FACTOR X DEFICIENCY

AN INHERITED BLEEDING DISORDER

AN INFORMATION BOOKLET

Canadian Hemophilia Society
Help Stop the Bleeding

Canadian Association of Nurses in Hemophilia Care
Association Canadienne des Infirmieres et Infirmiers en Hemophilie

Acknowledgements

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This booklet provides general information on factor X deficiency only. The Canadian Hemophilia Society does NOT practice medicine and does not suggest specific treatments. In all cases, we suggest that you speak with a doctor before you begin any treatment.

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Introduction

Factor X (pronounced 10) deficiency is a very rare blood coagulation disorder with complications that vary with the severity of the disorder. This deficiency is not well known, even among health professionals. People affected by this deficiency and those close to them have very little written information about it. This booklet therefore seeks to provide information for people trying to cope with this health problem. It explains the causes of the deficiency, symptoms, possible complications, and available treatments.

Discovery

Two independent research groups identified factor X deficiency for the first time during the 1950s. In 1956 Telfer and his colleagues reported a young 22-year-old patient named Prower who presented bleeding problems because of a factor X deficiency; in 1957, Hougie and his colleagues then described an abnormal coagulation profile in a 36-year-old male.

Laboratory experiments conducted at the time showed that mixing samples of blood from Prower and Stuart did not correct the coagulation problem. This lead to the understanding that the two individuals were lacking the same coagulation factor. This missing coagulation factor was named Stuart-Prower Factor. It is now known simply as factor X.

What is factor X?

Factor X is a protein in the blood. It plays a key role in the coagulation cascade, the chain reaction that is triggered when a blood vessel is damaged. Blood is carried throughout the body in a network of blood vessels. When we are injured, the blood vessels may break at the surface, as in the case of a cut. Or they can break deep inside the body, causing a bruise or 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 components responsible for coagulation come together to form a plug at the break. Coagulation factors are required to hold the plug (or homeostatic plug) in place and form the permanent clot.

There are four steps involved in forming a plug:

Step 1 The blood vessel is damaged.

Step 2 The blood vessels contract to restrict the blood flow to the damaged area.

Step 3 The platelets stick to the walls of damaged vessels and spread out, which is called *platelet adhesion*. These platelets then emit chemical signals that activate other nearby platelets so that they clump together at the site of the damage in order to form a plug, the *homeostatic plug*. This is called *platelet aggregation*.

Step 4 The surface of these activated platelets forms a base on which blood coagulation can take place. The coagulation proteins circulating in the blood (including factor X) are activated at the surface of the platelets to form a fibrin clot which looks something like a mesh. This is the permanent clot. (See **Figure 1**)

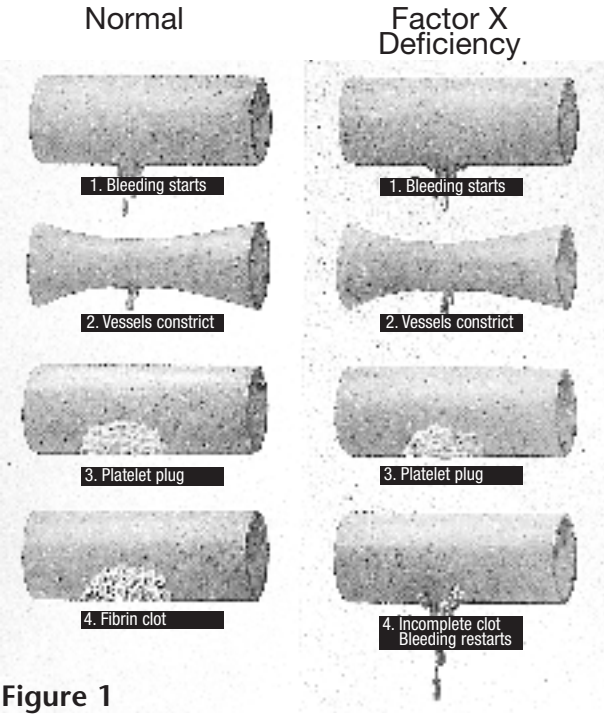

Figure 1

These proteins (Factors I, II, V, VIII, IX, X, XI, XII and XIII, as well as Von Willebrand factor) are triggered in a kind of domino effect, a chain reaction that is called the coagulation cascade.
(See **Figure 2**)

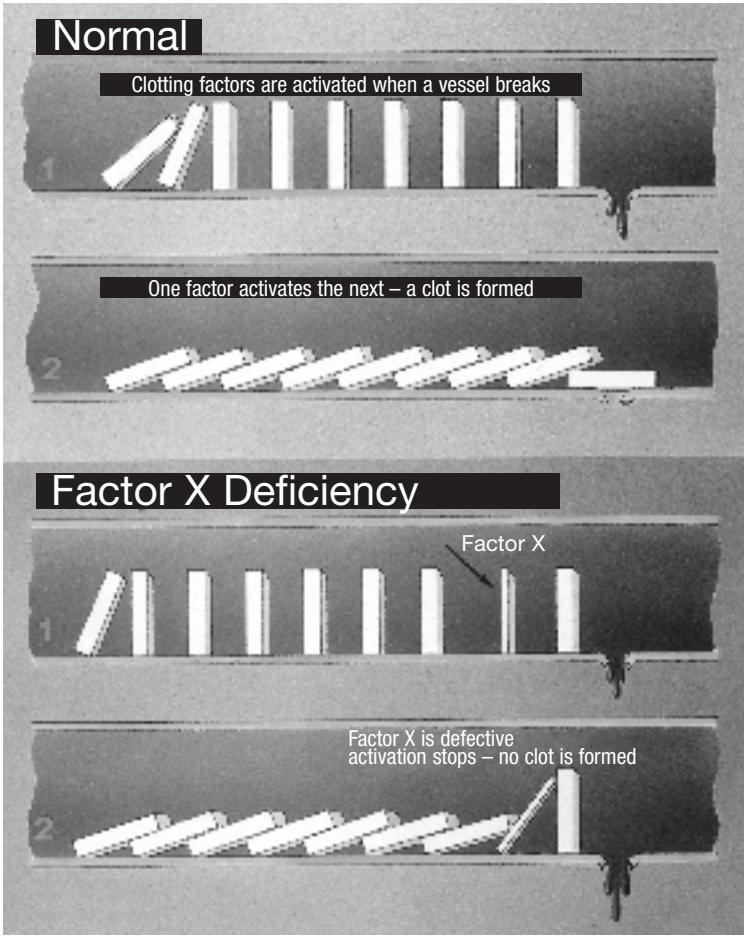

Figure 2

Activation by contact

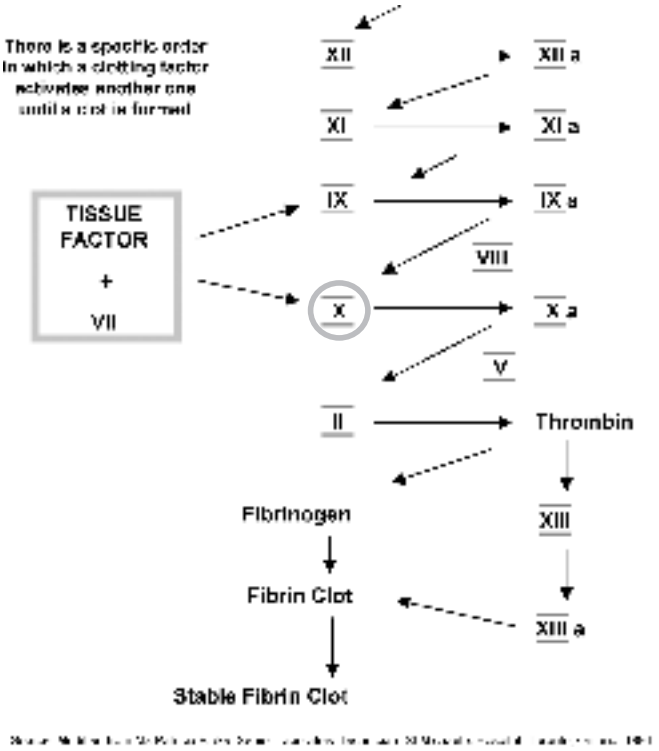

Figure 3

Take a look at **Figure 3**. It is a good illustration of the coagulation cascade. Factor X is activated by other coagulation factors (XII becomes XIIa, XI – XIa, IX- IXa, VIII and lastly, X). Note that Factor IXa normally activates FX to FXa (a – stands for activated). Factor Xa then activates other blood proteins, including FV, and Factor II (prothrombin) which is converted to thrombin. This chain reaction allows the coagulation process to continue.

If one of the coagulation factors is absent or deficient, the chain reaction is broken, and the bleeding is not controlled.

Is factor X deficiency common?

No, FX deficiency is extremely rare. Actually, it is considered the rarest of all coagulation deficiencies. To date, only 50 cases have been identified worldwide. It is estimated that the deficiency affects fewer than 1 in 500,000 people.

Factor X deficiency is more common in parts of the world where there is more consanguinity (marriages between people in a single family).

How is factor X deficiency inherited?

Factor X deficiency is an inherited bleeding disorder. It is passed from parent to child at the time of conception. It is an *autosomal recessive* disorder. This means that each parent must pass on a defective gene in order for the child to manifest the disorder. When only one of the two parents is a carrier of the gene responsible for factor X deficiency and it is passed on to a child, the child will not be affected.

A carrier is someone who carries the defective gene without being affected by the disorder. In order for a person to be affected by factor X deficiency, he or she must have inherited two defective genes, one from the mother and one from the father. Both parents must therefore be carriers.

If a person inherits the defective gene from only one of the parents, he/she will be a carrier. His/her factor X level will be lower than normal. Symptoms of the disease may be absent or only slightly present.

Each cell of the body contains structures called chromosomes. A chromosome is a long chain of chemicals known as DNA. This DNA is arranged into about 30,000 units called genes. These genes determine such things as the colour of a person's eyes. In the case of factor X deficiency, one of these genes has a defect. The defective gene in factor X deficiency is on a chromosome that does not decide the sex of the child. This means that factor X deficiency can affect females as well as males.

The five illustrations below show how FX deficiency can be passed on for each pregnancy.

Figure 4 shows what can happen when both parents are carriers. There is one chance that the child will be normal, one chance that it will have the disorder, and there are two possibilities that the child will be a carrier.

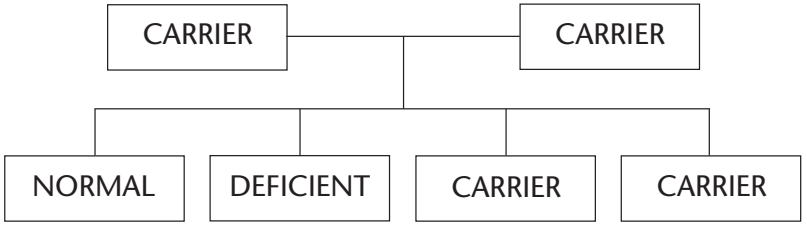

Figure 4

Figure 5 shows what can happen when both parents have FX deficiency. All their children will also have FX deficiency.

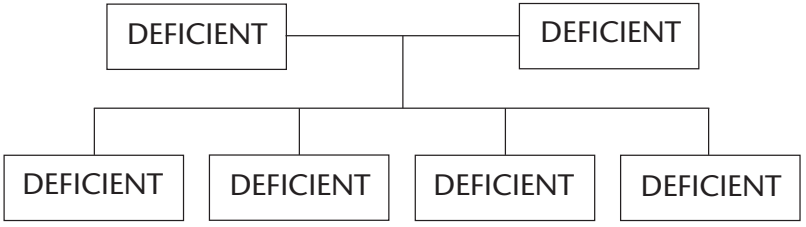

Figure 5

Figure 6 shows what can happen when one of the parents has the disorder and the other is normal. All their children will be carriers of FX deficiency.

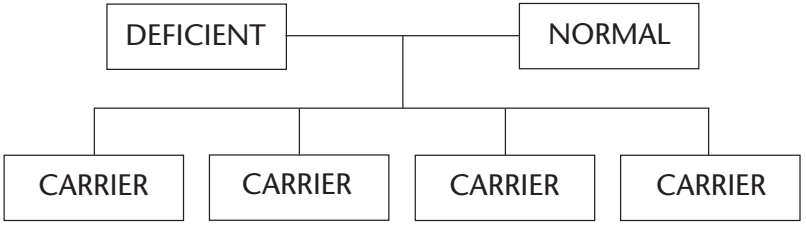

Figure 6

Figure 7 shows what can happen when one of the parents is a carrier and the other is normal. There are two possibilities that the child will be a carrier and two possibilities that it will be normal.

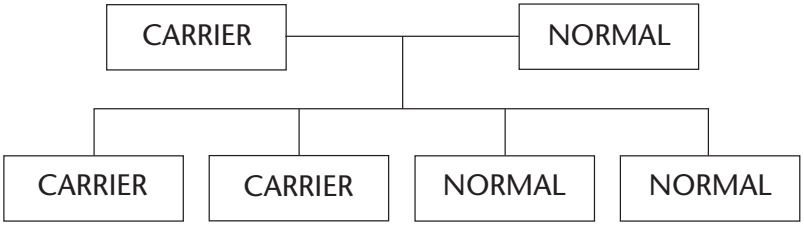

Figure 7

Figure 8 shows what can happen when one of the parents has the disorder and the other is a carrier. There are 2 possibilities that the child will have the disorder and 2 possibilities that it will be a carrier.

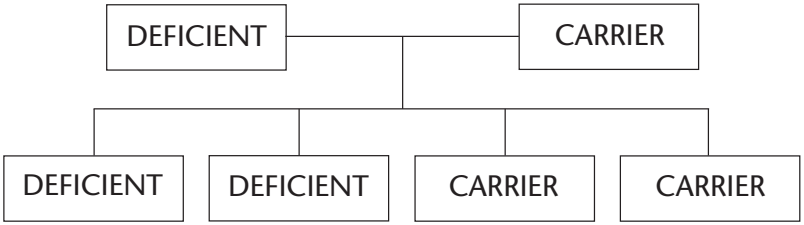

Figure 8

Note: *There is another form of factor X deficiency that is not inherited (from birth) but is acquired. There are various causes. Since factor X is synthesized by the liver, severe liver disorders may be involved, as well as a reduction of vitamin K produced by intestinal flora. Other causes, such as burns in children, topical application of thrombin, and leukemia, have also been reported. Under these conditions, over a lifetime a person can develop antibodies that destroy the body's own factor X. This bleeding disorder is also extremely rare.*

What tests are done to diagnose factor X deficiency?

When someone presents symptoms that suggest there may be a bleeding disorder, doctors will usually prescribe a series of tests to determine whether the person:
1. has a coagulation disorder; and
2. if so, what kind?

To identify factor X deficiency the following blood tests are used:

a. Prothrombin time (PT, also called INR). In the event of a factor X deficiency the result of this test is abnormal.
b. If prothrombin time is abnormally long, the physician will then ask for a Factor X assay to determine the level present in the blood.
c. Tests of family members

Symptoms of factor X deficiency

The symptoms are different for each individual. However, we can assume that the lower the FX level, the more severe the symptoms.

FX LEVEL	SYMPTOMS
More than 10% of normal FX in blood	Little bleeding
1 to 10% of normal FX in blood	Light to moderate bleeding
Less than 1% of normal FX in blood	Severe bleeding

The main symptoms are as follows:

- bleeding from the umbilical cord (frequent)
- bleeding after circumcision
- bleeding into joints
- nosebleeds
- internal hemorrhaging (bruises) at the slightest trauma
- bleeding into soft tissues and muscles
- gastrointestinal bleeding (stomach and intestines)
- increased and longer menstrual bleeding
- blood in urine (hematuria)
- intracranial bleeding
- spontaneous abortion in the first quarter
- bleeding in mothers after childbirth
- bleeding during and after surgery
- bleeding after a trauma

Intracranial bleeding is quite rare in persons with FX deficiency. However, when it does occur, it has a tendency to recur.

Similarly, persons with FX deficiency will not necessarily have bleeding into their joints, although those who do have bleeding may develop long-term complications.

Recognizing Bleeding

It is strongly recommended that people who suffer from FX deficiency learn to recognize the signs and symptoms of bleeding that can threaten their lives or the integrity of a limb so that they can react adequately and in a reasonable time.

People with a light to moderate deficiency should pay special attention to this. They often show little concern, since their symptoms are fairly rare, and they tend to forget their condition. As a result, they are more at risk of not recognizing a major bleed.

The following information describes the main kinds of bleeding that can occur in persons affected by coagulation disorders. The information is taken in part from a Canadian Hemophilia Society publication, *All About Inhibitors*.

TYPE OF BLEEDING	SIGNS AND SYMPTOMS	RECOMMENDATIONS
HEAD (bleeding in the brain is very serious)	• headache • blurred or double vision • nausea and vomiting • mood or personality changes • drowsiness • loss of balance • loss of fine motor coordination • loss of consciousness • seizures	All unusual signs and symptoms should be reported to the medical team so treatment can be given as soon as possible.
NECK	• pain in the neck or throat (swelling, difficulty swallowing, difficulty breathing)	A throat infection could cause bleeding.
CHEST	• pain in the chest • difficulty breathing • coughing, blood in spittle	This kind of bleeding is extremely rare.
ABDOMEN (stomach)	• pain in the abdomen or lower back • nausea or vomiting • blood in the urine • blood in the stool or black stool	All signs and symptoms of this nature should be reported to the medical team so treatment can be provided as soon as possible.
SOFT TISSUE	• redness in the affected area • a bruise increases in size (hematoma) • pain	
JOINT	• pain when a limb is used or even at rest, not necessarily with a bruise (hematoma) • joint swelling and warmth • child agitated or cries when moving a joint • loss of mobility in a joint, hesitation moving, especially in children	Improperly treated and/or poorly healed bleeding can lead to chronic disorders such as hemophilic arthritis.

Treatment

Treatment consists of intravenous administration of blood products. The following table lists the different products used, suggested dose, counter-indications, recommendations for pregnancy and, lastly, a few warnings.

PRODUCT	DOSAGE	COUNTER-INDICATIONS	DURING PREGNANCY	WARNINGS
Fresh frozen plasma	Attack dosage: 10 to 20 ml/kg intravenous Maintenance dosage: 3 to 6 ml/kg intravenous every 12-24 hours	Hypersensitivity documented Known allergy	Usage safe during pregnancy	Viral contaminations and infection are possible but not very probable owing to screening tests performed on blood products
Prothrombin concentrates are concentrates made from "pooled" human plasma. They contain FII, VII, IX and X; C proteins; and a small amount of heparin to protect against thrombosis (clot formation)	Dosage must be set according to the severity of bleeding; Usual dosage: 50 to 125 IU/kg. Maximum: 2 to 3 doses in the first 36 – 48 hours because of risk of thrombosis		Safety not documented for use during pregnancy	Risk of thrombotic complications and hypersensitivity reaction Do not use with antifibrinolytic agents
Vitamin K	Used mainly for patients with an acquired FX deficiency			

As in the case of anyone with a rare bleeding disorder, treatment in the home is a possibility. Affected people (or parents of an affected child) can learn to self-administer coagulation factor (or administer it to a child) at home if their condition requires it. It is impossible to make general recommendations on this aspect of care, given that the condition is so rare. However, it is important that the affected individual discuss this possibility with his or her care team.

Similarly, it may be advisable to keep enough factor concentrate at home so that if the patient needs to go to the emergency room, he or she will have an initial dose of product to start control of bleeding.

Visiting the emergency room

If the person thinks that he or she is bleeding, it is important to contact the hemophilia/bleeding disorder treatment centre. Outside opening hours, the person should go to the emergency room. Because factor X deficiency is an extremely rare condition, the duty physician may not be very familiar with managing this bleeding disorder. Consequently, to prepare for a visit to the emergency room, it is strongly suggested to bring along all documents that can explain the condition and the recommended treatment. If an initial dose of coagulation factor is on hand, do not leave it at home. Measures like this will make the trip to the emergency room go much more smoothly. The number one goal is to always control bleeding episodes as soon as the first symptoms appear.

Problems specific to women

Pregnancy in women affected by rare bleeding disorders (such as FX deficiency) is often associated with spontaneous abortion, detachment of the placenta, and premature childbirth.

Researchers Kumar and Mehta (1994) have documented four pregnancies in a woman with factor X deficiency. Her first two pregnancies resulted in the birth of two premature babies at 21 and 25 weeks. Both babies died during the neonatal period. She received fresh frozen plasma for acute bleeds during the two pregnancies. In addition, during her second pregnancy, the mother received prothrombin complex concentrate (PCC – containing factor X) as a preventive measure during the last two terms of her pregnancy.

At the very start of the third and fourth pregnancies, she received prothrombin complex concentrate as a preventive measure. She then gave birth to two babies at 34 and 32 weeks of gestation. Both children survived.

Women may also present abundant and longer menstruations (menorrhagia). When bleeding is abundant, various treatments, such as oral contraceptives or tranexamic acid (Cyclokapron), may be useful. Tranexamic acid (Cyclokapron) is taken orally to help stabilize the clot and better control bleeding.

Some women may have to use FIX concentrate (PCC or prothrombin complex) to control menstrual flow. These women can learn how to self-infuse with concentrate, which they can then administer themselves either when menstrual flow is abundant, or regularly at each menstruation. The benefits and risks of self-infusion should be discussed on an individual basis. We again stress the fact that it is impossible to make any recommendations, given the rare nature of the condition. A “case by case” analysis is thus essential.

Healthy living

The recommendations for healthy living are the same as for anyone with or without a coagulation factor deficiency:

- Follow a regular program of physical activity suited to lifestyle and capability. Maintaining adequate muscle mass can reduce the risk of bleeds.
- Use high quality sports equipment appropriate for any sport (helmet, elbow pads, kneepads, proper shoes, etc.). The most often recommended sports are swimming and cycling.
- Eat a well-balanced diet; maintain normal weight.
- Get enough sleep.
- Drink alcohol in moderation only.
- Don't smoke.

It is important to mention that contact sports like boxing, football, and hockey should be avoided due to the risk of serious injury.

Prevention

Never take aspirin. Aspirin increases the risk of bleeding by inhibiting platelet function.

Consult the healthcare team before taking any herbal medicinal supplements or vitamins and so-called natural products sold over the counter.

Take care of teeth in order to avoid having drastic dental care as far as possible. See the dentist regularly. The hemophilia treatment centre can recommend dentists who are familiar with coagulation disorders.

If surgery or any other invasive procedure (a procedure in which there is an intrusion into the body with an instrument) is necessary, contact the treatment centre in advance to obtain adequate preventive treatment.

Wear a *MedicAlert* bracelet or chain at all times on which the type of coagulation problem is engraved.

If planning a trip, let the hemophilia treatment centre know. They will tell you what precautions to take.

Always stay in touch with the hemophilia treatment centre.

Vaccination

The Canadian Paediatric Society publishes regular updates on recommended vaccinations for children. We feel that it is important to follow these recommendations. However, certain precautions should be taken to avoid a bleed at the site of an injection. The nurse at the Hemophilia Treatment Centre can provide information about precautions to take.

Additional vaccination

It is recommended that anyone likely to receive blood derivatives as part of a treatment be vaccinated against hepatitis A and B. This is a simple, effective, available and readily accessible preventive measure.

As a result of different viral inactivation procedures, today's blood derivatives are considered safe. However, one can never be too careful, so this recommendation should not be ignored.

The comprehensive care team

As the name suggests, a hemophilia comprehensive care team provides most of the medical services required by a child or adult with an inherited bleeding disorder.

The team is composed of several professionals, including:

- a medical director, usually a hematologist
- a nurse coordinator
- a physiotherapist
- a social worker
- a psychologist
- a pediatrician

The team works closely with other specialists – a surgeon, an orthopedist, a rheumatologist, a dentist, and a geneticist, among others. The purpose of this multidisciplinary team is to ensure the well being of the patient and, in the case of a child, the parents as well.

Conclusion

Factor X deficiency is an extremely rare, inherited or acquired bleeding disorder. It affects both men and women, as well as people of all races and ethnic origins.

Those affected by the condition may experience life-threatening bleeds. However, treatments now exist that make it possible to control bleeds.

It is essential that people affected by this deficiency be medically followed in a treatment centre that specializes in bleeding disorders, such as a hemophilia treatment centre.

For more information

You can obtain a list of Hemophilia Treatment Centres by contacting the National Office of the Canadian Hemophilia Society at the following address:

Canadian Hemophilia Society
625 President-Kennedy Avenue
Suite 505
Montréal, Québec H3A 1K2
Telephone: (514) 848-0503
Toll free: 1-800-668-2686
Email: chs@hemophilia.ca
Web site: www.hemophilia.ca

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Bleeding Disorders Info Center, www.hemophilia.org

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Canadian Hemophilia Society
Help Stop the Bleeding

Canadian Association of
Nurses in Hemophilia Care
Association Canadienne des
Infirmieres et Infirmiers en Hemophilie