EXHIBIT A

Hemophilia

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Symptoms & causes | Diagnosis & treatment | Doctors & departments | Care at Mayo Clinic

Overview

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Hemophilia is a rare disorder in which your blood doesn't clot normally because it lacks sufficient blood-clotting proteins (clotting factors). If you have hemophilia, you may bleed for a longer time after an injury than you would if your blood clotted normally.

Small cuts usually aren't much of a problem. If you have a severe deficiency of the clotting factor protein, the greater health concern is deep bleeding inside your body, especially in your knees, ankles and elbows. That internal bleeding can damage your organs and tissues, and may be life-threatening.

Hemophilia is a genetic disorder. Treatment includes regular replacement of the specific clotting factor that is reduced.

Symptoms

Signs and symptoms of hemophilia vary, depending on your level of clotting factors. If your clotting-factor level is mildly reduced, you may bleed only after surgery or trauma. If your deficiency is severe, you may experience spontaneous bleeding.

Signs and symptoms of spontaneous bleeding include:

- Unexplained and excessive bleeding from cuts or injuries, or after surgery or dental work
- Many large or deep bruises
- Unusual bleeding after vaccinations
- Pain, swelling or tightness in your joints
- Blood in your urine or stool
- Nosebleeds without a known cause
- In infants, unexplained irritability

Bleeding into the brain

A simple bump on the head can cause bleeding into the brain for some people who have severe hemophilia. This rarely happens, but it's one of the most serious complications that can occur. Signs and symptoms include:

- Painful, prolonged headache
- Repeated vomiting
- Sleepiness or lethargy
- Double vision
- Sudden weakness or clumsiness
- Convulsions or seizures

When to see a doctor

Seek emergency care if you or your child experiences:

- Signs or symptoms of bleeding into the brain
- An injury in which the bleeding won't stop
- Swollen joints that are hot to the touch and painful to bend

If you have a family history of hemophilia, you may want to undergo genetic testing to see if you're a carrier of the disease before you start a family.

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Causes

When you bleed, your body normally pools blood cells together to form a clot to stop the bleeding. The clotting process is encouraged by certain blood particles. Hemophilia occurs when you have a deficiency in one of these clotting factors.

There are several types of hemophilia, and most forms are inherited. However, about 30% of people with hemophilia have no family history of the disorder. In these people, an unexpected change occurs in one of the genes associated with hemophilia.

Acquired hemophilia is a rare variety of the condition that occurs when a person's immune system attacks clotting factors in the blood. It can be associated with:

- Pregnancy
- Autoimmune conditions
- Cancer
- Multiple sclerosis

Hemophilia inheritance

In the most common types of hemophilia, the faulty gene is located on the X chromosome. Everyone has two sex chromosomes, one from each parent. A female inherits an X chromosome from her mother and an X chromosome from her father. A male inherits an X chromosome from his mother and a Y chromosome from his father.

This means that hemophilia almost always occurs in boys and is passed from mother to son through one of the mother's genes. Most women with the defective gene are simply carriers and experience no signs or symptoms of hemophilia. But some carriers can experience bleeding symptoms if their clotting factors are moderately decreased.

Risk factors

The biggest risk factor for hemophilia is to have family members who also have the disorder.

Complications

Complications of hemophilia may include:

- **Deep internal bleeding.** Bleeding that occurs in deep muscle can cause your limbs to swell. The swelling may press on nerves and lead to numbness or pain.
- **Damage to joints.** Internal bleeding may also put pressure on your joints, causing severe pain. Left untreated, frequent internal bleeding may cause arthritis or destruction of the joint.
- **Infection.** People with hemophilia are likelier to have blood transfusions, increasing their risk of receiving contaminated blood products. Blood products became safer after the mid-1980s due to screening of donated blood for hepatitis and HIV.
- **Adverse reaction to clotting factor treatment.** In some people with severe hemophilia, the immune system has a negative reaction to the clotting factors used to treat bleeding. When this happens, the immune system develops proteins (known as inhibitors) that inactivate the clotting factors, making treatment less effective.

By Mayo Clinic Staff

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