Prothrombin (factor II) deficiency

Information for families

Great Ormond Street Hospital for Children NHS Foundation Trust

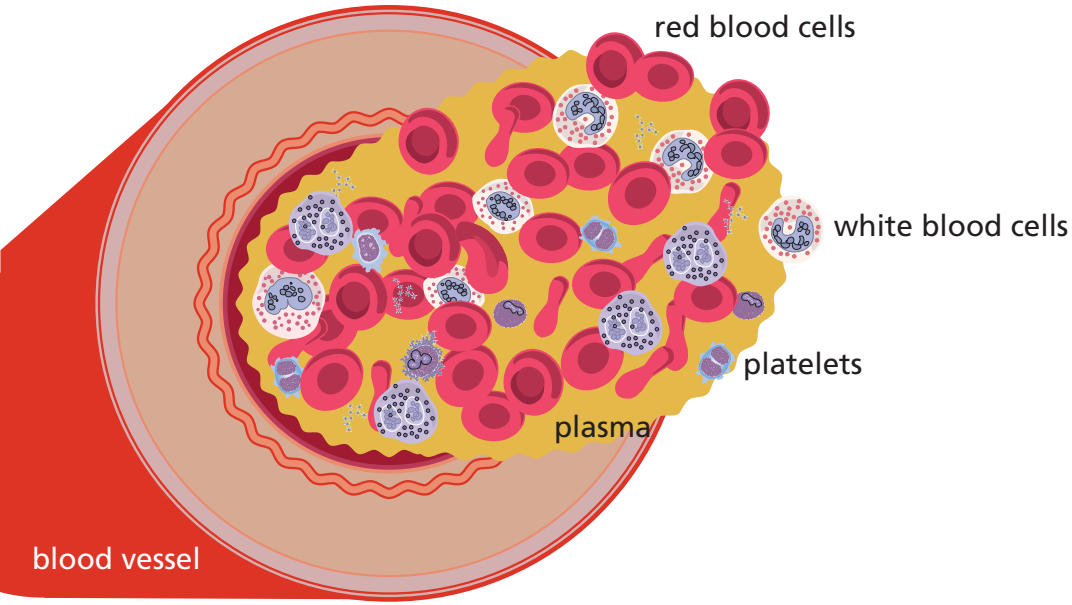
Prothrombin (factor II) deficiency is a type of clotting disorder. A specific protein called prothrombin is missing from the blood so that injured blood vessels cannot heal in the usual way. This information from Great Ormond Street Hospital (GOSH) explains the causes, symptoms and treatment of inherited prothrombin deficiency and where to get help. There is also an acquired form of prothrombin deficiency but this is not covered in this information sheet.

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 prothrombin deficiency?

Prothrombin deficiency affects only one person in every million. The specific coagulation factor that is missing or reduced in people with prothrombin deficiency is prothrombin or factor II. This plays an important role in clotting as it is responsible for making thrombin, which in turn forms the fibrin mesh that stops bleeding.

There are two main types of prothrombin deficiency:

- **Hypoprothrombinaemia** – where reduced amounts of prothrombin are produced by the body, which can cause mild, moderate or severe bleeding, depending on the amount of prothrombin present.
- **Dysprothrombinaemia** – this is where the amount of prothrombin produced is normal but it does not work properly.

The severity of symptoms ranges from mild to severe depending on the amount of prothrombin present in the blood and its activity.

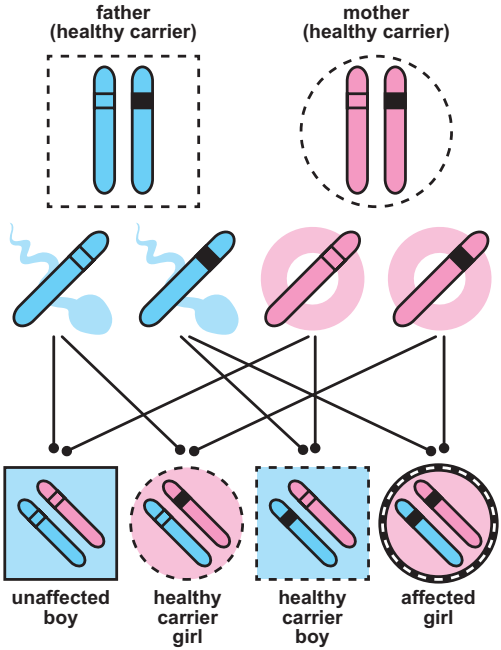
What causes prothrombin deficiency?

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. Prothrombin deficiency is caused by a mutation (change) on the F2 gene which contains the instructions for making the prothrombin protein. The mutation affects how much prothrombin is produced or how well it works.

Prothrombin deficiency is inherited in an autosomal recessive manner. 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 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 prothrombin deficiency as their Factor II levels can be half that of an unaffected person. This may or may not need treatment.

If someone with prothrombin deficiency has children, the mode of inheritance is different. For instance, if both parents have prothrombin deficiency, all their children will also have the condition. If only one parent has prothrombin deficiency, the chances will differ again.

What are the signs and symptoms of prothrombin deficiency?

Symptoms of the prothrombin deficiency often appear soon after birth when the umbilical cord is still present leading to prolonged bleeding. Circumcision or other neonatal surgery can also lead to prolonged bleeding.

Other forms of bleeding can also occur, such as nose and mouth bleeds. Internal bleeding, such as inside the brain or muscles and joints can also occur. Women with prothrombin 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.

Milder forms of prothrombin deficiency (where the levels of prothrombin are reduced but less significantly) may only be discovered when bleeding continues after surgery or injury.

How is prothrombin deficiency diagnosed?

Prothrombin 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, prothrombin deficiency can be diagnosed using a sample of blood for testing in the laboratory. The level of prothrombin or factor II 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 prothrombin deficiency treated?

The treatment options for prothrombin deficiency vary depending on the level of prothrombin in the blood and its activity. For instance, treatment may not be needed at all in some people. In many cases, what treatment is needed is on an on demand basis to treat symptoms as they occur rather than preventative (prophylaxis). Prothrombin has been developed from plasma and is now available as an injection.

If symptoms are severe enough to require preventative (prophylaxis) treatment, Prothrombin Complex Concentrate (PCC) derived from human plasma may be needed to replace the missing or reduced Factor II. Treatment may be required as part of planning for an operation or treating an injury. An alternative is an infusion of fresh frozen plasma (FFP) during the operation and afterwards rather than the factor concentrate.

It is important that people with prothrombin 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.

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.

What happens next?

Children and young people with prothrombin deficiency have a normal life span. If symptoms are mild or not present, no adjustment to everyday life will be needed, although it is always helpful to be aware of prothrombin deficiency.

If levels of prothrombin are very low or absent, 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. Bleeds into the brain can be life-threatening if not recognised and treated promptly.

It is may be advisable to wear a medical alert identity necklace or bracelet to alert health care professionals about having prothrombin 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.

Children and young people with prothrombin 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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