessary use of blood products.
• Provide optimal preparation for anaesthesia, surgery, pregnancy, childbirth and postpartum care.
• Provide counselling and support.
Team members

The primary members of a multi-disciplinary women’s clinic team include:

- a hematologist
- a gynaecologist
- an obstetrician and
- a nurse coordinator who arranges testing and meetings with the specialists.

Access to proper diagnostic testing is imperative. Lab technicians work closely with specialists in coagulation since some tests are very sensitive and must be properly done to have an accurate diagnosis. This team can meet with the patient to plan a therapeutic approach, and provide support and advice to a family physician. All carriers should be referred to a women’s clinic, if one exists, by their physician. At times, this will be the only consultation that a carrier may need, apart from childbirth.

Women with bleeding disorders may not always need to be seen by both the gynaecologist and the hematologist, but can be oriented to one or the other depending on their special needs. Referrals to other departments, such as orthopedics, Ear/Nose/Throat and dentistry can be coordinated by the HTC, and treatment discussed with the hematologist to take into account the special needs of carriers of hemophilia.

Before any coagulation investigation, carriers with abnormal menstrual bleeding should have a complete personal and family history and physical examination, including a gynaecological examination (not always necessary in adolescents). The introduction of a graphic scoring system for menstrual bleeding has resulted in a more practical means of quantifying excessive menstrual bleeding, the most common complaint in carriers.

As a mother I was expected to diagnose bleeding episodes my son was having. I can’t imagine why I would not be competent to know when I was bleeding.
(See Chapter 4, Symptomatic Carriers.) This can be sent to the patient for completion before her first visit to the clinic, along with a questionnaire on her personal and familial bleeding history.

While a multidisciplinary women’s clinic is the ideal model, most hospitals have yet to officially integrate such a clinic into their Hemophilia Treatment Centre. Women may be seen on an individual basis, and referred to the gynaecology department. The HTC can then work closely with this department to develop a treatment program for a carrier who is experiencing menstrual problems or who will be giving birth.

While HTCs are becoming more and more aware of the importance of bleeding experienced by carriers, there are, unfortunately, still occasions when the bleeding is not recognized and proper treatment not provided.

**MEDICAL OPTIONS FOR CARRIERS**

**Hormone therapy**

Oral contraceptives raise the levels of factor VIII and von Willebrand factor (VWF) in the blood. For many women who are carriers of hemophilia A and who suffer from menorrhagia, this hormone therapy alone is effective in reducing menstrual bleeding to normal.

Oral contraceptive therapy will not improve factor levels for women with deficiencies in factor IX (hemophilia B); however, they can be helpful even for these women by regulating the menstrual periods and reducing the flow of blood.
Other hormone therapies may be prescribed when oral contraceptives are contraindicated or not well tolerated by some women. These include progesterone. They work by thinning the lining of the uterus. This makes it less prone to heavy bleeding. However, these products cannot be taken for long periods of time.

More recently, another mode of chronic progestin delivery to the endometrium has become available in the form of an intrauterine system (IUS). It is called Mirena. Mirena releases 20 g of levonorgestrel per day, which effectively suppresses endometrial growth and significantly reduces menstrual bleeding, clotting, and dysmenorrhea. This device has been extensively evaluated in women with severe menorrhagia awaiting hysterectomy. Use of the Mirena IUS reduced menstrual blood loss by between 74% and 97% and resulted in 64% to 82% of women subsequently cancelling their hysterectomies. General acceptance of this device is excellent but, as with any therapy, side effects are possible.

**Desmopressin**

Desmopressin is a synthetic drug which is a copy of a natural hormone. It acts by releasing von Willebrand factor (VWF) stored in the lining of the blood vessels. The increased VWF in turn transports extra factor VIII and thus increases factor VIII levels. Desmopressin is not made from blood.

Desmopressin is another good alternative for hemophilia A carriers.
Desmopressin can be taken in three different ways:

- It can be injected into a vein. Most often, the brand name for this kind of desmopressin is DDAVP.
- It can be injected under the skin. This product is called Octostim.
- It can be taken by nasal spray. This form of desmopressin is called Octostim Spray.

Since desmopressin acts by releasing VWF stored in the body, one cannot “go to the well” too often. A sufficient amount of time, usually 12 to 24 hours, must elapse between doses of desmopressin to allow the body to rebuild its stores. In major surgery, desmopressin alone may not be enough to control bleeding. In such a case, a person may also require clotting factor concentrates.

Desmopressin is of no benefit to carriers of hemophilia B (factor IX deficiency).

Desmopressin can sometimes have some mild side effects. These are:

- facial flushing
- mild headache
- nausea and abdominal cramps.

Desmopressin is an anti-diuretic, that is, it can make the body retain water and decrease the body’s salt level. Therefore, doctors recommend that after receiving desmopressin people drink only enough fluid to satisfy thirst. Repeated doses of DDAVP should be avoided.
If a person has a very bad headache or has not been able to pass water 24 hours after taking desmopressin, she should go to the Hemophilia Treatment Centre or emergency room for help.

**Anti-fibrinolytic agent (Cyklokapron)**

Cyklokapron (tranexamic acid) is a drug that helps to hold a clot in place once it has formed. It acts by stopping the activity of an enzyme, called plasmin, which dissolves blood clots.

Cyklokapron does not help to actually form a clot. This means it cannot be used instead of desmopressin or factor concentrates. It can be used to hold a clot in place in mucous membranes such as:

- the inside of the mouth
- the inside of the nose
- inside the intestines (the gut)
- inside the uterus (the womb).

Cyklokapron has proven very useful for women with bleeding disorders. It is used:

- before dental work
- when a person has mouth, nose and minor intestinal bleeding
- for women with heavy and/or prolonged menstrual bleeding.

For women with menorrhagia, Cyklokapron can be started on the first day of menstrual bleeding and taken for 5 days in a row. It can even be combined with the use of desmopressin. Cyklokapron comes in tablet form.
Cyklokapron can sometimes have some mild side effects. These are:

- nausea
- sleepiness
- dizziness
- diarrhoea
- stomach pain.

These mild side effects go away when...

- the person stops taking the drugs
- the doctor reduces the dosage.

Note: In factor VIII deficiency hemophilia, high hormone levels increase the quantity of clotting factor, thus improving coagulation. Knowing this, carriers can time dental appointments (or any medical intervention) to coincide with their mid-cycle (ovulation) when hormone levels are at their highest. There is no hormonal change in carriers of hemophilia B.

**Clotting factor concentrates**

Safe and effective clotting factor concentrates are available, if required, for carriers of hemophilia A and B.

Factor concentrates can be used...

- when desmopressin, hormone therapy and anti-fibrinolytic drugs are not effective
- for surgery or
- after serious accidental injury.
Factor VIII and IX concentrates are genetically-engineered, recombinant (synthetic) products. This means that they are not made from human plasma. They do not transmit viruses. As a result, these concentrates are the treatments of choice for hemophilia A and B carriers.

Clotting factor concentrates are injected into a vein. They can be administered at a clinic, doctor’s office or emergency room. Many people with severe bleeding disorders learn to inject them at home.

Complementary medicines

There are a number of complementary medicines and practices that may help alleviate bleeding and pain for some symptoms. (See Chapter 8, Complementary and Alternative Medicine.)
SURGICAL OPTIONS FOR MENORRHAGIA

For some women, the medical treatments described above will not work. Heavy, prolonged bleeding during the menstrual cycle will continue. For these women, surgery is an option. Surgery, however, is a big step. Women should have all the information before making their decisions. These are some of the options.

Uterine ablation (endometrial ablation)

The purpose of this operation is to destroy the lining of the uterus. This is the endometrial tissue which bleeds so much during menstruation. The operation is done through the vagina so no surgical cutting is needed. The uterine lining is burned away. Hormone therapy is given in the two months before the operation to reduce endometrial growth. A woman cannot have children after this operation.

This is a new operation but success rates are promising. Fifty percent of women have no more menstrual bleeding and a further 35% of women have much less menstrual bleeding.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The operation involves no surgical cutting so there is much less chance of bleeding than with a hysterectomy.</td>
<td>• Unlike with medical treatment, the woman can no longer have children.</td>
</tr>
<tr>
<td>• The operation can be done in a doctor’s clinic. Therefore, the woman does not have to stay in hospital.</td>
<td>• The operation may have to be repeated.</td>
</tr>
<tr>
<td>• The recovery time is much shorter than with a hysterectomy.</td>
<td>• In about 10% of women, this operation does not reduce bleeding.</td>
</tr>
<tr>
<td>• The success rates are promising.</td>
<td>• There are rare complications to the operation.</td>
</tr>
</tbody>
</table>
**Hysterectomy (Removal of the uterus)**

The purpose of this operation is to remove the uterus so that menstrual bleeding stops once and for all. Sometimes, the ovaries and the fallopian tubes are removed as well.

This operation is often recommended to women with menorrhagia even before testing for a bleeding disorder has been done. This means that some women lose the ability to have children when their bleeding could be successfully treated.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>• Hysterectomy stops menstrual bleeding once and for all.</td>
<td>• Unlike with medical treatment, the woman can no longer have children.</td>
</tr>
<tr>
<td>• It may be the only option for women who do not respond to medical treatment, and for whom uterine ablation is not effective.</td>
<td>• A hysterectomy is a major operation. In women with bleeding disorders, there is increased risk of bleeding both during and after the operation. This can be managed with factor concentrates.</td>
</tr>
<tr>
<td></td>
<td>• The recovery time is much longer than with a uterine ablation.</td>
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<td></td>
<td>• The operation may require a stay in hospital.</td>
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</tbody>
</table>
Laparoscopic endometrial removal (To remove endometrial tissue outside the uterus)

The purpose of this operation is to remove endometrial tissue which has formed outside the uterus. This tissue bleeds during menstruation. The bleeding can cause pain in the pelvis and abdomen. Two small incisions are cut in the abdomen. Two tubes are inserted - one a tiny camera, the other a tube by which the endometrial tissue is cut out.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• This operation can reduce pain and bleeding in the woman who does not respond to hormone therapy or other medical treatment.</td>
<td>• While not a major operation, a woman with a bleeding disorder will need appropriate preparation which may include factor concentrates.</td>
</tr>
</tbody>
</table>

Oophorectomy (Removal of the ovaries)

The purpose of this operation is to stop bleeding from the ovaries. This bleeding may happen even when...
• a woman is having hormone therapy to reduce menorrhagia
• a uterine ablation has been done or
• a partial hysterectomy has been done.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• It can reduce bleeding and pain.</td>
<td>• An oophorectomy is a major operation.</td>
</tr>
<tr>
<td></td>
<td>• If both ovaries are removed, women can no longer have children.</td>
</tr>
<tr>
<td></td>
<td>• If both ovaries are removed, women need to take hormones until the age of menopause.</td>
</tr>
</tbody>
</table>
Dilation and Curettage (D&C)

The purpose of this operation is to scrape and clean the lining of the uterus. This may need to be done to diagnose another problem or after a miscarriage; however, for women with menorrhagia, it will not be effective in reducing bleeding. In fact, the opposite is probably true. The D&C will remove any existing platelet plugs and fibrin clots and make the bleeding worse.
This chapter describes:

- alternative or holistic treatments people can turn to in order to complement their conventional medical care
- many natural and pharmaceutical products that can actually cause or worsen bleeding in carriers of hemophilia A and B.
There are a number of alternative or holistic treatments people can turn to in order to complement their conventional medical care. These practices take into account not only the physical aspect of a person's health care, but also the person as a whole, including lifestyle, and mental, spiritual and emotional health. This holistic approach is preventive in nature, working to eliminate the underlying causes of a problem. However, any pre-existing medical condition, such as hemophilia, needs to be taken into account when dealing with complementary therapies. If a practitioner says he can cure hemophilia or that only his medication should be taken, he is not to be trusted. Always make sure that any alternative caregiver is a licensed professional, especially when this implies taking medication of any kind.

The information in this section is intended as an informative and practical guide to how complementary therapies might be integrated into one's life. This information is not intended as a substitute for professional advice and guidance by a qualified health practitioner. It's also important to let one's doctor know about any alternative medication one is using, because this knowledge may help prevent potentially dangerous combinations.

I'd like to know more about Vitamin K and other interactions of “natural health products” and bleeding disorders.
COMPLEMENTARY PRACTICES

Stress Reduction Techniques

Many people with hemophilia claim to bleed more often in times of stress. When looking for a practitioner for support in reducing or dealing with stress in life, it should be kept in mind that everyone is different and each person prefers a different method.

Meditation and visual imaging
Many health care professionals in the western world are now making use of the age-old techniques of meditation to supplement standard treatments. Even if a serious illness cannot be cured, meditation puts the person in control, enabling her to cope with the disease and the treatment, and lessen the stress that affects her health.

Meditation is found to contribute significantly to the empowerment of patients for self-healing. A meditative state increases levels of serotonin and melatonin, our “feel good” hormones, important neurotransmitters and neuropeptides that influence mood and behaviour in many ways. Melatonin has been linked to regulation of sleep, and early research indicates it may have anti-carcinogen effects and enhance the immune system. Meditation has been associated with increases in antibody titres to influenza vaccine, positive emotional states and improved immune function. There has also been evidence that a physiological link among mood, stress and hormones exists for healing wounds. Studies on prayer have found similar benefits, including improved healing time and better than expected outcomes for patients.
**Aromatherapy**
Aromatherapy involves the use of essential oils and other aromatic compounds from plants for the purpose of affecting a person’s mood or health. An example is peppermint oil applied to the temples to treat headaches. As people with bleeding disorders should avoid most headache medications, this creates a natural alternative.

**Massage**
Massage is a wonderful therapy for stress release, as well as a treatment for muscle pain. It is important to notify any Registered Massage Therapist of one’s bleeding disorder, as deep tissue and muscle massage can cause bleeding. Gentle massage techniques can still be extremely effective, and feel wonderful too!

As massage is not a regulated health profession under the Health Professions Act in all provinces, clients are encouraged to inquire if their massage therapist is a member in good standing of a professional association, and then investigate the organization’s entry requirements and find out if therapists need to fulfill continuing competence requirements.
Complementary practices

Ayurvedic medicine
Ayurvedic medicine originated in India and has been practiced there with great success for thousands of years. It has a strong preventive aspect, aiming to keep the person healthy, as well as working to restore health and balance. Ayurveda not only focuses on the physical aspects of health, but also the balance between the physical, emotional, spiritual and psychological self.

Ayurvedic treatments consist not only of herbs and diet therapy but may also involve physical, behavioural and spiritual practices.

Naturopathic medicine
Naturopathic medicine is a primary health care profession, which focuses on prevention and uses natural methods to promote healing. Naturopathic doctors (NDs) see the patient as a whole person and recognize that disease is not always isolated to a physical cause. Thus, NDs consider the emotional, spiritual, mental and physical aspects of a person when diagnosing and developing a treatment plan. They use a combination of clinical nutrition, botanical (herbal) medicine, homeopathic medicine, joint assessment and re-alignment, physical therapies, acupuncture and Asian medicine, and lifestyle counselling. Therapies are used to stimulate the body’s self-healing abilities. Naturopathic doctors are trained in pharmacology and pathology; they have a good understanding of how the body works, and are aware of potential drug interactions.

Look for a naturopathic doctor who is registered with both the national and provincial licensing boards. See www.cand.ca for more information.
CHAPTER 8 Complementary and Alternative Medicine

Traditional Chinese/Asian medicine
Traditional Asian medicine or TAM includes systems such as Traditional Chinese medicine (TCM), Japanese and Korean medicine. Treatments may include the use of acupuncture, acupressure, diet and lifestyle modifications, and Eastern botanical medicine. In many cases, acupuncture can be done safely in a person with a bleeding disorder. Many other aspects of this broad system of medicine can be helpful.

The following designations are used for a licensed professional: Doctor of Traditional Chinese Medicine, Dr.TCM; Registered TCM practitioner, R.TCM.P.; Registered TCM herbalist, R.TCM.H.; and Registered Acupuncturist, R.Ac.

Homeopathy
Homeopathy uses gentle remedies to support a person’s natural homeostatic forces, to regain balance and restore health. Homeopathic remedies can be used with all allopathic medication. Homeopathic remedies cannot replace conventional treatments for hemophilia. It is safe to try a remedy. At worst, there will simply be no improvement.

Homeopaths may have training ranging from a 2-week course to a 4-year doctoral degree. Naturopaths are also trained in homeopathy. Some medical doctors have also taken training.

Botanical medicine
Botanical medicine is medical treatment through the use of plants. Many common medications available today were originally developed from knowledge of botanical medicine. The more herbs are concentrated into powders and extracts in pill form, the more they start having side effects. Remember: more is not always better. The trick is to learn what is enough, and know what one is taking, and why.
Practitioners include conventional doctors, traditional Asian medicine/Chinese medicine, master herbalists and naturopathic doctors.

Many herbs can be combined to support an overall decrease in tendency to bleed. These need to be combined with the support of a professional and in conjunction with a medical doctor and pharmacist to ensure there are no interactions with current medications. Uses people with bleeding disorders may have for systemic herbs include the treatment of heavy periods with herbs taken just prior and during menstrual flow, as well as preparation for surgery. Consult a professional for more information.

**REMEDIES THAT ARE CONTRAINDICATED FOR PEOPLE WITH BLEEDING DISORDERS**

With heart disease being a leading killer in North America, remedies such as nutritional supplements and Western and Eastern Botanicals to improve blood flow and decrease the chances of forming a clot are becoming more and more common. Below is a list of herbs and nutrients to be cautious with. It is not an exhaustive list, so any remedy one chooses to take should still be overseen by a medical professional.

Note: Eastern herbs can go by more than one name so particular caution is advised when using Eastern herbs.

Alcohol – Thins the blood and increases the risk of bleeding.

Aspirin – Can cause gastro-intestinal upset and bleeding, among other side effects. Acetaminophen (Tylenol) is a safe choice for those with bleeding disorders.
Danshen – Used regularly in China to treat disorders such as cardiovascular disease and cerebral vascular problems. Danshen can affect hemostasis by inhibiting platelet aggregation and interfering with the coagulation cascade.

Dong Quai (Chinese Angelica) – Used most commonly in supporting gynaecologic disorders, including dysmenorrhea. Can cause bleeding, and so should be avoided in women with bleeding disorders.

Ephedra Ephedrine/ Ma Huang – This herb has proven to be dangerous in even moderate doses and, among many other adverse effects, can increase arterial pressure and increase the risk of cerebral hemorrhage.

Fenugreek/Trigonella foenum-graecum – Traditionally used to treat gastro-intestinal conditions such as constipation and dyspepsia. Can cause increased bleeding and bruising.

Feverfew (Tanacetum parthenium) – Acts as a vasodilator, thus can worsen a bleeding situation. Shown to inhibit the release of arachidonic acid, a precursor for many prostaglandins and other substances involved in the clotting cascade. Feverfew has also been shown to inhibit the binding of platelets to collagen, which is an important step in the extrinsic pathway of the clotting cascade.

Garlic (Allium sativum) – Used in capsule form to reduce hypertension and high cholesterol. Case reports of unexpected or increased surgical bleeding, prolonged bleeding time, and impaired platelet aggregation. Note: garlic as a food is safe.

Ginger (Zingiber officinale) – Inhibits platelet formation. Safe from food sources, but should be avoided in capsule form.
Ginkgo Biloba – A herb used to improve circulation. Method of action: thins the blood.

Ginseng/ Panax ginseng (all forms) – Widely used as a stimulant and blood sugar regulator. Possible side effects include nose bleeds (epistaxis). Drug interactions with MAO inhibitors (depression) and oral hypoglycemics and insulin.

Horse Chestnut/Aesculus hippocastanum – Most commonly used for treatment of varicose veins and hemorrhoids. Can cause severe bleeding and bruising, due to antithrombotic activity of aesculin.

Ibuprofen (Advil, Motrin) – See Aspirin above.

Jingui Huayu, Blood Circulator – Chinese medicine uses this time-honoured formula to promote micro-circulation. Works to prevent clot formation and inhibit platelet aggregation.

Kava/Piper methysticum (Kava-Kava) – Used mainly to treat anxiety. Long term use causes decreased platelet and lymphocyte counts.

Matricaria recutita (chamomile) – Used as a calming, soothing, anti-inflammatory herb, chamomile can cause bleeding, and decreased absorption of other medications. 1-2 cups/day, 3-4 times/week is of no concern. Avoid use in pregnancy and breast feeding.

Omega 3 Essential Fatty Acids – Used to decrease risk of cardiovascular disease. Method of action: thins the blood. Additional supplementation beyond the minimum for good health (2-3 servings of fish/week, and/or 1-2 Tbsp ground flax seed/day) is not recommended.
Papaya/Papain – Used like Bromelaine (for weight loss) as a natural anti-inflammatory and digestive enzyme. It is purported to work in a similar fashion, thus similar restrictions are recommended.

Pineapple/Bromelaine – Used as a natural anti-inflammatory and digestive enzyme, its method of action is: enhancing serum fibrinolytic activity, inhibiting fibrinogen synthesis, degrading fibrin and fibrinogen, and influencing prostaglandin synthesis. Thus, this should not be used as a supplement, and only eaten in moderate amounts (1-2 slices, 1-2 times/week and not 2 days in a row), avoiding the core which is the most rich in Bromelaine.

Vitamin E – Inhibits platelet formation. Safe from food sources, should be avoided in capsule form.

**CONCLUSION**

It is important to take excellent care of the whole person – mind, body and spirit. There are many different ways that a person can support her health, from regular exercise, finding happiness in everyday life and reducing stress to taking an active part in her own health through knowledge about both medical and alternative treatments.
This chapter explores some of the quality-of-life issues a carrier may face, including:

- the impact on young girls
- possible loss of faith in the medical system
- career repercussions for carriers
- the repercussions on sexuality and family life
- exercise and fitness
- the impact of having a child with hemophilia.

It ends with suggestions on where to find help and support.
This chapter is based on the experiences of carriers who spent much of their lives undiagnosed and untreated. Once a carrier starts to receive proper treatment for her hemophilia-related health problems, she can take control of her life, and many of these complications will be diminished or completely eliminated and, consequently, her quality of life improves.

**IMpact on Young Girls**

A significant proportion of adolescents presenting with excessive bleeding have been found to have a bleeding disorder. Excessive menstrual bleeding starting at menarche (the first few menstrual periods) is a particularly frightening problem for young girls with inherited bleeding disorders. Menarche is brought on by a surge of hormones that provoke the initial menstrual cycles. Young girls are not at ease discussing personal hygiene problems, and the treatment team will have to be sensitive to their needs.

It may be difficult for a girl to leave the house for extended periods due to the pain, excessive bleeding and fear of staining clothing that she can experience during her periods. She may miss school or family and social gatherings because of these symptoms, and be unable to take part in scheduled events. It can be awkward for a girl to explain to her friends why she needs to stay home every month or why she can’t go to a sleepover, and especially difficult to explain to a male teacher why she may have to leave during a class. Puberty is naturally associated with anxiety, and for young girls the problems they may experience due to a bleeding disorder can add to their stress. A young girl’s self-image and confidence can be negatively affected if she experiences shame and embarrassment due to menorrhagia. She should be assured she is not a lesser person because of her

I was always afraid of bleeding through my clothing. I never wore anything but dark coloured slacks or skirts. And I still do to this day!
condition. Other than the bleeding, she is a “whole” person. Oral contraceptives are regularly used to manage heavy periods. For adolescents, however, this treatment carries psychological and social implications. So as to ensure proper compliance, the physician should be sensitive to and discuss the concerns of the parents and the teenager with regard to birth control pills. For many teens, the issue of future fertility is a concern. Cultural, religious and ethnic differences must also be respected.

Without proper treatment, young girls may have difficulty managing the physical pain and discomfort associated with their menstrual cycle and spend large amounts of time lying in bed. Some may develop a dependency on pain medication. Because of days missed from school each month, some young girls may have difficulty keeping up with schoolwork and this could limit their achievement and, in turn, their choice of career opportunities. It is helpful for the Hemophilia Treatment Centre team to send a letter, with the girl’s consent, to the school explaining the condition and her special needs.

Anemia can cause problems of self-image, as well as limit physical activity and social interactions. Constant use of medication for anemia can cause other health problems. Adolescents feel sensitive about personal image and undergo rapidly changing emotional states. Allowances must be made for strong reactions, including denial, and support should be offered. If the carrier has low factor levels, she should understand how this can lead to other possible bleeding complications.

Preventive treatment can usually help reduce or eliminate the effects of menorrhagia on a young carrier’s quality of life. Early diagnosis and treatment can help her develop a sense of mastery over her own health, and allow her to have a full life.
LOSS OF TRUST

While many women begin having bleeding problems including menorrhagia as young as 9 years of age, the average age of diagnosis is 25. At this point, they’ve been living with the consequences of this undiagnosed and untreated problem for years. Their bleeding symptoms were often ignored or dismissed, and no testing was done for a bleeding disorder, at times despite the fact that hemophilia was known to occur in the family. A woman may have informed her doctor of other bleeding symptoms and was told that the problems were “all in her head.”

This failure to recognize and accurately diagnose carrier status can lead to a sense of mistrust in health care providers and contribute to feelings of anger and blame directed at health care professionals in general. A young woman can experience a sense of hopelessness, feeling that nothing can be done to change her situation. She may be fearful that she won’t be able to get proper treatment if the need ever arises. Over time, hopelessness can give rise to depression.

CAREER REPERCUSSIONS FOR ADULT CARRIERS

The impact of personal health

Being a symptomatic carrier of hemophilia A or B can affect career choices. 57% of carriers experience menorrhagia, compared with 10% of the general population. A woman may be required to take several days off work each month if she can’t get her bleeding under control. She may need to advise her employer of her condition and design a flexible schedule that allows for time off if it becomes necessary. While engaging in a physically
demanding career is possible, it may be more challenging if a woman suffers from anemia. Some career choices may have to be altered or eliminated.

**Having a child with hemophilia**

Having a child with hemophilia may require a woman to choose a career with some built-in flexibility. Job security can be affected by the need to leave work on a regular basis. She may have to take her son to the hospital or give him an emergency infusion. There will be days that he is unable to attend school or day care. This means that someone will need to remain home or make arrangements for alternate childcare.

Because of a sense of guilt and responsibility she may feel for bringing a child with hemophilia into the world, a woman may think she has to stay home to take care of her child. She sometimes doesn’t feel that anyone else, including her partner, can take care of their child as well as she can. She may be fearful that something will happen to her son when he’s in someone else’s care and, as a result, stay home and become a full-time parent. Becoming a full-time parent can be a very fulfilling and rewarding experience, but it is important to explore the reasons for deciding to stay home full-time. Staying home because of fear or guilt is not an emotionally healthy decision for either the mother or child.
Sexuality is often not discussed within the healthcare setting. The attitude and comfort levels of both clients and healthcare workers influence how likely it is that discussions about sexuality occur.

A young woman who has experienced menorrhagia since her first period may have developed some embarrassment and shame around her monthly period.

These experiences can affect a young girl’s emerging sexuality because her sexual centre, which is both the site of her menses and the area where her sexuality emerges, can become associated with shame and embarrassment.

The opportunity to express and enjoy a satisfying sex life can be affected if a woman experiences heavy and/or frequent periods, painful ovulation or mild bleeding or bruising during intercourse. Fatigue due to anemia can also reduce a woman’s interest in sexual activity. A sexual partner may be afraid of hurting a woman who is a carrier. This may lead to an avoidance of lovemaking or any sexual activity.

Open and honest communication is essential for all couples so that these issues can be addressed before they become problematic. Sexuality is an important part of life, involving how one feels about and expresses being a female, as well as the many physical ways in which one can experience closeness with a partner. There are numerous resources couples can turn to for help, including their family physician, the hemophilia centre team, or local health centres. There are marriage counsellors who can help a couple work through their problems and offer simple solutions to help improve their lives.
A Guide for Carriers of Hemophilia A and B

CHAPTER 9  Carriers’ Quality of Life

REPERCUSSIONS ON FAMILY LIFE

As with any couple, different parenting styles can put a strain on a marriage. This is heightened when a child with a chronic disorder is born. A deep-seated sense of guilt and responsibility can cause a mother of a child with hemophilia to be overly permissive or overprotective. She may consistently take responsibility for their son’s treatment. Her partner may feel left out of the relationship.

Marital relationships can become strained for a number of reasons. A carrier who experiences gynaecological problems may also become depressed, angry, irritable and tired during her period and lash out at her partner. He is likely to take her behaviour personally and either lash back or withdraw to avoid conflict. Either reaction leads to a disconnection between the partners.

Fatigue due to anemia might make the woman less able to maintain her commitments to parenting, household responsibilities, or their relationship, and this can put additional pressure on her partner to carry more of the responsibilities. Again, if these issues are not discussed, resentment can develop.

Having to take time off work to attend to a child’s frequent medical needs may lead to disagreements about who will be responsible. This can lead to resentment if one partner consistently has to take on more responsibility than the other. Conversely, if a parent isn’t allowed to take part in the child’s medical care, he/she will lack confidence in his/her ability as a parent and feel excluded.

In addition to feeling guilty for having transmitted hemophilia to my son, I felt guilty for missing work and tried to make up for it by being the “superwoman” that does everything for everybody. Also, I felt guilty for making my husband live with hemophilia because of my carrier status (although he NEVER EVER mentioned it and did nothing to make me feel guilty). After 3 years of being the guilty party and the superwoman, a major burn-out has kept me from working for the past 5 months.
Intimate marital relationships require a lot of time, attention, touch and sacrifice. Constantly placing the child’s needs ahead of the relationship can cause frustration and anger, leading to resentment that can directly or indirectly be aimed at the child. Priorities must be made clear and lines of communication kept open.

EXERCISE AND FITNESS

During their menstrual cycles, carriers may have a tendency to discontinue their regular exercise routine if they are bleeding heavily, in pain or fatigued because of anemia. One can work out on an exercise machine at home or take a brisk walk and be able to return home regularly if a change in pads or tampons is needed. Other types of exercise, such as stretching, yoga or calisthenics, can be done at home using a DVD or videotape for encouragement.

THE IMPACT OF HAVING A CHILD WITH HEMOPHILIA

When parents of children with chronic health conditions are asked, “How do you cope? How do you deal with assessments, home care, medical visits and the worry?” they usually reply, “What choice do I have?” Every child is born with unique qualities, which gradually become apparent as he/she grows up. Some are more challenging than others.

In most cases, the parents of a child with a bleeding disorder can trace the condition directly back to the mother and her family. This can result in guilt and/or blame. It can also be an opportunity to gain inspiration from a family who showed strength in difficult times.

A Guide for Carriers of Hemophilia A and B
"I did not invite my mother to a hemophilia-related event for over fifteen years. I was angry at her for years and blamed her for passing on the hemophilia gene. I have since apologized to her and told her how sad and sorry I was that I kept her away."

"When I first found out I was a carrier, I felt a little guilty but soon afterwards I realized that I didn’t do anything wrong during my pregnancy; somehow I was chosen."

"At the time of the child’s diagnosis

When a male child is diagnosed with hemophilia there can be a sense of guilt; there was something the mother did that caused this to happen. Hemophilia is an inherited genetic condition; we have no control over what genes we pass on. In fact, of the 30,000 genes in our body, we all have several genes that do not work; we just don’t know which ones.

Understandably, many families need support in adjusting to the situation, whether or not they knew their family member’s carrier status. Resource material such as All About Hemophilia: A Guide for Families may be provided, and they can be connected with their local hemophilia chapter. This support can be an invaluable resource for newly diagnosed families with hemophilia. The HTC can also offer to arrange for genetic counsellors or social workers to meet with the family. Throughout this process, the healthcare providers attempt to develop open communication with the family, communication that is non-judgmental and empathetic. In this way, decision-making by the family is informed and autonomous, and in keeping with their values and beliefs.

"The early years

Once parents have adjusted to the diagnosis of a bleeding disorder in one of their children, who is probably still quite young, they need to remind themselves about the kind of person they’d hoped their child would become, before the diagnosis of hemophilia. Wasn’t he to be a person who was happy in his family, had good friends, did enjoyable activities, became an independent adult who contributed to his community, and had children of his own some day? Can that still not be the case?"
Does the presence of hemophilia and the mother’s carrier status really affect the career or family plans each parent had?

Parents’ dreams for their children are always modified. The hoped-for opera singer is tone deaf; the future doctor wants to be a teacher...

Some carriers develop depression or anxiety because of the deeply rooted sense of responsibility and guilt for passing on the hemophilia gene. As a parent, it is difficult to infuse a child because of the pain one is causing him. A mother may anticipate the next bleed or infusion with fear and anxiety. She may also become depressed if her son expresses his anger towards her when he discovers that she passed on the hemophilia gene to him, or when he is in pain, or when she directs him into activities which are “safer,” rather than letting him do the same activities as his friends. It is essential not to dismiss his feelings or to suggest he shouldn’t feel this way. He must be permitted to express his true feelings, and be able to have an open and honest discussion on the subject.

Accidents which lead to bleeds should be de-dramatized and normalized. After all, they are part of the development of any child with or without hemophilia. They should be faced with serenity and without guilt or recrimination. The child is already living with the consequences of the bleed—possibly pain and restrictions on activity—and is learning what he should do to avoid such events in the future. This will help the child take charge of his condition with fewer complications. The idea is not that the child must suffer through many crises—this, after all is not under our control—but rather, that he can face them with confidence in his ability to cope. The way we face these inevitable problems is something that is under our control.
The older child

A child needs to be trusted. He must be allowed to explore his own limits. This will strengthen his sense of responsibility and ability. Parents should trust in the child’s capacity to care for himself. It is natural that the trust a parent places in his or her child will translate into the child’s own self-confidence.

It is far more important that a child’s strong points be reinforced than that all risks be avoided. Keeping the lines of communication open and listening to the child is more important than talking to him. This will give the child the ability to face the challenges that hemophilia will present to him in life. The greater his resources to face adversity, the better his adaptation will be, and the better prepared he will be to cope with other challenging situations.

Siblings

Research indicates that siblings of children with a chronic disorder often grow up in a situation of considerable stress, but without the cognitive and emotional maturity to deal with their experiences. They can be confused by their own reactions, which may include anger and jealousy towards the affected child and their parents. If these feelings are not expressed and dealt with, these children can be at risk of developing anxiety, depression, somatic concerns and low self-esteem.

On the other hand, if siblings are supported from an early age, they are more likely to develop resilience, reach their own potential and also contribute to the quality of life of their sibling with a chronic disorder. Dealing with siblings of a child with a chronic disease sometimes requires the help of a social worker or family counsellor.
Extended family and friends

Other family members, such as grandparents, and friends are sometimes fearful for the child and afraid to look after him, and therefore are not able to offer help and support to the parents. Information sessions can be arranged for them through the Hemophilia Treatment Centre to explain this medical problem. They can be reassured about their ability to help care for the child, thus increasing the possibility that they will be better able to be part of the parents’ support network.

FINDING HELP AND SUPPORT

Through education available from the Hemophilia Treatment Centre, the Canadian Hemophilia Society and its local chapter, and from the extended family, parents will gradually move into a position of control. Carrier mothers and their partners will accept the reality of hemophilia and their ability to manage it, while raising their child and his/her siblings to become confident, capable adults. If one or both parents feel overwhelmed by the demands of family life with hemophilia, the HTC can put them in touch with a social worker, psychologist or genetic counsellor who will help them work through their problems.

Here are a number of tips to consider when raising children with hemophilia.

• Allow yourself the time to adjust to this news.
• Accept support that is offered.
• Accept that there are some things a person can’t change.
• We are not alone. It can be tough at times, but challenges can be overcome and life can be normal to a certain extent.
• Take things day by day.
• Remember that many other people have gone through this before. They thought they would never cope but they learned how and went on to have happy, fulfilling lives. Most are more than willing to help.
• Don’t be secretive about hemophilia. There’s no shame in it.
• Retain a sense of humour.
• Remember that guilt is not a helpful feeling.
• Be confident in your intuition. Trust your instincts about your child.

Coming to terms with hemophilia takes time. Occasionally, parents need to cry, to mourn the “normal” child they expected and admit their fear of what the future could hold. It is part of a period of adjustment. Once hemophilia is acknowledged and dealt with, parents see their child anew, and embrace the fun and excitement of watching a life take shape. One day they’ll look at their little boy and he will seem “normal.” Hemophilia will just be one element of what makes him who he is.

A close, cooperative relationship with the team from the Hemophilia Treatment Centre will help reduce medical problems related to carrier status, including help for any emotional or psychological issues that arise. Local chapters of the Canadian Hemophilia Society are a source of information and support.
This final chapter focuses on some of the key strategies in coping with hemophilia as a carrier and taking control:

- getting proper care and treatment
- being informed
- building a support network
- advocating for quality care
- registering at a Hemophilia Treatment Centre.
GETTING PROPER CARE AND TREATMENT

Appropriate care and treatment for carriers of hemophilia A and B will help eliminate many of the problems that affect them. This is especially true when it comes to gynaecological and obstetric problems. In most cases, the impact that pain, menorrhagia and anemia have on a carrier’s quality of life can be reduced. This frees the carrier from many uncomfortable and painful situations she might experience, allowing her to live a full life. Knowledge of her carrier status, as well as conception and delivery options, allows her to make informed decisions on these subjects, giving the carrier more control over her life as an active participant in her own medical care.

A recent study shows that carriers of factor VIII and IX hemophilia with factor levels as high as 60% experience bleeding episodes unrelated to menstrual or obstetrical events. These include bleeds following injury or surgery, after dental procedures and epistaxis (heavy and/or prolonged nosebleeds).

When bleeding does occur, women need to know that expert consultation and treatment is available to them, just as it is for males with mild hemophilia. For most carriers, the simple fact of knowing their factor levels is sufficient and they can take preventive measures if they ever undergo surgery or suffer an injury. The medical team can be consulted if any suspicious bleeding occurs. However, if bleeding other than that of a gynaecological or obstetrical nature in carriers isn’t acknowledged by the HTC, women can be frustrated when they demand specialized hematological services. A woman who has a son with hemophilia may hesitate to insist on treatment, fearing repercussions for her son, even if she logically knows this is unlikely, and so suffers the personal consequences of lack of treatment which can include pain and/or joint damage.
BEING INFORMED

People cannot advocate for themselves without being informed of their condition. The first step for carriers and parents of young carriers who want to advocate for services is to learn about hemophilia and its implications for carriers. In order to make informed decisions, they must know what their needs and options are.

There are a number of articles about carriers of hemophilia, including the practice guidelines of the Society of Obstetrics and Gynaecology of Canada: Gynaecological and Obstetrical Guidelines of Women With Inherited Bleeding Disorders. The CHS Web site has this document along with other information on women and bleeding disorders. See under both Bleeding Disorders and Educational Material.

BUILDING A SUPPORT NETWORK

There are a number of ways to develop a support network.

• Speak with other women in your family to learn about their experiences as carriers.
• Get in touch with the local chapter of the Canadian Hemophilia Society. They may hold women’s sessions or put carriers in touch with each other.
• If there are no support groups, ask that a workshop or informal gathering for carriers be included in the next chapter family weekend or Annual General Meeting.
• Get involved in the planning.
ADVOCATING FOR QUALITY CARE

Symptomatic carriers need to know how to get access to care and treatment. They need to advocate for themselves or their daughters. Here are a few tips to getting the treatment needed.

- Arrange for a personal meeting with the nurse coordinator and the hematologist to discuss concerns. Have your factor levels measured.
- Talk to the hemophilia treatment centre team. If they have a clinic established for women, access to other specialists should be possible.
- If the clinic team is not open to providing services, contact the local chapter of the CHS and ask them to organize a session for women with bleeding disorders. Offer to help. Get assistance from the national level of the CHS.
- Once the session has taken place, arrange a meeting with women who participated to discuss the next step in advocating for services.
- Encourage all women with a bleeding disorder or who have a daughter who is a carrier to contact the Hemophilia Treatment Centre and ask for specialized consultants to be included in the team, or ask them to agree to work as consultants with other specialists, especially if surgery is indicated.
- If appropriate, ask to be officially registered with mild hemophilia at the HTC. This is controversial for many clinics, so each carrier will need to discuss this with her doctor. (See below.)
- Work out a treatment plan in case emergency treatment or preventive care is ever needed.
- Carry a FactorFirst card in your wallet.
Every person has a different way of dealing with a medical condition. The important thing is to make sure that the carrier’s needs are understood and that a treatment plan is developed. The security of knowing that proper treatment is available if needed will allow one to breathe easier.

REGISTERING AT A HEMOPHILIA TREATMENT CENTRE

It is important that carriers register at a hemophilia treatment centre, even if they do not have abnormal symptoms of bleeding. Registration at a hemophilia treatment centre allows a carrier to:

- get accurate information about hemophilia from the comprehensive care team
- get appropriate blood tests and genetic testing that can only be done at specialized centres
- have access to the newest treatments if necessary
- find out about the latest research on hemophilia.

Some carriers may decide not to have their daughters or themselves registered with mild hemophilia, fearing that this label will cause problems with insurance coverage. This is a legitimate concern. A frank discussion with the HTC team will allow the parents or the carrier to make this decision. This is a personal choice and the final decision should be made by the patient.
Knowledge is power. For women who inherit the gene for factor VIII or factor IX hemophilia, knowing the possible repercussions this status can have on their own physical and psychological well-being can mean the difference between being in control of their lives, and having a bleeding disorder control their lives.

A close relationship needs to be established between the female carrier of hemophilia and the multidisciplinary team at the Hemophilia Treatment Centre. Proper care and support will allow girls and women to enjoy life fully, and be confident that they will have access to the same high standard of care and treatment others in the bleeding disorders community have come to know and trust.
For more information or to get in touch with a Hemophilia Treatment Centre, contact:

Canadian Hemophilia Society National Office
625 President Kennedy, Suite 505
Montreal, Quebec H3A 1K2
Tel: (514) 848-0503
Toll-free: 1 800 668-2686
Fax: (514) 848-9661
E-mail: chs@hemophilia.ca
Website: www.hemophilia.ca

Hemophilia Treatment Centres

British Columbia

- Hemophilia Program of British Columbia - Adult Division
  St. Paul's Hospital Room 259, Comox Building
  1081 Burrard Street
  Vancouver, British Columbia V6Z 1Y6
  Tel: (604) 682-2344, ext. 63026/63745
  After hours: (604) 682-2344
  Fax: (604) 806-8784

- Hemophilia/Hematology
  Rm 1A13 - BC Children's Hospital
  4480 Oak Street
  Vancouver, British Columbia V6H 3V4
  Tel: (604) 875-2345 ext. 5335
  Pager: (604) 875-2161
  After hours: (604) 875-2161
  Fax: (604) 875-2533

Alberta

- Southern Alberta Hemophilia Program
  Alberta Children's Hospital
  2888 Shaganappi Trail NW
  Calgary, Alberta T3B 6A8
  Tel: (403) 955-7311
  After hours: (403) 955-7211
  Fax: (403) 955-7393

- Dr. John Akabutu Comprehensive Centre for Bleeding Disorders
  8440 112th Street, CSB 7-109
  University of Alberta Hospitals
  Edmonton, Alberta T6G 2B7
  Tel: (780) 407-6588
  Pager: (780) 445-1683
  Fax: (780) 407-2605
HEMOPHILIA TREATMENT CENTRES

ONTARIO

• Hamilton Health Sciences Corporation
  McMaster Division
  1200 Main Street West
  Hamilton, Ontario L8N 3Z5
  Tel: (905) 521-2100 #75978/75970
  24 hour: (905) 521-2100 #76443
  Fax: (905) 521-2654

• Bleeding Disorders Program
  London Health Science Centre
  Victoria Hospital Rm E4-201
  800 Commissioners Road East
  London, Ontario N6A 5W9
  Tel: (519) 685-8500 ext. 53582
  Pager: #15358
  Fax: (519) 685-8543

• Hemophilia Program
  Thunder Bay Regional Hospital
  Science Centre
  980 Oliver Road
  Thunder Bay, Ontario P7B 6V4
  Tel: (807) 684-6550
  Fax: (807) 684-5906

• Comprehensive Hemophilia Care Centre
  St. Michael's Hospital
  30 Bond Street
  Toronto, Ontario M5B 1W8
  Tel: (416) 864-5129
  Pager: (416) 685-9404/9478
  After hours: (416) 864-5431
  Fax: (416) 864-5310

• Hemophilia Program
  Hospital for Sick Children
  Hematology/Oncology Clinic, Ward 8D
  555 University Avenue
  Toronto, Ontario M5G 1X8
  Tel: (416) 813-5871
  Pager: (416) 377-9716
  After hours: (416) 813-7500
  Fax: (416) 813-7221

• Hematology Clinic
  Children's Hospital of Eastern Ontario
  401 Smyth Road
  Ottawa, Ontario K1H 8L1
  Tel: (613) 737-7600 ext. 2368
  Fax: (613) 738-4846

• Regional Comprehensive Care Centre for
  Hemophilia and Hemostasis (Adult)
  The Ottawa Hospital, General Campus
  501 Smyth Road, Box 248
  Ottawa, Ontario K1H 8L6
  Tel: (613) 737-8252
  After hours: (613) 722-7000
  Fax: (613) 737-8157

• Hemophilia Program, Sudbury &
  North-Eastern Ontario
  Laurentian Site of HRSRH
  41 Ramsey Lake Road
  Sudbury, Ontario P3E 5J1
  Tel: (705) 522-2200 ext. 3264
  Fax: (705) 523-7077

• South Eastern Ontario Regional Inherited
  Bleeding Disorders Program
  Kingston General Hospital, Douglas 3
  Kingston, Ontario K7L2V7
  Tel: (613) 549-6666 ext. 4683
  Fax: (613) 548-1356
  After hours: (613) 548-3232, Page
  hematologist on call

SASKATCHEWAN

• Saskatchewan Bleeding Disorders Program
  Royal University Hospital
  103 Hospital Drive Box 113
  Saskatoon, Saskatchewan S7N 0W8
  Tel: (306) 655-6504
  After hours: (306) 655-1000
  Fax: (306) 655-6426

MANITOBA

• Manitoba Bleeding Disorders Program
  Health Sciences Centre
  FE349-685 William Avenue
  Winnipeg, Manitoba R3E 0Z2
  Tel: (204) 787-2465
  Pager: (204) 787-2071 #3346
  Fax: (204) 787-1743

• Hemophilia Program
  Hospital for Sick Children
  Hematology/Oncology Clinic, Ward 8D
  555 University Avenue
  Toronto, Ontario M5G 1X8
  Tel: (416) 813-5871
  Pager: (416) 377-9716
  After hours: (416) 813-7500
  Fax: (416) 813-7221

• Hematology Clinic
  Children's Hospital of Eastern Ontario
  401 Smyth Road
  Ottawa, Ontario K1H 8L1
  Tel: (613) 737-7600 ext. 2368
  Fax: (613) 738-4846

• Regional Comprehensive Care Centre for
  Hemophilia and Hemostasis (Adult)
  The Ottawa Hospital, General Campus
  501 Smyth Road, Box 248
  Ottawa, Ontario K1H 8L6
  Tel: (613) 737-8252
  After hours: (613) 722-7000
  Fax: (613) 737-8157

• Hemophilia Program, Sudbury &
  North-Eastern Ontario
  Laurentian Site of HRSRH
  41 Ramsey Lake Road
  Sudbury, Ontario P3E 5J1
  Tel: (705) 522-2200 ext. 3264
  Fax: (705) 523-7077

• South Eastern Ontario Regional Inherited
  Bleeding Disorders Program
  Kingston General Hospital, Douglas 3
  Kingston, Ontario K7L2V7
  Tel: (613) 549-6666 ext. 4683
  Fax: (613) 548-1356
  After hours: (613) 548-3232, Page
  hematologist on call
HEMOPHILIA TREATMENT CENTRES

QUEBEC

• Clinique d’hémophilie CHUS - Hôpital Fleurimont
  3001, 12e avenue Nord
  Sherbrooke (Québec) J1H 5N4
  Tel: (819) 346-1110 ext. 14560
  Fax: (819) 820-6492 / (819) 564-5434
  (hématologie)

• Montreal Children’s Hospital
  2300 Tupper St., Suite A-216
  Montréal (Québec) H3H 1P3
  Tel: (514) 412-4420
  Fax: (514) 412-4424

• Centre d’hémophilie - 1re vidéootron
  Hôpital Ste-Justine
  3175, chemin de la Côte Ste-Catherine
  Montréal (Québec) H3T 1C5
  Tel: (514) 345-4931 #6031
  Pagers: (514) 415-5573/5584/5807
  After hours: (514) 345-4788
  Fax: (514) 514-345-7749

• Quebec Centre for Coagulation Inhibitors
  Centre d’hémophilie - 1re vidéootron
  Hôpital Ste-Justine
  3175, chemin de la Côte Ste-Catherine
  Montréal (Québec) H3T 1C5
  Tel: (514) 345-2360
  Fax: (514) 345-4828

• Centre régional de l’hémophilie de l’est du Québec
  Hôpital de l’Enfant Jésus
  1401, 18ave Rue Local J-S066 (sous-sol)
  Québec (Québec) G1J 1Z4
  Tel: (418) 649-5624
  Fax: (418) 649-5996
  After hours: (418) 649-0252

NEW BRUNSWICK

• South East Regional Health Authority Hemophilia Clinic
  135 MacBeath Avenue
  Moncton, New Brunswick E1C 6Z8
  Tel: (506) 857-5465 / 857-5467
  Pager: (506) 558-7158
  Fax: (506) 857-5464

• Inherited Bleeding Disorder Clinic
  Saint John Regional Hospital
  P.O. Box 2100,
  400 University Avenue
  Saint John, New Brunswick E2L 4L2
  Tel: (506) 648-7286
  Fax: (506) 648-7379

NOVA SCOTIA

• Pediatric Bleeding Disorder Clinic
  IWK Health Centre
  PO Box 9700
  6th Floor Ambulatory IWK Site
  5850 University Avenue
  Halifax, Nova Scotia B3K 6R8
  Tel: (902) 470-8752 / 470-8819
  Pager: (902) 470-8888 #1982
  After hours: (902) 470-8394
  Fax: (902) 470-7208

• Hereditary Bleeding Disorders Program (Adult)
  Victoria General Hospital Site
  Queen Elizabeth II Health Sciences Centre
  Rm: 4020 Centennial Building
  5820 University Avenue
  Halifax, Nova Scotia B3H 1V8
  Tel: (902) 473-5612
  Fax: (902) 473-7596

NEWFOUNDLAND

• Eastern Health Corporation
  Health Sciences Centre
  Janeway Site, Room 2J755
  300 Prince Philip Drive
  St. John’s, Newfoundland A1B 3V6
  Tel: (709) 777-4388
  Fax: (709) 777-4292
acetaminophen A drug used to relieve pain. A common brand name is Tylenol®. Acetaminophen does not affect platelet function and is safe for use in people with hemophilia.

acetylsalicylic acid (ASA) The active ingredient in Aspirin® and many other over-the-counter pain relievers and cold remedies, such as Entrophen®, Anacin®, Norgesic®, 222’s, 282’s, CoricidinCold®, Coricidin D®, Robaxisal® and Midol®. This drug affects platelet function and should not be used in people with hemophilia.

activated partial thromboplastin time A basic screening test for clotting problems. However, it is not very reliable in the diagnosis of mild and moderate hemophilia A.

amniocentesis A test used to detect abnormalities in the foetus. A small sample of fluid from the amniotic sac inside the womb is taken out, using a needle. The amniotic fluid contains cells from the foetus, which are examined for defects.

anaesthesiologist A physician who specializes in controlling pain and consciousness during surgery.

annovulatory cycle An anovulatory cycle is a menstrual cycle in which ovulation fails to occur.

antibody A substance produced in the blood by the body’s immune system to defend against other harmful substances.

anti-diuretic A substance that makes the body retain water.

anti-fibrinolytic A drug (Cyklokapron) that helps to hold a clot in place once it has formed by stopping the activity of an enzyme, called plasmin, which dissolves blood clots.

aromatherapy A therapy that involves the use of essential oils and other aromatic compounds from plants for the purpose of affecting a person’s mood or health.

arthritis Inflammation of the joint. In addition to inflammation of the synovial lining, there is also damage to the cartilage and bones of the joint surfaces. In hemophilia, arthritis is caused by repeated bleeding into the joint cavity.

AHCDC The Association of Hemophilia Clinic Directors of Canada.

Ayurvedic medicine A practice used in India for thousands of years that not only focuses on the physical aspects of health but also on the balance between the physical, emotional, spiritual and psychological self.

bleeding disorder A disease in which the body is unable to form blood clots as quickly or as effectively as normal. The family of bleeding disorders includes, hemophilia A, hemophilia B, von Willebrand disease, platelet function disorders and a variety of rare factor deficiencies. The disorder may be hereditary or acquired.

bleeding time The time required for a minor cut to stop bleeding.

blood clotting The process of forming a permanent clot to repair a damaged blood vessel. It includes four steps: vasoconstriction, platelet aggregation, platelet adhesion, and the formation of a fibrin plug.

blood clotting proteins Substances that circulate in the bloodstream, necessary in blood clotting. They include factors I, II, III, V, VII, VIII, IX, X, XI, XII, XIII and von Willebrand factor.

blood platelets Tiny cell fragments, less than 1/10,000 of a centimetre in diameter, circulating in the blood. There are 150 to 400 billion platelets in a normal litre of blood. Platelets are first to arrive at the site of a break in a blood vessel wall. They play an important role in stopping bleeding by clumping together, thereby beginning the repair of injured blood vessels.

blood type The particular kind of blood each person has. The types are A, B, AB and O.

botanical medicine A practice in which medicines are delivered in the form of plants.

CANHC The Canadian Association of Nurses in Hemophilia Care.

carrier A woman whose chromosomes include the gene for hemophilia. She can transmit hemophilia to her sons. Her daughters can be carriers.
CHS The Canadian Hemophilia Society

chromosome A long chain of chemicals known as DNA, which is arranged into hundreds of units called genes. Genes determine such things as the colour of a person’s eyes.

chorionic villus sampling A type of pre-natal testing for hemophilia. A very small sample of the chorionic villus (part of the placenta) from inside the womb is taken out and tested in the lab.

Christmas Disease Another term for hemophilia B or factor IX deficiency, named after Stephen Christmas, a Canadian with hemophilia who was the first person to be diagnosed with the disorder.

classical hemophilia Another term for hemophilia A or factor VIII deficiency.

clotting factor concentrate A lyophilized preparation of clotting proteins, which is dissolved in sterile water for infusion to correct a coagulation disorder. The concentrates can be manufactured from human plasma or by recombinant technology. Concentrates exist to correct deficiencies in factors I, II, VII, VIII, IX, X, XI, XIII and von Willebrand factor.

clotting factor modification A process by which the factor VIII or IX molecules are intentionally modified to make them better for the treatment of hemophilia, for example, by extending their half-life.

clotting factor purification The manufacturing steps whereby factor VIII or IX proteins are separated from other substances including bacteria and viruses in a series of physical and chemical purification processes.

clotting factor therapy The treatment in which clotting factors are infused into the bloodstream of a person with hemophilia to replace those that are missing, and temporarily correct the coagulation disorder. Also called factor replacement therapy.

coaulation A complex process that makes it possible to stop torn blood vessels from bleeding. The four stages in the coagulation process are vasoconstriction, platelet adhesion, platelet aggregation and the formation of a fibrin plug by clotting factor proteins.

coagulation cascade The chain reaction in which clotting factors, which are tiny plasma proteins, link to form a chain, called fibrin, around the platelets at the site of a break in a blood vessel wall.

coaulation laboratory A laboratory which is specialized in doing the many tests needed to correctly diagnose the different coagulation disorders, including hemophilia A and B.

coaulation testing The many tests needed to correctly diagnose the different coagulation disorders, including hemophilia A and B.

comprehensive care All of the medical services needed by a person with hemophilia and his/her family for the treatment of bleeding and related conditions. This care is provided at a Hemophilia Treatment Centre.

comprehensive care team The team of people involved in the care of a person with hemophilia. They include a medical director, nurse coordinator, physiotherapist, social worker, caregiver and patient or family member. Other health professionals are added to the team as needed.

cyklokapron An anti-fibrinolytic drug (tranexamic acid) that helps to hold a clot in place once it has formed by stopping the activity of an enzyme, called plasmin, which dissolves blood clots.

desmopressin A synthetic drug which is a copy of a natural hormone. It acts by releasing VWF stored in the lining of the blood vessels. Desmopressin is not made from blood. It can be called DDAVP, Octostim, Octostim Spray and Stimate Nasal Spray.

dilatation & curettage (D&C) An operation is to scrape and clean the lining of the uterus.

direct mutation testing A test to identify the presence of the actual hemophilia mutation.

dNA deoxyribonucleic acid DNA works as the building blocks of our genetic make-up. The DNA in each chromosome is arranged in thousands of units called genes. Each one of the genes directs the body to produce certain proteins, including clotting proteins.

dNA linkage studies The technique of following markers (or normal variations in the DNA) which are within and/or surround the hemophilia gene. Linkage analysis may be able to provide information about carrier status, with a certain degree of probability.
DNA polymorphism testing A test for genetic markers (or polymorphisms) that are close to, and follow, the mutant genes that cause hemophilia.

DNA testing A process to discover if a woman is a carrier of hemophilia. There are two kinds of DNA testing: DNA polymorphism testing and direct mutation testing.

dysmenorrhea Pain during the menstrual period.

endometriosis A condition in which endometrial tissue forms outside the uterus, for example, around the abdomen. When a woman menstruates, endometrial tissue, wherever it is in the body, bleeds.

epidural A type of local anaesthesia in which a needle is placed into the spine to freeze the lower part of the body.

episiotomy A procedure sometimes done during childbirth in which the skin is cut near the vagina to avoid tearing.

epistaxis Bleeding from the nose.

factor VIII A protein in the blood that is essential for clotting. Factor VIII levels are low in people with hemophilia A.

factor VIII deficiency hemophilia See hemophilia A.

factor IX A protein in the blood that is essential for clotting. Factor IX levels are low in people with hemophilia B.

factor IX deficiency hemophilia See hemophilia B.

factor assay A test done to measure the level of clotting factors in the bloodstream of a person. The standard used is 100%. People without hemophilia vary between 50% and 150%. People with severe hemophilia A or B have less than 1% of the normal quantity of factor VIII or IX.

factor concentrates See clotting factor concentrates.

factor purification See clotting factor purification.

factor replacement therapy See clotting factor therapy.

fibrin clot The clot which forms in the last stage of the coagulation process.

gamete intra-fallopian transfer A technique in which gametes (the female’s eggs and the male’s sperm) are washed and placed via a catheter directly into the woman’s fallopian tubes.

gene Tiny structures of DNA which determine such things as the colour of a person’s eyes. Hemophilia is caused by an abnormal gene on the sex chromosome.

gene therapy A treatment involving the delivery of a normal copy of the clotting factor gene to the patient’s cells.

genetic counsellor A person who understands genetic testing and is trained to work with couples who are planning to have a baby, or who are already pregnant.

genetic disorder A disease that is caused by a gene that does not work normally. Genetic disorders like hemophilia can be passed from generation to generation.

geneticist A person who studies genes and how people inherit diseases.

genetic mutation The specific mistake in the gene.

genetics The study of how genes are passed from one generation to the next.

gonadal mosaicism This occurs when a part of the gonadal cells of an organism have different genotype than the rest of the cells, usually because of a mutation that occurred in an early stem cell that gave rise to all or part of the gonadal tissue. If these cells have sustained a new mutation that causes a heritable disease like hemophilia, then it is possible for two healthy parents to have an offspring suffering from the disease.

gynaecologist A physician who specializes in the woman’s reproductive system.

half-life The time taken for half of the infused clotting factor activity to disappear from the bloodstream of a person with hemophilia.

hemarthrosis A bleed into a joint.

hematologist A physician specializing in diseases of the blood.

hematology The medical specialty dealing with diseases of the blood.
hematology laboratory A laboratory that does a wide range of blood tests.

hematoma A localized swelling filled with blood resulting from a break in a blood vessel.

hematuria Blood in the urine, caused by bleeding in the kidneys.

hemoglobin A substance in the red cells of blood, responsible for carrying oxygen.

hemophilia A term used to describe bleeding disorders caused by low levels of factor VIII or IX (hemophilia A and B). The term can also be used more broadly to describe the family of bleeding disorders, including VWD.

hemophilia A Genetic disorder characterized by frequent bleeding into joints, muscles and tissues. The prolonged bleeding is caused by low levels of factor VIII. The disease is also called classical hemophilia and factor VIII deficiency.

hemophilia B Genetic disorder characterized by frequent bleeding into joints, muscles and tissues. The prolonged bleeding is caused by low levels of factor IX. The disease is also called Christmas Disease and factor IX deficiency.

hemophilia treatment centre (HTC) A medical clinic that provides comprehensive care for people with hemophilia.

hemorrhage The escape of blood from blood vessels, either on the surface of the body or internally.

hepatitis A An acute viral disease transmitted because of poor hygiene or dirty water.

hepatitis B A viral disease which in 5% to 10% percent of cases becomes chronic. It is transmitted by sexual contact and the exchange of contaminated needles. In very, very rare cases it can still be transmitted by fresh blood components.

hepatitis C A viral disease which in 60% to 80% percent of cases becomes chronic. It is transmitted by the exchange of contaminated needles. In very, very rare cases it can still be transmitted by fresh blood components.

hepatologist/gastroenterologist A physician specializing in diseases of the liver.

home care The care of the person with hemophilia at home, rather than in hospital. This includes the home administration of desmopressin or factor concentrate by the person with hemophilia or a family member.

homeopathy A practice that uses gentle remedies to support a person’s natural homeostatic forces.

hormone A secretion in the blood that stimulates organs into action.

hormone therapy The administration of oral contraceptives or other hormones (progesterone) to raise factor VIII levels or reduce menstrual bleeding.

hysterectomy An operation to remove the uterus.

immune tolerance therapy The therapy to attempt to get rid of inhibitors in hemophilia A. Also called tolerization.

infusion The administration of clotting factor concentrates intravenously using a syringe and butterfly needle, or using a central venous access device, such as a port-a-cath.

inherited condition A disorder which is caused by a genetic mutation and which is transmitted from one, or both, of the parents to the child at the time of conception.

inhibitors Antibodies produced to eliminate factor VIII or IX or other clotting factor proteins, seen as foreign by the body’s immune system.

intravenous Into the vein.

in-vitro fertilization The technique in which eggs are retrieved from the woman and fertilized in the laboratory with the sperm from the woman’s partner.

iron deficiency anemia A condition caused by low hemoglobin levels because of blood loss, leading to fatigue and lack of energy.

joint bleed Caused by a tear in the synovium, blood escapes from the blood vessels and gradually fills the joint cavity.

joint disease Synovitis and arthritis. This disease in hemophilia is caused by repeated bleeding into joints. It is most common in knees, ankles and elbows.

laparoscopy An operation to remove endometrial tissue that has formed outside the uterus.
lyonization The process in which a woman’s X gene that has the hemophilia mutation dominates the normal X gene in the production of factor proteins. This is also called X-inactivation. Lyonization leads to factor levels below 50% of normal.

menometrorrhagia Heavy bleeding at irregular intervals during the menstrual cycle.

menopause The time in a woman’s life when menstrual periods permanently stop.

menorrhagia Bleeding during the menstrual cycle which is heavier than normal or lasts longer than normal.

metrorrhagia Bleeding throughout the menstrual cycle.

mid-cycle pain Pain occurring during ovulation, which can be due to bleeding from the ovary at the site of ovulation.

mild hemophilia A genetic coagulation disorder characterized by bleeding after trauma or surgery. The level of factor VIII or IX in the bloodstream is from 5% to 40% of normal.

moderate hemophilia A genetic coagulation disorder characterized by bleeding after minor injury, more serious trauma or surgery. The level of factor VIII or IX in the bloodstream is from 1% to 5% of normal.

mucous membrane An extension of the skin inside the body - for example, the insides of the mouth, the nose, the intestines (the gut) and the uterus (the womb).

mutant gene A gene with a mistake in its structure.

mutation The specific mistake in the gene.

mutation analysis The process of analyzing the DNA to find the specific change in either the factor VIII or factor IX gene that is responsible for hemophilia.

naturopathic medicine A practice that focuses on prevention and uses natural methods to promote healing.

nurse coordinator A key member of the comprehensive care team. Usually she/he is the coordinator of the comprehensive care team. She/he schedules appointments, answers patients’ telephone calls, performs infusions at the clinic and teaches people about hemophilia.

obligate carrier The daughter of a man with hemophilia who is necessarily a carrier.

obstetrician A physician who specializes in conception, pregnancy and childbirth.

oophorectomy An operation to remove the ovaries.

partial thromboplastin time A routine blood test which often gives normal results in people with bleeding disorders.

pediatrician A doctor who takes care of children, from birth to age 18.

perimenopause The period in a woman’s life before natural menopause, when her hormones are “in transition.” It is characterized by a gradual decrease in progesterone and estrogen, but hormone fluctuations are common. This period can last from 3-10 years before menopause.

physiotherapist A key member of the comprehensive care team. The physiotherapist is a person who is trained to keep a person’s muscles and joints healthy. She/he can give advice on how to prevent or limit bleeding. She/he can help patients to understand what a bleed is, whether a bleed is serious or not, and what to do to get better after each muscle or joint bleed. The physiotherapist can also give advice on how to be active and physically fit.

physiotherapy The use of exercise to stay fit or rehabilitate weakened muscles and damaged joints.

plasma The portion of blood that contains clotting factor proteins, including factor VIII and IX, as well as immunoglobulins and albumin.

plasmin A substance in the blood that dissolves blood clots after the blood vessels have healed.

platelets Small cells less than 1/10,000 of a centimetre in diameter circulating in the blood, which stick to and spread on the walls of the damaged blood vessel to promote clotting.
platelet adhesion The clumping together of platelets at the site of a tear in a blood vessel wall.

platelet aggregation By emitting chemical signals calling for help from other platelets and from clotting factors, like factor VIII and factor IX, the spreading platelets release substances that activate other nearby platelets which then clump at the site of blood vessel injury to form a platelet plug.

potential carrier A woman whose mother is known to be a hemophilia carrier. The daughter has a 1-in-2 chance of being a true carrier.

pre-implantation genetic diagnosis The technique in which a biopsy of a single cell of the embryo is conducted to determine if it is affected by hemophilia. This done in combination with in-vitro fertilization.

prophylaxis Regular infusions of clotting factor concentrates, usually 1, 2 or 3 times a week. This is done in order to prevent bleeding episodes from happening.

prothrombin time A routine blood test which gives normal results in people with mild hemophilia.

recombinant A series of procedures used to join together (recombine) DNA segments. In hemophilia, this process combines the human gene for making factor VIII or IX with the cell lines of the Chinese hamster ovary or baby hamster kidney to manufacture clotting factor concentrates.

self infusion The administration of clotting factor concentrates by the person with hemophilia himself. This is done intravenously using a syringe and butterfly needle.

severe hemophilia A genetic coagulation disorder characterized by spontaneous bleeding and bleeding after minor injury, more serious trauma or surgery. The level of factor VIII or IX in the bloodstream is less than 1% of normal.

social worker A key member of the comprehensive care team. The social worker’s job is to help parents, siblings and the child himself deal with the impact that hemophilia can have on their lives.

thrombin A substance that aids in blood clotting, formed by a chain reaction of clotting factor proteins.

tolerization The therapy to attempt to get rid of inhibitors in hemophilia A. Also called immune tolerance therapy.

tranexamic acid An antifibrinolytic drug (Cyklokapron®) that helps to hold a clot in place once it has formed by stopping the activity of an enzyme, called plasmin, which dissolves blood clots.

uteroablation An operation to destroy the lining of the uterus. The operation is performed through the vagina. The uterine lining is burned away.

vasoconstriction The first stage in blood clotting in which the blood vessel constricts to reduce the flow of blood to the damaged area.

viral inactivation The process used to kill or eliminate viruses that might be present in plasma-derived blood products. Chemical techniques such as treatment with solvent detergents, and physical techniques such as heat treatment, filtration and other purification technologies, are used.

von Willebrand disease (VWD) A family of inherited diseases in which the blood clots more slowly than normal.

von Willebrand factor (VWF) The clotting protein that is deficient in VWD. The VWF is either present at lower than normal levels or it does not work properly.

VWF: antigen The test that measures the level of von Willebrand factor.

X-inactivation The process in which a woman’s X gene that has the hemophilia mutation dominates the normal X gene in the production of factor proteins. This is also called lyonization. X-inactivation leads to factor levels below 50% of normal.


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