MANY FACES OF HEMOPHILIA B:
CHALLENGES AND OPPORTUNITIES
FOREWORD

In 2005 the B2B (hemophilia B patient to hemophilia B patient) program was created as a platform to empower individuals with hemophilia B through peer support and education. The B2B program is a sharing of firsthand accounts about everyday life from those living with hemophilia B. The original objectives of the B2B program remain today:

1. Address the challenges of having hemophilia B, especially those evident when transitioning from one life stage to another
2. Help strengthen the internal support system and educational network within the hemophilia B community

As part of the B2B program, a series of books were produced with content provided by members of the hemophilia B community. The books offer snapshots of peer-to-peer life experiences from people with hemophilia B, including young adults, mature adults, parents of infants and toddlers, preschoolers, and adolescents.

The books also include insight from medical professionals who treat children and adults with hemophilia B. The five previous B2B books are: Young Adults and Hemophilia B, Learn From Experience: A Guide for Mature Adults, Navigating the Preteen Years, Hemophilia B in Early Childhood, and Hemophilia B: Your Point of View. Each book offers tips from members of the hemophilia B community in their words, through their stories, about dealing with daily challenges one may face when living with hemophilia B.

In this book, the sixth book in the B2B series, Many Faces of Hemophilia B: Challenges and Opportunities, you will find discussions about the clinical challenges and complications of hemophilia B that affect daily lives of people with hemophilia B. You’ll also find valuable guidance from medical professionals who are dedicated to helping families and individuals living with hemophilia B. Their educational insight into the many faces of hemophilia B may help you gain a deeper knowledge of the
challenges often faced with this disorder. By sharing some of their current thinking in areas such as women and bleeding disorders, human immunodeficiency virus (HIV) and/or hepatitis C, and hemophilia B in the aging population, you may gain a clearer understanding of some of the challenges of hemophilia B. You may also find it helpful to share this book with other family members to help broaden their awareness of the many faces of hemophilia B.

On behalf of Pfizer Inc, The Coalition for Hemophilia B, Inc., and the B2B Advisory Board, we would like to extend our gratitude to the members of the hemophilia B community who contributed to this book. Your time, knowledge, and personal stories about life with hemophilia B are greatly appreciated: Wayne Cook, Becky VanSant, and Elizabeth VanSant.

We would also like to thank the professionals involved with hemophilia care who shared their insights about hemophilia B: Andra James, MD, MPH, Edward Kuebler, LCSW, and Thomas Truncale, DO, MPH, CIME.

The views and opinions expressed in this book are those of an advisory board comprising patients, parents, and hemophilia care specialists within the hemophilia B community, and are not necessarily those held by Pfizer Inc.

The information in this book should in no way replace the advice of your health care professional. Be sure to talk with your physician, nurse, or hemophilia treatment center (HTC) staff regarding any form of medical advice or treatment.
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GALLERY
Open
“If one is master of one thing and understands one thing well, one has at the same time, insight into and understanding of many things.”

Vincent van Gogh (1853-1890)
A chronic disorder may present a challenge to psychosocial adjustment for both the patient and his or her family. Facing this challenge may become more difficult for everyone when unexpected complications to the disorder arise. If your family is already taking advantage of a comprehensive care team at a hemophilia treatment center (HTC), you may know that one of the benefits for individuals with hemophilia B, in addition to improved medical and quality-of-life outcomes, is early detection of complications.

Even though great progress has been made in the care and treatment of hemophilia B, people with the disorder still face certain risks and complications. One of the early complications that can occur when children are first exposed to clotting factor concentrates is the development of inhibitors against the factor product infused to prevent or stop bleeds. Other complications of hemophilia B may include pain with bleeding events, excessive menstrual bleeding in females (menorrhagia), prolonged bleeding following surgery, bleeding into the joints or muscles, HIV/acquired immune deficiency syndrome (AIDS) and hepatitis C (HCV), and the management of comorbidities (the coexistence of two or more disease processes) in the aging hemophilia B population.

Building awareness throughout the hemophilia B community that encourages early detection of complications is important. Most of the hemophilia population has severe hemophilia; however, individuals with moderate hemophilia and individuals with mild hemophilia are also at risk for bleeding, especially after surgery or trauma.

Throughout your life stages, you may or may not experience any of the complications discussed in this book. However, it’s important for you to be aware of them and to discuss any new signs and symptoms with your physician immediately. Guidance, support, and treatment are available to help you manage the clinical challenges of hemophilia B.

The objectives of this book are to:
- Provide an overview of complications and challenges of hemophilia B that might appear throughout different life stages
- Offer insight and tips from individuals with hemophilia B who have experienced complications from the disorder and challenges in their daily lives
- Suggest resources to help you manage social and/or treatment issues that may arise during your life stages

The first estimate of hemophilia-related, disability-adjusted life years (DALYs) in the United States indicates that control of hemophilia can potentially result in a gain of 1 healthy year of life for every 2700 people in the population.
HEMOPHILIA B—AN OVERVIEW OF CLINICAL CHALLENGES

In recent decades, great progress has been made in the care and treatment of persons with hemophilia B. However, people with the bleeding disorder still face certain risks, complications, and challenges including:

- Inhibitor development
- Pain with certain types of bleeds
- HIV and/or hepatitis C
- Bleeding disorders in women
- Emerging challenges in the aging hemophilia B population
- Preparing for elective surgery—presurgical and postsurgical care

The low prevalence of inhibitor development after factor IX (FIX) replacement therapy means that experience in managing individuals with this complication is limited. The physician may be faced with the unique features of anaphylactic reactions following FIX concentrate administration in individuals who develop FIX inhibitors.5

Another complication faced by people with bleeding disorders, but rarely discussed, is pain. Pain has been an invisible presence yet it casts a net beyond the person who is directly affected. It is an added burden on top of the many already faced by people with hemophilia B and their families.6

One of the largest therapeutic problems during the continuous treatment of patients with hemophilia A and B are viral infections, such as hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, and other infective diseases, which can be transmitted by the transfusion of blood products.7

The availability of effective antiviral drugs to treat HIV and HCV, the advent and proliferation of safer factor concentrates, and the comprehensive care provided though the HTC network are the main factors contributing to improved health for older patients with hemophilia. However, increasing numbers of people with
hemophilia are middle-aged and older, and they face the same age-related health issues as the general population. The impact of these risks on people with hemophilia is unclear.8

Bleeding problems among women are often unrecognized or misdiagnosed. While they are a common problem, very little information is available regarding gynecological complications in hemophilia B. However, in recent years, many studies into the management of women with bleeding disorders have been undertaken.9 Approximately 10% of carrier females are at risk for bleeding (even if the affected family member has mild hemophilia B) and are thus symptomatic carriers, although signs and symptoms are usually mild.10

Inherited or acquired bleeding disorders may present with unexplained excessive bleeding at the time of dental extractions, surgery, or trauma.11 A systematic approach may be adopted when assessing a patient with a bleeding history so that a sound presurgical and postsurgical treatment plan can be put in place to ensure adequate precautions are taken and additional factor IX is on hand for prevention of bleeding during and after surgery.

Compliance Can Help to Prevent Complications
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Thomas Truncale, DO, MPH, CIME, is a pulmonary and critical care physician at the University of South Florida. He and his wife have four children, three boys and a girl. Two of their sons have hemophilia: a 12-year-old and a 3-year-old. There is no family history of hemophilia that they’ve been able to identify, and his wife has three brothers. The 12-year-old son was first diagnosed with hemophilia A when he was 15 months old and just beginning to walk.
When asked about the challenges of complications with hemophilia B, including inhibitor development, Dr. Truncale explained, “When high doses of factor are given early on in life, strict monitoring must take place to identify an inhibitor immediately. When this is done, factor amounts can be increased or decreased immediately to prevent an inhibitor from forming. Because factor is degraded over time, the monitoring should continue over a period of about 6 months.”

Dr. Truncale also stated, “Parents need to monitor children closely. If a child is getting factor and bleeding, or complaining of burning or pain, they must be looked at immediately because this could be a sign of an inhibitor forming. If an inhibitor does develop, the family should make an effort to take precautions to prevent further development.” He also said, “It’s most important for a child to be checked for antibodies (inhibitors) presurgery and have factor levels monitored throughout surgery and after surgery.”

Dr. Truncale noted that inhibitors are more common in hemophilia A than in hemophilia B. However, because of the rareness in hemophilia B, treatment and prevention of inhibitors are less studied. As a result of this, inhibitors in hemophilia B take a long time to treat. “The causes for inhibitor development are not defined. The best identification of someone likely to develop an inhibitor is found in the genetic system of a family,” states Dr. Truncale. “For this reason, it is most important that families monitor a child with hemophilia B to watch for inhibitor development, and if any signs or symptoms appear, seek immediate medical attention.” There are medical treatments available for inhibitors.
A common long-term complication of hemophilia B is permanent damage to joints and muscles caused by repeated bleeding episodes. As a result, accurate diagnosis and treatment are critical to the health of the patient. Since hemophilia B patients frequently self-infuse, an understanding of the need for adherence to prescribed therapy is necessary to reduce the risk of long-term complications. In Dr. Truncale’s opinion, compliance is generally pretty good with hemophilia B management, but there are some barriers that you should be aware of:

1. A reduction or disappearance of bleeding signs and symptoms
2. Not enough time for treatment
3. Forgetfulness
4. Difficulty with peripheral vein access
5. Social and family stresses

Most of these issues can be resolved with patient education and care through your HTC. Dr. Truncale stresses, “Awareness of the importance of compliance to treatment regimens to avoid complications in the hemophilia B patient is the most important thing parents can do for their child with hemophilia B.”
INHIBITORS

What are inhibitors?
People with hemophilia B use treatment products called factor-clotting concentrates. This treatment improves blood clotting and is used to stop or prevent a bleeding episode. Currently, the biggest risk from receiving factor concentrate is that of developing inhibitors.

Inhibitors (substances that restrain or retard physiological, chemical, or enzymatic action) develop when the body’s immune system stops accepting the factor (factor IX for hemophilia B) as a normal part of blood. The inhibitors stop the factor from working. This makes it more difficult to stop a bleeding episode.

In the case of hemophilia B, development of inhibitors against the factor product infused to prevent or stop bleeds may occur when children are first exposed to clotting factor concentrates. The presence of a new inhibitor should be suspected in any patient who fails to respond clinically to clotting factors, particularly if he has been previously responsive.

Inhibitors are much less frequently encountered in hemophilia B, occurring in less than 3% of affected individuals.

In all cases, inhibitors render treatment with replacement factor concentrates difficult.

Inhibitor measurement should be done in all patients who have been intensively treated for more than 5 days, within 4 weeks of the last infusion.

Inhibitors should be assessed prior to surgery or if recovery assays are not as expected, and when clinical response to treatment of bleeding is suboptimal in the postoperative period.

What causes inhibitors?
Scientists do not know exactly what causes inhibitors. Risk factors that have been shown in some studies to possibly play a role include:

- Age
- Race/ethnicity
- Type of hemophilia gene defect
- Frequency and amount of treatment
- Family history of inhibitors
- Type of factor treatment product
- Presence of other immune disorders

How are inhibitors diagnosed?
A blood test is used to diagnose inhibitors. The blood test measures inhibitor levels (titers) in the blood. The amount of titers is measured in Bethesda units (BU). The higher the number of Bethesda units, the more inhibitor is present. “Low titer” inhibitor has a very low measurement; usually less than 5 BU. “High titer” inhibitor has a very high measurement; usually much higher than 5 BU.

Inhibitors are also labeled “low responding” or “high responding,” based on how strongly a person’s immune system reacts or responds to repeated exposure to factor concentrate. When people with high-responding inhibitors receive factor concentrates, the inhibitor titer measurement increases quickly. The increased inhibitor titer prevents the factor clotting concentrates from stopping or preventing a bleeding episode. Repeated exposure to factor clotting concentrates will cause more inhibitors to develop.
Allergic reactions in hemophilia B patients with inhibitors

Up to 50% of hemophilia B patients with inhibitors may have severe allergic reactions, including anaphylaxis, to factor IX administration. Thus, newly diagnosed hemophilia B patients, particularly those with a family history and/or with genetic defects predisposed to inhibitor development, should be treated in a clinic/hospital setting capable of treating severe allergic reactions during the initial 10 to 20 treatments with FIX concentrates. Reactions can occur later but may be less severe.\textsuperscript{15}

Gene therapy for hemophilia B: a look at the future

You have probably heard of gene therapy at one time or another. People interested in treating human diseases, by transferring genes to make essential molecules that some people cannot make for themselves, have long been interested in hemophilia B. Transfer of the gene that codes for the production of factor IX has now been successfully carried out in a small number of patients. Results from a trial carried out in Europe and the United States showed that gene transfer in six men with severe hemophilia B, who were producing clotting factor IX at less than 1% of normal levels, raised their factor IX, and that four of the six men remained free of spontaneous bleeding without any administration of factor IX.\textsuperscript{17}
PAIN IN HEMOPHILIA B

“People who live with hemophilia B and other bleeding disorders are veterans in the acute care of bleeds. They are, however, strangers in the uncharted waters of effective pain management.”

What causes pain in hemophilia B?
In the hemophilia B community, a new bleeding episode is recognized primarily because it causes pain. Active bleeding into a joint or muscle causes acute pain.

Chronic pain is caused by long-term joint or muscle damage. This type of pain mainly affects older people with hemophilia B who suffer more from arthritis. Acute pain is a signal that something is wrong, and it is usually one of the earliest signs and symptoms of a bleed. A bleed that is ignored will go on to put pressure on muscles and other structures in the body. This will then make the pain get much worse. Even if there are no obvious signs of bleeding, such as swelling, clotting factor therapy is recommended.

How is pain treated in hemophilia B?
The aim of pain control within the first few hours of a bleeding episode is relief of suffering. With chronic pain control there is the added goal of maintaining daily function. A balance among the efficacy of pain relief, the side effects, if any, and the ability to be as functional as possible is the final goal of pain management.

Giving clotting factor concentrate to stop the bleeding as soon as a problem is identified can relieve pain from a bleed.

Bleeds in the muscles or soft tissues can be treated by using a form of first aid called RICE (Rest, Ice, Compression, Elevation).

During a bleed, the affected area should be rested—no walking if the bleed is in the knee, no lifting if the bleed is in the elbow. To lessen pain or swelling, apply ice to the affected area—10 to 15 minutes every 2 hours is recommended.

Applying pressure (compression) to the area can also help to slow the bleeding—such as using an elastic bandage. Always check with your local HTC for the proper way to apply the bandage. Elevating or raising the injured limb (arm or leg) above the heart will help to slow the bleeding.
It is always a good idea to check with a doctor if there are any questions about how to control a bleed.

If the regular treatment of clotting factor does not seem to relieve the pain, contact your physician immediately.

**Can painkillers be given to relieve pain?**

A wide range of interventions can be used to help manage chronic pain in patients with hemophilia B. Nondrug treatments include acupuncture, biofeedback, cognitive-behavioral therapy, distraction, exercise programs, guided imagery, hydrotherapy, hypnosis, integrative therapy, physical therapy, therapeutic massage, and transcutaneous electrical neurostimulation. Drugs that can be used to treat pain include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), cyclo-oxygenase inhibitors and morphine (and related drugs).\(^\text{19}\) It is important to note that conventional NSAIDs are associated with a risk of gastrointestinal complications, including ulcers, bleeding, and perforation. Due to the risk for bleeding, NSAIDS should not be used by hemophilia patients during bleeding episodes.\(^\text{19}\) In addition, many of the painkillers that are available at the pharmacy without a prescription contain acetylsalicylic acid, the active ingredient in aspirin. People with hemophilia B must not take products that contain aspirin. Aspirin stops platelets from grouping together to make a clot. Its use will make the bleeding worse.\(^\text{14}\)

**What is the impact of pain on the family?**

Pain can affect people and their families emotionally, socially, academically, financially, and spiritually. Families in the bleeding disorder community have adapted to the physical demands of their condition by educating themselves about their particular situation, learning to do home treatments, and by learning about safe activities.\(^\text{6}\)

Effective pain management is a new frontier for comprehensive care teams at the HTCs.\(^\text{6}\)

**How is pain assessed at the HTC?**

The first step in treating pain is through assessment. If the pain is acute, new bleeding may be suspected. If the pain is chronic, persistent tissue damage may be likely.

An individual’s experience of pain is affected by his age, physical condition, gender, culture, attitude toward life, and personal and family supports.

The result of the pain assessment influences the choice of treatment.

In children, pain and distress coexist. Distress is often a manifestation of pain, but distress can also reflect fear, anxiety, separation from family, and agitated behavior. Unfortunately, young children do not have the vocabulary to tell us when something is wrong. Severe pain results in crying and inconsolability, but lesser pain may cause withdrawal, decreased activity, and irritability. Parents are key to the recognition of a child’s pain. There is no gadget to measure pain—it must be evaluated by asking questions and observing behavior.
Types of Bleeds
Bleeding episodes in hemophilia B that threaten life, limb, or function are:

Intracranial or Head Bleeds
A bleed into the brain is very serious. The signs and symptoms include headache, blurred vision, nausea or vomiting, mood or personality changes, drowsiness, loss of balance or coordination, weakness or clumsiness, stiffness of the neck, loss of consciousness, and seizures.18

Nose, Mouth, and Throat Injuries
Injury or infection in the nose, mouth, or throat causes blood to fill the tissues. As the tissues swell with blood, they can press on the airway, making it smaller or closing it completely. It is important to watch out for pain in the neck or throat, swelling, difficulty swallowing, and difficulty breathing.18

Chest Injuries
Injury to the chest may cause bleeding in the lungs, heart, and major blood vessels. Bleeding in the lung tissues forces blood into the spaces that normally contain air, making it difficult to breathe. Signs and symptoms are pain in the chest and difficulty breathing.18

Abdomen
Injury to the belly area, including the stomach, spleen, and intestines, could result in massive bleeding from an organ or major blood vessel. Pain in the abdomen or lower back, nausea, and/or vomiting are signs and symptoms to watch out for.18

All of these bleeds require a call to your doctor, immediate intervention, or a trip to your local emergency room.

Additional Types of Bleeds
Joint Bleeds
Joint bleeds, also called hemarthroses, are one of the most common kinds of bleeding for a person with hemophilia.20 A joint bleed may begin with a warm, tingling, and/or burning sensation that is usually followed by pain, decreased movement, and swelling of the joint.20,21 Recurring bleeds in a joint can cause permanent damage by destroying the synovial membrane and the cartilage at the end of bones.21

The knee is the joint most often involved in hemarthroses in people with in hemophilia. Severe pain, impaired function, and restricted movement are indications for total knee replacement (TKR). The long-term success of TKR in patients with hemophilia is equivalent to that in patients without this disease and this intervention substantially improves quality of life.22

Urinary Tract Bleeds
About 66% to 90% of people with hemophilia B have bleeding in the urinary tract, also called hematuria, at least once in their lives.21 A symptom to watch for includes dark red urine.18
Iliopsoas Bleeds
Iliopsoas bleeds occur in the muscle of the pelvic area, near the hip. This type of bleed can damage the nerves of the thigh muscle, thereby limiting a person's movement. If an iliopsoas bleed is left untreated, it can cause heavy blood loss and permanent damage.21

Compartment Bleeds
Compartments are closed-in spaces, such as in the forearm muscles. When a person bleeds deep inside these closed spaces, the blood settles in this area and puts pressure on the nerves and blood vessels within the muscle. If left untreated, compartment bleeds can cause permanent nerve damage and sometimes a loss of limb.21 Signs and symptoms to watch for include pain and tingling in the fingers or toes.18

Bruising
Bruises are another common bleeding symptom in people with hemophilia B. Some bruises can be mild and heal on their own with ice, and others may not. Please seek medical attention for bruises that are very painful, grow larger over time, limit movement, or affect sensitive critical areas.18

Mouth Bleeds
Mouth bleeds, such as those caused by biting the lip or tongue, a torn frenulum, new teeth coming in, or a dental procedure, are very common in people with hemophilia B.20 They can be very serious because persistent mouth bleeding can cause severe anemia.18

Please speak with a medical professional to learn when to seek medical care.
“As I look back over more than 30 years of caring for women, I realize that too often, I looked for a reason for excessive bleeding that had nothing to do with the clotting cascade. I was convinced it was something simple that would resolve with time. Awareness that it might be a bleeding disorder is the key element needed to start the process of discovery,” said Ruth Ann Kirschman, WHNP-BC, women’s health nurse practitioner and member of the NHF Women with Bleeding Disorders Task Force.

While women with bleeding disorders are at risk for the same obstetrical and gynecological problems that affect all women, women with bleeding disorders are disproportionately affected by conditions that manifest with bleeding. Optimal management involves the combined expertise of hemostasis experts and obstetrician-gynecologists.24

Menorrhagia, or heavy menstrual bleeding, is the most common symptom that they experience. Not only is menorrhagia more prevalent among women with bleeding disorders, but also bleeding disorders are more prevalent among women with menorrhagia. According to Andra James, MD, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina, “Women with bleeding disorders appear to be at an increased risk of developing hemorrhagic ovarian cysts and possibly endometriosis. Women suspected of having a bleeding disorder or being a carrier of hemophilia should be offered diagnostic testing before getting pregnant to allow for appropriate preconception counseling and pregnancy management.”24

What is a bleeding disorder?

A bleeding disorder occurs when a person’s blood does not clot (stop bleeding) properly. Women are more likely to notice the symptoms of a bleeding disorder because of heavy or prolonged bleeding during their menstrual periods and after childbirth. Heavy bleeding affects more than 10 million American women each year. A CDC study found that bleeding disorders were diagnosed in nearly 11% of women with heavy menstrual bleeding.25

What are the signs and symptoms of a bleeding disorder?

- Bleeding for more than 7 days from the time bleeding begins before it completely stops
- Flooding or gushing of blood that limits daily activities, such as housework, exercise, or social activities
- Passing clots that are bigger than a quarter
- Changing a tampon or pad, possibly even both, every hour or more often on heaviest day(s)
- Prolonged bleeding episodes from
  - Dental surgery, other surgery, or childbirth
  - Frequent nosebleeds that last longer than 10 minutes
  - Bleeding from cuts or injury that last longer than 5 minutes
  - Easy bruising that occurs weekly, are raised, and are larger than a quarter in size25

Note: If you have signs and symptoms of a bleeding disorder, it is important to get a proper diagnosis and treatment from a specialist called a hematologist. In the United States, there is a network of HTCs that provide comprehensive care to patients with hemophilia and other bleeding disorders. HANDI, the National Hemophilia Foundation’s information resource center, can provide information on bleeding disorders and the nearest HTC. Contact HANDI at handi@hemophilia.org.26
Blood clots are formed by a cascade of clotting factor activations: the activated form of one clotting factor catalyzes the activation of the next. Thus, very small amounts of the initial factors suffice to trigger the cascade, ensuring a rapid response to trauma.27
Who is a carrier of hemophilia?

A carrier of hemophilia is a female who has an abnormal X chromosome carrying the hemophilia gene. One of her two X chromosomes has a mutation of the factor IX gene, resulting in decreased levels of clotting factor IX.\(^{28}\)

Females have two X chromosomes (XX). Males have an X chromosome and a Y chromosome (XY). The genes that produce factor IX are part of the X chromosome. Hemophilia is passed from generation to generation in a family through the X chromosome. An abnormal X chromosome can be inherited from a father who has hemophilia or a mother who carries a hemophilia gene and therefore is a carrier.\(^{28}\)

A female who has a factor IX gene mutation is called an **obligate carrier of hemophilia**. About 20% of obligate carriers have factor IX levels that are below the normal range. These carriers can have signs and symptoms similar to mild hemophilia. Some carriers have signs and symptoms similar to severe hemophilia, but this is quite rare.\(^{28}\)

A female who has lower than normal clotting factor levels and has signs and symptoms of factor deficiency is called a **symptomatic carrier of hemophilia**.\(^{28}\)

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**Figure A**

A father with hemophilia B will pass the defective gene to his daughters, making them carriers. His sons, however, will not be affected because they get their X chromosome from their unaffected mother.\(^{29}\)

**Figure B**

In a mother who is a carrier, there is a 50% chance her daughter will be a carrier also. If she has a son, there is a 50% chance he will have hemophilia B because she has one “affected” X chromosome.\(^{29}\)
How are carriers of hemophilia diagnosed?

Different tests are used to measure a potential carrier’s factor levels and to test for carrier status. Access to proper diagnostic testing at an HTC is important.²⁸

- Factor IX clotting assay—measures the amount of factor IX clotting activity in the blood. This test can help determine if a female is at greater risk of having bleeding problems because her factor IX clotting activity level is close to or below the normal range (her clotting factor activity level is between 40% and 60%).²⁸
- Genetic testing—determines the exact factor VIII or IX gene mutation in a carrier. This test can identify the specific hemophilia mutation in 90% to 99% of cases. This type of test can be used for preimplantation or prenatal diagnosis to determine whether or not an embryo or fetus carries the genetic mutation, inherited from a father with hemophilia or a mother who is a carrier.²⁸

Before any type of factor clotting assay or genetic testing is done, a potential carrier is usually given a complete physical examination and review of her personal and family medical history.²⁸

Carriers of Hemophilia

You are a possible carrier of hemophilia if you are the:
- Daughter of a carrier of hemophilia
- Mother of a child with hemophilia and no one else in the family has hemophilia or is a carrier of hemophilia
- Sister, mother, maternal grandmother, aunt, niece, or cousin of female carrier of hemophilia or a male with hemophilia²⁸

You are an obligate carrier of hemophilia if you are the:
- Daughter of a man with hemophilia
- Mother of a child with hemophilia and at least one other person in the family has hemophilia (brother, maternal grandfather, uncle, nephew, or cousin)
- Mother of a child with hemophilia and have a family member who is a carrier of hemophilia (mother, sister, maternal grandmother, aunt, niece, or cousin)
- Mother of two or more children with hemophilia²⁸

You are a symptomatic carrier of hemophilia if:
- Your factor IX level is below the normal range or within the lower range of normal and you have signs and symptoms similar to mild hemophilia²⁸
What is a symptomatic carrier?
A symptomatic carrier is a female who:
- Has the abnormal gene that causes hemophilia B
- Experiences a bleeding tendency
  - About one in 10 carriers have factor IX levels lower than normal
  - In rare cases, the factor level will be very low: carriers with factor levels of 5% to 40% have bleeding tendencies similar to males with mild hemophilia; carriers with factor levels lower than 4% have bleeding tendencies similar to men with moderate to severe hemophilia.

The lower the factor level, the more susceptible a carrier is to bleeding problems.

What types of bleeding can occur in symptomatic carriers?
Bleeding in carriers is grouped into two general categories:
- Gynecological and obstetrical bleeding
- Other types of bleeding

Gynecological and obstetrical bleeding
- Menorrhagia—heavy bleeding during a menstrual period and/or prolonged menstrual bleeding (more than 7 days)
  - One of the most common gynecological signs or symptoms experienced by carriers of hemophilia
  - Common cause of iron deficiency, anemia, and decreased quality of life in affected women
  - Especially pronounced when a carrier first starts her period
- Metrorrhagia—abnormal/irregular vaginal bleeding
  - Occurs beyond normal menstrual period (between end of one menstrual period and beginning of next)
  - Variations in duration of bleeding and amount of blood loss
- Dysmenorrhea—painful menstruation
  - 50% of carriers experience moderate to severe menstrual pain
  - Possibility that heavier menstrual flow contributes to amount of pain experienced by some carriers during menstruation
- Mittelschmerz—mid-cycle abdominal pain
  - During ovulation at middle of the menstrual cycle (halfway between end of last period and beginning of next) when ovaries release new egg into fallopian tubes
  - Carriers of hemophilia are more likely to have this pain due to bleeding at ovulation
- Corpus luteum—hemorrhagic ovarian cyst
  - Carriers of hemophilia are more likely to have significant bleeding at ovulation
– Prolonged bleeding into an ovarian cyst causes it to expand, causing pelvic or abdominal pain
– At risk of rupturing around time of menstruation, causing internal bleeding and sudden pain in lower abdomen

■ Hemoperitoneum—bleeding into the abdominal cavity
– Bleeding into pelvic tissues, ligaments, and abdominal or pelvic cavities
– Bleeding into abdominal or pelvic cavities is serious and requires urgent medical attention

■ Postpartum bleeding—bleeding after childbirth
– Carriers of hemophilia are at risk of heavy bleeding with childbirth
– Bleeding complications during pregnancy are unusual (factor IX levels usually remain unchanged throughout pregnancy)

– Risk of hemorrhage within the first 24 hours following childbirth is 4% to 5% for noncarriers; this increases to 22% for carriers

Are there any other types of bleeding?
A symptomatic carrier has a higher tendency to bleed than the average person.

■ Bleeding signs and symptoms similar to those seen in males with mild hemophilia include:
– Easy bruising
– Prolonged bleeding from minor wounds
– Prolonged nosebleeds (epistaxis)
– Prolonged bleeding after tooth extraction
– Significant bleeding after trauma or surgery
How are bleeds in symptomatic carriers managed?

Signs and symptoms and types of bleeding that carriers have in common with males with hemophilia are usually treated in the same way. Gynecological and obstetrical types of bleeding experienced by symptomatic carriers require particular attention and treatment.28

Treatment options for bleeds in symptomatic carriers are usually considered on an individual basis taking into account the carrier’s age, gynecological issues, and reproductive plans. Treatment options include28:

- Menorrhagia and metrorrhagia—similar to the treatment for noncarriers except that the use of anti-inflammatory drugs, such as ibuprofen (Advil®), is not recommended for carriers because they increase bleeding. Other medical treatment options for menorrhagia are either hormonal or nonhormonal28
  - Women who have had a proper gynecological evaluation and who are either not effectively managed with hormonal therapy or want to become pregnant may consider treatments including DDAVP (1-desamino-8-D-arginine vasopressin), antifibrinolytic drugs (aminocaproic acid tranexamic acid), and clotting factor concentrates24
- Dysmenorrhea and mittelschmerz—usually involves anti-inflammatory drugs, such as ibuprofen (Advil®), but these should be avoided in carriers. Pain medication, such as acetaminophen (Tylenol®) and parecetomol and codeine-based medications (Empracet® and Tylenol® with codeine), can be used since they do not increase bleeding28
- Hemorrhagic ovarian cysts—usually managed conservatively without surgery in carriers of hemophilia using combined hormonal contraception or an antifibrinolytic agent, such as tranexamic acid or factor concentrates28
- Abdominal bleeding—usually requires treatment with factor concentrates28
- Childbirth and postpartum bleeding—management of carriers during childbirth is best carried out using a multidisciplinary approach28
  - Referral for prenatal and obstetrical care at a medical center where there are specialists in high-risk obstetrics and a hematologist with expertise in hemostasis28
  - Gynecological and obstetrical care for carriers is available through most hemophilia treatment centers, and some HTCs now have a multidisciplinary clinic for women with bleeding disorders28

Is a person’s quality of life affected if they are a symptomatic carrier?

Factors that may affect a carrier’s quality of life include:

- Age at which carrier is diagnosed
- Carrier’s history of bleeding signs and symptoms, such as frequent nosebleeds, easy bruising, or heavy menstrual periods, and whether bleeding problems have affected her school, work, and/or social life for a long time
Informed decision making—why it’s important to YOU

Diagnosis and knowledge of the options and strategies for treating female bleeding signs and symptoms allow carriers and family members to make informed decisions. This knowledge also allows a carrier to control how the bleeding disorder affects her quality of life and actively participate in her own medical care.\textsuperscript{28}

It’s important for carriers to register at a hemophilia treatment center, even if the carrier does not have abdominal bleeding signs and symptoms. Registering at the HTC allows her to:

- Get accurate information about hemophilia B and being a carrier from the comprehensive care team
- Get appropriate blood tests and genetic testing and counseling that can only be done at specialized centers
- Work out a treatment plan with the care team, including guidelines for emergency care or preventive treatment
- Have access to up-to-date information and the newest treatments related to carriers
- Learn about the latest research on hemophilia B\textsuperscript{28}

Project Red Flag and Victory for Women

Project Red Flag was the National Hemophilia Foundations’ public awareness campaign that educated women and their health care providers about the signs and symptoms of bleeding disorders and encouraged proper diagnosis and treatment.\textsuperscript{30} In the United States, 1.5 to 4 million women have a bleeding disorder.\textsuperscript{31}

NHF launched a new women’s health and bleeding disorder initiative at their 62nd annual meeting in New Orleans, Louisiana on November 11-13, 2010. It is called Victory for Women with Bleeding Disorders, and it builds and expands upon the former Project Red Flag. NHF wants all women in the United States to be able to raise their fingers in the “V” sign for “victory.” The idea behind Victory for Women is that only when all women are aware of the signs and symptoms of bleeding disorders can they achieve success.\textsuperscript{32}

The expanded program, Victory for Women, aims to:

- Raise awareness outside the bleeding disorders community
- Develop educational resources and programs for women with bleeding disorders
- Increase advocacy efforts
- Support research
- Collaborate with partners\textsuperscript{32}

More information about the Victory for Women initiative can be obtained by visiting www.victoryforwomen.org.
A Letter to All Women—Heavy Bleeding Should Not Be Ignored

Andra James, MD, MPH
Director, Women’s Hemostasis and Thrombosis Clinic
Associate Professor of Obstetrics & Gynecology
Division of Maternal Fetal Medicine
Associate Professor of Medicine
Duke University Medical Center
Durham, North Carolina

Nearly 1% of the population suffers from bleeding disorders, yet many women don’t know they have one because physicians aren’t looking for the condition, according to researchers at Duke University Medical Center.

“Hemophilia B carriers concern us as a group,” says Dr. James. “OB/GYN physicians think hemophilia B carriers don’t have problems, and as a result, don’t get referred to genetic counseling during pregnancy.” Because of a lack of anticipation by the physician that the infant may have additional needs, there may not be enough FIX available after surgery. Hemophilia B carriers, who have low FIX levels, need to be evaluated for a potential bleeding disorder during pregnancy, so that arrangements can be made for delivery to take place at a facility where physicians who treat bleeding disorders are available. In addition, all of a carrier’s children should be evaluated for a bleeding disorder, including boys and girls.

“Heavy bleeding should not be ignored,” says Dr. James. “When a woman’s blood can’t clot normally, the most obvious sign is a heavy period.” Women with a history of flooding during their period and heavy periods requiring treatment for anemia are an indication that a checkup is needed. Dr. James advises women with either of these situations to see their physician to have their factor levels checked or seek out a hemophilia treatment center for a complete checkup.

Unfortunately, when faced with these scenarios, most physicians aren’t suspecting a blood-clotting problem is to blame. “Sometimes they think hormones are the cause, or fibroids,” says Dr. James. “In some cases they recommend removal of the uterus or offer another gynecological explanation when the real contributing factor is a blood clotting disorder.”

An international expert consortium specifically outlined the definitive signs and symptoms that may signal the presence of a bleeding disorder in women. The guidelines aren’t just for physicians. “Women who suffer from heavy menstrual cycles should be on the lookout for these signs and symptoms as well,” says Dr. James. “About 25% of women with heavy menstruation may have an undiagnosed bleeding disorder,” she said.

Without the laboratory test, the consortium says women and physicians should be on the lookout for the following:

- Heavy blood loss during menstruation
- Family history of bleeding disorder
- Notable bruising without injury
- Minor wound bleeding that lasts more than 5 minutes
- Prolonged or excessive bleeding following dental extraction
- Unexpected surgical bleeding
- Hemorrhaging that requires blood transfusion
- Postpartum hemorrhaging, especially if it occurs more than 24 hours after delivery.
“Too often women think heavy bleeding is okay because the women in their family—who may also have an undiagnosed bleeding disorder—have heavy periods as well,” states Dr. James. “We want women who continually experience abnormal reproductive tract bleeding, specifically heavy menstrual bleeding, to be alert to these other signs and symptoms and approach their physicians about being evaluated.”

Medical and Scientific Advisory Council (MASAC) Guidelines for Perinatal Management of Women With Bleeding Disorders and Carriers of Hemophilia A and B

Bleeding in the peripartum period is a major issue for women with bleeding disorders. Now that more women with bleeding disorders are being identified, it is important that guidelines be established for the management of these women during pregnancy, labor and delivery, and in the postpartum period to minimize the risk of bleeding-related complications.

1. Preconception genetic counseling: Girls and women who are at risk for being carriers of hemophilia A and B and other severe bleeding disorders should have their bleeding disorder status determined before they become pregnant.

2. Pregnancy management: Pregnancy should be managed by a multidisciplinary team of specialists, including a coagulation disorders specialist, an obstetrician, and an anesthesiologist, all of whom are knowledgeable in the management of women with bleeding disorders.

3. Labor and delivery management: Women with bleeding disorders are at risk of bleeding complications during pregnancy and the postpartum period. Women should give birth in a facility that has the appropriate laboratory, pharmacy, and blood bank support.

4. Method of delivery: While the majority of infants of hemophilia carriers can be safely delivered vaginally, the outcome of labor cannot be predicted, and a spontaneous (nonoperative) vaginal delivery cannot be guaranteed. Therefore, obstetricians caring for women who are carriers of hemophilia should discuss with the woman the maternal and fetal risks of a vaginal delivery versus a planned cesarean delivery; the option of a planned cesarean should be recommended when an affected or potentially affected infant is anticipated.

5. Umbilical cord blood sampling: Umbilical cord blood should be obtained through proper technique at the time of delivery in order to avoid venipuncture of the infant and to ensure that the neonate is tested early.

6. Postpartum management of the mother to prevent bleeding: Obstetricians and midwives routinely take precautions to prevent postpartum hemorrhage, and this is especially important in women with bleeding disorders. The third stage of labor should be actively managed to reduce blood loss and reduce the incidence of postpartum hemorrhage.
**BECKY VANSANT**

Mother of Elizabeth who has hemophilia B
Advocate for all women with hemophilia B
Becky VanSant is a mother of three daughters ages 10, 14, and 18. Elizabeth, the 18-year-old, has severe hemophilia B and is the first person with hemophilia B in the family. Becky describes this as, “Elizabeth’s translocation is on the long arm of her X chromosome and her 14th chromosome. An equal size piece of each X chromosome and each 14th chromosome traded places. Therefore, her X has a piece of her 14th, and her 14th has an equal size piece of her X.” Becky and her husband, Jim, have been very proactive in seeking medical help that will be important to others as well in the future.

When Elizabeth was 3 months of age, she had a bruise on her chest. When Becky took her to the physician to have it checked, he did a finger-prick blood test. The bleeding from this test did not stop. In further analysis, the physician noted that Elizabeth’s FIX level was very low. Not only was the physician surprised at this, but Becky and her husband found this very difficult to believe because Elizabeth did not fit the profile. There was no information about girls being diagnosed with hemophilia B. Becky and Jim not only had difficulty accepting this diagnosis, but also found it difficult to explain to others that she did indeed have hemophilia B, including a nurse they met before Elizabeth’s surgery who was in the surgery waiting area. The nurse argued for some time with Becky that this was impossible. She was a tough sell and hard to convince that Elizabeth had hemophilia. This reaction was because most of the literature and teaching at the time centered around boys, not girls with hemophilia.

“When we began to go to an HTC, we found that the education about the genetics and the cause of Elizabeth’s hemophilia helped us, and we started to get involved. The support from the HTC was more valuable than anything in our acceptance of the diagnosis. Before that, we felt like we were really alone because everyone and everything pertained to boys,” Becky stated. “It took time for people to focus on the diagnosis and not on the gender. In time we became part of the hemophilia B community, and everyone accepted Elizabeth as a person, just like the others who had hemophilia B.

Becky feels that over the past 18 years, the educational information for women with bleeding disorders has increased quite a bit. She has become very proactive in her efforts to build awareness with as many women as she meets. She tells them, “If you have bleeding issues, get your levels checked because there might be a reason for this.” “I do see more women speaking up now and things are changing in the hemophilia B community,” Becky says.

As a teacher, she has had an impact on some of her previous students who are now in college and call her with statements professors have made such as, “Women can’t have hemophilia.” Becky believes that little by little awareness will continue to build that hemophilia B is not necessarily gender-specific. “Instead of focusing on gender, if your factor levels are low, you are a hemophiliac. If you are a symptomatic carrier, you are a mild or moderate hemophiliac.”

Becky says, “When we first joined the hemophilia B community, everyone was shocked. Now it is okay. We’re finally in the place where women are accepted as a part of the community, and we are no longer alone.”
HEMOPHILIA B DOESN’T DEFINE ME—
IT’S A PART OF WHO I AM

Elizabeth VanSant

18 years of age
Loves golf and music
Has severe hemophilia B
When Elizabeth was in third and fourth grades, she was very angry that she had hemophilia B. “There was a stage when I was so angry. I am over that now, and in order to do what I want to do, I just accept it and move on. I don’t talk about it much at all. My classes at school are all single gender, so it has not been an issue.” Her hemophilia B has only impacted her physical education classes at school.

Elizabeth is self-infusing and is doing well. The ability to self-infuse is an important skill for Elizabeth as she heads off to college.

The hemophilia B community is much more accepting of Elizabeth and other women with a bleeding disorder now. Elizabeth has been doing what she can to inform others about women with hemophilia B and how she is coping. When she was in New York she spent time talking with other children with hemophilia about the disorder and how they can manage daily challenges. She credits her family with being a great support for her and says her sisters think it is kind of cool that she is doing her own self-infusing.

When asked about her future, she said that she is already thinking about how she will need to consider specific jobs and insurance plans. She said she may consider becoming a teacher, and shared that she loves music and golf. “I love golf, but I am not in to many other sports. I am more of a musical person; I play the piano, the flute, and the guitar.” Elizabeth has plans like any other teen. She says, “I’ll progress normally like anyone else. Hemophilia B doesn’t define me, it’s only a part of who I am.”
CLINICAL CHALLENGES IN THE AGING HEMOPHILIA B POPULATION

The availability of safe replacement clotting factor concentrates together with effective antiviral drugs to treat HIV and HCV viruses and the provision of care at designated hemophilia treatment centers have resulted in a new phenomenon in hemophilia B management—the aging patient.8

"Today, increasing numbers of persons with hemophilia B are middle-aged and older, and they face the same age-related health issues as the general population. The impact of these risks on people with hemophilia B is unclear, and there is a lack of available information about how to manage comorbidities that uniquely affect older persons with hemophilia B, including cardiovascular disease, liver disease, cancer, renal disease, and joint disease."8 Obesity is a particularly important problem for patients with hemophilia. People with hemophilia who are overweight or obese face the same problems as such individuals in the general population. There are also additional concerns with obesity in hemophilia. Arthropathy (joint damage) occurs more often in overweight and obese individuals with hemophilia who have decreased range of motion that is correlated in a higher body mass index.35

Older persons with hemophilia B face many challenges related not only to hemophilia B but also associated with aging. They may often have known risk factors for cardiovascular disease, such as hypertension and HCV infection, which may counteract any protective effects gained from the hypocoagulable state. Arthritis and joint disease are common and contribute to disability and pain.36

The high prevalence of HCV infection has led to an increased risk for liver failure and hepatocellular (kidney) carcinoma. Renal function and urological disorders are a concern in these patients.36 The risk for chronic kidney disease and acute renal failure is also increased in people with hemophilia, with the risk of death from renal failure as high as 30 to 50 times higher than the general population. HIV infection in people with hemophilia appears to play an important role in this increased risk.37

The use of routine procedures for general health maintenance in the elderly (eg, colonoscopy) can be more complex in patients with hemophilia B due to the inherent risk of bleeding, and serious disorders, such as malignancies, can be overlooked if signs and symptoms of abnormal bleeding are attributed to hemophilia B, rather than to cancer.36

Patients with hemophilia may also be at increased risk for the development of osteoporosis (abnormally high bone loss with aging). Multiple factors may contribute to increased risk for this condition, including hemarthrosis and arthropathy, long periods of immobility that contribute to increased bone resorption, and inflammation associated with HCV and/or HIV infection.38

Stay in Control

- Control stress—stress can have a negative effect on the immune system, which is already compromised in a large segment of the hemophilia B population because of HIV
- Know your disorder—learn all you can about the disorder and conditions that affect your life and health. Then you will be capable of informed decision making
- Maintain a good relationship with your comprehensive care team—take an active role in the treatment and management of your health care
- Keep an ongoing list of questions and signs and symptoms—bring this list with you when you go to medical appointments
Don’t Let Your Hemophilia Card Get Out of Date
Edward Kuebler, LCSW
Gulf States Hemophilia and Thrombophilia Center
Houston, Texas

Edward Kuebler, a member of the comprehensive care team at Gulf States Hemophilia and Thrombophilia Center in Houston, Texas, works with families and individuals in the hemophilia B community. He is familiar with many of the life stages of this disorder, from newly diagnosed infants up to and including the aging population, who have lived with hemophilia B their entire lives.

Aging considerations common to everyone else create additional challenges for those with hemophilia B. If you or a family member has hemophilia B, many of these complications may seem insurmountable to you as you age. Ed Kuebler encourages, Be assured that you have the skill base to manage them. You already know how to do this as you have through all of the life transitions you have gone through before today.”

Mr. Kuebler is very clear about how important it is for you to be involved in your own medical care, “It’s important that you let your hemophilia treatment center team know what you need. Don’t try to manage everything yourself. This is for you now; this is your time, and we are there to help you. If you have any concerns at all, don’t hesitate to speak with any of us at the HTC. We will make sure that you have all the help and support you need.”

“You have been the frontier group for young people with hemophilia B, and they recognize this. They look to you as mentors to guide them through difficult stages. You’ve paved the way forcing better treatment protocols, comprehensive care centers, increased awareness of hemophilia B throughout the population, and in many cases, you understand more about hemophilia B and its treatment than most health care providers,” Mr. Kuebler states.

However, you are the first aging population with hemophilia B, and you do need someone to guide you when you are undergoing procedures or moving into uncharted territory. A comprehensive treatment team will coordinate your care with your internist and any other specialists your care may require. Members of the team will be there to help you before and after.

It’s important now that you help to educate the hemophilia B community and build awareness that people with hemophilia B, who are in their senior years, make life as normal as possible as they age. Encourage them to stay strong and fit, and talk to the hemophilia treatment center team about ways to design their own wellness program.

There’s no reason why aging people with hemophilia B shouldn’t live normal, active, fulfilling lives. The support is there for you when and if you need it. It’s up to you to stay in the game.

- Stay positive—treat problems as challenges that can be solved and not as insurmountable obstacles
- Stay strong and fit—this is one of the best things anyone can do to counteract aging
- Be with the things and people you love—laugh often and do the things you love
ME, I’M ABOUT TO START A NEW CHAPTER IN MY LIFE

Wayne Cook

Hemophilia B patient

Age 50
Wayne Cook, president of the Coalition for Hemophilia B, Inc., father of three, golfer, car enthusiast, a person with hemophilia B, and a long-time mentor to the hemophilia B community, tells us very clearly, “I want to live a long, happy life. I want to do the things I love. I am now about to start a new chapter in my life.”

Wayne was diagnosed with hemophilia B when he was 6 years old after a head injury called attention to his bleeding disorder. At that time, he was treated with fresh frozen plasma and spent days in the hospital. Wayne reminds us, “Medicine has come a long way since then in how they diagnose and treat hemophilia B.” His initial treatment was managed by the family physician, and it wasn’t until 1985 that Wayne became a patient at a hemophilia treatment center.

“I don’t focus on hemophilia B. The quality of factor products today has helped us to lead better lives, and I am very proactive with my own care. I always take care of myself. I infuse as prevention, if I am doing something that may cause a bleed,” states Wayne. Because of his health issues, Wayne was not able to exercise much, and he developed a weight problem. This in turn led to other health problems unrelated to hemophilia B. When asked how he manages to lead such an active life anyway, Wayne said, “My hemophilia B is second nature to me now. I go for checkups every 6 months, and I am too busy with my life to let hemophilia B rule me.”

Wayne is an aging person with hemophilia B. He has lived through many life stages to get where he is today. He has other medical problems in addition to hemophilia B, including cardiology issues. Wayne has been through several surgeries. He was asked how he managed all of this while raising a family and how he is managing life now as an aging person with hemophilia B. Wayne’s strongest advice to other aging persons with hemophilia B is, “Communicate with every member of your care team all the time. Become your own advocate and insist that they speak with you and each other about your care.” Before Wayne enters into any surgery, he gets the treatment team together to discuss his physical condition, what FIX he is taking and how much. “Communication between the doctors is so important,” says Wayne. He will always stay in contact with all of his physicians and ask them if there is anything special he has to do. He keeps an ongoing list of all his medications with him at all times and stays much attuned to any signs and symptoms that he notices when they develop. “As we age, problems do develop, and letting your physician know right away is the best way to deal with them,” Wayne advises.

When asked what advice he might have for other aging persons with hemophilia B, Wayne offered:

- Be your own advocate in your care. Communicate everything to your physicians, as issues will develop as you age
- Don’t be afraid to travel. Take your FIX and all your other medications with you, and if possible, investigate where you could obtain medical care if you need it, such as at a hemophilia treatment center or a hospital. Sometimes, I contact my physicians and ask if there is anything special I should do. I also carry a letter with me from my primary care physician explaining my health situation and the medications I take
- Plan for your financial future. Because we have hemophilia B, we never thought we would live to be seniors, so we didn’t plan ahead. People with hemophilia B who are over age 50 really need to begin thinking about all of this. Find a financial advisor to help you. Make sure you have a will. Look into how and where you will manage your senior years. I have made all of my own plans, so I took the burden off my family
- Get out there, get involved, and enjoy living your life to its fullest
It is important to get diagnosed as soon as possible—do not wait for a serious bleed in the midst of an emergency.\textsuperscript{13}

The consequences of having hemophilia depend on the severity of the disorder. The level of clotting factor activity determines the severity. Normal clotting factor activity is described as 100%, but can be anywhere within the range of 50% to 150%.\textsuperscript{13}

In people with hemophilia, the clotting factor activity is lower than normal. The lower the clotting factor activity level, the more frequent the bleeding.\textsuperscript{13}

### Classification of Hemophilia\textsuperscript{14}

<table>
<thead>
<tr>
<th>Classification of hemophilia</th>
<th>Percentage of clotting factor activity</th>
</tr>
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<tbody>
<tr>
<td>Severe</td>
<td>Less than 1%</td>
</tr>
<tr>
<td>Moderate</td>
<td>1% to 5% of normal</td>
</tr>
<tr>
<td>Mild</td>
<td>5% to 30% of normal</td>
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</tbody>
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People with severe hemophilia can have frequent bleeding episodes and bleeding into major joints, muscles, and soft tissues.\textsuperscript{13}

People with moderate hemophilia usually have fewer bleeds than those with the severe form. Their bleeds are frequently the result of minor trauma, such as a sports injury. However, some people with moderate hemophilia, especially those with a factor IX level of 1% to 2%, can have bleeding into joints and muscles without a known cause of trauma. This is similar to people with severe hemophilia.\textsuperscript{13}

People with mild hemophilia rarely have unexplained bleeding episodes. When there are any, they are the result of serious injury, surgery, or dental extractions. Because of this, some people with mild hemophilia remain undiagnosed until they have a significant trauma or undergo surgery. In these patients, not knowing a bleeding disorder is present may lead to extreme blood loss, which can be serious.\textsuperscript{13}

If you or your family physician suspects your child has a bleeding disorder, it is important to go to a hospital that specializes in diagnosing and treating bleeding disorders, such as a hemophilia treatment center. Specialists there can take a careful clinical and family history of bleeding and do the laboratory tests for diagnosis. It is important to get diagnosed as soon as possible—do not wait for a serious bleed in the midst of an emergency.\textsuperscript{13}
SURGERY TAKES A TEAM—BE PROACTIVE BEFORE YOU HAVE ELECTIVE SURGERY

“Adequate hemostasis (the stoppage of bleeding or hemorrhage) during surgery and postoperative rehabilitation is crucial, as development of a wound hematoma may jeopardize long-term outcomes. Success depends not only on appropriate drug therapy but also on preoperative preparation and adequate perioperative surveillance. Preoperative assessment of vascular status is very important, and strong motivation on the part of the patient, the surgeon, and the hematologist is needed to ensure a satisfactory result.”

YOU know your child and yourself better than anyone. Be proactive about your medical needs and insist that your physician, surgeon, and you communicate about your hemophilia B before surgery. Make sure that all know what factor IX you are taking and how much you are taking. Also, make sure that there is enough on hand to prevent any problems after surgery. Surgery takes a team!

Here are a few suggestions to help you prepare before surgery:
- Interview your surgeon. He or she should have experience operating on people with bleeding disorders and understanding potential complications
- Get a second opinion. Most insurance companies encourage second opinions; for some procedures, they may be mandatory
- Find out who your surgical support team is. If the hematologist overseeing your care is not your usual physician, make an appointment to discuss your needs and concerns
- Ask about factor coverage. These days, most replacement surgeries are done under continuous infusion
- Meet with the anesthesiologist to discuss pain management. Discuss any previous reactions to anesthetics or prescription pain medications
- Ask how long you will be in the hospital. Make arrangements for help at home once you are discharged
WHAT DOES THE FUTURE HOLD FOR HEMOPHILIA B?

In January 2009, W. Keith Hoots, MD, became the director of the Division of Blood Diseases and Resources at the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) in Bethesda, Maryland. Prior to this appointment, Dr. Hoots received the National Hemophilia Foundation’s Outstanding Service Award in 2004. He also chaired NHF’s Medical and Scientific Advisory Council (MASAC) from 2001 to 2007. In his new position, he will have an opportunity to make a greater impact on bleeding disorders research and treatment.42

Dr. Hoots feels that a promising research area for the bleeding disorders community is the way that cells interact with proteins in response to injury. “I hope this will result in a more complete understanding of all the elements that interact to produce normal clotting in response to injury,” he says. “This knowledge could then direct new avenues of research to enhance clotting in the face of too much bleeding or to reduce clotting activation when thrombosis is most likely to occur.”42

In the next decade, Hoots says challenges include continuing to improve quality of life with better and longer-acting factor concentrates and exploring the role that gene transfer could have in treating or curing bleeding disorders.42

In December of 2011, a paper published in *The New England Journal of Medicine* reported the first unequivocal evidence of success in gene therapy for hemophilia B. Six patients with severe hemophilia B responded to injections of a normal factor IX gene. The first patient treated with a low-dose injection has maintained levels of 2% for more than 16 months, while another patient receiving the highest dose maintained levels that fluctuated between 8% and 12% for 20 weeks. All six patients showed benefit from the factor IX gene administration.17,43

The researchers involved in this study stated that “this study documents a critical step toward [eliminating the need for long-term intravenous infusions] and shows that sustained therapeutic expression of a transferred factor IX gene can be achieved in humans.” The study concluded that “this gene-therapy approach, even with the associated risk of transient hepatic dysfunction, has the potential to convert the severe bleeding phenotype into a mild form of the disease or to reverse it entirely.”43
RESOURCES

Arizona Hemophilia Association
North American Camping Conference of Hemophilia Organizations (NACCHO)
Phone: 888-754-7017
Web site: www.naccho.com

Canadian Hemophilia Society
Phone: 800-668-2686
Web site: www.hemophilia.ca

Centers for Disease Control and Prevention (CDC)
Hemophilia Treatment Centers
Web site: www.cdc.gov/ncbddd/hemophilia/HTC.html

The Coalition for Hemophilia B, Inc.
Phone: 212-520-8272
Web site: www.coalitionforhemophilia.org

Hemophilia Federation of America (HFA)
Phone: 800-230-9797
Web site: www.hemophiliafed.org

Pfizer Hemophilia’s HemMobile™
HemMobile™ is an app to log infusions, track bleeds, and more. Created with essential patient and caregiver input, this is one app designed with the community in mind. Visit HemophiliaVillage.com for more information.

National Heart, Lung, and Blood Institute
Phone: 301-592-8573
Web site: www.nhlbi.nih.gov

National Hemophilia Foundation (NHF)
Phone: 800-424-2634 (42-HANDI)
Web site: www.hemophilia.org

Patient Services Inc. (PSI)
Phone: 800-366-7741
Web site: www.patientservicesinc.org

World Federation of Hemophilia (WFH)
Phone: 514-875-7944
Web site: www.wfh.org

Pfizer provides a wealth of programs and services to support consumers. Please visit us at Pfizer.com for further information.
REFERENCES


This book was funded by Pfizer Inc and distributed in partnership with The Coalition for Hemophilia B, Inc.

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