Irish Haemophilia Society

# Von Willebrand Disorder

# Contents




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## What is Von Willebrand disorder (vWD)?

Von Willebrand disorder (VWD) is a bleeding disorder which affects the blood's ability to clot. If your blood doesn't clot, you can have bleeding symptoms. Some of the most common symptoms are easy bruising, frequent and prolonged nosebleeds, prolonged bleeding after some dental procedures, prolonged bleeding post-surgery or traumatic injury. For women, heavy or prolonged menstrual bleeding and prolonged bleeding after childbirth.

Your body makes lots of different clotting proteins that help you to stop bleeding, one of which is called von Willebrand factor (vWF). In vWD, either your body does not make enough vWF which can be referred to as a "quantitative" (i.e. not enough) problem or the vWF doesn't work as well as it should which is referred to as a "qualitative", (i.e not as effective). Bleeding happens when you damage a blood vessel. Normally, your body responds by fixing the damage in the blood vessel wall, stopping the bleeding. The body's first response to stop the bleeding, uses small cells called platelets (PLATE-lets) that clump together at the location of injury to plug the hole in the blood vessel. VWF acts like glue to help the platelets stick together and to the blood vessel wall to stop the bleeding.

One of the other important roles vWF also has, is carrying clotting Factor VIII (8). This is another important protein that helps your blood to clot. vWF carries the Factor VIII from other parts of the blood to the area where the blood vessel is damaged. Some people with low von Willebrand factor, may also have low levels of Factor VIII levels which can sometimes delay a diagnosis, due to this being slightly more complex.

## How is it vWD inherited?

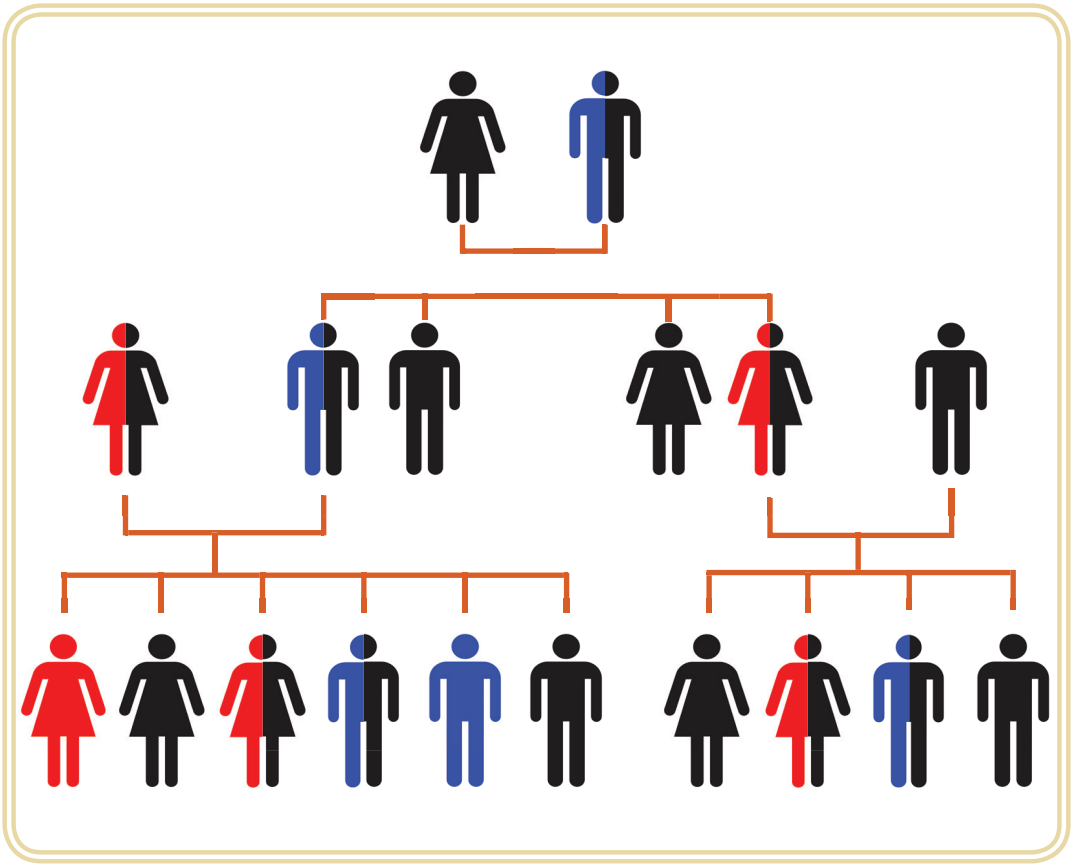
Normal vWF levels are greater than 0.50 IU/mL. This can sometimes be referred to as "50%" level. Some people may have lower levels of vWF but experience no bleeding. This is common in people who are blood group O as their vWF levels are naturally lower.

People who experience bleeding with mildly lowered vWF levels (0.30-0.50 IU/mL) have a condition called "Low vWF". While people with Low vWF are born with low levels, the inheritance pattern, how it is passed down from parent to child, is not well understood and other family members can be affected differently.

If your vWF level is less than (0.30 IU/mL ("30%") you have a diagnosis of von Willebrand Disorder (vWD). In this case, it almost always inherited (passed down) from a parent to a child. vWD can be passed down from either the mother or the father, or both, to their son or daughter (Fig 1).

The son or daughter of a parent with vWD has a 50% chance of having vWD. The "type" of the vWD, indicates how the condition is passed down. In type 1 and 2, if one parent has vWD and does pass it to their child, then that child will have the condition. In type 3, the child usually inherits the condition from both parents. Even if, both parents have vWD, the child could get either a mild or severe form of the vWD based on how the condition is passed on. People with vWD can have different experiences of bleeding, depending on their "type" and even within "types", some people may experience bleeding more than others.

# VON WILLEBRAND DISORDER INHERITANCE



**KEY**

Normal Male

Male with mild vWD or unaffected

Male with severe vWD

Normal Female

Female with mild vWD or unaffected

Female with severe vWD

# Low vWF and types of von Willebrand Disorder (vWD)

### Low von Willebrands Factor (Low vWF)

This is the most common condition, affecting 60% of people identified with reduced vWF levels (Fig 2). Recent research in Ireland, on people with Low vWF identified that bleeding, in particular easy bruising, may be problematic in patients with Low vWF. In the same research, women with heavy periods were also identified as a group who may have problems due to low vWF. As a result, some people with low vWF levels have bleeding symptoms like people with vWD and may need to have treatment if they are having surgery or other invasive procedures. Women with low vWF may also need treatment to help with management of heavy periods.

# Types of von Willebrand Disorder?

If you have von Willebrand factor (vWF) levels, less than 0.30 IU/mL( 30%), your doctor will do additional tests to figure out what type of von Willebrand Disorder (vWD) you have. This is important as treatment options, responses to treatment and monitoring differ between types of vWD.

### Type 1

People who have type 1 vWD have much lower levels of vWF than expected because their body either doesn't make enough vWF or breaks it down too quickly. Doctors often refer to this as a "quantitative" issue. This means the quantity or the amount of vWF available in the body is not enough. Type 1 is the most common form of those diagnosed with vWD, with about 3 out of 4 people who have VWD, being diagnosed with type 1.

### Type 2

People with type 2 vWD will make vWF but the quality of the vWF produced is not as good as normal vWF, so it doesn't work well. This can often be referred to as a "qualitative" problem. Type 2 can be further subdivided depending on which part of the vWF is not working correctly (type 2A, 2B, 2M or 2N). Different types of mutations (changes) cause each type. Of those diagnosed with vWD, about 1 in 4 have type 2.

### Type 3

People who have type 3 vWD usually have, extremely low levels of vWF. As they do not have enough vWF to carry factor VIII around their body, their factor VIII levels are also low, and they may experience bleeding like people with haemophilia. Type 3 is the most serious form of vWD, but it is rare affecting about 1 in 500,000 people.

## What are the symptoms?

The symptoms of vWD and their severity, mostly depend on the type of vWD you have. Many people have some of the following symptoms and may not know they have vWD.

**Common symptoms include:**

- Frequent large bruises from minor bumps or injuries.
- Frequent or prolonged nose bleeds.
- Prolonged bleeding from gums after dental procedure.
- Heavy or prolonged bleeding from a cut.
- Prolonged or heavy bleeding after injury.

**Less common symptoms:**

- Joint or muscle bleeding
- Gastrointestinal bleeding (bleeding in stomach or gut)

**For women:**

- Heavy or prolonged menstrual bleeding
- Heavy bleeding after surgery or childbirth.

### Type 3 vWD

People who have type 3 vWD may also have more frequent bleeding into muscles or joints than the other types of vWD. This can occur after minor injuries or over exertion, you might not even notice, and it may appear that the bleeding started for no reason.


## How is it diagnosed?

vWD can be difficult to diagnose and may require a couple of tests to be sure. Type 3 vWD can cause major bleeding problems very early, it is mostly diagnosed, early as infants or children, and quickly. Some people with type 2 may have bleeding and bruising which are seen at a younger age and can be diagnosed early on in life, due to things like intramuscular injections used in vaccinations.

People with Low VWF or type 1 vWD may not have day to day bleeding problems and as a result, may not be diagnosed until they have severe bleeding after surgery, dental procedures or injury.

### Medical history

Your doctor will ask questions about your medical history and your family's medical history such as:

- Have you had any bruising as result of a little or no injury; especially if you could feel a lump under the bruise?
- Have you had any nosebleeds that happened for no reason; especially ones

that were very heavy or lasted for more than 10 minutes despite pressure on the nose; or any nosebleeds that needed medical attention?
- Have you had any bleeding from a small wound that lasted more than 15 minutes?
- Have you had any prolonged, heavy or repeated bleeding that required medical care after surgery or dental procedures, such as extractions?
- Have you used any medicines that might cause bleeding or increase the amount of bleeding; like non-steroidal anti-inflammatory drugs (NSAID's- some examples e.g. Aspirin, Brufen, Nurofen, and Ponstan).

**For women**

- Have you had heavy or prolonged menstrual bleeding; maybe ones where you have seen large clots?
- Have you had heavy bleeding or prolonged bleeding after childbirth?

## Physical examination

Your doctor may do a physical exam to look for unusual bruising or recent bleeding.

## Blood tests

While testing has improved in recent years, no single test can diagnose vWD. Specialised blood tests, usually performed only in specialised Haemophilia / Inherited Bleeding disorder treatment centres are required. (See list of Centre's and contact details on Page 21) Blood tests may include:

- Tests of how much VWF is in your blood (Von Willebrand Factor Antigen)
- Tests of how well your VWF is working such as GpIb tests, Collagen binding activity and a von Willebrand Factor Ristocetin Cofactor activity.
- Factor VIII level. This is checked with VWF since Factor VIII level may also be low.

vWF levels can be affected by stress, illness, and hormones, so you may need to have these tests more than once to confirm or exclude a diagnosis. It can be useful to know your vWF and FVIII levels, as it will help you find the information that is most suitable to you.

## How is it treated?

Bleeding such as bruising, minor cuts and some nosebleeds can often be controlled using simple first aid measures such as R.I.C.E (Rest, Ice, Compression and Elevation). If bleeding continues in cases liked continued heavy or prolonged nosebleeds, some dental procedure, during or after surgery or after injury, other treatment options may be needed.

For young women, treatment such as hormonal contraceptives or the intrauterine devices (IUD's. e.g. Mirena coil) may be used as bleed prevention for heavy or prolonged bleeding. There are also surgical options if required

**Please contact your Haemophilia Treatment Centre for advice:**

- If you need a dental extraction
- If you need intramuscular injections
- If you need surgery
- If you are injured

**For women**

- If you are pregnant
- If you are having a hysterectomy

## Treatment options

- Desmopressin (DDAVP)
- Tranexamic Acid (Cyklokapron)
- Fibrin glue
- Factor replacement therapy

**For women**

- Hormonal Contraceptives
- Intrauterine Devices

## Desmopressin (DDAVP)

Desmopressin (DDAVP) is a synthetic drug, identical to a hormone found normally in the body. It is not used in children under the age of 2 years or in adults over the age of 55 years.

## How does it work?

DDAVP stimulates your body to release your own stores of clotting factors Factor VIII and VWF into the blood stream. This helps to boost vWF levels for up to 12-24 hours. If necessary, the dose of DDAVP can be repeated after 12 hours. As DDAVP is asking the body to release stored FVIII and vWF, if you have used it within the last 12 hours, the body doesn't have the chance to rebuild its stores, so repeated doses may not be as effective.

## DDAVP Trial

Some people do not respond to DDAVP. If this is the case, it is important to know this for your future treatment options. Treatment centres, hence suggest doing a DDAVP trial to find out if you are a "responder", a "partial responder" or a "non-responder".

The trial generally takes 3 hours for children and 6 hours for adults and some

children. Blood samples are taken before and hourly after DDAVP infusion up to four hours. Occasionally a blood test will be needed on the following day. The response to DDAVP will be reported as one of the three following categories:

**Responder:** Your body responds well to DDAVP, resulting in a boost in VWF levels. DDAVP will be the treatment option for procedures and some bleeding episodes.

**Partial responder:** Your body responds only partially to DDAVP, resulting in a minor boost in VWF levels. This may be enough to cover minor procedures and minor bleeding episodes. An alternative treatment will be necessary for major procedures and major bleeding episodes.

**Non-responder:** Your body doesn't respond to DDAVP. An alternative treatment will be necessary for all procedures and all bleeding episodes.

## How is DDAVP given?

DDAVP is available as an intravenous injection which is often used in treatment centres and if needed at home can be available as a subcutaneous injection. For the intravenous injection it is slowly injected over thirty minutes to one hour.

## Before DDAVP administration

**Please inform your nurse / doctor of the following:**

- Any known reaction to this or any other medication
- If you take diuretics, medication for high blood pressure or any other medications, including over the counter medications and herbal remedies
- Pregnancy or breastfeeding
- Any significant medical problems including:
    - heart disorder
    - kidney disorder
    - cystic fibrosis
    - epilepsy

## Side Effects of DDAVP

Some people can experience flushing (reddening of skin or face) or increased heart rate during the infusion. If this occurs, please tell your team; often this will settle if DDAVP is given slower.

**Other occasional side effects include:**

- Headache
- Stomach pain and nausea
- Allergic reactions
- Decrease in blood pressure

In the elderly and in people with cardiovascular disease, DDAVP can cause more serious side effects and may not be recommended.

## Fluid Intake

Adults should not drink more than 1 to 1.5 litres (approximately 8 to 10 cups) in the twenty-four hours following DDAVP. A child's fluid intake is restricted to 75% of normal daily fluid requirement in the 24 hours following DDAVP.

DDAVP can cause fluid to be retained by the body it is important to restrict fluid intake after the infusion of DDAVP. You will pass less urine in the 24 hours after the infusion. If you find you are passing little urine in 24 hours following the DDAVP treatment you should contact your Haemophilia centre.

Treatment with DDAVP without reducing fluid intake may lead to fluid retention, dilution of salt in the blood, and in more severe cases, epileptic seizures. If these side effects occur, your doctor may advise an alternative treatment to DDAVP.

## Tranexamic acid (Cyklokapron)

Tranexamic acid (also known as Cyklokapron) is an anti-fibrinolytic agent. This means that it slows the breakdown of blood clots. It is used to prevent or treat bleeding from mucous membranes such as the inside of the mouth, nose, gut or womb. It may be given before dental work, for nosebleeds. It is often used in treating prolonged or heavy menstrual bleeding.

It may be used alone or in combination with DDAVP and von Willebrand factor

replacement therapy. Tranexamic acid does not help to form a clot. This means it cannot be used instead of DDAVP factor replacement therapy.

**It can sometimes have side effects, which include;**

- Nausea
- Dizziness
- Diarrhoea
- Stomach pain

### Fibrin Glue

Fibrin glue is made from synthetic copies of two proteins, fibrinogen and thrombin, which are normally found in the body. Fibrin glue can be put directly to the site of bleeding. It is especially useful in tooth extractions

### Factor replacement therapy

Factor concentrate is given into a vein to replace the missing vWF to allow clotting to take place. There are two types of factor replacement available for vWD. The first is made from pooled human plasma, (which is screened for blood-borne viruses such as HIV and hepatitis B and also treated to destroy viruses). This also contains FVIII. The newest option is recombinant vWF (rvWF) which is engineered in a laboratory. The type of product used can be dependent on the type of bleeding that you are being treated for, as well as the type of vWD you have.

### Hormonal Contraceptive therapy

Hormonal contraceptives reduce menstrual bleeding by thinning the endometrium and possibly increasing factor VIII and von Willebrand factor levels. They have an added advantage of controlling ovulation bleeding and midcycle pain. Hormonal contraceptives currently available include combined oral contraceptive pill (COC), transdermal contraceptive patches, oral progestogens, Progestin-only pills or implantable, Gonadotropin-releasing hormone (GnRH) analogues.

Most women who use hormonal contraceptives have very few or no side effects. Serious side effects of hormonal contraceptives include high blood pressure, liver abnormalities and clots. Women with inherited bleeding disorders, however, may have a lower risk of clotting. Side effects that some women experience are nausea, headaches, dizziness, breast tenderness and mood changes. Some of these side

effects improve over the first 3 months. If the side effects continue the doctor may prescribe a different brand of hormonal contraceptive.

### Intrauterine device (IUD, e.g. Mirena®)

An IUD has been shown to be useful for reducing menstrual blood loss in women with bleeding disorders. The licensed duration of use in Ireland is five years i.e. once inserted it may stay in place for 5 years. Side effects may be irregular bleeding or spotting, especially within the first 6 months. There is a potential risk of bleeding at the time of insertion and preventative treatment with a haemostatic agent may be required.

## Living with vWD

Tell your healthcare providers doctor, nurse, physiotherapist, dentist, and pharmacist that you have vWD. Your dentist can ask your Haemophilia Centre whether you need medication before dental procedures to reduce bleeding.

You also may want to tell other people about your condition, like your occupational health nurse and, personal trainer or sports coach. Anyone who cares for you or your child with vWD (teacher, crèche etc.) could benefit from knowing as this will allow them to act quickly and appropriately if you or your child have an injury.

Your treatment centre will supply you with an alert card that you should carry with you in case of injury or bleeding. In case of a serious accident or injury, this should help to ensure that the healthcare team treating you will know that you have vWD.

### Medications

Avoid over the counter medicines that can affect blood clotting, such as Aspirin, Ibuprofen, and other non-steroidal anti-inflammatory drugs (NSAIDs). Always check with your doctor before taking any medicines.

## Exercise, fitness and sports

Try to be physically active and maintain a healthy weight. Physical activity helps keep muscles strong and flexible. This helps to prevent damage to muscles and joints. Always stretch before exercising. Contact sports are recommended to be avoided in case of injury.

Talk with your treatment centre if you are thinking about a new sport. If you are starting a new exercise program, slowly build up and if necessary, discuss more intense programs with the treatment centre.

## Travel

Find out the contact details of Treatment Centres in the places that you are visiting. Information is available from your Treatment Centre, Irish Haemophilia Society and World Federation of Hemophilia (www.wfh.org). Take up-to-date written medical information, including diagnosis and the name and phone number of your Treatment Centre. Haemophilia treatment centres provide treatment for people with haemophilia, von Willebrands and all inherited bleeding disorders.

## Women with reduced vWF Levels

### Preparing for your first period

Your body releases hormones, causing your period to start every month. In teenage girls, these hormones may not be as well controlled as in adults and this can result in unpredictable, heavy, or irregular periods. While this is a normal part of your body maturing, it also means that for girls with Low vWF or vWD, their periods can be very heavy from the outset. Frequent or heavy bleeding can lead to fatigue, poor concentration, iron deficiency or anaemia.

It is important that your daughter(s) understands everything there is to know about getting her first period, so that she can ask for help if needed. Some parents may have undiagnosed vWD and their own monthly menstruation may be considered as heavy, so it's a good idea for your daughter(s) to learn to get to know what a

normal period looks like.

It is also important that you take the time to explain to your daughter, that because of her bleeding disorder her period may be heavy, but that there are treatments available that can help. Your doctor may give you tranexamic acid tablets to have at home, just in case your daughters period starts and is heavy. If you or your daughter needs additional support with managing heavy periods, contact your treatment centre straight away.

## Menstruation

It can be difficult to tell if menstrual bleeding is heavy. Comparing yourself to other women in the family can be misleading as they, too, may also have low vWF levels or VWD without knowing it. The following should alert a woman to a potential problem:

- Bleeding which lasts longer than 7 days, requires you to change pads or menstrual cup every 2 hours or passing clots >1-euro size)
- Unpredictable bleeding
- Menstrual bleeding which affects daily activity (needing time off work / school)

There are lots of useful and effective treatment options for women with heavy menstrual bleeding. If heavy periods are not managed, women can become fatigued, iron deficient or anaemic so it is important to discuss your periods with your doctor if you are concerned.

Doctors may discuss using hormonal contraceptives or intrauterine devices (IUDs) as treatment for the prevention of bleeding, and anti-fibrinolytic drugs, like tranexamic acid, may also be useful for women with heavy menstrual bleeding. In severe cases or in the time between coming off a hormonal therapy and trying to get pregnant, other options such as prophylaxis with factor replacement might be considered to prevent heavy bleeding.

## Pregnancy and childbirth

Pregnancy can cause blood levels of vWF to increase in many women, but the level will depend on your type of vWD. It is important to inform your treatment centre when you become pregnant and they will arrange to see you and plan your delivery with you and your obstetrician. In some cases, gentle delivery methods may be

necessary if the baby is at risk of having vWD.

The highest risk of bleeding for women with Low vWF and vWD is in the 3-6 weeks after the baby is born as the pregnancy related rise in vWF blood levels reverses. If you notice new or heavier vaginal bleeding at this time you should contact your treatment centre for advice.

## Menopause

Just like the start of menstrual life, when menopause begins, hormone regulation can again become erratic. This can result in new onset of unpredictable and heavy menstrual bleeding. Again, treatment options are available and should be discussed with your centre. It is also important to remember that you can still become pregnant during the menopause and contraception is advised for 2 years after your periods stop for women under 50 years old or for one year in women over 50 years of age.

**Irish Haemophilia Society**

*Representing people living with haemophilia, von willebrand's and other inherited bleeding disorders*

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For women with bleeding disorders, more information can be found in the Irish Haemophilia Society booklet 'Women and Bleeding Disorders' or our website, haemophilia.ie.

# Haemophilia / vWD Treatment Centres in Ireland

## Adults

**National Coagulation Centre, St. James's Hospital, Dublin 8**
Director: Dr. Niamh O Connell
Tel: (01) 416 2141 / 4162142
E-Mail: ncc@stjames.ie

## Children

**Children's Health Ireland at Crumlin, Dublin 12**
Director: Dr. Beatrice Nolan
Haemophilia nurse specialist Tel: (01) 4096939 / 4096940
Tel: (01) 4096100 pager 8731 / 8732 / 8733

After 6pm and at weekends
Tel: (01) 4096100 ask for haematology doctor on call

Non urgent enquiries: haemophilia.dept@olchc.ie
E-Mail : haemophilia.dept@olchc.ie

## Adults & Children

**Cork University Hospital**
Director: Dr. Cleona Duggan
Tel: 021-492 2278 direct line. Hospital line 021-4546400 bleep 719
E-Mail: hcd@hse.ie

After 5pm and at weekends
Tel: 021-4546400 ask for haematology team on call

**Galway University Hospital**
Director: Dr. Ruth Gilmore
Tel: 021-492 2278 direct line. Hospital line 021-4546400 bleep 719

After 5pm and at weekends
Tel: 021-4546400 ask for haematology team on call

# NOTES

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