Factor XI deficiency

Information for families

Great Ormond Street Hospital
for Children NHS Foundation Trust

Factor XI deficiency (also known as Haemophilia C, plasma thromboplastin antecedent deficiency or Rosenthal syndrome) is a 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 XI deficiency and where to get help.

What is a clotting disorder?

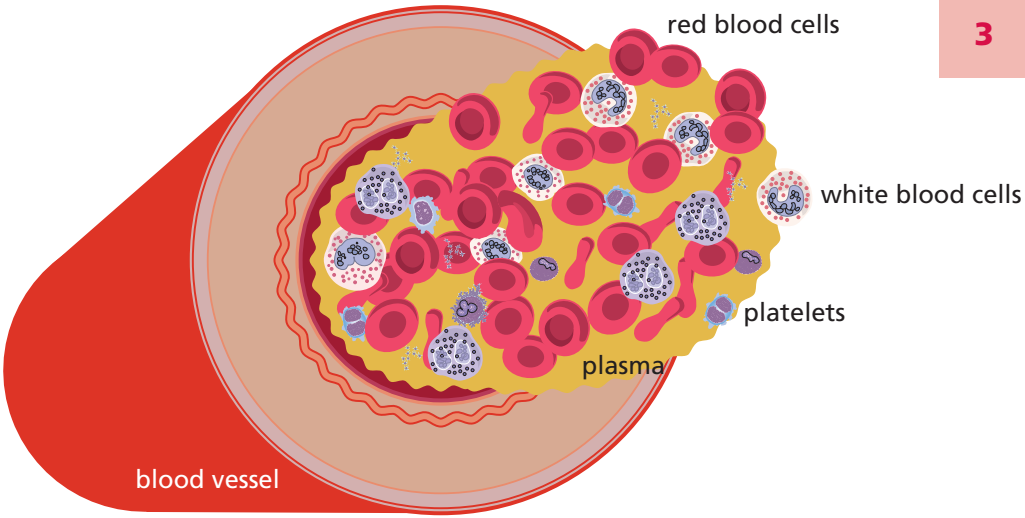
A clotting (or coagulation) disorder is a medical condition where a specific protein is missing from the blood.

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 XI deficiency?

Factor XI deficiency is a rare clotting disorder, affecting around 1 in 100,000 people worldwide, most commonly in Ashkenazi Jewish populations. The specific coagulation factor that is missing or reduced is Factor XI. Factor XI is important for producing thrombin protein that converts fibrinogen to fibrin during the clotting process.

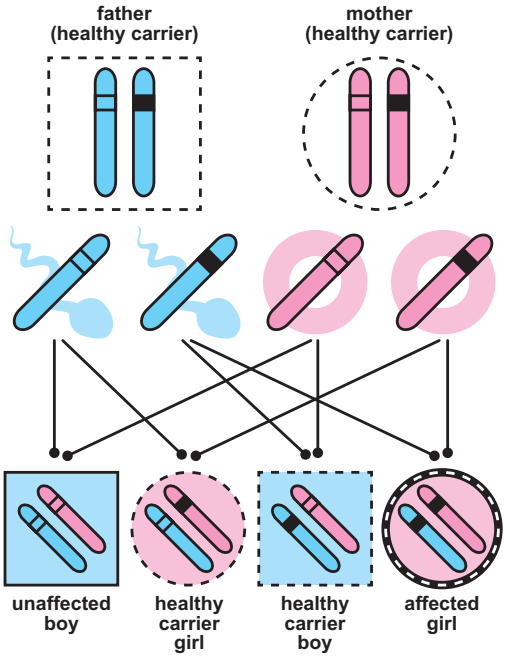


What causes Factor XI deficiency?

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 XI deficiency is caused by a mutation (change) on the F11 gene, which is inherited in an autosomal recessive manner. This means that a person has to inherit the faulty gene from both parents to develop the disease in a severe form.. 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

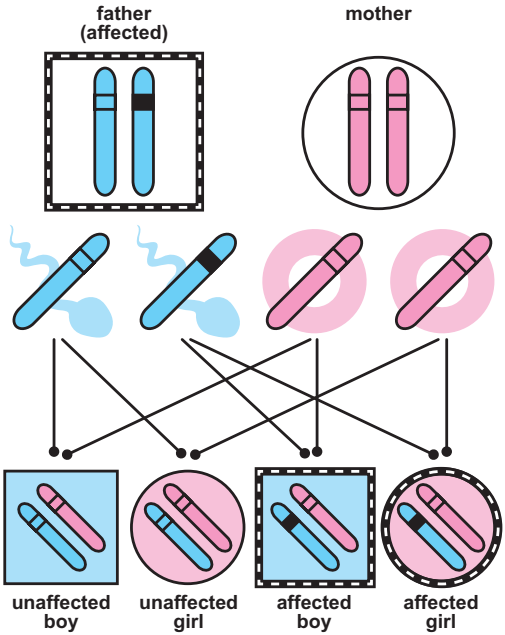


People who carry one copy of the faulty gene are said to be a 'carrier'. The majority of carriers are healthy but occasionally 'affected carriers' may show mild symptoms of Factor XI deficiency, which may or may not need treatment.

Factor XI deficiency is more common in Ashkenazi Jewish people where it affects a higher proportion of the population. It seems to be passed on in an autosomal dominant manner – that is, a person only has to inherit one copy of the faulty gene to develop the disease.

Each pregnancy carried a:

- 50 per cent chance of having an unaffected child
- 50 per cent chance of having an affected child



What are the signs and symptoms of Factor XI deficiency?

Most people do not show symptoms of Factor XI deficiency. The severity of symptoms is not always linked to the levels of Factor XI in the blood as shown in laboratory tests. People with mild Factor XI deficiency can still have serious bleeding episodes whereas other people with severe Factor XI deficiency do not have bleeding problems at all.

Factor XI deficiency may be suspected when abnormal bleeding occurs when the umbilical cord is cut after birth, after surgery such as circumcision or dental treatment, such as tooth extraction. Bleeding into the muscles or joints is unusual.

Women with Factor XI deficiency can have heavy menstrual periods. Pregnancy should be carefully planned as there is an increased risk of early miscarriage or extended bleeding following childbirth.

How is Factor XI deficiency diagnosed?

Factor XI 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.

Factor XI deficiency can be diagnosed using a sample of blood for testing in the laboratory. A test to measure how long a sample takes to clot may suggest a clotting disorder, which would then be investigated further. The level of Factor XI in the blood will be checked and doctors will try to identify the gene mutation as well, as this can be helpful for assessing risk of inhibitor development (antibodies made by the body against FXI treatment).

How is Factor XI deficiency treated?

If symptoms are not problematic, treatment may not be needed. In many cases, what treatment is needed is on an on demand basis to treat symptoms as they occur rather than preventative (prophylaxis). Factor XI has been developed from plasma and is now available as an injection.

Treatment may be required as part of planning for an operation or treating an injury. An infusion of fresh frozen plasma (FFP) can be given during the operation and afterwards. Fibrin glue can be used to treat skin injuries. Alternatively, a medicine called tranexamic acid can be given to make blood clots more stable.. This is given by mouth, intravenously or topically (applied to the skin).

It is important that people with severe forms of Factor XI deficiency should not use Non-Steroidal Anti-Inflammatory Drugs (NSAIDs such as ibuprofen) as this 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.

Females may have to take additional measures to make their monthly periods manageable. Options can include taking tranexamic acid before and during her periods, taking the contraceptive pill or having an intra-uterine device (IUD) inserted (for women who have had children).

Children and young people with Factor XI 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?

Children and young people with Factor XI deficiency have a normal life span. 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. It may be advisable to wear a medical alert identity necklace or bracelet to alert health care professionals about having Factor XI deficiency – details are available via the support organisation. Any surgery or future pregnancy will need careful planning in advance so it is important that all health care professionals involved are aware.

As Factor XI 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 XI deficiency may 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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