



## INFORMATION FACT SHEET

### Haemophilia: General Information

#### What is Haemophilia?

Haemophilia is an inherited bleeding disorder in which the blood fails to clot normally. People with haemophilia lack the normal levels of “clotting factors” which are particular proteins that are necessary to the blood clotting mechanism. Haemophilia A (Classical Haemophilia), the more common type of haemophilia, is due to a deficiency of factor VIII (factor 8). Haemophilia B (Christmas Disease) is caused by a deficiency in factor IX (factor 9).

Both disorders cause bleeding into the joints, muscles and other soft tissues, sometimes spontaneously. It is a common misconception that people with haemophilia may bleed to death from the most minor of cuts. This is not the case; a person with haemophilia simply bleeds for longer but not more than a person with normal clotting.

There are also other related bleeding disorders, the most common of which is von Willebrand's, and rare factor deficiencies (for information on these see pages 5, 6, 7, & 8).

#### How is Haemophilia Inherited?

In nearly all cases haemophilia is an inherited condition although in about one third of all cases of haemophilia there is no previous history of the condition in the family. This means that the condition has arisen as a spontaneous mutation, this may occur in the person with haemophilia or in his mother. It is also possible to acquire haemophilia (see page 5). Haemophilia is termed a “sex linked recessive” condition. While only males have the condition, it is passed through the female line in the family. Females can either have normal or low levels of factor VIII or IX. Women with low levels may experience bleeding problems similar to those described for people with moderate haemophilia below.

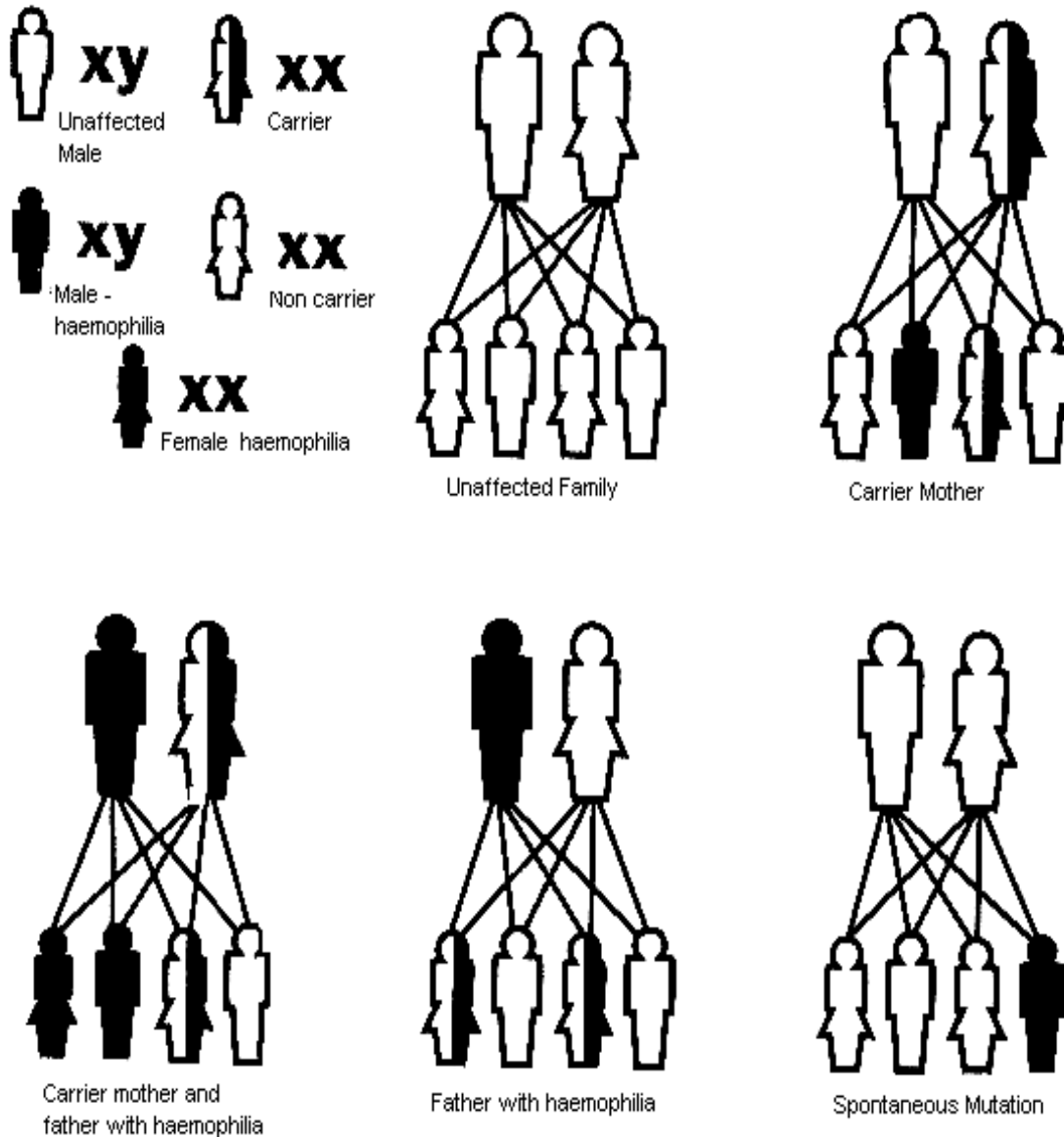
The genes for both factor VIII and IX are found on the female sex chromosome (the X chromosome). Two chromosomes determine the sex of an individual. These are the X and Y chromosome's. Females have two X chromosomes (XX), and males have an X and Y chromosome (XY). The faulty gene that causes haemophilia is on the X chromosome. A child will inherit a chromosome from each parent.

- ◆ If the mother carries the haemophilia gene and the father does not suffer from the condition, there is a 50:50 chance of a male child having haemophilia, as he will inherit one of his mothers X chromosomes. If it is the faulty one he will have haemophilia. If the child is female there is also a 50:50 chance that she will carry the haemophilia gene, as she will inherit an X chromosome from her mother.
- ◆ If the mother is not a haemophilia carrier, but the father has haemophilia, a female child will be a carrier, as she will have a normal X chromosome from her mother and a faulty X chromosome from her father. A male child will not be affected, as he will inherit his father's normal Y chromosome and his mother's normal X chromosome. The son cannot pass haemophilia on to future generations.
- ◆ However, in a third of all cases of haemophilia there is no previous history of the condition in the family. This means that the condition has arisen as a spontaneous mutation.

The inheritance can appear complex at first. It is important to understand it properly so that families where there is haemophilia present and get accurate advice and support (see chart 'How haemophilia is inherited').

Tests are available to determine if a female carries the haemophilia gene (see Haemophilia Gene Carrier fact sheet).

### How Haemophilia is Inherited



### Levels of Haemophilia

Haemophilia A and B are classed as mild, moderate, or severe depending on the level of clotting factor in the individuals blood e.g. having less than 2% is classified as severe.

A person with moderate (factor levels of between 2 – 10%) or severe haemophilia can suffer bleeds following minor trauma. Bleeds can also occur spontaneously. Internal bleeding into joints, muscles and soft tissues can cause considerable pain, and disability. These bleeds may be life threatening if not effectively treated.

A person with mild haemophilia (factor levels of between 10% and normal = 50%) will usually have few problems and will only require treatment for their condition after major tooth extraction, surgery or following trauma.

### What are the symptoms or signs of a bleed?

Babies seldom have problems before they reach the crawling/walking stage, around nine months. These activities will produce the inevitable knocks which can cause bruising or bleeds into joints. Painful swelling or reluctance to use an arm or leg is an indication that a bleed has occurred.

As children grow they learn to recognise that a bleed may be occurring. Aches, tingling or irritation in an affected area are often experienced when a bleed begins. If treatment is not administered there follows pain and stiffness, limitation of use of the arm or leg, the site of the bleed will get hot, swollen and progressively more tender. It is important to rest a joint, as this will help the healing process following treatment.

A joint, which has been affected by repeated bleeds, can become weak. This is known as a target joint and is prone to frequent bleeding episodes.

### What is the Treatment?

Haemophilia A and B are treated by replacing the missing clotting factor. Treatment consists of an injection of factor concentrate into a vein. Genetically engineered recombinant factor VIII and IX are the treatment of choice for children with haemophilia – this reduces the child's exposure to human blood products and to blood borne viruses. Adults are treated with plasma derived products.

A person with mild or moderate haemophilia A will in most cases be treated “on demand” following trauma or before surgery. Minor cuts and scratches do not usually pose problems. A little pressure and a plaster will usually do. In some cases DDAVP (Desmopressin) can be used as this stimulates the body to release factor VIII. Although people with mild and moderate haemophilia have bleeds infrequently, it is recommended that they attend their haemophilia centre for at least annual review.

Modern treatment for people with severe haemophilia aims to prevent bleeding and joint damage. For children and young people this involves “prophylactic” treatment (injections two or three times a week to keep clotting factor levels high enough to stop spontaneous bleeds). The amount of factor prescribed will depend on the baseline level of factor and body weight. For emergency treatment/treatment on demand a single injection is usually enough to control a bleed.

Most minor bleeds can be treated in the home (home treatment). Parents can be trained to inject their children and the children will eventually learn to give themselves injections. School and work attendance is more regular and the individual has greater control of his life. Thanks to the introduction of home treatment people with haemophilia have regained their independence and do not need to attend the haemophilia centre for all their treatment needs.

Hospital stays are infrequent and are usually only required for special treatment such as bleeds caused by trauma to the head.

Treatment and care of people with haemophilia remains very specialised; and is carried out in specialist haemophilia centres within NHS hospitals. There are two types of centres: comprehensive care centres which are larger and offer a full range of medical and related services and haemophilia centres which tend to have smaller number of patients and are not able to offer the comprehensive range of services. See 'Where do I go for treatment?'

### **Is treatment safe?**

In the 1970's and early 1980's many people with haemophilia were infected with HIV and/or Hepatitis C viruses through contaminated blood products. All blood donations are now screened for these viruses. Coagulation concentrates are now treated in a number of ways during manufacture in order to destroy any harmful viruses. The processes include heat treating, and/or the addition of a solvent and detergent mixture. Patients should also be vaccinated against Hepatitis A and B.

The introduction of genetically engineered (recombinant) products offers an even greater margin of safety. In March 1998 the Department of Health decided that recombinant factor concentrates should be used by all children under 16 years. This followed the recall of blood products contaminated by a donor infected with variant Creutzfeldt-Jakob disease (vCJD). Also in 1998 the government began importing plasma from the USA for the manufacture of plasma derived factor concentrates to reduce the risk of transmission of CJD through blood products. The USA has not had any recorded cases of Bovine Spongiform Encephalopathy (BSE), the disease in animals, which is believed to cause vCJD in humans. The transmission of vCJD through blood products is thought to be theoretical and there are no known cases of anyone with haemophilia having been infected with vCJD through blood products or having died from vCJD.

### **What does the future hold?**

The prospects for children with haemophilia are excellent. Children with haemophilia now face few limitations. They can participate in most sports (they should avoid contact sports such as rugby) and most jobs are open to them.

Advances in genetic science mean that the use of gene therapy to treat haemophilia is a real possibility for the future.

### **Where do I go for treatment?**

There are two types of treatment centre for haemophilia, haemophilia centres and comprehensive care centres (CCC). Haemophilia centres provide care, information and support for people with haemophilia.

Comprehensive care centres offer a complete range of treatment and diagnostic services. These are centres of excellence with greater expertise than haemophilia centres. Staff with specialist knowledge are available to deal with treatment requirements such as; haematologists, nurses, dentists, physiotherapists, and orthopaedic surgeons. Comprehensive care centres are available in most areas, although you may have to travel some distance to reach the nearest one. For further information see the Haemophilia Alliance's National Service Specification available for The Haemophilia Society. Because haemophilia is a lifelong condition, it is important that you receive continued supervision by a specialist medical team at a comprehensive care centre. People with haemophilia should be registered with and regularly reviewed at a comprehensive care centre. To register with a comprehensive care centre ask your GP to refer you or contact your nearest centre and make an appointment. For a list of haemophilia centres and comprehensive care centres contact the Haemophilia Society.

**Other bleeding disorders: All the following bleeding disorders affect males and females equally.**

### **Acquired Haemophilia**

This is a very rare disorder with an incidence of about 2 new cases per million of the population per year. It happens when the body's own immune system develops antibodies which attack the factor VIII in a person who has no history of a bleeding disorder. It can occur in women in the late stages of pregnancy or just after giving birth. More usually it occurs in middle aged or elderly people. Sometimes, those affected may be suffering from cancer, autoimmune conditions such as rheumatoid arthritis and drug reactions. Treatment involves treating the bleed and getting rid of the antibody causing the problem. It should always be carried out in a haemophilia centre and preferably a comprehensive care centre.

### **Von Willebrand's**

The medical term for the condition is von Willebrand's Disease (vWD). Von Willebrand's (vW) is a blood clotting disorder which is usually inherited. Von Willebrand's factor is one of the proteins in the blood that works to make blood clot. In vW either there is a shortage of von Willebrand's factor, or there is something wrong with its structure so that it does not work properly. Because of these problems, it takes longer for the blood to clot and for bleeding episodes to stop. It affects 1% of the population of the UK.

Von Willebrand's is usually less severe than haemophilia. Most people are diagnosed with a mild form of vW. The severe form of vW is uncommon.

Von Willebrand's is mostly a genetic condition. This means it is passed down through the genes from parent to child. The abnormal gene in vW is on one of the regular chromosomes, not one of the sex chromosomes (like haemophilia), vW affects males and females.

For further information about von Willebrand's contact The Haemophilia Society see page eight for details.

### **Other Factor Deficiencies**

There are a number of factor disorders which affect the clotting mechanism. Factors are important proteins in the blood, which facilitate clotting. If a factor is missing, present in lower than normal levels, or not working properly, it can obstruct the coagulation cascade. This is the chain reaction that is set in motion when there is an injury to a blood vessel.

#### Factor I (one) (Fibrinogen) deficiency

Is a rare inherited bleeding disorder. It is caused by either a low level of fibrinogen in the blood, or fibrinogen that does not work properly.

Fibrinogen is a protein in the blood that helps platelets in blood clotting. Platelets clump together to block leaks in blood vessels. Without fibrinogen, this happens much more slowly.

There are three types of factor I deficiency:

Afibrinogenemia – In this disorder, there is a complete absence of fibrinogen which causes serious bleeding episodes.

Hypofibrinogenemia – In this disorder fibrinogen is present in lower than normal levels. Bleeding problems can be mild, moderate or severe.

Dysfibrinogenemia – In this type fibrinogen levels are normal. However, the fibrinogen does not work properly. People rarely have bleeding problems; they can even have the opposite – thrombosis (blood clots in the bloodstream).

Treatment, usually fibrinogen concentrates, is normally given only when bleeding occurs or to prevent bleeding before operations.

Factor II (two) (Prothrombin) deficiency

Is caused by either a lower than normal amount of prothrombin in the blood, or prothrombin which does not work properly.

Prothrombin is a protein in the bloodstream, important to the clotting process. Prothrombin is changed into Thrombin, which is important for making the final clot, by an active form of factor X.

There are two types of factor II deficiency:

Congenital – A hereditary condition where children are born with this problem. This deficiency is very rare. Approximately 30 cases reported in the world to date.

Acquired – This disorder is acquired later in life. It is caused by an antibody following other diseases or the intake of certain medication. Acquired prothrombin deficiency is common.

Factor V (five) deficiency

Is a rare inherited bleeding disorder. It is also known as *Owren's Disease* and *parahemophilia*. Factor V is a protein in the blood called a *cofactor*. It speeds up the formation of prothrombin and meshes with prothrombin and Factor Xa on the surface of platelets at the site of a blood vessel injury.

Factor V deficiency is usually a fairly mild disorder which causes nose and mouth bleeds and bruising. It is treated only when bleeds occur, with fresh human plasma – there is no factor V concentrate.

Factor VII (seven) deficiency

Is very rare and also goes by the name *Alexander's Disease*. Factor VII is a trace protein in the blood. It is activated by tissue thromboplastin and turned in factor VIIa (the "a" stands for "activated"). Factor VIIa in turn activates factor X (ten) and factor IX (nine), allowing the clotting process to continue.

In factor VII deficiency there are lower factor levels than normal or the factor is missing altogether.

There are two types of this deficiency:

Inherited factor VII deficiency which is a lifelong condition.

Acquired factor VII which is a result of other physical disorders and may only last a short time.

Factor VII deficiency can vary from being a very mild bleeding disorder through to a very severe one. Treatment will depend upon the severity of the bleeding – in those who bled frequently factor VII concentrate can be given two to three times per week to stop bleeds occurring.

Factor X (ten) deficiency

Also known as *Stuart-Prower Deficiency*, is an inherited bleeding disorder. It is caused by either low levels of factor X in the blood or factor X which does not work properly.

Factor X is activated (switched on) by other clotting factors and changes into factor Xa (the "a" standing for "activated"). Factor Xa then activates other blood proteins including factor VII, and prothrombin (factor II), which changes to thrombin. This chain reaction allows the clotting process to continue.

Factor X is one of the rarest factor deficiencies known, with only 50 cases being reported in the world.

Factor X deficiency can cause severe bleeding even in people with relatively good factor X levels – particularly following injury or trauma. Treatment will depend upon the severity of the bleeding. There is not a factor X concentrate, but factor X is in some of the combined factor concentrates and these may be used to treat bleeding – as may fresh human plasma.

#### Factor XI (eleven) deficiency

Also known as *Haemophilia C*. It is a trace protein in the blood. Factor XI helps in the activation of Factor IX (nine), another blood protein essential in the clotting process.

Factor XI deficiency is generally quite rare affecting 1 in 100,000 people, except within the Ashkenazi Jewish community where it is much more common.

Some patients with virtually undetectable levels of factor XI rarely bleed, whilst others with relatively normal levels can bleed quite heavily. Treatment will be given with either factor XI concentrates or fresh human plasma.

#### Factor XII (twelve) deficiency

First identified in 1955 and is also known as *Hageman Factor*. Factor XII was thought to be very rare affecting 1 in 1 million people but in the last few years it appears to be one of the most common abnormalities of blood clotting. This may be because new techniques within the laboratory are making it easier to detect.

Factor XII is either inherited, or can occur spontaneously. The symptoms of bleeding are extremely rare in factor XII deficiency. In fact the opposite is sometimes true. The person has a tendency to form blood clots in the blood stream. This can be very serious.

Factor XII deficiency rarely causes bleeding. In the rare instances of treatment being required this is given as fresh human plasma, no factor XII concentrate is available.

#### Factor XIII (thirteen) deficiency

Factor XIII is the factor that stabilises fibrin. Fibrin is made of strands that form the permanent clot on the surface of the broken blood vessel. Without factor XIII the clot is not solid. After several hours or days the clot breaks up and bleeding starts again.

Factor XIII is very rare estimated at affecting 1 in 3 million people. Like factor XII, factor XIII is an “autosomal recessive” disorder. Both parents carry the faulty gene and pass the deficiency on to their children – this results in a severe bleeding disorder in the child, often presenting with bleeding from the umbilical cord shortly after the baby is born. The parents may have a mild disorder themselves.

Factor XIII deficiency is treated by giving factor XIII concentrate. This stays in the blood for a very long time – so an injection once a month is enough to prevent most bleeds from occurring.

For further information contact the Haemophilia Society.

### **Inhibitors**

Our immune system protects from foreign invaders such as bacteria and infectious organisms by recognising them as foreign and destroying them by making an antibody. Sometimes the immune system cannot distinguish between beneficial foreign proteins such as clotting factors and those which are harmful such as bacteria. To the immune system all

foreign proteins are harmful, so it produces antibodies that bind to the foreign protein triggering the white blood cells to destroy it.

People with haemophilia lack factor VIII or IX. Treatment for this is replacement of the missing clotting factor. However, sometimes the body recognises the replacement-clotting factor as a foreign protein and produces antibodies to it. These are known as inhibitors because they consume the clotting factor and inhibit its action.

Inhibitors present a major problem in only a few people with haemophilia. Between 35 and 45% of people with haemophilia develop inhibitors when they first start treatment. Therefore, most inhibitors occur in small children, most disappear of their own accord within a few weeks, but some remain and make treatment more complex. If someone has not developed an inhibitor within the first 100 treatments, the risk of developing one later is very small. Inhibitors become a long-term clinical problem for between 10 and 20 per cent of people with severe haemophilia A and for between 3 and 16 per cent of people with haemophilia B.

The amount of antibody produced varies from person to person. Some produce a lot, this is called a high *titre* response; others produce only a little and are called low *titre* responders. Fortunately, most people do not produce any clotting antibodies at all.

A blood test can determine if a person has developed an inhibitor. Inhibitors vary in the way they work, so their effects and the response to treatment differ from person to person.

There have been major improvements in the treatment inhibitors. Most bleed can now be treated successfully, despite the presence of the inhibitor, with one of several alternative therapies: either high doses of human factor VIII or IX, recombinant factor VIIa (these are the treatments of choice for children), or porcine factor VIII (factor VIII made from pigs blood – for patients with haemophilia A) and prothrombin complex concentrates.

Further information can be found in 'Haemophilia and Inhibitors' available from the Haemophilia Society see page 10 for details or take a look at our website at [www.haemophilia.org.uk](http://www.haemophilia.org.uk)

#### **For further information:**

The Haemophilia Society  
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Tel: 020 7831 1020  
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Email: [info@haemophilia.org.uk](mailto:info@haemophilia.org.uk)  
Web site: [www.haemophilia.org.uk](http://www.haemophilia.org.uk)

The Volunteer Telephone Support Network:  
Need a listening ear? Talk in confidence to  
someone with similar experiences.  
Freephone: 0800 018 6068

World Federation of Hemophilia (WFH)  
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Website: [www.wfh.org](http://www.wfh.org)

## Reading List

- Living with Haemophilia, by Dr Peter Jones, 1995
- Haemophilia and School, produced by the Haemophilia Society, 1997
- Haemophilia Information for Teachers & Playgroup Leaders. Compiled by Chris Titley, Clinical Nurse Specialist, Coventry Haemophilia centre, 2000
- Everyday a Milestone (video). Produced by the Haemophilia Society, 1998
- A Guide for Women Living with von Willebrand's. Produced by the Haemophilia Society, 2001
- A Guide for Women & Girls with Bleeding Disorders. Produced by the National Hemophilia Foundation (USA), 1998
- UK Haemophilia Centre Directory. Produced by BPL, 1999, revised 2004
- Raising a child with Haemophilia; A Practical Guide for Parents. By Lauren Kelley, 1999
- Go For It – Sport. Published by the World Federation of Hemophilia, 1998
- Haemophilia Alliance National Service Specification for Haemophilia (2001).
- Hepatitis C (HCV) Booklets
  - Being There: A guide for parents of young people with hepatitis
  - Living Life to the Full: A guide for young people (14 and older) on learning to live with hepatitis C
  - Alive and Kicking: A guide for young adults on living well with hepatitis C
  - Meeting the Challenge: A guide for adults with hepatitis C

Fact sheets covering a number of topics are also available from the Society. For a full publications list contact the Society.

The Haemophilia Society has a range of books on haemophilia specifically for children. If you would like a full list of our publications or to order a publication from those listed above, contact Tom on 0208 7380 0600. E-mail: [info@haemophilia.org.uk](mailto:info@haemophilia.org.uk). You can visit our website at [www.haemophilia.org.uk](http://www.haemophilia.org.uk)

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The fact sheet can only give basic general information drawing on medical opinion and evidence available at the time of writing. Different people may give you different advice on certain issues and there may be some variations in the way care is managed in different hospitals and in different areas. It is important that you contact your own doctor(s) and nurses(s) for further information and advice on your own individual circumstances.