FACTOR VII 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 infirmières et infirmiers en hémophilie

Second Edition
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PREFACE

We are pleased to present the second edition of the information booklet *Factor VII deficiency: An inherited bleeding disorder*.

This booklet has been written in order to inform people with factor VII deficiency and their families about the disorder.

The information presented in this document was accurate at the time of publication. The authors and editors do not assume responsibility for any problems that may arise related to its practical clinical application.
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Introduction

Learning that you have factor VII deficiency is not easy. Learning your child has this disorder can be even more difficult. Feelings of insecurity and frustration are common. To make it even more challenging, factor VII deficiency is a very rare disease.

This booklet has three main goals. The first is to provide individuals with factor VII deficiency and their families with information on the disease and its treatment. The second goal is to raise awareness of the signs and symptoms of bleeding. Thirdly, it describes the comprehensive care team, just in case there are any problems.

This booklet will not provide you with all the answers you need. As medical care must always be personalized, your best source of information is the comprehensive care team at your bleeding disorder treatment centre. Nevertheless, it can serve as a reference that we hope will be useful and help people with factor VII deficiency deal with the disease.
How factor VII deficiency is genetically inherited

Factor VII deficiency is an inherited bleeding disorder. It is passed on from parent to child at conception. The bleeding problem is caused by an abnormal gene.

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 VII deficiency, one of the genes on chromosome 13 has a defect.

The defective gene in factor VII deficiency is on a chromosome that does not decide the sex of the child. This means that factor VII deficiency can affect females as well as males. In this way, it is unlike other bleeding disorders such as factor VIII deficiency, also called hemophilia A or classic hemophilia, in which the defective gene is sex-linked – and therefore primarily affects males.

A carrier is a person who carries a single defective gene but is not affected by the disease. In order for a person to inherit factor VII deficiency, one parent must have severe factor VII deficiency and the other parent must be a carrier, or both parents must be carriers. In such cases, the child can inherit two defective factor VII genes, one from the mother and one from the father.

Approximately 1 in 1,000 people is a carrier of the defective factor VII gene. However, because both parents need to be carriers of the defective gene in order to pass on the disease, severe factor VII deficiency is extremely rare – it occurs in 1 in 500,000 people.
The following four figures illustrate how factor VII deficiency can be passed on.

**Figure 1** shows what can happen when a carrier of factor VII deficiency has a child with another carrier. There is a 1-in-4 chance that the child will have severe factor VII deficiency, a 1-in-2 chance that the child will be a carrier, and a 1-in-4 chance that the child will not have the disease.

**Figure 2** shows what can happen when someone with severe factor VII deficiency has a child with a non-carrier. The child will be a carrier, but will not have the disease.
Figure 3 shows what can happen when someone with severe factor VII deficiency has a child with a carrier. There is a 1-in-2 chance that the child will be a carrier. There is also a 1-in-2 chance that the child will have severe factor VII deficiency.

Figure 4 shows what can happen when a carrier of factor VII deficiency has a child with a non-carrier. There is a 1-in-2 chance that the child will be a carrier and a 1-in-2 chance that the child will not have the disease.
Diagnosis

Factor VII deficiency is often diagnosed when a newborn has a bleeding episode soon after birth, sometimes following circumcision. However, in many cases, factor VII deficiency is diagnosed later in childhood or even in adulthood. When a patient shows signs of abnormal bleeding, the doctor normally orders a small blood sample in order to measure the length of time it takes for blood to clot. A prolonged clotting time suggests that there may be a factor deficiency. The diagnosis is made by a clotting factor test to determine the specific factor deficiency, in this case factor VII, and its severity.
Degree of severity of factor VII deficiency

The severity of factor VII deficiency depends on the level of factor VII in the bloodstream. If factor VII is completely absent or present at a very low level, a person has a severe deficiency. In general, the lower the factor VII level, the greater the severity of symptoms of the disease, and vice versa.

There are several variations of factor VII deficiency. Some people, for example, have almost no factor VII in their blood, which explains why they can have severe bleeds. However, bleeding symptoms vary widely and do not always correspond to the level of factor VII in the bloodstream. For example, some people with severe factor VII deficiency may rarely have bleeding episodes.

Equally, people with only a mild or moderate deficiency (2% to 10% of the normal level of factor VII) can suffer from bleeds. As they do not often have bleeding problems, they may have difficulty identifying the signs and symptoms of a bleed. It is therefore equally important that these individuals receive care in a centre that specializes in bleeding disorders.

If you have factor VII deficiency, even if it is mild, you must immediately report any suspicious symptoms to your bleeding disorder treatment centre. The nurse coordinator will help you determine the exact nature of the problem.
Cause of bleeding in factor VII deficiency

Blood is carried throughout the body in a network of blood vessels. When tissues are injured, a blood vessel can rupture and result in leakage of blood. Blood vessels can rupture near the surface, as in the case of a cut, or they can rupture deep inside the body, causing an ecchymosis (bruise) or internal hemorrhage.

Clotting, or coagulation, is a complex process that stops an injured blood vessel from bleeding. As soon as a blood vessel wall ruptures, the components responsible for coagulation come together to form a clot, sort of a plug where the blood vessel is ruptured. There are several steps involved in forming a clot:

- **Blood platelets**, which are very tiny cell fragments, are the first to arrive at the rupture. They clump together and stick to the wall of the injured vessel.
- These platelets then emit chemical signals that call for help from other platelets and from clotting factors.
The clotting factors, tiny plasma proteins including factor VII, link to form a chain called fibrin. The strands of fibrin cross-link to weave a mesh around the platelets. This prevents the platelets from drifting back into the bloodstream. **Figure 4**

Factor VII is a trace protein found in the blood. It plays a role in the coagulation cascade, the chain reaction that is set in motion to produce fibrin when there is an injury to a blood vessel. Factor VII is activated, or “turned on” by tissue factor and turned into recombinant factor VIIa (“a” stands for “activated”). Factor VIIa in turn activates other factors, allowing the clotting process to continue and produce a solid clot. If any of the clotting proteins is absent, the chain reaction is broken, and clotting occurs more slowly, or not at all. **Figure 5**
Common bleeds in people with factor VII deficiency

Here are the types of bleeding that typically occur, in descending order of frequency, in people with factor VII deficiency:

- Heavy/prolonged menstrual bleeding (*menorrhagia*)
- Nose bleeds (*epistaxis*)
- Gum bleeds (*gingivorrhagia*)
- Frequent and easy bruising (*ecchymosis*)
- Gastrointestinal bleeding (e.g., black stools, bright red vomit)
- Muscle bleeds (*hematoma*)
- Joint bleeds (*hemarthrosis*)
- Blood in urine (*hematuria*)
- Bleeding into the brain or spinal cord (central nervous system)

This list is not exhaustive. Other types of bleeding can also occur. If you suspect there is bleeding or discomfort of uncertain cause, do not hesitate to contact the bleeding disorder treatment centre. They will help you assess the situation and respond appropriately.
Signs and symptoms of bleeds

A person with factor VII deficiency must be aware of the signs and symptoms of specific bleeds, some of which are potentially life-threatening.

Caution: Head, neck, chest, abdomen

Bleeds that affect the head, neck, thorax (chest), or abdomen (belly) can be life-threatening and require immediate medical treatment such as factor VII or recombinant factor VIIa treatment. It is important to realize that these bleeds can occur following an injury or spontaneously (without apparent reason). Any accident, injury or abnormal symptoms should be reported immediately and without delay to bleeding disorder treatment centre.

Head

The brain, protected by the skull, controls all the vital functions of the body. A head bleed is very serious and requires immediate medical attention. Symptoms may occur immediately or over several hours.

*Signs and symptoms:*

- Headache
- Problems with vision (eyesight)
- Nausea and vomiting
- Personality changes
- Drowsiness
- Loss of balance***
- Loss of fine motor coordination (clumsiness)***
- Fainting***
- Convulsion***

***These symptoms develop over time in the case of a serious head injury. If any of these symptoms occurs, seek immediate medical treatment.
Neck
The tissues of the throat are extremely *vascular*. This means that they contain many veins and arteries that carry blood. A small injury or infection can cause an accumulation of blood in these tissues, which compresses the respiratory tract. This makes breathing difficult and can even block the airway completely.

*Signs and symptoms:*
- Pain in the neck or throat
- Swelling
- Difficulty swallowing
- Difficulty breathing

Thorax (chest)
The chest cavity (thorax) contains the lungs, the heart, and many large blood vessels. Bleeding into the lung tissues traps blood inside the air sacs that normally hold oxygen. This makes breathing difficult.

*Signs and symptoms:*
- Pain in the chest
- Difficulty breathing
- Coughing or spitting up blood

Abdomen (belly)
The stomach, spleen, liver, and intestines are but four of the organs found in the abdominal cavity. An injury in this area can cause extremely serious bleeding in the organs or from a large blood vessel. Failure to treat this type of bleed could be fatal.

*Signs and symptoms:*
- Abdominal pain or lower back pain
- Nausea and vomiting
- Presence of blood in urine
- Presence of blood in stools or black stools
Ecchymosis (bruises)
Bruises are often very visible but are generally not dangerous and rarely require treatment.

Signs and symptoms:
- Discolouration: The skin reddens quickly then changes colour over time (green, yellow, black).
- Swelling: Swelling is caused by the accumulation of blood under the skin. If possible, use a pen or marker to outline the swelling in order to be able to track its progress. The blood accumulation is rather soft to the touch and tends to seep inward and the swelling flattens or diminishes as the blood is reabsorbed (healing). Bruises should not swell larger than the size of an egg.
- Warmth

Muscle and joint bleeds
Muscle and joint bleeds must be assessed without delay so that there is prompt treatment in order to avoid effects of bleeding such as permanent joint pain caused by the deterioration of cartilage (hemophilic arthropathy), or loss of skin sensation in the affected area due to nerve compression during a muscle bleed.

Signs and symptoms:
- Pain at rest or with mobilization. Loss of movement of the affected limb, limping, unexplained crying by a young child.
- Warmth due to the accumulation of blood in a joint or muscle.
- Swelling, which can be measured using a tape measure or string in order to assess an increase or decrease in the joint or muscle bleed. An effective way to take measurements is to use a pen or marker to outline the swollen area and monitor change in size over time.
Basic first aid to treat bleeds

This section describes how to treat minor and moderate bleeds in joints and in tissues.

Rest and elevation are two ways of lessening pain and discomfort due to a bleed.

It is important to note that while ice and compression have long been recommended for treating minor and moderate bleeding into joints and soft tissues, these methods have now been questioned. Therefore, when bleeding occurs, it is important to contact the bleeding disorder treatment centre for guidance on how best to treat it.

Rest – Rest a leg by using crutches or a wheelchair and minimize walking as much as possible. Rest an arm by using a scarf or sling for support.

Elevation – Raise the affected limb above the heart to reduce swelling. This will also improve blood circulation.

If ice is recommended:

Ice – Use an ice pack or a bag of frozen vegetables wrapped in a damp towel. Never apply ice directly to the skin. Apply the ice pack for about 15 minutes at a time, every 2 hours.

If compression is recommended:

Compression – Wrap the injured joint in an elasticized bandage using a figure-eight pattern. Watch for signs of numbness, cold, sharp pain, or a change of colour in the fingers or toes. These are signs that the blood circulation has been cut off. If any of these signs occur, remove the bandage and rewrap it less tightly.

The bleeding disorder treatment centre team will provide support during these bleeding episodes. Do not hesitate to contact them when bleeding occurs – treatment with factor VII or recombinant factor VIIa concentrate may be needed.
A major bleed into a muscle can cause permanent damage to the affected limb. The muscles and arteries can be compressed by the accumulation of blood. If a muscle bleed is suspected, contact the treatment centre immediately. In addition, if you apply compression, watch carefully for the signs described above that the bandage is too tight and cutting off blood circulation.

**Nose bleeds (epistaxis)**

Many people with factor VII deficiency get frequent nose bleeds. If this is your case, please advise the team at your bleeding disorder treatment centre.

**First aid for nose bleeds**

- Remain calm.
- Sit upright and pinch the soft part of the nose, where the cartilage meets the bone.
- Breathe through the mouth and hold for 10 to 15 minutes.
- If the nose bleed continues, keep applying pressure. If bleeding lasts more than 30 minutes or if the bleeding recurs often in the following days, contact the bleeding disorder treatment centre to discuss the treatment options, such as tranexamic acid (Cyklokapron® oral prescription tablets).

**Gum bleeds**

To prevent gum bleeds, good dental hygiene with regular toothbrushing and flossing is essential. If despite these efforts, gums bleed regularly, contact the bleeding disorder treatment centre to discuss treatment options, such as tranexamic acid (Cyklokapron®).
Gastrointestinal bleeds
Gastric bleeding is caused by a lesion in the stomach or intestines; the blood then mixes with stool. Gastric bleeding can occur insidiously and symptoms may not appear until several days after the start of blood loss. Therefore, it is essential to contact the bleeding disorder treatment centre as soon as any of these symptoms appear in order to receive appropriate medical treatment and avoid blood transfusion or hospitalization.

*Signs and symptoms:*
- Black stool.
- Bright blood in stool.
- Stomach discomfort (cramps).
- Vomiting that is blood-stained or has appearance of "coffee."
- Unexplained fatigue.

Blood in urine (hematuria)
The presence of blood in urine is a common occurrence among people with bleeding disorders. In most cases, drinking plenty of water and rest are sufficient to eliminate the problem (drink at least two litres per day). At the first sign of hematuria, contact the bleeding disorder treatment centre. Never take tranexamic acid (Cyklokapron®) when hematuria occurs because it can cause serious kidney damage.
Heavy/prolonged menstrual bleeding (menorrhagia)
Women with factor VII deficiency may have heavy and prolonged menstrual bleeding which can sometimes be controlled using hormonal treatment such as oral contraceptives. Other medical treatment options include the hormonal intrauterine device (Mirena®) or tranexamic acid (Cyklokapron®) taken during menstruation. If these methods are ineffective, intravenous treatment with factor VII and recombinant factor VIIa concentrate can be used during menstruation. Menorrhagia is not a condition that must be tolerated. It is important to contact the bleeding disorder treatment centre to get good care and find the right solution to reduce bleeding symptoms and enable better quality of life.

Pregnancy and childbirth
During pregnancy, all women experience a slight increase in their factor VII level. It can be assumed that the same increase in levels occurs in pregnant women with factor VII deficiency. This slight increase during pregnancy does not, however, remove the potential risk of a significant hemorrhage during or after childbirth. A pregnant woman with factor VII deficiency must be followed by a bleeding disorder treatment centre because a specific treatment plan may be needed during childbirth.
Treatment options: Clotting factor concentrates

Treatment with clotting factor concentrates can temporarily raise bloodstream factor VII levels high enough to stop bleeding. This is called factor replacement therapy and is administered intravenously. There are currently two treatments available: recombinant activated factor VII (rFVIIa) and plasma-derived factor VII (FVII). These safe and efficacious products are available in Canada; your hematologist will discuss which product is the best choice for you or your child.

**Recombinant factor VIIa** is made in the laboratory using recombinant technology – it is not made from human blood (plasma). Its half-life* is 2 to 4 hours. This product can be stored at room temperature. It is available in Canada under the brand name NiaStase RT®.

**Plasma-derived factor VIIa** is made from human plasma from blood donors. Donors are carefully selected and each blood donation is tested to ensure that it contains no known viruses. The factor is then treated to remove viruses that may still be present. Its half-life is approximately 6 hours. This product must be stored in the refrigerator. The product available in Canada is FVII Baxter®.

*Half-life is the time it takes for the concentration of the factor in the bloodstream to be reduced by half.

Factor VII concentrates can be infused to prevent or control bleeds.
Other medications

Tranexamic acid (Cyklokapron®) is available in oral tablets and as a solution for intravenous infusion. It is used for mucosal bleeding (nose, mouth, gastrointestinal tract, uterus and vagina).

Hormonal treatment such as the oral contraceptive pill thins the uterine lining, reducing menstrual bleeding.

Physical activities and exercise

Contact sports are not recommended because of the high risk of serious injury, particularly to the head, muscles and joints.

The type of sports and physical activities recommended or prohibited will vary from one person to another, and will depend on factors such as the severity of disease and the person’s bleeding history. The physiotherapist at the bleeding disorder treatment centre is the ideal person to consult about appropriate sports and physical activities.

Vaccination

A child with factor VII deficiency should be vaccinated on a timetable set by the pediatrician or family doctor. By precaution it is recommended that anyone receiving plasma-derived factor concentrates should be vaccinated against hepatitis A and hepatitis B.
**The comprehensive care team of the inherited bleeding disorder treatment centre**

As the name suggests, the bleeding disorder 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:

- the medical director, usually a hematologist
- the nurse coordinator
- the physiotherapist
- the social worker and/or psychologist

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

**Conclusion**

People with a severe deficiency can experience serious bleeding. The bleeding disorder can be treated with medications such as factor VII concentrates to control bleeding episodes. It is important that people with bleeding disorders be followed by a centre that specializes in the treatment of bleeding disorders.
References


For more information

You can obtain a list of bleeding disorder treatment centres from the Canadian Hemophilia Society Website (www.hemophilia.ca) or by contacting:

Canadian Hemophilia Society
Telephone: 514-848-0503
Toll-free: 1-800-668-2686
chs@hemophilia.ca

This brochure provides only general information on factor VII deficiency. 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.