14 Symptomatic Carriers of Hemophilia

This chapter provides answers to these questions:

- What is a carrier of hemophilia?
- How does a woman become a carrier of hemophilia?
- How are carriers of hemophilia diagnosed?
- What is a symptomatic carrier?
- What is the range of clotting factor levels for symptomatic carriers?
- What types of bleeding can occur in symptomatic carriers?
- How is bleeding in symptomatic carriers managed?
- How does being a symptomatic carrier affect a person's quality of life?
- What should be done to ensure that a carrier gets proper medical care?
- Are there specialized programs for carriers of hemophilia?

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Introduction

Being a carrier of hemophilia can have a significant impact on a person's health, well-being and quality of life. This chapter describes the symptoms and types of bleeding that can occur in carriers. It also explains the different diagnostic tests, treatment options and resources available to women with bleeding disorders. Carriers can develop bleeding problems at different stages such as menstruation, pregnancy or childbirth. Therefore, it is recommended that carriers be followed at a hemophilia treatment centre (HTC) or a multidisciplinary clinic for women with bleeding disorders.

■ What is a carrier of hemophilia?

A *carrier of hemophilia* is a female who has an abnormal X chromosome carrying the hemophilia gene. One of her two X chromosomes has a mutation of the factor VIII or factor IX gene, resulting in decreased levels of clotting factor VIII or IX, respectively. Carriers often do not show symptoms of hemophilia because although one X chromosome is abnormal, the other X chromosome generally works as normal to produce factor VIII or IX. However, some carriers do experience bleeding problems and this can affect their physical and/or emotional well-being and their quality of life.

A female who has a factor VIII or IX gene mutation is called an *obligate carrier of hemophilia*. Most obligate carriers produce almost normal amounts of factor VIII and IX. This protects them from having bleeding problems and symptoms of hemophilia.

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About 20 per cent of obligate carriers have factor VIII or IX levels that are below the normal range. These carriers can have symptoms similar to mild hemophilia. Some carriers have symptoms similar to severe hemophilia but this is quite rare. A female who has lower than normal clotting factor levels and has symptoms of factor deficiency is called a *symptomatic carrier of hemophilia*.

Recent research shows that carriers can have bleeding problems even if their factor levels are close to or within the normal range. For these reasons, carriers of hemophilia should be followed at a HTC.

You are a **possible carrier of hemophilia** if you are the:

- daughter of a carrier of hemophilia
- mother of a child with hemophilia and no one else in the family has hemophilia or is a carrier of hemophilia
- sister, mother, maternal grandmother, aunt, niece or cousin of a female carrier of hemophilia or a male with hemophilia

You are an **obligate carrier of hemophilia** if you are the:

- daughter of a man with hemophilia
- mother of a child with hemophilia and at least one other person in the family has hemophilia (brother, maternal grandfather, uncle, nephew or cousin)
- mother of a child with hemophilia and have a family member who is a carrier of hemophilia (mother, sister, maternal grandmother, aunt, niece or cousin)
- mother of two or more children with hemophilia

You are a **symptomatic carrier of hemophilia** if:

- your factor VIII or IX level is below the normal range or within the lower range of normal and you have symptoms similar to mild hemophilia

Did you know...

that one-third of cases of hemophilia are the result of new genetic mutations?

☞ *See also "**What is a symptomatic carrier?**" and "**What is the range of clotting factor levels for symptomatic carriers?**" later in this chapter.*

How does a woman become a carrier of hemophilia?

Females have two X chromosomes (XX). Males have an X chromosome and a Y chromosome (XY). The genes that produce factor VIII and IX are part of the X chromosome. Hemophilia is passed from generation to generation in a family through the X chromosome. An abnormal X chromosome can be inherited from a father who has hemophilia or a mother who carries a hemophilia gene and therefore is a carrier.

Clotting factor levels in carriers are independent of the severity of hemophilia in related males. In fact, even carriers within the same family can have very different factor levels, ranging from very low to normal.

Genetic mutation inherited from father who has hemophilia

If a man with hemophilia has a boy with a woman who does not carry a hemophilia gene (both her X chromosomes are normal), the child will not have hemophilia. This is because he inherits his Y chromosome from his father and a normal X chromosome from his mother. However, if the child is a girl, she will carry the hemophilia gene. This is because she inherits her father's abnormal X chromosome with the hemophilia gene and a normal X chromosome from her mother. A female who carries a hemophilia gene is called an obligate carrier. If she shows symptoms of hemophilia, she is a symptomatic carrier.

Possible outcomes when the father has hemophilia and the mother does not carry a hemophilia gene.

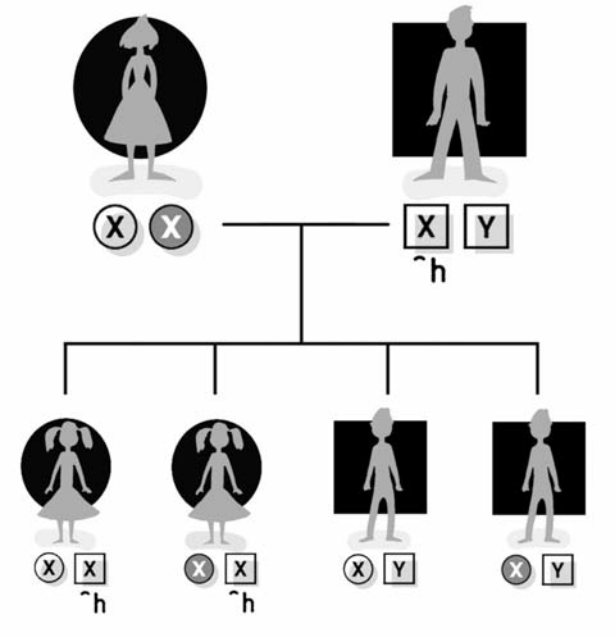

Figure 1

Genetic mutation inherited from mother who is a carrier

If a woman who is a carrier (one of her two X chromosomes is abnormal because it carries a hemophilia gene) has a child with a man who does not have hemophilia, there is a 50 percent chance that the child will inherit the mother's abnormal X chromosome (and equally a 50 percent chance that the child will not inherit the abnormal X chromosome — inheriting the mother's normal X chromosome instead). The 50 percent chance of inheriting the mother's abnormal X chromosome applies equally whether the child is a boy or a girl. If a boy inherits his mother's abnormal X chromosome, he will have hemophilia. If a girl inherits her mother's abnormal X chromosome, she will also be a carrier. If she shows symptoms of hemophilia, she is a symptomatic carrier.

"Prior to our son being born we hoped he'd be unaffected… but he has hemophilia. We've had great support and no issues we couldn't handle."

Possible outcomes when the father does not have hemophilia but the mother is a carrier.

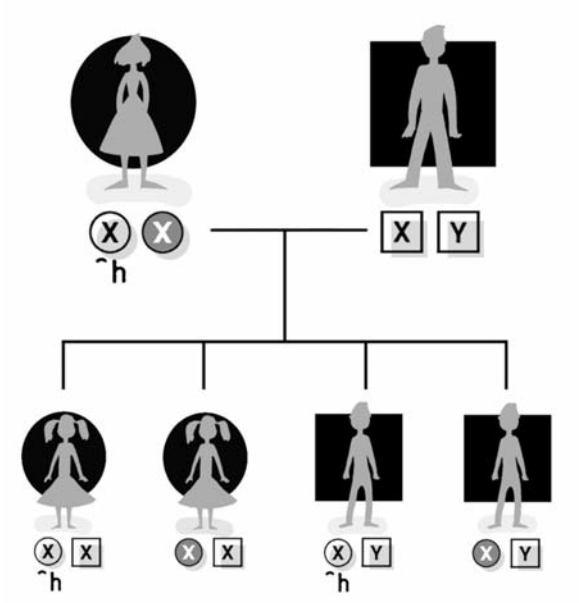

Figure 2

For more information on the inheritance of hemophilia, see **Chapter 2, How A Child Gets Hemophilia.**

How are carriers of hemophilia diagnosed?

Different types of tests are used to measure a potential carrier's factor levels and to test for carrier status. Access to proper diagnostic testing at a hemophilia treatment centre is essential. This is because some carrier tests are very sensitive and must be properly done to ensure an accurate diagnosis.

"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."

The following tests are used in the diagnosis of carriers of hemophilia:

- **Factor VIII clotting assay –** This test measures the amount of factor VIII clotting activity in the blood. Having normal clotting factor activity does not guarantee that someone is not a carrier. That's because most carriers have factor levels within the normal range (defined here as above 40%) while only about 20 percent of carriers have factor levels below the normal range. This test does not determine beyond all doubt whether a female is a carrier. However, it can help determine whether a female is at greater risk of having bleeding problems because her factor VIII clotting activity level is close to or below the normal range (her clotting factor activity level is between 40% and 60%).

  Many factors can affect the results of a factor VIII clotting assay. High hormone levels during pregnancy or from taking oral contraceptive pills can increase factor VIII levels. Factor VIII levels can also be affected by physical and mental stress, exercise and infections. While it is impossible to avoid all of these influences, they should be taken into consideration.

- **Factor IX clotting assay –** This test measures the amount of factor IX clotting activity in the blood. Test does not determine beyond all doubt whether a female is a carrier. However, it can help determine whether a female is at greater risk of having bleeding problems because her factor IX clotting activity level is close to or below the normal range (her clotting factor activity level is between 40% and 60%). Factor IX clotting activity levels are not affected by hormones, stress, exercise and infection the way that factor VIII clotting activity levels can be affected.

- **von Willebrand factor antigen test (VWF antigen) –** The VWF antigen test measures the amount of von Willebrand factor in the blood. This test is done so as to rule out von Willebrand disease as the cause of low factor VIII levels or as the cause of bleeding in hemophilia A.

- **Genetic testing –** Genetic testing determines the exact factor VIII or IX gene mutation in a carrier. This test can identify the specific hemophilia mutation in 90 to 99 percent of cases. This type of test can be used for prenatal diagnosis to determine whether or not a fetus carries the genetic mutation, inherited from a father with hemophilia or a mother who is a carrier. Results are most predictable if DNA from a family member who has hemophilia is available. DNA is the building block of genes and can be extracted from a blood sample.

  Genetic testing for hemophilia is covered by provincial health insurance. Females who are identified as obligate carriers because they have a parent with an abnormal X chromosome (a father with hemophilia or a mother who is a carrier), or as possible carriers because there is a family history of hemophilia (a male member of the family has previously been identified with hemophilia or a female family member has shown symptoms of bleeding problems) are eligible for DNA testing. Genetic testing is complex and not available in all HTCs; when available, it may take many months to get results.

"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."

- **Mutation analysis –** This test involves laboratory analysis of the genes responsible for hemophilia. The test looks for changes in either the factor VIII or factor IX gene. If the specific gene mutation in the person with hemophilia is known, accurate carrier testing by mutation analysis can be carried out on female family members. When the mutation can be identified (in 90 to 99 percent of cases), mutation testing is 100% accurate.

  The laboratory begins the analysis by looking for the most common type of mutation in hemophilia — an *inversion* in factor VIII (half of males with severe hemophilia A have an inversion in their factor VIII gene). If an inversion is not found, then the laboratory needs to do further testing looking for other less common mutations, which may be more complex and time-consuming.

- **DNA linkage analysis –** If the specific mutation is not known, DNA linkage analysis is the next step. This involves following DNA markers (genetic markers) that are either within and/or surround the hemophilia gene. Linkage analysis is not direct testing — it does not identify the specific mutation or clotting factor activity level. However, DNA linkage analysis can provide information about the specific "pattern" of the factor VIII or IX gene mutation. This genetic pattern provides information about carrier status with a certain degree of probability. DNA samples from family members, both with and without hemophilia, are necessary.

Before any type of factor clotting assay or genetic testing, a potential carrier should have a complete physical examination and review of her personal and family medical history.

What is a symptomatic carrier?

"I was so focused on my son's condition that I never thought about my own symptoms and the need to be registered at an HTC."

A symptomatic carrier is a female who has the abnormal gene that causes hemophilia A or B and who also experiences a bleeding tendency. About 1 in 10 carriers have factor VIII or IX levels that are lower than normal. In rare cases, the factor level will be very low. Carriers with factor levels of 5% to 40% have bleeding tendencies similar to males with mild hemophilia. Carriers with factor levels lower than 4% have bleeding tendencies similar to men with moderate to severe hemophilia.

In general, the lower the factor level, the more susceptible a carrier is to bleeding problems. Approximately 20 percent of carriers are symptomatic to some degree, including some who have near normal factor clotting activity (40% to 60%).

☞ *For more information on the genetic causes of carriers of hemophilia, see "***How does a woman become a carrier of hemophilia?***" earlier in this chapter and* **Chapter 2, How A Child Gets Hemophilia**.

What is the range of clotting factor levels for symptomatic carriers?

Normal clotting factor activity in the average person (a non-carrier who does not have a bleeding disorder) is said to be 100%. People who do not have a bleeding disorder can have a factor level anywhere from 50% to 150% — this is considered the normal range.

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Carriers have clotting factor levels ranging anywhere from 5% to 200% of normal. The average factor level among carriers is 60%. Although a level of 40% is usually used as the upper limit for defining mild hemophilia, recent research has shown that carriers can have bleeding symptoms similar to mild hemophilia even if their factor levels are close to normal (within the range of 40% to 60%). Carriers with even lower levels can experience more severe bleeding symptoms.

The level of clotting factor that a carrier produces results from the balance between her normal X chromosome and her abnormal X chromosome carrying the hemophilia gene. This balance is determined by a genetic process called *lyonization* or *X-inactivation*, whereby either one of a carrier's two X chromosomes is randomly inactivated during development.

If the balance favours inactivation of the carrier's normal X chromosome, her factor VIII or IX level will likely be low — that's because the abnormal X chromosome with the hemophilia gene will dominate. However, if the balance favours inactivation of the carrier's abnormal X chromosome carrying the hemophilia gene, her factor VIII or IX level will likely be within the normal range —that's because the normal X chromosome will dominate. If inactivation occurs equally between the normal and the abnormal X chromosomes, the carrier is expected to have 50% factor VIII or IX level. This is because the normal X chromosome should work as normal to produce clotting factors (the normal X chromosome is responsible for producing 50% of the total clotting factor level).

This X-inactivation process is why, although the average carrier is expected to have a 50% factor VIII or IX level, there is actually a wide range of factor levels seen in carriers (from less than 1% to more than 150% of normal).

MYTH:

GIRLS CAN NEVER HAVE SEVERE HEMOPHILIA.

REALITY:

In very rare cases, girls can have severe hemophilia. This is usually caused by lyonization, or X-inactivation.

What types of bleeding can occur in symptomatic carriers?

In general, the severity of the bleeding manifestations in symptomatic carriers is related to the carrier's factor level. So the lower the factor level is, the more severe the carrier's bleeding symptoms are likely to be.

Bleeding in carriers is grouped into two general categories: gynecological and obstetrical bleeding, and other types of bleeding. This chapter focuses on gynecological and obstetrical bleeding since this type of bleeding is particular to carriers and females with hemophilia. Other types of bleeding are described only briefly in this chapter since they are also seen in individuals with hemophilia and are discussed in detail in other chapters.

"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."

☞ *For more information on bleeding symptoms in mild hemophilia, see* **Chapter 4, Management of Bleeds**, *and* **Chapter 9, Mild and Moderate Hemophilia**.

Gynecological and obstetrical bleeding

Heavy/prolonged menstrual bleeding (menorrhagia)

Menorrhagia refers to heavy bleeding during a menstrual period and/or prolonged menstrual bleeding (more than seven days). It is one of the most common gynecological symptoms experienced by carriers of hemophilia. Menstrual bleeding can be heavy in terms of the amount of blood loss during the period and/or due to a prolonged menstrual period (more than seven days). One in three women miss substantial time from school or work due to menorrhagia. It is also a common cause of iron deficiency, anemia and decreased quality of life in affected women. Heavy menstrual bleeding can be especially pronounced when a carrier first starts her period and can sometimes lead to hospitalization.

Abnormal/irregular vaginal bleeding (metrorrhagia)

Metrorrhagia refers to abnormal/irregular bleeding that occurs beyond the normal menstrual period. The abnormal bleeding occurs sometime in the interval between the end of one menstrual period and the beginning of the next, with variations in the duration of bleeding and amount of blood loss. If bleeding is heavy, bed rest and/or hospitalization may be required.

Painful menstruation (dysmenorrhea)

Although some pain during menstruation (menstrual periods) is a common complaint among women in general, about 50 per cent of carriers experience moderate to severe menstrual pain called *dysmenorrhea*. It is possible that heavier menstrual flow contributes to the amount of pain experienced by some carriers during menstruation.

"I'd like to have known about my carrier status much sooner… maybe something could have been done for my heavy periods throughout my life."

Mid-cycle abdominal pain (*mittelschmerz*)

During ovulation at the middle of the menstrual cycle (halfway between the end of the last period and the beginning of the next), carriers and non-carriers alike can experience abdominal pain when the ovaries release a new egg into the fallopian tubes. Mid-cycle abdominal pain is referred to as *mittelschmerz* (the German word for "middle pain"). Carriers of hemophilia are more likely to have mid-cycle abdominal pain than non-carriers due to bleeding at ovulation.

Hemorrhagic ovarian (corpus luteum) cyst

During ovulation, a small amount of bleeding can occur when the egg is released from its follicle (the fluid-filled sac in which an egg develops). This bleeding can cause a type of cyst to form on the ovary, referred to as a *corpus luteum cyst*. Carriers of hemophilia are more likely to have significant bleeding at ovulation. Prolonged bleeding into an ovarian cyst causes it to expand, eventually causing pelvic or abdominal pain. Furthermore, an ovarian cyst is at risk of rupturing around the time of menstruation, causing internal bleeding and sudden pain in the lower abdomen. This is called a *hemorrhagic ovarian cyst*.

Bleeding into the abdominal cavity (hemoperitoneum)

Bleeding can occur into the pelvic tissues and ligaments, and sometimes into the abdominal and pelvic cavity. This is called *hemoperitoneum*. Bleeding into the abdominal and pelvic cavity is a serious and possibly life-threatening situation, and requires urgent medical attention.

Bleeding after childbirth (post-partum bleeding)

Carriers of hemophilia A and B are at risk of heavy bleeding with childbirth. However, bleeding complications during pregnancy are unusual. In fact, factor VIII levels increase and low levels in carriers often normalize during pregnancy due to the favourable effect of pregnancy hormones. This is not the case though for factor IX levels, which usually remain unchanged throughout pregnancy. In general, the risk of hemorrhage within the first 24 hours following childbirth is four to five percent for non-carriers. This risk increases to 22 percent for carriers.

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Carriers of hemophilia A and B are also at higher risk of having delayed hemorrhage following childbirth (bleeding that occurs after the first 24 hours after childbirth). About 11 percent of carriers experience delayed bleeding after childbirth compared to 1 percent of women in the general population.

Delayed bleeding in carriers of hemophilia A typically occurs 5 to 10 days after childbirth, when the carrier's factor VIII returns to its baseline level. However, delayed bleeding can sometimes occur after 10 days and up to two weeks post-delivery. Carriers of hemophilia B can also experience delayed bleeding although factor IX levels remain unchanged during pregnancy and after childbirth.

"I wasn't surprised when I got the carrier results. Growing up, I was prone to nosebleeds and bruised easily, and I suspected it was somehow related to hemophilia."

Other types of bleeding

A symptomatic carrier has a higher tendency to bleed than the average person. Symptomatic carriers generally have bleeding symptoms similar to those seen in males with mild hemophilia. These symptoms include:

- Easy bruising
- Prolonged bleeding from minor wounds
- Prolonged nose bleeds (epistaxis)
- Prolonged bleeding after tooth extraction
- Significant bleeding after trauma or surgery

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Bleeding into joints and into muscles is not very common in carriers of hemophilia except in cases where the factor level is very low (less than 4%). Carriers with factor levels below 4% can have bleeding patterns similar to those seen in males with moderate and severe hemophilia. However, some carriers with factor levels above 4% can have joint and muscle bleeds following relatively minor trauma. Recent research has shown that the risk of prolonged bleeding (more than five minutes) from small wounds or after surgery can be twice as high for symptomatic carriers than for non-carriers from the same family.

☞ *For more information, see* **Chapter 9, Mild and Moderate Hemophilia.**

How is bleeding in symptomatic carriers managed?

Did you know...

that 57% of carriers of hemophilia A and B experience heavy, prolonged menstrual bleeding?

The symptoms and types of bleeding that carriers have in common with males with hemophilia are treated in the same way. But symptomatic carriers can also experience gynecological and obstetrical types of bleeding. These are distinctly different from the bleeding symptoms seen in males with hemophilia, and require particular attention and treatment.

Treatment for gynecological and obstetrical bleeding

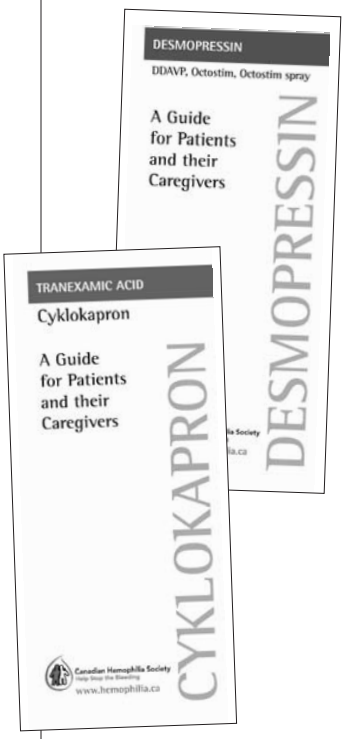
Treatment of menorrhagia and metrorrhagia

The treatment of menorrhagia and metrorrhagia for carriers is similar to the treatment for non-carriers — except that the use of anti-inflammatory drugs such as ibuprofen (Advil®) is not recommended for carriers because they increase bleeding. Other medical treatment options for menorrhagia are either hormonal or non-hormonal. These treatment options should be considered on an individual basis taking into account the carrier's age, gynecological issues and reproductive plans. If bleeding is heavy and prolonged, bed rest and/or hospitalization may be required.

- **Hormonal treatment –** Carriers who would like to preserve fertility but do not foresee a pregnancy in the near future should consider hormonal treatment. Hormones can be used alone or in combination with non-hormonal treatment. The most common hormonal approaches include the combined oral contraceptive pill (estrogen and progestin), progestins alone, or the levonorgestrel intrauterine system (Mirena® IUS). The levonorgestrel intrauterine system (Mirena® IUS) is a device that is implanted into the uterus to control menstrual bleeding through the release of hormones into the lining of the uterus. Hormones help decrease the thickness of the lining of the uterus thus decreasing menstrual bleeding.

- **Antifibrinolytic medication –** Carriers who wish to preserve fertility and also plan to get pregnant soon, can be given non-hormonal treatment. This generally consists of the use of antifibrinolytic drugs such as tranexamic acid (Cyklokapron®) and/or desmopressin (DDAVP). Antifibrinolytic drugs prevent the rapid breakdown of blood clots, a natural bodily process that appears to be increased in women with heavy menstrual bleeding.

- **Desmopressin (DDAVP) –** This medication helps raise factor VIII levels by increasing von Willebrand factor. Carriers who do not respond to treatment with antifibrinolytics and DDAVP, including carriers with severe factor deficiency, should be treated with factor concentrates. (Another antifibrinolytic agent is epsilon amino caproic acid — also called Amicar® or EACA — but this product is no longer available in Canada.)



"I didn't know about the possibility that I could bleed after surgery."

- **Surgical treatment –** Carriers who have completed childbearing and do not wish to preserve fertility can consider hormonal and non-hormonal treatments as well as surgical approaches. Surgical approaches include removal of the lining of the uterus (*endometrial ablation*) and removal of the uterus (*hysterectomy*). Surgical options should especially be considered for women who have abnormalities of the uterus or for carriers who have not responded to other types of treatment. It is imperative to properly prepare the patient before surgery to prevent bleeding complications following the surgical procedure.

Treatment of dysmenorrhea and *mittelschmerz*

Treatment of painful menstrual periods and mid-cycle abdominal pain in the general female population usually involves anti-inflammatory drugs such as ibuprofen (Advil®) but these should be avoided in carriers. Pain medication such as acetaminophen (Tylenol®) and parecetomol and codeine-based medications (Empracet® and Tylenol® with codeine) can be used since they do not increase bleeding. Combined oral contraceptives and the levonorgestrel intrauterine device (Mirena® IUS) also reduce pain during menstruation, possibly by decreasing blood flow.

Treatment of hemorrhagic ovarian cysts

Hemorrhagic ovarian cysts are best managed conservatively without surgery in carriers of hemophilia using an antifibrinolytic agent such as tranexamic acid (Cyklokapron®), DDAVP or factor concentrates. The combined estrogen and progestin oral contraceptive pill can be used to suppress ovulation and prevent recurrences.

Treatment of abdominal bleeding (hemoperitoneum)

Bleeding into the abdominal cavity usually requires treatment with factor concentrates. Occasionally, when there is only a small amount of abdominal bleeding, treatment with DDAVP can be given but must be closely monitored.

Childbirth and post-partum bleeding

Management of bleeding of carriers of hemophilia during childbirth is best carried out using a multidisciplinary approach. Carriers who are at risk of severe bleeding during childbirth should ideally be referred for prenatal and obstetrical care at a medical centre where there are specialists in high-risk obstetrics and a hematologist with expertise in hemostasis. Gynecological and obstetrical care for carriers is available through most hemophilia treatment centres, and some HTCs now have a multidisciplinary clinic for women with bleeding disorders.

Prior to giving birth, all carriers should meet with an anesthetist to discuss pain control options for the delivery. Decisions on treatment prior to delivery should be based on the coagulation studies in the third trimester. If coagulation parameters and factor levels are normal by the time of delivery, regional anesthesia (*epidural*) is considered safe. DDAVP can be used to increase factor VIII levels in carriers of hemophilia A whose levels are not normalized at term. Factor concentrates should be considered in carriers with very low factor levels prior to delivery. In general, 50% factor VIII and IX levels are recommended prior to delivery.

It is also recommended to keep factor levels above 50% for three days following vaginal delivery or five days following delivery by caesarean section. Hemorrhage immediately after childbirth is managed with DDAVP and/or antifibrinolytics agents (tranexamic acid). Factor concentrates are usually only necessary when bleeding is severe or does not respond to first line treatments. Delayed hemorrhage after childbirth is usually managed with

DDAVP, hormones and /or antifibrinolytic agents (tranexamic acid). Carriers who have a high risk of bleeding after childbirth can be given oral contraceptives or tranexamic acid to prevent bleeding. Counselling and early medical consultation are essential for optimal treatment of post-partum bleeding.

The mode of child delivery in carriers of hemophilia is controversial. Most experts have long considered vaginal delivery as the standard for carriers of hemophilia. Recently, caesarean section has been revisited as an alternative to vaginal delivery for carriers of babies with severe hemophilia. The risk and benefits of vaginal delivery versus caesarean section for carriers should be considered on an individual basis taking into account both maternal and fetal factors. Ideally this decision should be discussed with a multidisciplinary team of an HTC.

Treatment for other types of bleeding

Bleeding symptoms in carriers similar to those seen in males with mild hemophilia (nose bleeds, bleeding from minor cuts, and bleeding after surgical and dental procedures) are treated in the same way. Antifibrinolytic agents such as tranexamic acid (Cyklokapron®) are generally sufficient to treat these types of bleeding. Antifibrinolytic agents can also be used to prevent bleeding due to surgical and dental procedures, used either alone in carriers of hemophilia A or B or in combination with DDAVP in hemophilia A carriers. DDAVP helps raise factor VIII levels by increasing von Willebrand factor.

Carriers who do not respond to treatment with antifibrinolytics or DDAVP are treated with factor VIII or IX concentrates. Factor concentrates can also be used to prevent bleeding in carriers with severe factor deficiency, especially before major surgery. The treatment approach for bleeding in these carriers should be individualized for each patient following discussion with the care team.

☞ *For more information on the treatment of mild bleeding, see* **Chapter 9, Mild and Moderate Hemophilia**.

How does being a symptomatic carrier affect a person's quality of life?

The quality of life experienced by symptomatic carriers is affected by a number of variables. Quality of life is a subjective measurement that depends on the individual experience of each carrier, her support system and her attitude towards life. Factors that can affect quality of life include:

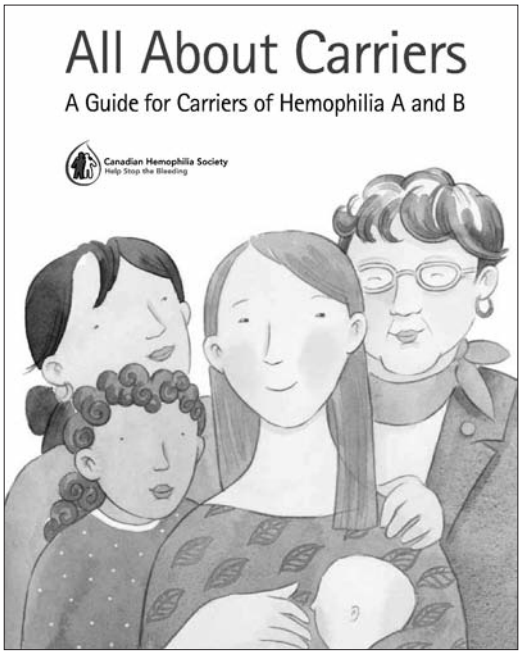
- The age at which a carrier is diagnosed — a younger person generally has more time to adjust to the information than someone who is only diagnosed after the birth of her first child.
- The carrier's history of bleeding symptoms such as frequent nose bleeds, easy bruising or heavy menstrual periods, and whether the bleeding problems have affected her school, work and/or social life for a long time.
- The length of time for the diagnosis of carrier status to be made, which can sometimes be a long and frustrating journey through an uninformed healthcare system.
- The attitudes within a family with a history of bleeding disorders regarding the diagnosis of a carrier in the family.

The reality of the impacts of being a carrier of an inherited bleeding disorder should not be minimized. The consequences are far-reaching, from the health issues for symptomatic carriers to the impact on a young couple considering whether to have children, and the emotions such as guilt and sadness experienced by some mothers who have children with hemophilia.

"My daughter was only six when she was diagnosed, and she was very pleased to be a part of her brother's hemophilia."

Fortunately, once contact has been made with a hemophilia treatment centre, they will have access to clear, accurate information and proper treatment. Through contact with the various members of the care team, the carrier and her immediate or extended family members (depending on her age and wishes) will be able to gain control of many of the challenges presented by her medical condition. Through the HTC, she will also have the opportunity to learn about resources offered by the Canadian Hemophilia Society at the national and local levels, as well as information available through other related organizations.

As a carrier understands more about her condition, gains access to the treatment options available to women with bleeding disorders, and develops a trusting relationship with the care team, she will gain confidence in her ability to manage the bleeding disorder. With time, she will learn ways to minimize the impact of being a carrier on her quality of life. Eventually, if she has a child who has hemophilia or is a carrier, she will also be able to pass along a strong, confident attitude and optimism about living with a bleeding disorder.



What should be done to ensure that a carrier gets proper medical care?

Get appropriate care and treatment

It is important for carriers of hemophilia to get appropriate care and treatment to help control and prevent many of the bleeding problems that can affect them. This is important no matter what the carrier's age, but especially so when it comes to bleeding related to gynecological and obstetrical problems. In most cases, an appropriate treatment strategy can effectively reduce bleeding symptoms that have a significant impact on a carrier's quality of life, such as menstrual pain, menorrhagia and anemia. This frees the carrier from many uncomfortable and painful symptoms and potential bleeding problems, and allows her to have a better quality of life.

The ideal approach for treating carriers of hemophilia relies on a strong and collaborative relationship between the patient, her physician and the HTC team. It is important for carriers to remember that there are medical experts available who can provide good treatment and advice on how to manage their bleeding problems.

For most carriers, the simple diagnosis of a factor VIII or IX deficiency and their specific factor level is very helpful. Then they can become informed about preventive and treatment measures. It is important to remember that at any age, carriers can require medical treatment following a serious injury or surgery. For example, a child having surgery such as tonsillectomy or adenoidectomy (common procedures in children) would likely need treatment with factor concentrate and/or DDAVP before the procedure.

"When I found out that I was a carrier I was shocked and scared but at the same time it made my bleeding issues and problems with pregnancies understandable."

The HTC team should be consulted if any prolonged or unexpected bleeding occurs. Referrals to other departments (ear/nose/throat, dentistry, gynecology and obstetrics, etc.) should be coordinated by the HTC so that the hematologist can explain the appropriate treatment for the carrier.

Register at a hemophilia treatment centre

It is important for carriers to register at a hemophilia treatment centre, even if the carrier does not have abnormal bleeding symptoms. Registering at an HTC allows her to:

- Get accurate information about hemophilia and being a carrier from the comprehensive care team.
- Get appropriate blood tests and genetic testing and counselling that can only be done at specialized centres.
- Work out a treatment plan with the care team including guidelines for emergency care, or preventive treatment.
- Have access to up-to-date information and the newest treatments related to carriers.
- Learn about the latest research on hemophilia.

Some carriers of hemophilia sometimes decide not to register themselves or their daughters at an HTC fearing that this could cause problems with health insurance coverage. There can also be cultural or religious beliefs and circumstances that prevent a potential carrier from seeking carrier testing. For example, being a carrier of hemophilia can sometimes be a stigma that affects marital opportunities or the spousal relationship. A frank discussion with the HTC team will allow parents or the carrier to make an informed decision regarding carrier testing.

"We consulted the HTC for my daughter's heavy periods and bleeding after tooth extraction. Despite her levels being fairly high, we felt heard and supported."

☞ *For more information on carrier and prenatal testing see* **Chapter 2, How A Child Gets Hemophilia**.

Get informed and take control

Diagnosis and knowledge of the options and strategies for treating female bleeding symptoms (menorrhagia, dysmenorrhea, hemorrhagic ovarian cysts, post-partum bleeding, etc.) allow carriers and family members to make informed decisions. This knowledge also allows a carrier to control how the bleeding disorder affects her quality of life and actively participate in her own medical care.

Are there specialized programs for carriers of hemophilia?

Hemophilia treatment centres have recently come to recognize the importance of having an expert team to deal with the types of bleeding specific to carriers (such as menorrhagia, dysmenorrhea, postpartum bleeding, etc.). Some HTCs now have a multidisciplinary clinic for women with bleeding disorders.

Multidisciplinary clinic for women with bleeding disorders

The following healthcare professionals are the key team members of a multidisciplinary clinic for women with bleeding disorders:

- hematologist
- gynecologist
- obstetrician
- nurse coordinator

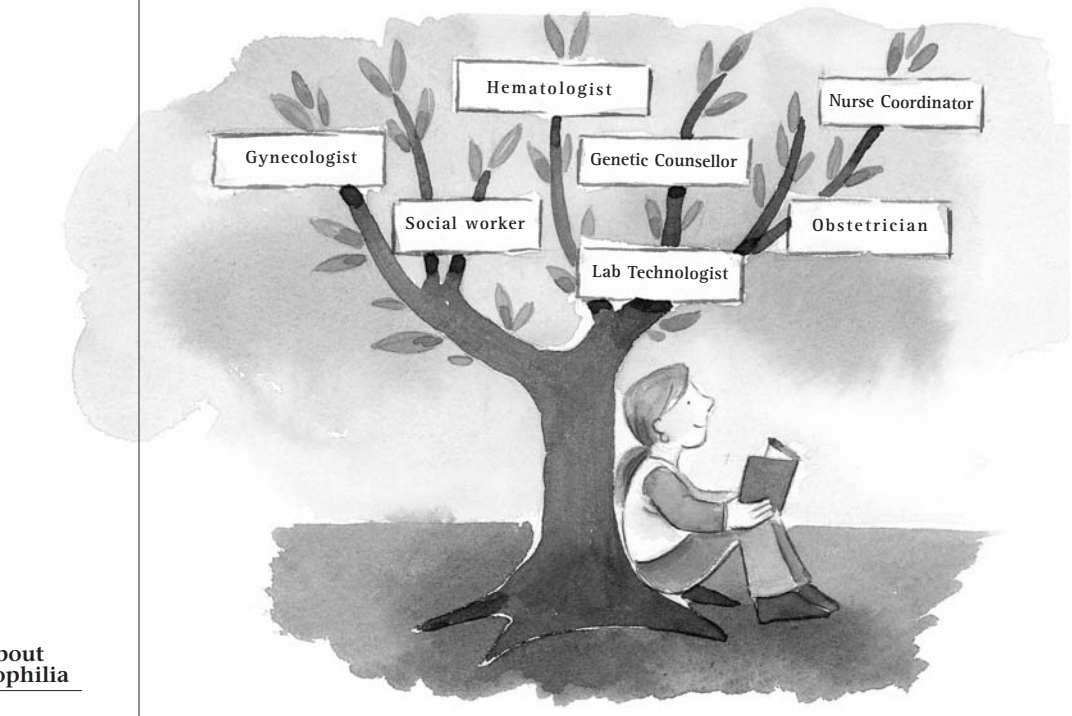
The multidisciplinary team will meet with the carrier and/or her family members to plan a treatment approach, and provide support and advice to the family physician.

"It is very important for women to understand that just because they haven't had any problems, doesn't mean they won't in the future: registering at an HTC could prevent disasters, such as in the case of an accident or emergency surgery."

14 Symptomatic Carriers of Hemophilia

The general objectives of a multidisciplinary clinic for women with bleeding disorders are to:

- Improve quality of life for women with bleeding disorders.
- Create a forum for discussion and the exchange of information among hematologists, nurses and other health professionals with expertise in women's bleeding disorders.
- Advance knowledge about treatment for women's bleeding disorders.
- Inform and educate physicians, carriers and women with bleeding disorders as well as the general public.



Specific objectives are to:

- Provide appropriate diagnostic testing and follow-up for women with bleeding problems and accurately identify underlying gynecological and hematological diseases.
- Provide appropriate treatment and preventative care for women with bleeding disorders.
- Reassess patient treatment strategies regularly.
- Avoid unnecessary surgery.
- Avoid unnecessary use of blood products.
- Inform women with bleeding disorders about how they need to prepare for anesthesia, surgery, pregnancy, childbirth and postpartum care.
- Provide genetic and psychological counselling and support.

All carriers of hemophilia should be referred by their physician to an HTC multidisciplinary clinic for women with bleeding disorders, if one exists in their region. However, while a multidisciplinary clinic for women is the ideal model, many hospitals have yet to officially integrate such a clinic into their HTC. In this case, carriers can be seen and followed individually at the HTC, and referred to the gynecology department as needed. The HTC team then works closely with the gynecologist or obstetrician to develop a treatment plan to address the carrier's specific bleeding symptoms and problems.

"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."

Conclusion

Health professionals are becoming more and more aware of the bleeding problems experienced by carriers of hemophilia. This has helped improve awareness of women's bleeding disorders and access to treatment. Anyone who thinks she may be a carrier of hemophilia, or whose doctor suspects she may possibly have a bleeding disorder, should go to a hemophilia treatment centre for proper diagnosis, treatment and follow-up care.