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Carl lives in Denmark
and has haemophilia A

Congenital Haemophilia

**A guide for people with congenital
haemophilia and their families***

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Congenital Haemophilia

If you have congenital haemophilia, you're not alone. It's a disorder present from birth, in which the blood cannot clot properly, so bleeding takes longer to stop than normal. Although it's considered to be rare, congenital haemophilia affects many thousands of people around the world.

Understanding your condition is important for staying well, to help you live life to the full. This booklet has been written to help further that understanding, supporting the information and care provided by your haemophilia centre.

As always, talk to your doctor or nurse at your haemophilia centre if anything is unclear. You can be sure that they will always be happy to help.

What types are there?

There are two main types of haemophilia, called haemophilia A and haemophilia B. To understand the differences between these, we first need to consider how the body normally stops bleeding.

Imagine someone cuts their finger in the kitchen. To prevent excessive blood loss, tiny cells in the bloodstream called platelets clump together and form a plug at the site of the injury. Substances in the body called clotting factors then undergo a chain reaction that acts to 'glue' this plug into place. It is this clotting process that stops the bleeding. Two of the clotting factors needed for this are factor VIII and factor IX ('VIII' is the Roman numeral for 8 and 'IX' is the Roman numeral for 9).

Haemophilia A and haemophilia B are defined by the absence or lack of factor VIII or factor IX, respectively:

As explained later in this booklet, haemophilia is passed down through families in such a way that it mainly affects males:

- Approximately 1 in every 4,000 males born will have haemophilia A
- Approximately 1 in every 20,000 males born will have haemophilia B

Your doctor or nurse at your haemophilia centre will be able to tell you which type of haemophilia you or your child has.

How is severity classified?

Haemophilia is classified as mild, moderate or severe, based on the amount of clotting factor activity in the blood. Factor levels can be expressed as a percentage of normal factor activity or as specific units of activity within an amount of blood:

	Percentage of normal factor activity in the blood	Number of international units (IU) per milliliter (ml) of whole blood
Mild haemophilia	5–40%	0.05–0.4 IU
Moderate haemophilia	1–5%	0.01–0.05 IU
Severe haemophilia	Less than 1%	Less than 0.01 IU

People with mild haemophilia may never have a bleeding problem, unless they have surgery or a major injury. Those with moderate haemophilia have a greater risk of prolonged bleeding e.g. after dental procedures. However, they rarely experience spontaneous bleeds – that is, bleeding that occurs without an obvious external cause. In severe haemophilia, spontaneous bleeds do occur. There may also be bleeding into muscles, joints and other parts of the body, which we will cover later in this booklet.

Congenital haemophilia

Haemophilia A

(also called 'Classic haemophilia')

Caused by an absence or lack of factor VIII and accounts for around 80% of haemophilia cases

Haemophilia B

(also called 'Christmas disease')

Caused by an absence or lack of factor IX and accounts for around 20% of haemophilia cases

What causes it?

Haemophilia is usually inherited – that is, passed to children from their parents. This passing on process is done via the parents' genes. Genes are like a biological instruction manual that tells the cells in the body how to develop (e.g. what hair and eye colour a person will have).

It is important to note, however, that haemophilia can sometimes occur when there is no family history of it. This is called sporadic haemophilia. Around 1 in 3 people with haemophilia A and 1 in 5 with haemophilia B did not get their condition through their parents' genes. It was caused by a change in their genes, not passed to them by their parents.

How is it passed through families?

To understand how haemophilia is inherited, we need to take a look at sex chromosomes. These are strands of genetic material found inside cells. There are two types of sex chromosomes, known as X and Y. All humans have a pair of these, which determines their gender. Males have an XY pair and females have an XX pair. Boys inherit their X chromosome from their mother and their Y chromosome from their father. Girls on the other hand inherit an X chromosome from each parent.

The genes or 'instructions' for making blood clotting factors are found on the X chromosome. Haemophilia is therefore described as an X-linked disorder. As girls have two X chromosomes, they usually receive a healthy gene on the second X

chromosome. This healthy gene will be dominant, so girls who inherit the gene for haemophilia are carriers of the disease, but don't usually show symptoms of it themselves. This is because their healthy gene can often code for the production of enough clotting factor to stop bleeding.

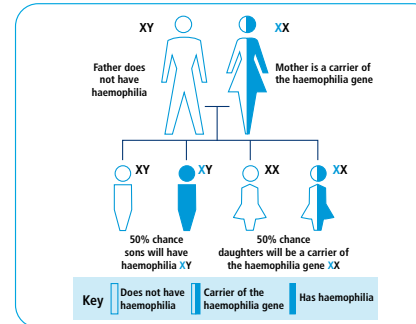
This is not always the case though, as some women who are genetic carriers of haemophilia do have bleeding symptoms. That is because they have low levels of factor VIII or factor IX, due to partial inactivation of their 'normal' functioning X chromosome. This is called lyonization. If their clotting factor levels are below 40%, they meet the diagnostic criteria for having haemophilia. In addition, bleeding symptoms can occur when factor levels are in the normal range, which is referred to as a symptomatic carrier state.

Things are different for males who inherit the gene for haemophilia, because they only have one X chromosome. This means they have no 'back up' instructions for making clotting factor. As a result, they cannot produce enough clotting factor – or are unable to make any at all – so their ability to stop bleeding is always compromised.

Will my children have it?

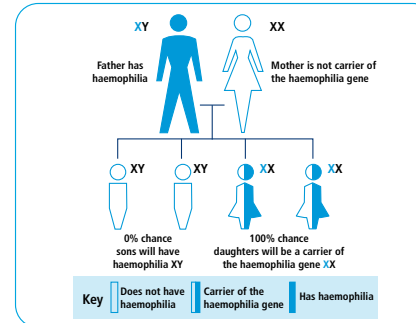
The likelihood of your child having haemophilia or being a carrier of it will depend on the genetics of both you and your partner, as shown in the following examples. Remember, however, that around one-third of people with haemophilia have no family history of the disorder. In these cases, haemophilia was caused by a change in their genes, rather than being passed to them by their parents.

Example 1. Mother is a carrier



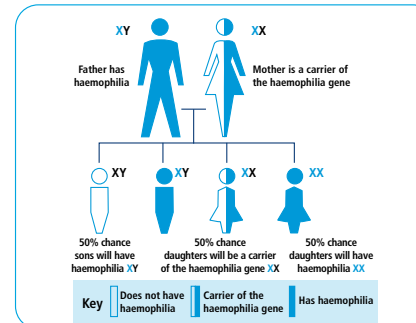
- Each son born to these parents has a fifty-fifty chance of having haemophilia
- Each daughter born to these parents has a fifty-fifty chance of carrying the haemophilia gene

Example 2. Father has haemophilia



- All daughters born to these parents will carry the haemophilia gene
- No sons born to these parents will have haemophilia

Example 3. Father has haemophilia and mother is a carrier



- Each son born to these parents has a fifty-fifty chance of having haemophilia
- Each daughter born to this couple has a fifty-fifty chance of having haemophilia. Any daughters that don't have haemophilia will carry the haemophilia gene.

Genetic counselling helps people to understand their likelihood of passing a disease onto their children, as well as offering advice and support. If you would like to know more, ask your doctor or nurse at your haemophilia centre about genetic counselling services in your area.

How is it diagnosed?

As haemophilia is usually inherited, some people have a family history of the disease. Because of this, they may seek genetic counselling and testing before or during pregnancy. The diagnosis of haemophilia usually begins with a review of a person's family history, particularly on the maternal side. In those with no family history of haemophilia, diagnosis often occurs after childhood injuries or procedures, such as immunisations or tooth extractions, when there is excessive bleeding.

The most important standardised tests of clotting are platelet count, prothrombin time (PT) and activated partial thromboplastin time (aPTT). Laboratory test results in newborns differ from adult results, as

babies are born with low vitamin K levels and receive a dose of vitamin K shortly after birth. Vitamin K affects clotting test results, which complicates diagnosis of haemophilia.

Platelet count and PT will be normal for age, but the aPTT will be prolonged in haemophilia A and B. Specific assays are performed on plasma samples to measure the amount of factor VIII or IX in an individual, to determine the level of deficiency and classify haemophilia severity.

Genetic testing plays a key role in identifying the mutation in people with haemophilia A or B. Genetic testing is often done in conjunction with a genetic counsellor, or with a specialist in a haemophilia treatment centre.

	Haemophilia A	Haemophilia B
Prothrombin time (PT)	Normal	Normal
Activated partial thromboplastin time (aPPT)	Prolonged	Prolonged
Platelet count	Normal	Normal
Factor level	Factor VIII less than 40%	Factor IX less than 40%
Genetic testing	Factor VIII gene abnormality	Factor IX gene abnormality

How do I spot a bleed?

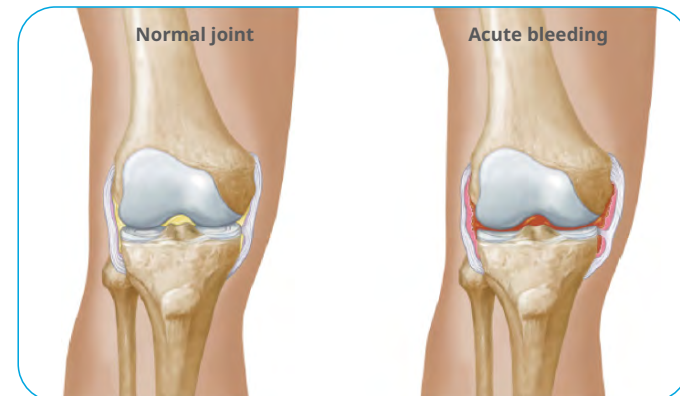
While external bleeding is usually easy to see, bleeds inside the body can be harder to recognise. Being able to spot bleeds quickly is very important, so that appropriate action can be taken without delay. This is particularly true for children, as they may be too young to say how they feel.

Some bleeds are clearly due to trauma, like a cut or fall. However, bleeds may also occur spontaneously in some people with haemophilia, with no obvious external cause. In this section, we will consider the type of bleeds that may occur and how to spot them.

Joint bleeds

There are many types of bleeds, but joint bleeds are the most common, accounting for 70–75% of all bleeding episodes. Joint bleeds happen when blood vessels in the tissue lining the joint (the synovium) are injured. The most common sites for joint bleeds are the knees, ankles and elbows. But bleeds can occur in any joint, including the shoulder, hip, hands and feet. Repeated joint bleeds can lead to joint damage, called arthropathy or haemophilic arthropathy.

During a joint bleed, the first sign may be a tingling or bubbling feeling. As the bleed progresses, there may also be limited motion, swelling, pain that worsens with time, or general difficulty moving the joint. You may eventually feel warmth on the skin covering the joint, or see swelling. However, these are late signs, which means that the bleeding has been going on for a while.



Muscle bleeds

Muscle bleeds happen when blood vessels in a muscle are injured. The cause of muscle bleeds is sometimes known, such as an injury, but spontaneous bleeds can also happen. The most common muscle bleeds occur in the calf, thigh and upper arm. But bleeds in the psoas muscle at the front of the hip and the forearm muscles also occur.

During a muscle bleed, the muscle swells and feels warm, stiff and painful. Bruising may be seen if the bleed is the result of trauma near the skin. Bleeds in muscles can put pressure on nerves and blood vessels, which is called a compartment syndrome. This causes tingling and numbness and may result in permanent damage. A muscle spasm may occur when the muscle tightens up to protect itself (called Volkmann's sign). Development of a compartment syndrome represents a serious bleed and your haemophilia treatment centre should be contacted immediately.

Head bleeds

Head bleeds can be just under the skin or inside the skull itself, in or around the brain. They are usually, but not always, caused by an injury. If you or your child suffers from a headache that seems to go on for longer than usual, or if there is an extreme lack of energy or sleepiness, it could point to a head bleed. Other symptoms include: trouble walking in a straight line or difficulty walking at all; vision problems; bleeding from the ears or nose; loss of consciousness; vomiting;

seizures and dizziness. Bleeding in the head is serious, so contact your haemophilia treatment centre immediately if you feel this might have happened.

Spine bleeds

Spine bleeds can occur spontaneously or as a result of injury. These bleeds put pressure on the spinal cord or the nerves going to the body, so arms or legs may feel weak – or there may be pain or tingling. Trouble with urination or bowel movements can also be a sign of pressure on the spinal cord from a bleed. Bleeding in and around the spine is serious, so contact your haemophilia treatment centre immediately if you suspect this may have happened.

Stomach and intestinal bleeds

Bleeds in the stomach and intestine, sometimes called gastrointestinal (GI) bleeds, can occur for a variety of reasons. They sometimes occur in conjunction with other medical problems, such as ulcers – or after endoscopic procedures. Symptoms include vomiting blood or black, syrup-like material that is sometimes described as looking like coffee grounds. Red or black bowel movements resembling tar can also occur. Bleeding in the stomach and intestines is serious, so contact your haemophilia treatment centre immediately if you suspect this may have happened.

Life-threatening bleeds

Contact your haemophilia treatment centre immediately if you suspect a bleed in the head, neck, throat or abdomen, as these are potentially life-threatening

Does age affect type of bleeding?

Taking normal growth and development into account is important for recognising the types of bleeds most likely to occur at different ages. Babies, for example, may undergo circumcision and receive vaccinations, while toddlers are likely to have bumps and bruises while learning to walk. In older children and adults, joint and muscle bleeds become more common, particularly those affecting the ankles, knees and elbows.

Adolescents and adults also have the potential for more serious muscle bleeds, such as bleeding in the muscles that run inside the pelvis, along the inner side of the hip bones (called the iliopsoas).

What treatments are available?

Haemophilia A and B can be treated by replacing the missing clotting factors. In people with haemophilia A, factor VIII (FVIII)

is replaced and in people with Haemophilia B, factor IX is replaced. This is done via intravenous injection for factor replacement therapy - that is, injected into a vein. Non-factor replacement therapy may involve a subcutaneous injection, under the skin.

There are broadly two approaches to treatment: on demand and prophylactic. On-demand treatment is given once a bleed has started, while prophylactic treatment is given to prevent bleeds from starting in the first place.

On-demand treatment

On-demand treatment, given when a bleed occurs, can be used in people with mild to moderate haemophilia and in some people with severe haemophilia. With an on-demand approach, less frequent injections may be needed, compared with prophylactic treatment. However, it's important to recognise bleeds promptly, then act quickly to reduce the risk of a bleed causing damage.

Desmopressin treatment

Some people with mild haemophilia A can be treated on-demand with desmopressin. This is a man-made form of a hormone that works by stimulating the release of a small amount of factor VIII that is stored in endothelial cells in the body.

Prophylactic treatment

Prophylactic treatment, sometimes called prophylaxis, is given at regular intervals to prevent bleeds from happening. As well as helping blood to clot, prophylaxis reduces the likelihood of long-term damage to the body due to bleeding. This is important, because people with severe haemophilia can experience spontaneous bleeds, without any external cause. Without prophylaxis, a person with severe haemophilia can have frequent bleeds into joints for example, resulting in long-term damage such as arthritis.

Prophylactic treatment can help people to get on with work or study without too much disruption. Prophylaxis may also mean fewer visits to a haemophilia centre for treatment, although this varies according to individual circumstances. It is important to remember, however, that prophylaxis involves regular administration of clotting factor, necessitating an ongoing commitment from the person with haemophilia themselves or their parent or carer.

World Federation of Hemophilia (WFH) definitions of clotting factor replacement therapy

Term	Definition
On-demand treatment	Treatment given at the time of clinically-evident bleeding
Primary prophylaxis	Regular continuous* treatment initiated in the absence of documented bone changes in the joints, determined by physical examination and/or imaging studies, and started before the second clinically evident large joint bleed and age 3 years.
Secondary prophylaxis	Regular continuous* treatment started after 2 or more bleeds into large joints (ankles, knees, hips, elbows and shoulders) and before the onset of joint disease documented by physical examination and imaging studies.
Tertiary prophylaxis	Regular continuous* treatment started after the onset of joint disease documented by physical examination and plain x-rays of the affected joints.
Intermittent (periodic) prophylaxis	Treatment given to prevent bleeding for periods not exceeding 45 weeks in a year

*Continuous prophylaxis is defined as the intent of treating for 52 weeks per year with patient adherence to administering a minimum prescribed number of infusions per week for at least 45 weeks a year.

Which treatment will I or my child receive?

Most people with haemophilia need preventative treatment (prophylaxis). This involves regular injections of the clotting factor that is missing or of a non-factor replacement therapy, which helps with the clotting process.* If your child has haemophilia, you will be shown how to give the injections. As they grow older, they will be taught how to do this themselves.

In some cases, injections may be given into a device called an implantable port, which can be surgically placed under the skin. This port is connected to a blood vessel near the heart, which avoids the issue of having to find a vein for injection. While prophylaxis is usually continued for life, a change to on-demand treatment may be possible in some cases.

It is important to note, however, that every person with haemophilia is unique, so an individualised approach is vital. The team at your haemophilia centre will work with you to design a treatment plan that meets the specific needs of you or your child.

How do I treat bleeding episodes?

The World Federation of Hemophilia (WFH) recommends immediate treatment once a bleed starts, ideally within 2 hours

if possible. The WFH also recommends additional support with **R**est, **I**ce, **C**ompression and **E**levation – known as **R.I.C.E.** Early treatment of bleeds may limit the amount of blood in the joint or in other bleed locations, which is very important. Be aware that a feeling of bubbling or tingling may be an early sign of bleeding, showing that it's time to treat. Don't wait for swelling or pain, which may indicate that a lot of blood has already entered the joint.

Pain management is also important and pain medicines (analgesics) are a key part of this. However, it's important to know which ones you can take and which you should avoid. You need to be sure that an analgesic won't interfere with your clotting factor medicine.

Some pain medicines containing aspirin can affect your platelets or blood clotting. The same is true for non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or naproxen. Avoid these medicines, as they might make the bleed worse. Many over the counter products contain aspirin or NSAIDs and some spices and herbal remedies can affect blood clotting too. Check with your doctor or nurse at your haemophilia treatment center to identify which pain medications, spices and herbal remedies you should avoid. You should also check with the pharmacist when buying over the counter products.

*Ask your health care provider for further information on new therapies.

Joint bleed and arthritis

Joint bleeding can lead to serious complications. That's because blood causes joint damage, first to the soft tissues (synovium) and then to the cartilage and bone. Failure to treat joint bleeds quickly may result in more blood entering a joint. Ultimately, joint damage may progress to chronic pain, affect joint motion and have a negative impact on walking and self-care. Learning to 'listen' to your body can help you to identify joint bleeds more easily, making earlier treatment possible.

When a joint bleed happens, you may experience the following:

- Pain or aching in the joint (this usually gets worse the longer the bleed goes untreated)
- Tingling or bubbling feelings in the joint
- Not wanting to move the joint
- Being unable to bend or straighten the joint normally (called a decreased range of motion)

When these symptoms are present, it's time to start treatment. As explained earlier, treatment should ideally be initiated within 2 hours of realising that a bleed has started. If the bleeding has gone on for a while, the joint will swell and feel numb; the skin around the joint could feel warm to the touch too. These are called late-symptoms. It is very important to treat joint bleeds early if possible, before late-symptoms occur.

When it comes to joint bleeds, there are some clear things to do and avoid:

ALWAYS

- ✓ Treat with clotting factor as soon as possible, ideally within 2 hours. With non-replacement therapy, please consult your haemophilia doctor or nurse quickly.
- ✓ Use Rest, Ice, Compression and Elevation (R.I.C.E) if possible
- ✓ Rest the joint as long as advised, then put a rehabilitation plan into place
- ✓ Ensure appropriate clotting factor use during recovery
- ✓ Set goals for restoration of movement as advised
- ✓ Measure progress by keeping a journal

NEVER

- ✗ Exercise a joint during an active bleed
- ✗ Return to a sport/activity following a bleed without discussing it with your doctor or nurse at your haemophilia centre
- ✗ Forget to exercise other parts of your body while resting the joint that is healing
- ✗ Do high-impact sports or lifting that may provoke a joint bleed

What if I need surgery?

Surgery is an issue that often causes anxiety for people with bleeding disorders. However, haemophilia treatment centers have

developed expertise around administration of clotting factors during surgery, enabling everything from simple tooth extractions to complex heart procedures.

Your haemophilia centre will consult with your surgeon and anaesthetist, as well as hospital pharmacists and blood banks to make sure that all is prepared in advance. You should always discuss the risks and benefits of any surgery with your surgeon and your doctor at your haemophilia treatment centre. In addition, always carry an emergency alert card and identification (e.g. medic alert bracelet) with you. This will alert medics if you are unconscious or unable to communicate, after a car accident for example.

Will I need orthopaedic surgery?

For some people with haemophilia, ongoing joint bleeding may result in joint damage, pain or limitations in function. This may ultimately require surgery to be considered. The decision regarding whether or not to have orthopaedic surgery should be made together with your haemophilia centre, surgeon and family, weighing up potential risks and benefits.

Orthopedic procedures which may be considered include:

Joint Repair (Synovectomy)

Synovectomy removes swollen tissue from the joint. It is performed once chronic inflammation of the joint lining (synovitis)

has happened. Your haemophilia treatment centre might recommend this procedure before permanent joint damage occurs. This may reduce the number of bleeds you have and help to slow progression of joint disease.

Joint Replacement (Arthroplasty)

The damaged bone and joint tissue are removed and replaced with metal, ceramic and plastic parts. This may involve the knee, hip, shoulder or elbow joint.

Joint Fusion (Arthrodesis)

Ankle fusion (arthrodesis) is performed to improve the ability to walk or bear weight. Two bones are joined together or fused with screws, steel rods or staples to relieve pain. However, the joint will no longer be flexible, so the the foot cannot be moved up or down after the procedure.

Elbow surgery

The elbow is a hinge joint consisting of 3 bones: the upper arm bone (humerus) and 2 forearm bones (radius and ulna). Elbow surgery may involve removing the damaged end of the radius, called radial head excision. Often, synovectomy will be done at the same time to remove damaged tissue. Although elbow replacement has been done, it is not as common as knee or hip replacement.

What are inhibitors?

To understand what inhibitors are, we first need to consider antibodies. Antibodies are proteins in the body that help to fight off foreign invaders, such as viruses. In haemophilia, the body doesn't have normal amounts of factor VIII or IX. So when someone with haemophilia is a baby, their body doesn't learn to recognise those proteins as being part of themselves. As a result, the body may mount an immune reaction when it comes into contact with replacement clotting factor, because it thinks this medicine is a harmful foreign invader.

This exposure to clotting factor, resulting in an antibody response, may occur in early childhood if you have severe haemophilia. Alternatively, it may occur later in life if you have mild haemophilia and need clotting factor treatment at some point (e.g. after surgery). Antibodies produced in response to an injection of clotting factor may have no effect on treatment. However, if antibodies block the activity of injected clotting factor, making it less effective, they are called inhibitors.

What causes inhibitors?

Inhibitor development can depend on many things. These include the type and severity of haemophilia, as well as having a family history of inhibitors. Haemophilia with inhibitors affects 20–30% of people with haemophilia A, for example, compared with up to 6% of those with haemophilia B.

People with severe haemophilia are more likely to get inhibitors than those with mild haemophilia, because their bodies make less factor VIII or IX and are thus more likely to see replacement clotting factor as foreign.

Having a family history of inhibitors could mean you are more likely to develop them. Your treatment centre may want to check your factor VIII or IX gene, to see what type of gene abnormality you have. This is done via a blood test and is called genotyping. Finding out whether you are at particular risk of developing inhibitors is important, as this information can be used to help to individualise treatment.

It is important to note that inhibitors don't exist at birth. They can only develop after someone with haemophilia has received replacement clotting factor. Most of the time, inhibitors appear within 3 to 70 exposure days (an 'exposure day' is a 24-hour period in which one of more doses of clotting factor treatment are given). In can take up to 150 exposure days for inhibitors to appear, but this is rare. Inhibitors may also occur in people with mild or moderate haemophilia who receive factor VIII or IX for the first time e.g. after receiving large amounts to treat a major injury.

What are the signs of inhibitors?

Signs of inhibitors include:

- Bleeding despite receiving clotting factor regularly
- Clotting factor for a bleed not working as expected
- Needing higher doses of clotting factor than usual
- Needing more injections of clotting factor than usual

You should contact your treatment centre to schedule a blood test if you suspect that you or your child may have inhibitors. Your haemophilia treatment may undertake a blood test called the Bethesda assay. This is used to detect inhibitors and assess reduction of factor VIII or IX activity. Results are given in 'titers' or 'Bethesda units (BUs).'

If you have inhibitors, you want your titers to be as low as possible. When an inhibitor is less than 0.5 BU, it is said to be negative, because the lowest amount the assay can test for is 0.5 BU. As your titer rises, more and more factor will be needed to overcome the inhibitor and stop the bleed. Once the titer reaches 5 BUs, almost no factor escapes the inhibitor, even if many times the normal dose is used. In this instance, normal replacement factor will not work and bypassing agents are needed instead. As the name suggests, these agents help blood to clot by bypassing the steps where factor VIII or IX are required. If such agents are needed, your haemophilia centre will

work with you to monitor the inhibitors and undertake an appropriate treatment plan.

How do inhibitors affect treatment?

Inhibitors are classified by titers (as explained in 'What are the signs of inhibitors?'). The following terms are used when considering the impact of inhibitors on treatment:

High titer inhibitor

Inhibitors of more than 5 BU are considered 'high titer'. No amount of factor VIII or IX administered will make the blood clot. Bypassing agents are then needed instead of factor VIII or IX (see 'What are the signs of inhibitors?').

Low titer inhibitor

Inhibitors of less than 5 BU are considered 'low titer'. In some cases, you could give more factor VIII or IX to overcome the inhibitor (e.g. give twice as much for a titer of 1 BU, four times as much for a titer of 2 BU, etc.). Sometimes, administering more factor can stimulate more antibodies to be produced, which is called an anamnestic response. Your haemophilia centre may test to see if your antibodies go up in response to giving clotting factor, to determine the best treatment option.

High responder

If your antibodies go above 5 BU in response to a test dose of factor, the term 'high responding inhibitor' is used. This means you probably need bypassing agents to control bleeding.

Low responder

If your antibodies don't really change in response to clotting factor, you may be able to treat with higher doses of factor VIII or IX. Depending on the titer, bypassing agents might still be necessary, or the volume/dose of factor VIII or IX may increase to such an extent that it makes more sense to treat with bypassing agents.

While inhibitors are less likely to occur in haemophilia B than haemophilia A, people with haemophilia B who do develop them can have a complication called anaphylaxis. This is a potentially life-threatening allergic reaction that includes difficulty breathing and changes in heart rate. Anaphylaxis can occur in up to 50% of people with haemophilia B with inhibitors if they are given additional factor IX. Because of the risks of anaphylaxis, the first few doses of factor IX are given in a haemophilia treatment centre, to keep a close watch for potential side-effects. As a kidney problem called nephrotic syndrome can also occur in people with haemophilia B who have inhibitors, ongoing monitoring of kidney function is also undertaken

What is Immune Tolerance Induction (ITI)?

Imagine a person has really bad hay fever. A doctor may try giving them increasingly concentrated injections of a solution made from grass pollen, so that their body gets used to it – that is, becomes tolerant to it. The aim is to help the person no longer have the

allergic reaction that causes hay fever. The same principle can be used in people with haemophilia who have inhibitors. In other words, their doctor will try and make their body tolerant to clotting factor again. This is called Immune Tolerance Induction (ITI).

In ITI for haemophilia A with inhibitors, large amounts of factor VIII are administered regularly over a period of up to several years, with the aim of eventually reinstating routine prophylaxis with factor VIII. ITI is far more complex in haemophilia B, due to the risks of anaphylaxis and nephrotic syndrome (see 'How do inhibitors affect treatment?'). ITI is thus usually restricted to people with haemophilia A.

What is infectious transmission?

In the 1960s, scientists found that the plasma in whole blood was rich in clotting factor proteins. This was a major discovery, which made it possible to treat patients with haemophilia by replacing the factor that they were lacking. Manufacturers found ways to pool donated plasma into factor concentrates, which proved to be clinically effective. Sadly, however, this occurred before science knew about transmission of diseases through blood donations. As a result, viral diseases such as HIV and hepatitis were unwittingly passed to people through the blood products that they received.

Scientists subsequently focused on improving blood product technology, to avoid the risk of infection. This included in-

depth screening, together with inactivation of viruses and other disease-causing agents in the donor blood supply. Another approach was to produce proteins in a way that doesn't need blood donations. This process involves inserting a small piece of human DNA into a cell from another animal, then growing these cells in large numbers.

As the process of adding in a specific gene is called recombination, factors made in this way are called recombinant proteins. This approach can be used to produce factor VIII or IX, which can then be purified and made into a medicine for injection. Recombinant products, together with novel viral screening and inactivation technologies, have virtually eliminated the risk of viral transmission from human sources.

How can I help stay healthy?

We all know the importance of regular exercise and good nutrition for helping to stay well. In fact, combining regular activity with a healthy diet is the key to protecting yourself or your child from joint disease, obesity and diabetes.

Overweight people in general are at increased risk of having cardiovascular problems later in life, such as high blood pressure, heart attacks and strokes. But for people with haemophilia, avoiding excess weight gain is particularly important. A healthy weight puts less stress on joints and may mean lower doses of clotting factor, given that dosage is based on bodyweight.

It is important to note that not all exercise causes bleeds. In fact, regular, low-risk activity under the supervision of your haemophilia treatment team can help to strengthen muscles, preventing bleeds and joint damage, as well as increasing stability and range of motion. Sports and activities that may be of interest include:

- Archery
- Fishing
- Golf
- Tai chi
- Swimming
- Badminton
- Table tennis
- Hiking
- Sailing
- Walking

Always follow the advice of your doctor or nurse at your haemophilia centre, who will be happy to advise you on suitable activities and sports. Also, when starting a new sport or activity, always 'listen' to your body. Some degree of discomfort may be expected, but if you experience a pain that is increasing, it's important to slow down or stop altogether. This is good advice for everyone, not just those with haemophilia.

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