

FACTOR XII 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

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This brochure provides general information 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

Severe Factor XII deficiency is a very rare condition and is not well known, even among health professionals.

The purpose of this booklet is to describe the deficiency with the hope that it will permit those affected to better understand the issues.

How Factor XII Deficiency is Inherited

Congenital Factor XII deficiency is an inherited coagulation protein deficiency disorder. This means that it is passed on from parent to child at the time of conception. The coagulation protein deficiency 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 XII deficiency, one of these genes has a defect.

The defective gene in Factor XII deficiency is on a chromosome that does not decide the sex of the child. This means that Factor XII deficiency can affect females as well as males.

A carrier is a person who carries the defective gene. This person may have few symptoms or no symptoms at all. In order for a person to inherit Severe Factor XII deficiency, both parents must be carriers. In such a case, the baby inherits two defective Factor XII genes, one from the mother and the other from the father.

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

The three illustrations below show how Factor XII deficiency can be passed on:

FIGURE 1 below shows what can happen when a carrier of Factor XII deficiency has children with another carrier. There is a 1 in 4 chance that a child will have severe Factor XII deficiency, a 1 in 2 chance that a child will be a carrier and a 1 in 4 chance that a child will not be affected.

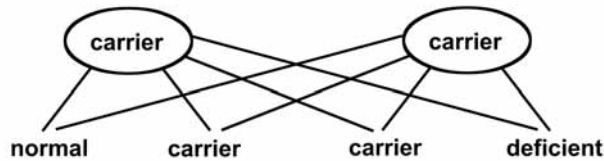


FIGURE 2 shows what can happen when someone with severe Factor XII deficiency has children with a non-carrier. All the children will be carriers, but the disease will affect none of them.

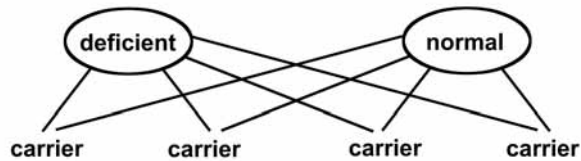
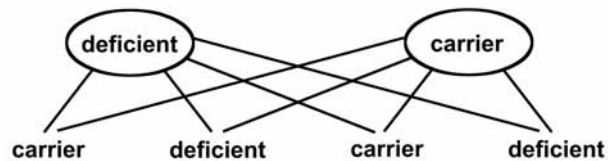


FIGURE 3 shows what can happen when someone with severe Factor XII deficiency has children with a carrier. There is a 1 in 2 chance that a child will be a carrier. There is also a 1 in 2 chance that a child will have a severe Factor XII deficiency.



What is Factor XII Deficiency?

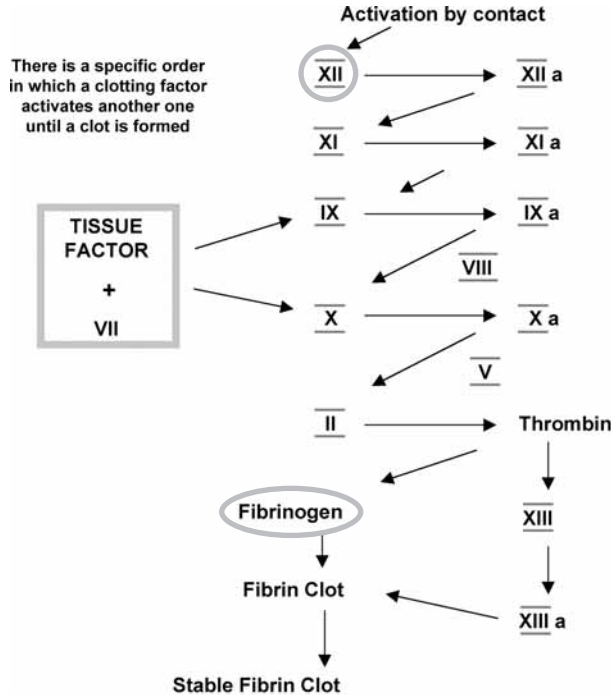
Factor XII deficiency is a rare inherited coagulation factor deficiency. It was first identified in 1955. Factor XII is also known as Hageman Factor, named after the patient in whom this condition was first diagnosed.

Factor XII is a protein in the blood. It plays a role in the coagulation cascade. Blood is carried throughout the body in a network of blood vessels. When tissues are injured, damage to a blood vessel may result in leakage of blood through holes in a vessel wall. The vessels can break near 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. There are several steps involved in forming a plug:

- Blood platelets, which are very tiny cell fragments, are the first to arrive at the break. They clump together and stick to the wall of the damaged vessel.
- These platelets then emit chemical signals calling for help from other platelets and from clotting factors.
- The clotting factors, which are tiny plasma proteins, lead to the deposition of fibrin, an efficient plug. The strands of fibrin join together to weave a mesh around the platelets.

The following diagram was devised by a Toronto laboratory technician. It shows the stages in clot formation in a way that makes it easier to understand the theoretical notions explained above.



Source: Modified from Ms Patricia Blake, Senior Laboratory Technician, St Michael's Hospital, Toronto, Ontario, 1994.

Factor XII is a protein involved in that complex process. It plays a role, as described before, in the chain reaction that is set in motion when there is an injury to a blood vessel.

Surprisingly, Factor XII deficiency does not lead to abnormal bleeding, even with major surgical procedures or trauma. Although Factor XII is part of the complex coagulation chain, a deficiency of Factor XII does not appear to be important in “real life” clotting.

The deficiency is somewhat of a medical mystery. It does not cause abnormal bleeding. It has been suggested that people with Factor XII deficiency may be at increased risk of forming blood clots in the bloodstream when they are not wanted. This is called “thrombosis,” and it remains unproven.

Incidence

Severe Factor XII deficiency is an extremely rare disorder. It affects only 1 in 1 million people. Factor XII levels are lower in patients of Asian descent than in other ethnic groups.

Diagnosis

Factor XII deficiency is usually discovered by accident in a patient through a routine coagulation blood test done prior to surgery or following a family history of coagulation problems.

The physician will order a blood test called PT and PTT. These tests measure the time it takes for a clot to form. In the case of Factor XII deficiency, the PTT will be markedly prolonged but the PT will remain normal. The coagulation time will be longer than normal. Following this abnormal result, the physician will then order specific Factor level, including a Factor XII level.

Symptoms

There are no symptoms of bleeding in Factor XII deficiency. The explanation for the lack of bleeding problems is unknown.

The opposite is sometimes true. It is suggested, but unproven, that patients may not be as well protected from thrombotic disease (clots forming in the blood vessels) as the normal population.

Treatment

Contrary to most other coagulation disorders, hemorrhaging and excessive bleeding are not associated with the deficiency. Therefore treatment is generally unnecessary. However, always notify your dentist, doctor and/or specialist of this problem in order to prevent a delay or even a cancellation of a surgical procedure.

Recommendation for the Patient with Factor XII Deficiency

Even though you will not have bleeding problems, it is important to wear a bracelet or a Medic-Alert type chain and a wallet card at all times. The wallet card will provide a summary of information relating to your condition.

It will inform the medical professionals of your coagulation disorder and your ability to form a clot within a normal time.

The Comprehensive Care Team

As the name suggests, a 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, and
- a social worker.

The team works closely with other specialists – a surgeon, an orthopedist, a rheumatologist, a dentist, a geneticist and a 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, the parents as well.

For More Information

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

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

References

1. Amesse C, Lacroix S, Lupien G. Canadian Hemophilia Society. Factor XIII Deficiency: An Inherited Bleeding Disorder, 2001.
2. Bernardi F, Marchetti G, Volinia S, Patracchini P, Casomato A, Girolami A, Conconi F. A Frequent Factor XII Gene Mutation in Hageman Trait. *Human Genetics Springer-Verlag.* 1988;80:149-151.
3. Colman RW. Contact Activatin Pathway: Inflammatory, Fibrinolytic, Anticoagulant Antiadhesive and Antiangiogenic Activities. In: Colman RW, Hirsch J, Marder VJ, Salsman EW, eds. *Hemostasis and Thrombosis Basic Principles and Clinical Practice*, Philadelphia: JB Lippincott Co, 1982: 111-115.
4. Colman RW. Deficiencies of Factor XII and Prokallikrein and High Molecular Weight Kininogen. In: Colman RW, Hirsch J, Marder VJ, Salsman EW, eds. *Hemostasis and Thrombosis Basic Principles and Clinical Practice*, Philadelphia: JB Lippincott Co, 1982: 1919-1920.
5. Harrington A, Lacroix S, Schwetz N. Canadian Association of Nurses in Hemophilia Care. *Acquired Hemophilia*, 2001.
6. Harrison's Online; Chapter 62: Bleeding and Thrombosis.
7. McDonough RJ, Nelson CL. Clinical Implications of Factor XII Deficiency. *Oral Surg. Oral Med. Oral Pathol.* 1989;68:264-266.
8. National Hemophilia Foundation. *Orientation Manual for Health Care Professionals: Factor XII Deficiency. (Hageman Factor)*, p19.

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