Von Willebrand disease

Von Willebrand disease (also called **von Willebrand disorder** or **VWD**) is an inherited bleeding disorder. People with VWD have a problem with a protein in their blood called von Willebrand factor (VWF) that helps control bleeding. They do not have enough of the protein or it does not work the way it should. This means that it takes longer for blood to clot and for bleeding to stop.

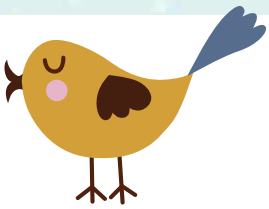
VWD is the most common inherited bleeding disorder worldwide. It affects both females and males equally. It is thought that up to 1 in 100 people have VWD, but most people with it have few or no symptoms and only a small number of them have been diagnosed. Many people with VWD may not know they have the bleeding disorder because their bleeding symptoms are very mild and it may cause little or no disruption to their life.

In comparison to the number of people with the mild form of VWD, the form of VWD causing moderate bleeding problems is uncommon, and the severe form of VWD is rare. But any bleeding that occurs with VWD needs to be assessed and treated.

How serious is VWD?

It depends on the type of VWD and the level of von Willebrand factor in the person's blood. Most people have such mild symptoms that they are not aware they have the disorder. Others only realise they have a bleeding problem when they have heavy bleeding after a serious accident or a dental or surgical procedure.

However, with all forms of VWD there can be bleeding problems. Some people with VWD bleed quite often, eg with



nosebleeds, bruising and heavy periods. A smaller number of people have the severe form of VWD and may also experience joint and muscle bleeds, similar to haemophilia.

There is no cure for VWD. It is a lifelong condition but with appropriate treatment VWD can be managed effectively.

Different types of VWD

There are three main types of von Willebrand disease. Bleeding symptoms can vary from person to person within each type.

Type 1 VWD is the most common form. Around 80% of people with VWD have this form. In type 1 VWD, the von Willebrand Factor (VWF) works normally, but there is not enough of it.

Symptoms are usually mild, depending on the level of VWF in the blood. However, some people with type 1 can have very low levels of VWF and have severe bleeding problems.

In **type 2 VWD**, the amount of VWF in people's blood is often normal but the VWF doesn't work properly. Type 2 VWD is divided into subtypes 2A, 2B, 2M and 2N. Certain subtypes may be treated differently, which makes knowing the exact type of VWD you have very important.

Type 3 VWD is very rare. People with type 3 VWD have very little or no VWF in their blood and also have low factor VIII (8) levels. Bleeding can occur often, be more severe and can also include joint and muscle bleeding.

It is important to remember that any bleeding is significant and is important even with a mild condition.

Bleeding symptoms of VWD

The symptoms of VWD vary greatly from person to person. Even members of the same family may have different symptoms. The type of VWD and the level of von Willebrand factor in the person's blood determine the severity and type of bleeding symptoms. However, there can be bleeding problems with all types of VWD. Bleeding often involves the mucous membranes, (the delicate tissues that line body passages) such as the nose, mouth, uterus, vagina, stomach and intestines.

The **more common symptoms of VWD** are:

- Frequent nosebleeds, or nosebleeds that are hard to stop
- Bruising easily
- Very heavy periods, or periods that last more than 8 days
- Bleeding for a long time from small cuts
- Bleeding from the gums, usually after trauma/injury
- Bleeding that continues for a long time after injury, surgery or dental work.

Less common symptoms that older people might experience are:

- Blood in faeces (poo) due to bleeding in the intestines or stomach
- Blood in urine due to bleeding in the kidneys or bladder.

People with severe forms of VWD, particularly type 3 VWD, may also have other bleeding problems similar to severe haemophilia, such as:

- Bleeding episodes that happen for no obvious reason
- Bleeding into joints and muscles which can cause swelling and pain.

Women with VWD sometimes have abnormally heavy bleeding in the first couple of weeks after giving birth. They may also have quite a bit of bleeding between periods with ovulation (when the ovary releases an egg).

Sometimes the kind of symptoms a person with VWD experiences can change over their lifetime. For example, as a child they may have nosebleeds and bruise easily, but find this occurs less often as they grow older. However, their type of VWD will not change.

How do you get VWD?

Von Willebrand disease (VWD) is usually inherited.

The way each of us makes von Willebrand factor (VWF) in our body is coded into one of our genes, called the VWF gene. This gene has been inherited from genetic information from both our mother and father.

If there is a mutation in the gene causing VWD, this can then be passed down from parent to child, in the same way as other genetic information like the colour of their hair or their eyes. The altered VWF gene is often called a *VWD gene*. A parent can pass on the altered VWF gene even if they don't have symptoms.

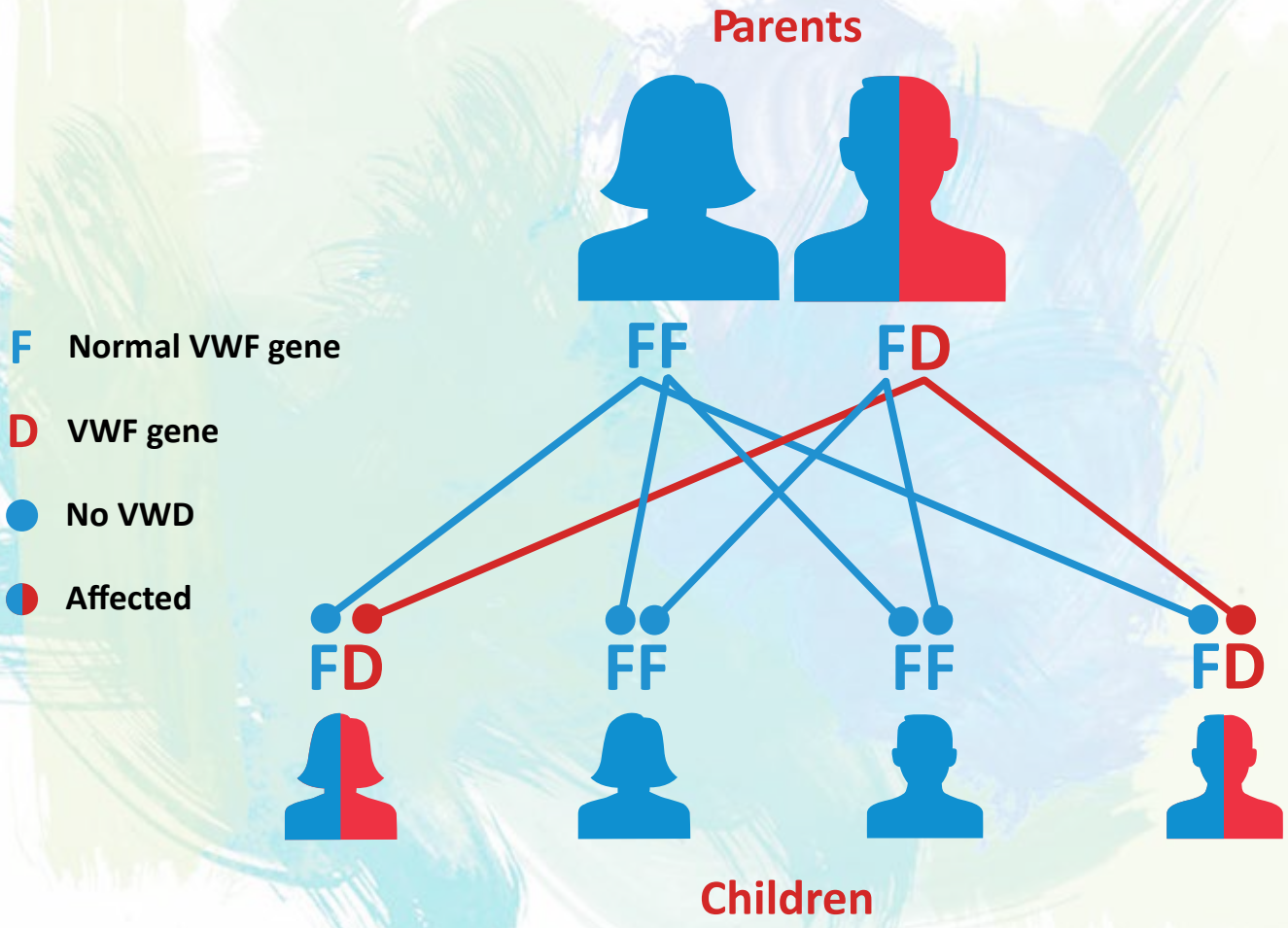
All of us have two copies of each gene, one inherited from each parent. Genes are carried in our chromosomes. The VWF gene is located on an ordinary chromosome (autosome), not on a sex chromosome, like haemophilia. Sex chromosomes decide whether we are male (XY) or female (XX). This means that VWD affects males and females in equal numbers, unlike haemophilia which usually occurs in more males than females – so both sons and daughters can inherit VWD. Their symptoms can be different to their parents or to their brothers and sisters.

How is VWD inherited?

There are two main inheritance patterns for VWD:

In most type 1 and type 2A, 2B and 2M VWD, the VWD gene is **dominant**.

Autosomal dominant inheritance pattern



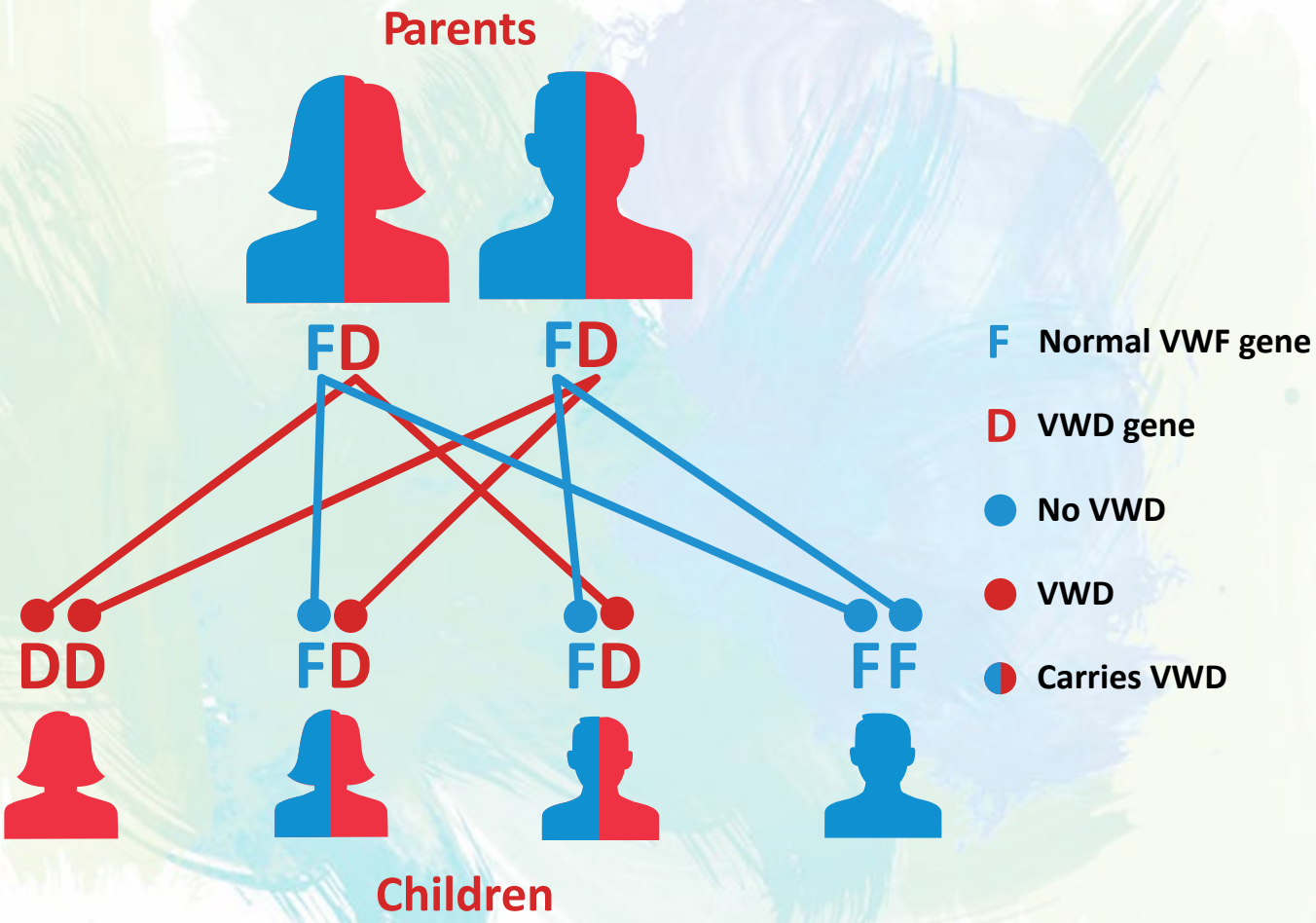
Inheritance of Von Willebrand Disorder Type 1, 2A, 2B, 2M

This means that if one parent has a VWD gene, they have a **1 in 2 (50%)** chance of passing the gene on to each of their children. They or their children may or may not have symptoms.

If a child who has inherited autosomal dominant VWD (eg, has type 1 or type 2A, 2B or 2M VWD) has children, each of their children has a **1 in 2 (50%)** chance of inheriting the altered VWF gene. Their children would typically have a symptom pattern similar to their affected parent.

In type 3 and type 2N, the VWD gene is **recessive**. If both parents carry this type of VWD, they may have no or mild symptoms.

Autosomal recessive inheritance pattern



Inheritance of Von Willebrand Disorder Type 2N and 3

Source: Adapted from Goodeve AC, James P. Von Willebrand disease. GeneReviews Oct 5 2017, viewed 1 August 2018. < https://www.ncbi.nlm.nih.gov/books/NBK7014/ >

With their children:

- There is a **1 in 4 (25%)** chance that their children could inherit a copy of the VWD gene from both of them and have symptoms, usually moderate to severe.

- There is a **1 in 2 (50%)** chance that their children will inherit only one copy of the VWD gene from them and carry the gene but may have no or only mild symptoms, like their parents.

- There is also a **1 in 4 (25%)** chance that their children will not inherit the VWD gene at all.

If a child has inherited autosomal recessive VWD (eg, has type 3 or type 2N VWD), their children will **ALL** inherit a copy of the altered VWF gene and are known as **obligate carriers**. Their children may or may not have symptoms.

If one member of a family is diagnosed with VWD, the doctor may recommend testing other members to see whether they have VWD as well.

"My mother was diagnosed with Von Willebrand's about 15 years ago after an operation and advised my sister and me to get tested. It turned out that I have Type 1 but my sister doesn't."

"In my family it seems as though everybody has it! Myself and two of my three brothers were diagnosed at birth, and recently we found out that my oldest brother also has it, although much more mildly. Since I have a more severe form, it's likely that my mum is also a carrier- she doesn't experience any bleeding problems herself, but her own mother was a severe bleeder."

No family history of VWD

Sometimes there is no family history of VWD. A baby can have a genetic mutation, or change in one of their genes, before they are born. Although their parents and their brothers and sisters do not have the VWD gene, the child will be able to pass the VWD gene on to their own children in the future.

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