

Factor XIII deficiency



Information for families

Great Ormond Street Hospital
for Children NHS Foundation Trust

Factor XIII deficiency is a type of clotting disorder. A specific protein is missing from the blood so that injured blood vessels cannot heal in the usual way. This information sheet from Great Ormond Street Hospital (GOSH) explains the causes, symptoms and treatment of Factor XIII deficiency and where to get help.

What is a clotting disorder?

A clotting (or coagulation) disorder is a medical condition where a specific protein is missing from the blood.

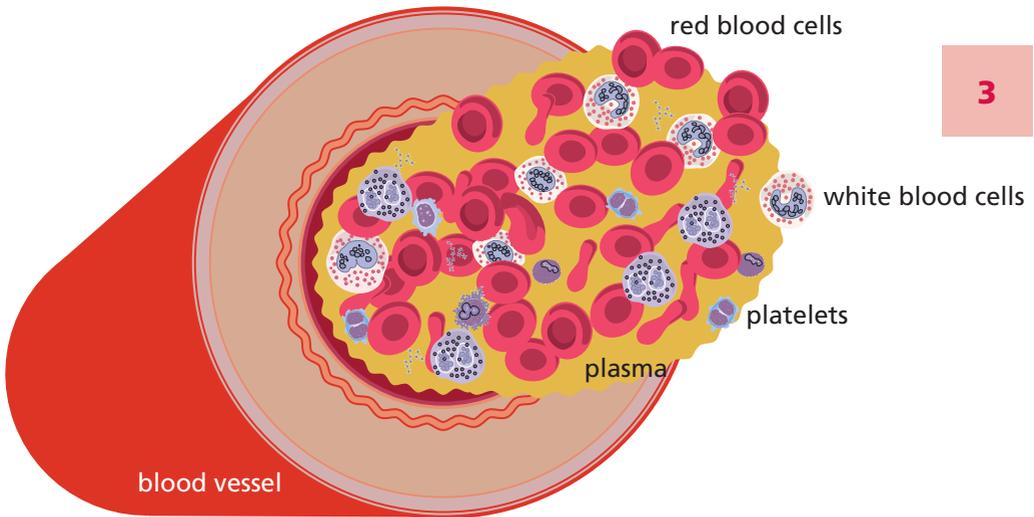
Blood is made up of different types of cells (red blood cells, white blood cells and platelets) all suspended in a straw-coloured liquid called plasma. Platelets are the cells responsible for making blood clot. When a blood vessel is injured, platelets clump together to block the injury site. They also start off a complicated chemical reaction to form a mesh made of a substance called fibrin. This complicated chemical reaction always follows a strict pattern – with each clotting protein (known as a coagulation factor) turned

on in order. When all of the factors are turned on, the blood forms a clot which stops the injury site bleeding any further.

There are a number of coagulation factors circulating in the blood, lying in wait to be turned on when an injury occurs. If any one of the factors is missing from the body, the complicated chemical reaction described above will not happen as it should. This can lead to blood loss, which can be severe and life-threatening. Each coagulation factor is given a number from I to XIII – they are always written as Roman numerals – and the effects of the missing factor will vary.

What is Factor XIII deficiency?

Factor XIII deficiency is one of the rarest types of clotting disorder affecting around 1 in every 5 million people worldwide. The specific coagulation factor that is missing or reduced in people with Factor XIII deficiency is Factor XIII. Factor XIII deficiency is different to other clotting disorders in that a clot forms after injury but it is unstable so breaks down and starts to bleed again. The severity of symptoms ranges from mild to severe depending on the amount of Factor XIII present in the blood and its activity. Factor XIII also seems to play an important role in wound healing, pregnancy and formation of new blood vessels but more research is needed to understand this better.



What causes Factor XIII deficiency?

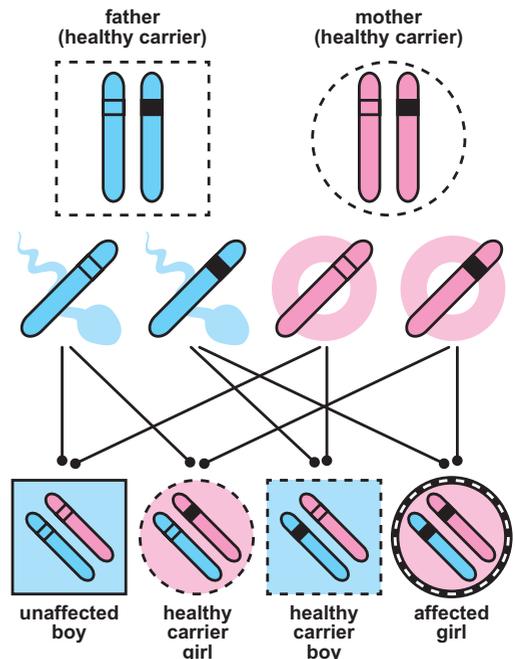
Human beings have about 30,000 to 40,000 different genes, each of which has a function in making an individual person. The genes are arranged in pairs (one of the pair from each parent) on 23 chromosomes – inevitably some of these genes are faulty. Factor XIII deficiency is caused by a mutation (change) on the F13A1 or F13B gene, both of which are inherited in an autosomal recessive manner. The mutation on the F13A1 gene is the most common type.

Autosomal recessive disorders mean that a person has to inherit the faulty gene from both parents to develop the disease. Autosomal recessive disorders are more common in areas of the world where marriage between close relatives is common.

Each pregnancy carries a:

- 75 per cent chance of having an unaffected child
- 25 per cent chance of having an affected child

People who carry one copy of the faulty gene are said to be a 'carrier'. The majority of carriers are healthy but occasionally, 'affected carriers' may show mild symptoms of Factor XIII deficiency as their Factor XIII levels can be half that of an unaffected person. This may or may not need treatment.



What are the signs and symptoms of Factor XIII deficiency?

Symptoms of Factor XIII deficiency often appear soon after birth when the umbilical cord is still present – a clot may form for a day or two but will quickly break down causing repeated bleeding.

This occurs in the majority of babies born with Factor XIII deficiency.

Bleeds inside the brain (intracranial haemorrhage) without trauma also occur in around one-third of people and unfortunately can be severe enough to be life-threatening. This is because the level in Factor XIII in the blood is too low to make the clot as described earlier.

Other forms of bleeding can also occur, such as nose and mouth bleeds and bleeding into the muscle tissue. Women with Factor XIII deficiency will often have heavy menstrual periods. Pregnancy should be carefully planned as there is an increased risk of early miscarriage or extended bleeding following childbirth. Men seem to have reduced fertility and a low sperm count.

How is Factor XIII deficiency diagnosed?

Factor XIII deficiency can be diagnosed before birth (prenatally) if there is a family history. There are several options for this including chorionic villus sampling (CVS) early in pregnancy or amniocentesis around 15 to 20 weeks or so.

After birth, Factor XIII deficiency can be diagnosed using a sample of blood for testing in the laboratory. However, the standard test to measure how long a sample takes to clot will show normal results. Another type of test will check how stable a blood clot is after it has formed, which will be abnormal in Factor XIII deficiency. The level of Factor XIII in the blood will also be checked and doctors will try to identify the gene mutation as well, as this can be helpful for planning future brothers and sisters and for testing other family members.

Imaging scans, such as MRI, CT or ultrasound scans may be used to identify any internal bleeds, for instance, inside a joint.

How is Factor XIII deficiency treated?

People with Factor XIII deficiency need to have preventative (prophylaxis) treatment.

Preventative treatment aims to replace the missing or reduced Factor XIII with a substitute derived from human plasma.

This is given regularly as an injection, sometimes into a central venous access device such as an implantable port.

Injections can be given at home which is less disruptive to family life.

Development of 'inhibitors' that mean the body fights off Factor XIII injections can be an extremely rare problem for people with Factor XIII deficiency. This will be checked regularly at review appointments. If inhibitors develop, additional injections will be needed.

It is important that people with Factor XIII deficiency should not use Non-Steroidal Anti-Inflammatory Drugs (NSAIDs such as ibuprofen) as this greatly increases the risk of bleeding. Other methods of pain relief should be used instead.

Caution is needed for injections as well – immunisations for instance, should be given subcutaneously (under the skin) rather than intramuscularly (into a muscle) to reduce the risk of a painful bruised swelling (haematoma) developing.

Children and young people with Factor XIII deficiency will need regular reviews at their specialist centre to check that they are responding to treatment and not experiencing any side effects. This review will usually involve a check-up from the physiotherapist and dentist as well.



What happens next?

Most children and young people with Factor XIII deficiency have a normal lifespan – the most common cause of death is a spontaneous intracranial haemorrhage. The introduction of replacement factors has greatly reduced the numbers of people developing blood borne viruses following transfusion. Some activities may need to be avoided – such as contact sports that carry a high risk of head injury for instance – but most day to day activities will cause few problems.

Women with severe Factor XIII deficiency should receive regular Factor replacement throughout pregnancy to reduce the risk of early miscarriage.

It is always advisable to wear a medical identity necklace or bracelet to alert health care professionals about having Factor XIII deficiency – details are available via The Haemophilia Society support organisation. Any surgery will need careful planning in advance as well so it is important that all health care professionals involved are aware.

As Factor XIII deficiency is a genetic condition that can be passed on from parent to child, it is possible to have genetic counselling before planning a family, both for affected individuals and unaffected carriers. Talk to us about a referral to our Clinical Genetics service.

Children and young people with Factor XIII deficiency will need life-long monitoring and treatment, so as your child approaches their teenage years, we will start to talk to them about getting ready to move on to adult health services. This is a planned process so that they become more independent as they grow older and able to manage their own health.

Further information and support

Call the **Haemophilia Comprehensive Care Centre** at GOSH on 020 7829 8837.

The **Haemophilia Society** offers support and advice to anyone affected by haemophilia or any other clotting disorder. Call their helpline on 020 7939 0780 or visit their website at www.haemophilia.org.uk

A wide range of resources is also available on the World Federation of Hemophilia website at www.wfh.org and UK-specific information regarding haemophilia, bleeding disorders and the National Haemophilia Database can be found via the United Kingdom Haemophilia Centre Doctors' Organisation website at www.ukhcdo.org. Useful details of Haemophilia Centres when travelling in Europe can be found at www.euhanet.org/centrelocator.

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