**Hemophilia A and B**

1. [What is Hemophilia?](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#whatis)
2. [Causes of Hemophilia](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#causes)
3. [Signs & Symptoms of Hemophilia](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#signs)
4. [Treatment of Hemophilia](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#treatment)
5. [Treatment Adherence in Hemophilia Care](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#adherence)
6. [Hemophilia Treatment Centers (HTCs) and Comprehensive Care](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#htc)
7. [Special Considerations](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#special)
8. [What Can IHTC Do For You?](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#doforyou)
9. [Resources](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#resources)
10. [References](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-a-and-b/#references)

**What is Hemophilia?**

Hemophilia is a rare bleeding disorder that results from reduced levels or lack of clotting factor VIII (FVIII; hemophilia A) or IX (FIX; hemophilia B). Normal blood clotting is a complex process that involves as many as 20 blood proteins called clotting factors. The shortage or absence of one of these factors, as happens in hemophilia, may disrupt the clotting process. Persons with hemophilia cannot form blood clots when needed to stop bleeding and therefore bleed longer than people without hemophilia, not faster. People with hemophilia experience abnormal bleeding – either after an injury or spontaneously-into their joints, muscles, and soft tissues. Bleeding into the joints and muscles is one of the distinctive signs of hemophilia. Minor cuts and scrapes are often not of great concern for people with hemophilia, but bleeding into the head, abdomen, kidneys, intestines, and major joints and muscle groups can be life- or limb-threatening.

**Types of Hemophilia**

The two most common types of hemophilia are FVIII deficiency (**hemophilia A**) and FIX deficiency (**hemophilia B**, or Christmas disease). According to the National Institutes of Health (NIH), both types of hemophilia are considered rare diseases, that is, they each affect fewer than 200,000 individuals in the United States.1 Both hemophilia A and B affect all races and ethnic groups equally. 2,3 ***Hemophilia A (FVIII deficiency)***2: Hemophilia A is the most common type of hemophilia. It occurs in about one in 5,000 male births and affects about 25,000 individuals in the United States. ***Hemophilia B (FIX deficiency)***3: Hemophilia B is the second most common type of hemophilia and is less common than FVIII deficiency. Hemophilia B occurs in about one in 25,000 male births and affects about 3,300 people in the United States. ***Hemophilia C (Factor XI deficiency): A Unique Bleeding Disorder*** Factor VIII and Factor IX deficiencies are the best known and most common types of hemophilia, but other clotting factor deficiencies also exist. Low levels of factor XI (FXI), another blood protein required for clot formation, cause hemophilia C, which is also known as plasma thromboplastin antecedent (PTA) deficiency or Rosenthal syndrome. Although also associated with bleeding, hemophilia C differs from hemophilia A and B in incidence, cause, bleeding tendency, and treatment. For more detailed information on hemophilia C, including treatment options and complications, [click here.](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/hemophilia-c/) The remainder of the hemophilia section will focus on hemophilia A and B.

**Severity of Hemophilia A and B**

Hemophilia is classified as mild, moderate, or severe depending on the amount of the clotting factor in a person’s blood.2,3 The normal range of FVIII and FIX is between 50% and 150%. Hemophilia severity is classified as follows:

| **Severity** | **Blood clotting factor level** |
| --- | --- |
| Normal | 50%-150% |
| Mild hemophilia | 6%-49% |
| Moderate hemophilia | 1%-5% |
| Severe hemophilia | <1% |

* In **mild hemophilia** (6% to 49% factor activity), bleeding typically occurs only after injury, trauma, or surgery. Patients may have very few symptoms otherwise. About 25% of the hemophilia population has mild deficiency.
* In **moderate hemophilia** (1% to 5% factor activity), bleeding tends to occur after minor injuries, though spontaneous bleeding episodes (i.e., without obvious cause) may occur. About 15% of the hemophilia population has moderate deficiency.
* Persons with **severe hemophilia** (<1% factor activity) may experience not only bleeding after injury, trauma, or surgery, but also spontaneous bleeding into joints and muscles. Recurrent bleeding into joints can cause hemophilic arthropathy, a joint disease that results in physical disability at a young age. About 60% of the hemophilia population has severe factor deficiency.

**Causes of Hemophilia**

Hemophilia is a genetic disease and is caused by a mutation within the genes for coagulation factors VIII or IX. In approximately 70% of cases, hemophilia is inherited from a parent, but in about 30% of patients, the family history may be absent or may not be apparent. In such cases, the condition is often caused by a spontaneous gene mutation at the time of fertilization.2,3 The gene causing hemophilia normally contains the instructions for the body to make clotting factor. This gene is carried on the X chromosome, which is called a sex chromosome. A person’s gender is determined by the pairing of two sex chromosomes (X and Y) inherited from their parents. Males have an **XY** pairing with one X chromosome inherited from the mother and one Y chromosome inherited from the father. Females have an **XX** pairing with one X chromosome inherited from the mother and one from the father. Men who have hemophilia will pass their Y chromosome to their sons and their X chromosome (with the altered gene) to their daughters. Sons, therefore, will not be affected by the father’s altered gene, but daughters will all be **carriers** (also known as**obligate carriers**), because they carry their father’s altered X chromosome. **Women carriers** have one X chromosome with the altered gene and one chromosome with a properly functioning gene. If a male child inherits his mother’s unaffected chromosome, he will not have hemophilia. If, however, he inherits his mother’s affected X chromosome, he will have hemophilia. If a female child inherits her mother’s affected X chromosome, she will be a carrier. As such, there is a 50% chance that a female carrier’s sons (XY) will have hemophilia (Figure 1).

**Figure 1: Hemophilia Inheritance – Carrier Mother and Father without Hemophilia**4



Image from: Darling D, ed. “Hemophilia.” The Internet Encyclopedia of Science. (Accessed December 29, 2009 at http://www.daviddarling.info/encyclopedia/H/hemophilia.html). Images used with permission. Males with hemophilia**cannot** pass the condition onto their sons, but **all of their
daughters**will be carriers (Figure 2).

**Figure 2: Hemophilia Inheritance – Father with Hemophilia and Mother Who is Not a Carrier**4



Image from: Darling D, ed. “hemophilia.” The Internet Encyclopedia of Science. (Accessed December 29, 2009 at http://www.daviddarling.info/encyclopedia/H/hemophilia.html). Images used with permission.

**Important Information for Female Carries of Hemophilia**

A carrier of the hemophilia trait can pass on the trait to her children but usually does not experience any symptoms herself. A woman is an obligate carrier of hemophilia if any of the following apply:

* She is the biological daughter of a man who has hemophilia,
* She is the biological mother of more than one son with hemophilia, or
* She is the biological mother of at least one son with hemophilia and has at least one other blood relative with the disorder.

It is recommended that women who are carriers or are at risk of being carriers have their clotting factor levels evaluated. This evaluation is available at the IHTC.

**Women with Hemophilia**

As an X-linked recessive trait, hemophilia occurs almost exclusively in males. There are circumstances, however, when females can experience bleeding symptoms.

1. **Symptomatic carriers:**In some cases, female carriers of hemophilia can have low (< 50%) levels of either FVIII or FIX and experience bleeding symptoms. Female carriers who have bleeding symptoms are called symptomatic carriers.
2. **Daughters of a father with hemophilia and a carrier mother:**In rare cases, it is possible for a female to have a father with hemophilia and a mother who is a carrier, and thereby inherit an affected X chromosome from both parents. Such daughters would therefore **have** hemophilia.
3. **Turner’s syndrome:**This is a rare chromosomal disorder in which females carry only one X chromosome. If these girls inherit the hemophilia gene, they will have hemophilia.

**Signs & Symptoms of Hemophilia**

The primary signs and symptoms of hemophilia are excessive/prolonged bleeding and easy bruising.5 Bleeding can be external or internal. The extent of these symptoms depends on the hemophilia type (A or B) and severity (mild, moderate, or severe).

* Persons with **mild hemophilia** (<6% – 49% factor level) may have excessive bleeding after dental procedures, accidents, or surgery, but do not typically have spontaneous bleeds as in severe hemophilia. In some cases, mild hemophilia causes so few symptoms that it is not diagnosed until adolescence or adulthood.
* Moderate and severe hemophilia are typically characterized by more frequent and severe bleeding complications as compared to mild hemophilia.

Males with severe hemophilia may bleed heavily after circumcision. In many cases where there is not a family history of hemophilia, the diagnosis is made due to excessive or prolonged bleeding after circumcision. Other common symptoms include the following:

* Joint bleeding;
* Soft tissue bleeding or bleeding after minor trauma;
* Easy or excessive bruising;
* Prolonged bleeding in the mouth from a cut or bite;
* Bleeding associated with surgery or invasive procedures

**Emergency Care**

Rarely patients can have bleeding within vital internal organs or structures. These are often **life-threatening bleeding events**. Symptoms of such **internal bleeding** can be difficult to recognize, so it is important that patients know what to look for. The four most serious bleed sites include6:

* ***Head*** – headache, neck pain, sleepiness, sensitivity to light, nausea, vomiting, loss of consciousness. There might also be no initial symptoms of a head bleed, so **PATIENTS MUST CONTACT THE HTC IMMEDIATELY IF EVEN MINOR HEAD TRAUMA OCCURS.**
* ***Neck/tongue*** – neck-swelling or tongue-swelling that may cause blockage of the airway and problems with breathing.
* ***Spinal cord*** – weakness, tingling, or pain in the arms or legs; difficulty with urination or bowel movements; back pain.
* ***Internal organs such as stomach, liver, spleen, intestine*** – blood in vomit, vomit that looks like coffee grounds, black tar-colored stools.

If you or your family member needs to visit the **emergency department (ED)**, be sure to contact the IHTC so we can help you get the best possible care. Visit our webpage on [Emergency Care](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/emergency-care/) to learn about what you should do, what you need to take to the ED, and what information you need to provide to the ED staff. Read the useful [IHTC’s Emergency Care Tips](http://www.ihtc.org/wp-content/uploads/2010/05/Emergency%20Care%20Tips.pdf) and keep it handy.

**Joint Bleeds**

Joint bleeds (called hemarthroses), which can be spontaneous or caused by trauma, are the main cause of chronic pain and disability in severe hemophilia.7 Chronic bleeding into the joints breaks down the joint lining (synovium) and causes joint damage. This results in the painful arthritic condition known as **hemophilic arthropathy**. Joint bleeds most often occur in the knees, elbows, ankles, or hips, but can occur in any joint. While joint bleeds can occur in all severities of hemophilia, **spontaneous joint bleeds tend to be most common in individuals with severe hemophilia. In individuals with moderate and especially with mild hemophilia, trauma or injury usually initiates joint bleeding.** Symptoms of joint bleeds are not always apparent right away. The first symptom is often tingling or tightness in the joint with no real pain or visible signs of bleeding. As bleeding continues, the joint swells and becomes warm to touch and painful to move. Swelling increases as bleeding continues and movement can be temporarily lost. Pain can be severe. Joint bleeds must be treated quickly and aggressively to prevent permanent joint damage. Untreated joint bleeds can be debilitating, as chronic pain, swelling, and permanent joint damage lead to limited mobility and decreased quality of life.

**Soft Tissue Bleeding**

Bleeding in muscular tissue is also called soft tissue bleeding. Bleeding in large muscle groups such as the hip flexors (iliopsoas muscle) can cause severe anemia and unstable blood pressure. Bleeding within compartments such as the forearm or lower extremity can cause **compartment syndrome**. Patients with compartment syndrome often have significant nerve and tissue damage with symptoms of pain, tingling or numbness. Compartment syndrome **requires immediate specific treatment** to control bleeding and, in some cases, measures to reduce the pressure on nerves and blood vessels.

**Diagnosis of Hemophilia**

The diagnosis of hemophilia is made with attention to the following:

1. Personal history of bleeding
2. Family history of bleeding and its inheritance pattern
3. Laboratory testing

The details about personal and family history of bleeding were discussed in earlier sections.

**Laboratory Evaluation**

In a patient with suspected hemophilia, screening coagulation tests along with mixing studies are performed. Once the diagnosis of hemophilia is established, the screening of other at-risk family members, including females, should be performed to diagnose other affected individuals and determine the clotting factor level of carriers. Genetic testing is available to identify the genetic change causing hemophilia. Genetic tests are particularly helpful in diagnosing the carriers in the family as they often do not experience symptoms and may have normal levels of the clotting factor. **Diagnosis of Hemophilia in Newborns** In newborns who experience bleeding from heel sticks, bruises or bleeding after an intramuscular injection, bleeding with circumcision, head bleeds, or bruising, diagnostic tests are needed. FVIII deficiency or hemophilia A can be diagnosed at birth because newborns should have normal levels of FVIII. In contrast, FIX levels are low during the newborn period and may take 6 months to reach normal levels. The diagnosis of mild FIX deficient hemophilia, therefore, may be more difficult in the newborn period, depending on the level of deficiency. It is often prudent to recheck the FIX values when the baby is 3 to 6 months old to confirm a diagnosis of mild hemophilia A or B. Until then, an infant with suspected hemophilia should be treated as if he did have hemophilia. Alternatively, genetic testing may be performed to confirm the diagnosis of hemophilia. The IHTC staff can advise physicians on which tests to order and how to interpret the results, especially for patients who are experiencing or have a history of abnormal bleeding. The IHTC provides a cord blood kit to diagnose hemophilia in newborns in families with known hemophilia. If the blood testing is performed on umbilical blood, care should be taken to avoid contamination with maternal blood. Cord blood testing may not always be accurate in mild hemophilia. **Prenatal diagnosis options** The following prenatal diagnosis options are available for women known to be carriers of hemophilia:

* Noninvasive fetal sex determination by ultrasound. Fetal sex determination provides information about the potential to have an affected male and may be helpful in making informed decisions about delivery.
* Invasive testing by chorionic villus sampling or amniocentesis. This testing provides definitive diagnosis of an at-risk fetus.

**Treatment of Hemophilia**

There is currently no cure for hemophilia. However, treatment has advanced remarkably in the past 30 years. Children with hemophilia who receive comprehensive treatment can now look forward to a near-normal life expectancy.8 **For individuals with mild hemophilia A**, the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation recommends that desmopressin (DDAVP) should be used whenever possible. DDAVP is available in both an injectable form (DDAVP Injection) and as a highly concentrated nasal spray (Stimate Nasal Spray). [Click here](http://www.ihtc.org/wp-content/uploads/2011/05/DDAVP_Check_List_and_Guidelines.pdf) to download the IHTC’s fluid restriction guidelines and other information on DDAVP/Stimate use. Desmopressin should not be used in some categories of patients. Children under the age of 2 years, pregnant women, and patients with mild hemophilia A in whom desmopressin does not provide adequate Factor VIII levels should be treated with factor concentrates. Hemophilia can also be well managed with infusion of manufactured clotting factor concentrates to replace the factor that is missing from the blood. This is called clotting factor replacement therapy.

**Clotting Factor Concentrates**

Clotting factor concentrates can be made using human plasma or through recombinant technology.

1. **Plasma-derived products:** plasma-derived products are made from human blood components such as donated plasma.
2. **Recombinant products:** recombinant factor products are made in a laboratory using recombinant technology. These products do not use human blood as a starting component. Recombinant products offer a safer option than plasma-derived products because they avoid potential blood-borne transmission of infectious diseases. In the United States, treatment with recombinant products, when available, is the standard of care.

Clotting factor is administered by placing a needle in the patient’s vein (venipuncture) or through a surgically implanted device called a Port-a-Cath (“port”). Treatment (“infusion”) with clotting factor stops or prevents bleeds by raising the patient’s factor level for a certain time period. Patients who need frequent infusions and their parents often learn to infuse at home, making treatment more convenient and accessible for the patient and family. IHTC nurses are experienced in training families and patients to home infuse. Patients usually receive clotting factor products from homecare companies or HTC pharmacy programs. As Indiana’s only federally recognized comprehensive treatment center, the IHTC operates a Public Health Service 340B Pharmacy Program. This program allows the IHTC to dispense factor at reduced prices. Visit the [IHTC Pharmacy Program](http://www.ihtc.org/patient/ihtc-pharmacy-program/) to learn more about how IHTC’s pharmacy program works on behalf of patients to lower costs and optimize the care those patients receive. **Patient Notification System** The IHTC encourages you to register with the Patient Notification System. This free, confidential, 24 hour communication system provides information on withdrawals and recalls of plasma-derived and recombinant therapies. To learn more about what this system is and how to register for this service, [click here.](http://www.ihtc.org/wp-content/uploads/2010/05/Patient%20Notification%20System.pdf)

**Hemophilia Treatment Regimens**

The amount of factor and the frequency of administration depend on several variables including bleeding severity and site; and the patient’s size (i.e., weight). There are two main categories of treatment for hemophilia. **Prophylactic Infusion Therapy (Prophylaxis)**The Medical and Scientific Advisory Committee (MASAC) of the National Hemophilia Foundation and the World Health Organization (WHO) recommend prophylactic (preventive) treatment for persons with severe hemophilia A or B.9 10Prophylactic therapy often involves regular administration of clotting factor 2 to 3 times per week to raise the factor level to a moderate range to **prevent** spontaneous bleeds or bleeds after minor injury. Prophylactic treatment requires a large amount of factor and frequent infusions. Due to the high cost of prophylaxis, health insurance coverage is vital for patients who use this treatment. The IHTC social worker is available to answer your questions about insurance and to help you through changes in your insurance coverage. To learn more about the types of prophylactic treatments and **IHTC’s prophylaxis clinic**, [click here](http://www.ihtc.org/patient/blood-disorders/bleeding-disorders/bleeding-disorder-clinics/#prophylaxisclinic).**Episodic Infusion Therapy (“On-Demand”)** Episodic treatment of hemophilia involves the use of clotting factor to treat acute bleeds after bleeding has started. In general, people with mild and moderate hemophilia, who tend to bleed less often, use episodic treatment. **Treatment Records Help You Take Charge of Your Health Care!** By keeping treatment records, you can take charge of your health care and help the IHTC provide the best care for you. ***What is a treatment record?*** A treatment record or infusion log is a way to document or record bleeding episodes and treatment in an organized manner. This record or log makes it easier to discuss health issues with your nurse and physician in clinic or when you have a concern. ***Why do I need to keep an infusion log?*** Keeping a treatment log maintains an accurate record of your bleeding episodes and treatment over a period of time. Trying to recall bleeding events and treatment is difficult and often inaccurate. Having accurate information available assists in the discussion and development of the best treatment plan for you. Additionally, many insurance companies **now require** treatment records of every bleeding episode and infusion for continued coverage of factor concentrate. ***What are my options?*** The IHTC currently has two recording options available. We would be happy to discuss either of these options with you further.

1. **ATHNadvoy:** This electronic treatment record system enables you to log bleeding events and treatments online through a computer. [Click here](http://www.ihtc.org/wp-content/uploads/2010/05/ATHNadvoy.pdf) to learn more about ATHNadvoy and how to register for this service.
2. **Infusion calendar:** This paper calendar is specifically designed by the IHTC team to document bleeding episodes and infusions in an easy to document and read format. [Click here](http://www.ihtc.org/wp-content/uploads/2011/05/Infusion_Calendar_Instructions.pdf) to download the IHTC’s instructions on how to use the infusion calendar.

***Is keeping a treatment record a requirement for my care?*** We recommend that everyone record their bleeding events and infusions to help the IHTC provide the best care possible. In addition, many insurance agencies now require these records. ***What happens to the records when I send them to the IHTC?*** Your treatment records will become a part of your medical record and can be accessed and viewed by the IHTC staff, or requested by you when you need them.

**Treatment Adherence in Hemophilia Care**