Von Willebrand disease is a type of clotting disorder – more common than the better known haemophilia. A specific protein is missing from the blood so that injured blood vessels cannot heal in the usual way. Von Willebrand disease is named after the doctor first described the condition in the early 20th Century. This information sheet from Great Ormond Street Hospital (GOSH) explains the causes, symptoms and treatment of Von Willebrand disease 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 Von Willebrand disease?

Like haemophilia, Von Willebrand disease is also a clotting disorder. However, in Von Willebrand disease, another protein called the Von Willebrand Factor is missing from the blood or does not work properly. It usually attracts the platelets to clump together to block the injury site. It also protects a specific coagulation factor called Factor VIII to stop it being removed from the blood plasma. Therefore, if someone has no or reduced Von Willebrand Factor they will have reduced levels of Factor VIII as well.

It is thought around one per cent of the UK population have reduced levels of Von Willebrand Factor, but this is rarely severe enough to cause problems or require treatment. It is diagnosed more in females than males due to menstruation and child birth.

There are four main types of Von Willebrand disease:

- **Type 1** – This is most common type of Von Willebrand disease and is the least severe with reduced levels of Von Willebrand Factor.
- **Type 2** – In this type, the Von Willebrand Factor is present but it does not work properly. Type 2 VWD is further divided into four different subtypes.
- **Type 3** – This is the least common type where there are very low levels of Von Willebrand Factor or it is completely absent and causes the most bleeding.
- **Pseudo Von Willebrand disease** is similar to Type 2 but the problems are with the platelets themselves rather than the Von Willebrand Factor.
There is also an ‘acquired’ type of Von Willebrand disease that can develop later in childhood, often as a result of another condition.

**What causes Von Willebrand disease?**

Von Willebrand disease is caused by a mutation (change) on the gene responsible for producing the Von Willebrand Factor (specifically at 12p13). In most cases, this mutation is passed on from parent to child but the manner in which this occurs depends on the type of Von Willebrand disease.

Types 1, 2 and pseudo-Von Willebrand disease are passed on in an autosomal dominant manner. This means that only one parent has to have the mutation to pass it on to a child. For each pregnancy, there is a one in two chance that the child will have Von Willebrand disease.

Type 3 is passed on in an autosomal recessive manner. This means that both parents have to have the mutation for their child to have the condition. For each pregnancy, there is a one in four chance that the child will have Von Willebrand disease.
What are the signs and symptoms of Von Willebrand disease?

In many cases, the condition is so mild that there are no noticeable symptoms. The severity of symptoms depends greatly on the level of Von Willebrand Factor (and therefore Factor VIII) in the blood. When the level of Von Willebrand Factor is low or absent or it does not work properly symptoms will be present, often early in life.

People with moderate to severe Von Willebrand Disease may bruise more easily than usual and may bleed for longer after injury or more severely following surgery or dental work. Generally only people with Type 3 Von Willebrand disease have spontaneous bleeds often from the nose or mouth and sometimes internally, for instance in the digestive system. Women with Von Willebrand disease often have heavy periods.
**How is Von Willebrand disease diagnosed?**

Many people with Von Willebrand disease may not be diagnosed if symptoms are not present or troublesome. When it is suspected, Von Willebrand disease 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. A clinical history of which symptoms are present and when will also help contribute to the diagnosis.

If there is a family history of Von Willebrand disease and the genetic mutation has been identified, the condition can be diagnosed prenatally (before birth) using chorionic villus sampling or amniocentesis.

**How is Von Willebrand disease 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). There are a number of options for treatment, the most common of which is desmopressin (also known as DDAVP®) which increases levels of Von Willebrand Factor and Factor VIII in the blood by releasing them from storage.

This is given as an injection under the skin or into a vein or as a ‘sniff’ up the nose. It does not work for every type of Von Willebrand disease (particularly type 3), so usually a test dose will be given at a specialist centre.

Alternatively, a medicine called tranexamic acid can be given to temporarily boost the proteins that stabilise blood clots. This is given by mouth, intravenously or topically (applied to the skin). Rarely, except in Type 3 Von Willebrand disease, is replacement Von Willebrand Factor required, but if it is, this is typically given as an intravenous infusion. The Von Willebrand Factor is taken from donated blood and screened carefully for blood-borne viruses. This tends to be suggested if desmopressin does not work.

It is important that people with Von Willebrand disease 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.

Females may have to take additional measures to make their monthly periods manageable. Options can include taking the contraceptive pill, having an intra-uterine device (IUD) inserted or taking desmopressin or tranexamic acid before and during her periods.
What happens next?
Children and young people with Von Willebrand disease 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 is always advisable to wear a medical alert identity necklace or bracelet to alert health care professionals about having Von Willebrand disease – 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 Von Willebrand disease is a genetic condition that can be passed on from parent to child, it is usual 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 Von Willebrand disease 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.