

Von Willebrand Disease: When is a “little” bleeding too much?

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Objectives

- To review the clinical presentation of von Willebrand Disease, its treatment and the prevention of bleeding episodes.
- To identify strategies to adapt the home and school environment to meet the needs of children with inherited bleeding disorders.
- To identify a network of coordinated support systems to promote independence in families with this chronic condition.

What is von Willebrand Disease?

- Von Willebrand disease is an inherited bleeding disorder-meaning you are born with it.
- Less than normal amounts of von Willebrand factor in the blood or von Willebrand factor that does not work as well as it should
- Effects the normal ability to form a blood clot
- Other parts of the clotting process do still work, however.

von Willebrand Disease (vWD)

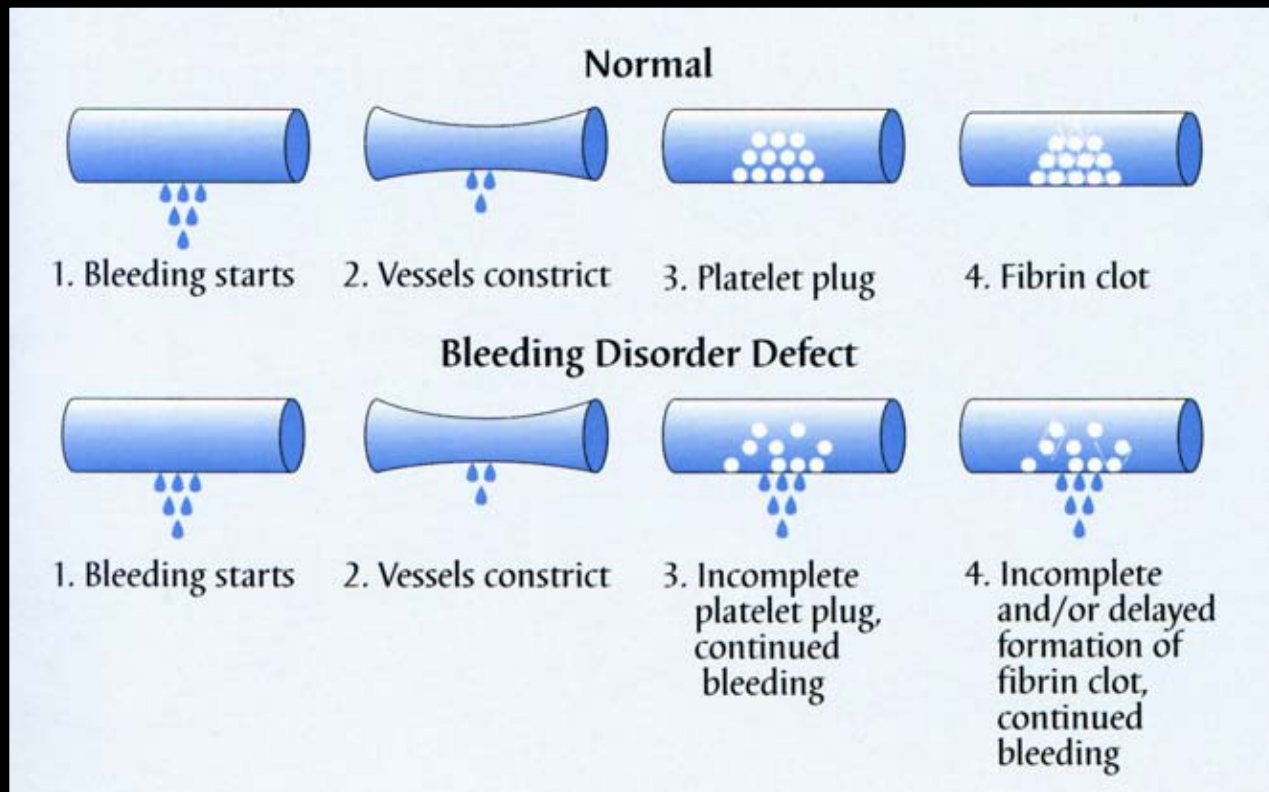
A person with von Willebrand disease does not bleed any faster than normal, but may bleed for a longer time.

(In some situations)

Normal Clot Formation

- Vasoconstriction (the blood vessel gets smaller)
- Platelets form a plug
- Other clotting factors make fibrin strands to make the platelet plug hold together better
- A clot forms
- The clot is dissolved when it is no longer needed

Clotting Illustration



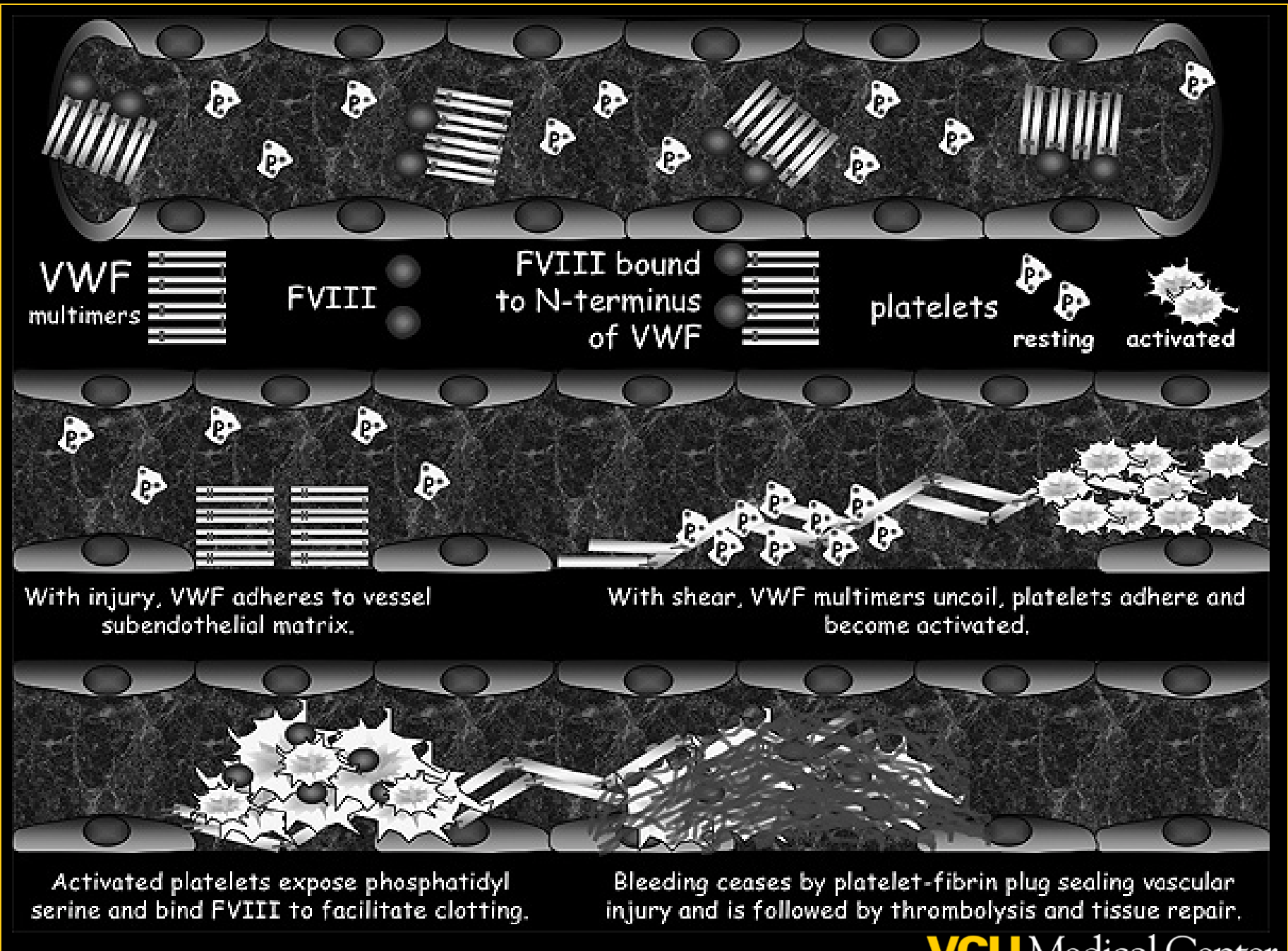
William J. *A guide for women and girls with bleeding disorders*. New York, NY: National Hemophilia Foundation. 1998:7-14.

Vasoconstriction

- Occurs spontaneously following injury to a blood vessel
- Slows and reduces flow of blood to injured area
- Prevents more blood loss
- Like pinching off a hose to decrease the water flow to a hole in the hose.

Platelet Plug Formation

- Platelets are round or oval-shaped, plate-like cells in the blood that
 - Rush to the injury site and begin to stick to the surface of the blood vessel where the hole is
 - Begin to stick to each other in groups and form a loose plug
- Plug is weak at this point without the stringy fibrin strands to strengthen it



Function of von Willebrand Factor in Clotting Process

- vWF is a glue-like protein needed for platelet plug formation
- Major functions
 - Serves as a bridge between platelets and injury sites in the blood vessel
 - Carries and protects one of the clotting factors (factor 8) in the blood that helps make the fibrin strands that strengthen the platelet plug

Kleinert D et al. *JOGMN*. 1997;26:271-276.
Ginsburg D, Bowie EJW. *Blood*. 1992;79:2507-2519.

Prevalence of vWD

- Most common inherited bleeding disorder
- Estimated to affect ~1% of the population (mostly type 1)
- Males and females of all races may be affected
- May be diagnosed at any age
- Symptoms generally mild and may not require frequent treatment with type 1

Kleinert D et al. *JOGNN*. 1997;26:271-276.

Ewenstein BM. *Annu Rev Med*. 1997;48:525-542.

Types of von Willebrand Disease

- Three different types of von Willebrand Disease:
Type 1, 2 and 3
- The severity of the bleeding problem will depend on the type of von Willebrand Disease

Type 1 vWD

- Most common type; in >80% of cases
- Quantitative defect
 - Normal structure and function of vWF
 - Mild to moderate decrease in amount of vWF in the blood stream
- Bleeding symptoms may be absent, mild, or moderate

Ewenstein BM. *Annu Rev Med.* 1997;48:525-542.

Image adapted from Vosburgh E. *Hosp Practice.* 1993;28:31-41.

Type 2 vWD

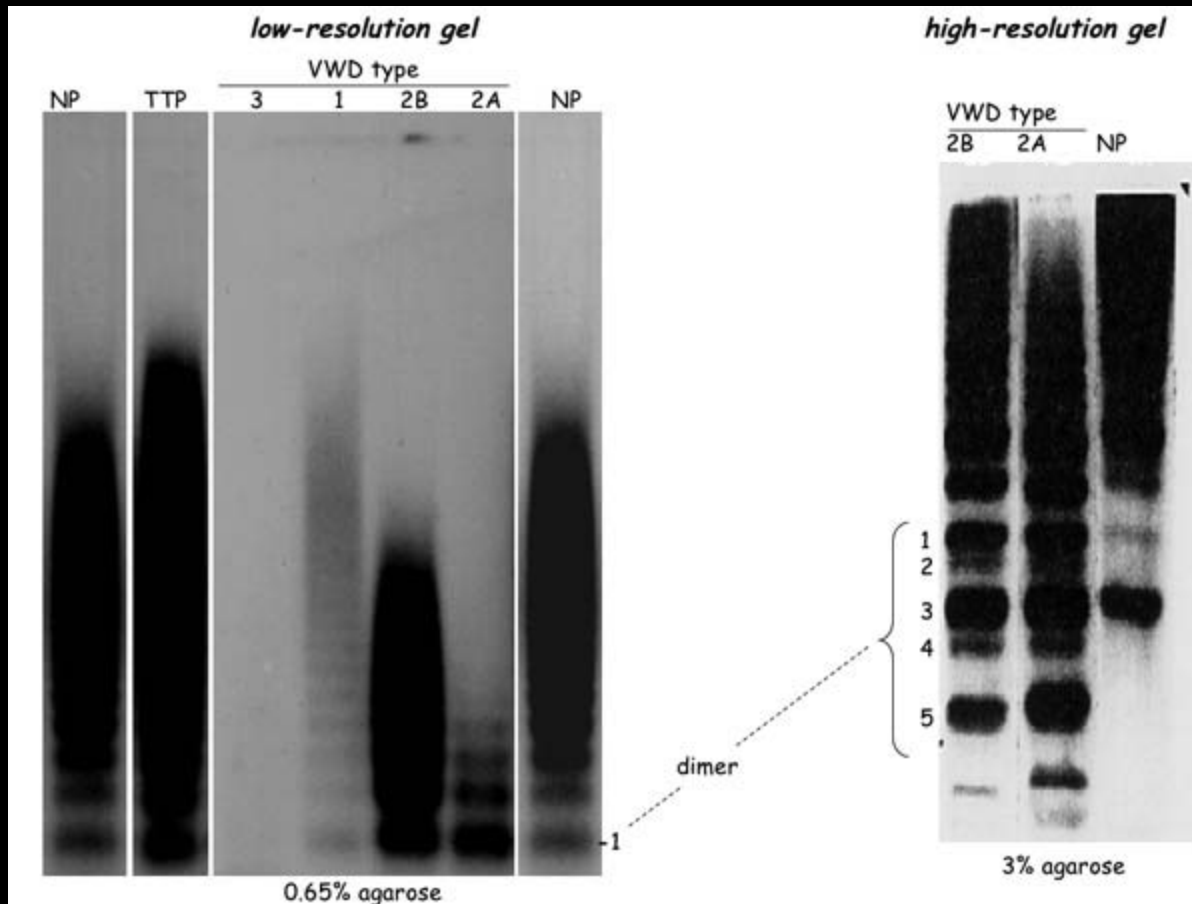
- Qualitative defect- vWf does not work right
- Bleeding symptoms can be mild to severe
- Several sub-types related to the actual defect in the vWf:8
 - related to the ability to bind with platelets or factor 8

Type 3 vWD

- Rare
- Quantitative defect-almost no von Willebrand factor
- Very low factor 8 level
- More severe bleeding symptoms seen in early childhood

Ginsburg D, Bowie EJW. *Blood*. 1992;79:2507-2519; Lak M et al. *Br J Haematol*. 2000;111:1236-1239. Sadler JE et al. *Thromb Haemostasis*. 2000;84:160-174.
Image adapted from Vosburgh E. *Hosp Practice*. 1993;28:31-41.

• Soft tissue and joint bleeds common



Clotting Defect in people with von Willebrand Disease

- The platelets do not stick together as well to form the platelet plug
- The fibrin strands needed to strengthen the platelet plug are not as strong because there is less factor 8 at the site of the injury. (one of the clotting factors needed to help make the fibrin strands)

vWD: Sites of Bleeding

Mucous membrane areas

- Nose (epistaxis)
- Mouth (gingiva)
- Throat
- Digestive tract
- Urinary tract
- Reproductive tract (uterus)

Most Common Types of Bleeding

Clinical Presentations of Symptoms

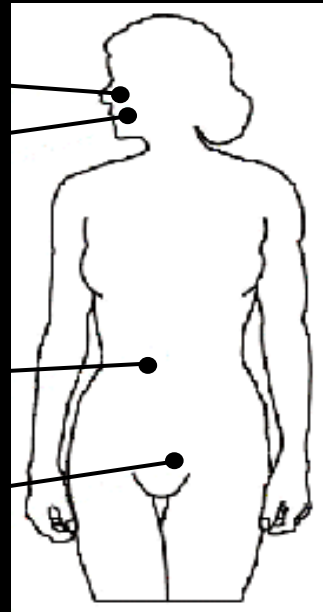
Nosebleeds

Mouth bleeding

GI bleeding

Menorrhagia

(Heavy periods)



Symptoms of vWD

- Bleeding after surgery (especially involving mucus membranes)
- Prolonged or excessive bleeding after dental procedures
- Prolonged bleeding after delivery of a baby
- Heavy, prolonged menstrual periods
- Easy, excessive bruising
- Nosebleeds
- May vary in each person from time to time, throughout life

Characteristics of Normal Menstruation

Normal menstruation

- Occurs every 28 ± 7 days
- Duration of flow 2 to 7 days
- Blood loss 25 to 69 mL/cycle
- With vWD, one or all of above can be greater, resulting in increased blood loss, iron deficient anemia

Characteristics of Menorrhagia

- Prolonged flow >7 days
- Blood loss >80 mL/cycle
- Passage of clots, flooding, staining of clothes and bedding

Incidence of Menorrhagia

Incidence in women with vWD:
~65%

This is >4 times higher
than in women without vWD.



MENSTRUAL FLOW CHART

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
JAN																																
FEB	X	X	X	X																					X	X	X	X	X			
MAR																																
APR	X	X	X	X	X	X																										
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Type of flow: Bleeding X Spotting S

Please have this chart with you when you call or visit your health care provider

WHAT IS A NORMAL PERIOD?

Normal Periods:

- ❖ Start before age 15
- ❖ Last one week or less
- ❖ Are between 21 and 42 days from the first day of one period to the first day of the next period
- ❖ When you bleed, you fill less than one pad per hour

If your periods are NOT “normal,” talk with your clinician.

WRITE YOUR PERIODS DOWN ON A CALENDAR

This information is provided to you as a courtesy through:

Cincinnati Children's Hospital Medical Center

Teen Health Center, Adolescent & Pediatric Gynecology

If you need an appointment, please call (513)636-4681

Causes of variance in Von Willebrand levels

- vWF levels may be increased with
 - Exercise, stress
 - Inflammation
 - Pregnancy, birth control pills, hormone replacement therapy
 - Smoking
 - Surgery, trauma, or blood transfusion
 - Childbirth

Sadler JE et al. *Thromb Haemost.* 2000;84:160-174.

Gill JC et al. *Blood.* 1987;69:1691-1695.

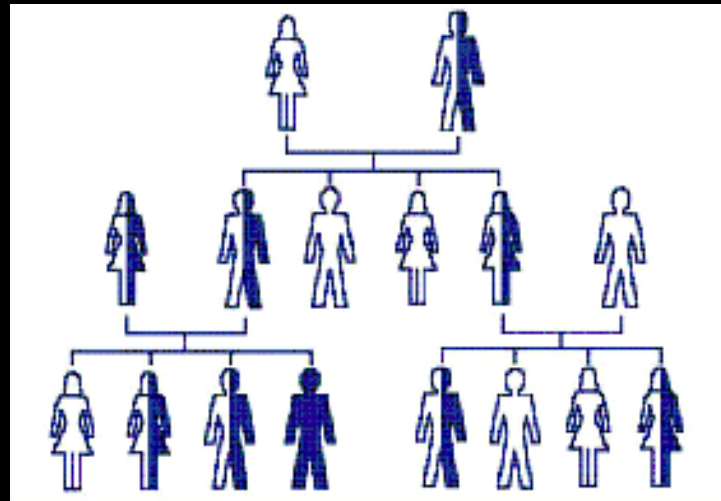
Causes of variance in Von Willebrand levels

- vWF levels may be decreased with
 - Menstruation
 - Hypothyroidism
 - Blood type O

Inheritance of vWD

- Gene is carried on chromosome 12
- Not sex-linked: both males and females can have the defect in the gene.
- Transmission is autosomal dominant or autosomal recessive
- Spontaneous mutations can occur, where there is no parent with the genetic defect

Autosomal Transmission



Inheritance Pattern by Type of von Willebrand Disease

- Type 1-
autosomal dominant-one parent has vWD and each child has a 50% chance of having vWD
- Type 2-
autosominal dominant or recessive
- Type 3-
autosominal recessive-both parents are carriers of the gene and have a 25% chance of a child with severe type 3

Spontaneous Mutation

- Change in gene occurs during prenatal development (in womb before birth)
- Occurs when neither parent has vWD
- Future inheritance pattern will be the same as in someone with a family history of vWD

Montgomery RR, Hilgartner MW. *Understanding von Willebrand Disease*. New York, NY: National Hemophilia Foundation; 1991.

Diagnosis of vWD

- Personal and family history of bleeding symptoms
- Blood work to check von Willebrand levels and type
- Type 1 disease often diagnosed later in life after extensive dental work or heavy menses.
- Often adult parent diagnosed after child found to have the disease

Suggested Questions for Screening Persons for a Bleeding Disorder

- Do you have a blood relative who has a bleeding disorder such as von Willebrand Disease or hemophilia?
- Have you ever had prolonged bleeding from trivial wounds, lasting more than 15 minutes or recurring spontaneously during the 7 days after the wound?
- Have you ever had heavy, prolonged or recurrent bleeding after surgical procedures, such as a tonsillectomy?

National Heart, Lung and Blood Institute, The Diagnosis, Evaluation and Management of von Willebrand Disease, 2007

Suggested Questions for Screening Persons for a Bleeding Disorder

- Have you ever had bruising, with minimal or no apparent trauma, especially if you could feel a lump under the bruise?
- Have you ever had a spontaneous nosebleed that required more than 10 minutes to stop or needed medical attention?

Suggested Questions for Screening Persons for a Bleeding Disorder

- Have you ever had heavy, prolonged or recurrent bleeding after dental extractions that required medical attention?
- Have you ever had bleed in your stool, unexplained by a specific anatomic lesion (such as an ulcer in the stomach or a polyp in the colon) that required medical attention?
- Have you ever had anemia requiring treatment or received a blood transfusion?

Suggested Questions for Screening Persons for a Bleeding Disorder

- For women, have you ever had heavy menses?
 - Presence of clots greater than an inch in diameter
 - Changing a pad or tampon more than hourly
 - Resulting in anemia or low iron level

Other considerations

- Liver or kidney disease
- Blood or bone marrow disorder
- High or low platelet count
- Taking aspirin, NSAIDS, clopidogrel (Plavix), warfarin or heparin

Treatment of vWD

- Treatment decision influenced by
 - Type of vWD
 - Severity of bleeding
- Minor bleeding may not require treatment

Recommended Treatments

- Desmopressin acetate (intravenous DDAVP, intranasal Stimate)
- Intravenous Factor concentrates with von Willebrand factor and factor 8 in them
- Amicar (oral medication)
- Birth control pills for heavy periods

Intranasal Desmopressin: Stimulate

- Intranasal DDAVP
- Convenient; may be administered at home or school
- Can be stored in refrigerator; stable at room temperature for up to 3 weeks
- Peak effect within 90 minutes of administration
- Usually causes a temporary rise in the amount of von Willebrand factor in the blood stream

Physician's Desk Reference®. 57th ed. Montvale, NJ:
Medical Economics Company, Inc; 2003.

Intranasal Desmopressin: Stimulate (cont)

- Dose
 - 1 spray in *either* nostril (one puff) if patient is less than or equal to 110 pounds (≤ 50 kg)
 - 1 spray in *each* nostril (2 puffs) if patient is greater than 110 pounds (50 kg)
- Stimulate challenge to document if you respond with increased von Willebrand factor in the blood after a dose

Physician's Desk Reference®. 57th ed. Montvale, NJ:
Medical Economics Company, Inc; 2003.

Side-effects of Stimate

- Fluid retention- need to decrease what you drink for 24 hours after a dose and drink fluids with sodium in them to prevent decreased blood sodium
- Facial flushing
- Headaches

Stimate: Desmopressin Acetate 1.5 mg/mL



Amicar (aminocaproic acid)

- Oral medication (pills or liquid)
- Helps keep clot from breaking down as quickly
- Especially good for use with dental work
- May be used along with Stimate or intravenous factor concentrates
- May cause stomach upset
- Do not give if blood in urine!

McEvoy GK. In: *AHFS Drug Information*[®]. Bethesda, Md: American Society of Health-System Pharmacists, Inc; 1999:1233-1352.

Treatment of Epistaxis (Nosebleeds)

- Treat with Amicar and/or Stimate if orders to do so
- Local measures: pressure, ice
- Nosebleed QR powder (OTC)
- If bleeding not stopped after 15 to 30 minutes, especially with bilateral heavy bleeding, needs medical attention
- Local prevention (humidity, saline gel, neosynepherine)

Hormonal Therapy for vWD

- Treatment with estrogen increases vWF levels in type 1 vWD
- Birth control pills can be useful in treating heavy menstrual periods
- A levonorgestrel intrauterine device. This is a contraceptive device that contains progestin. It's placed in the uterus (womb)
 - opposing estrogen induced growth of the endometrium or lining of the uterus.
- Endometrial ablation for women beyond childbearing or not interested in childbearing
- Not effective treatment for type 2 vWD as structural defect will not be corrected

Ewenstein BM. *Annu Rev Med.* 1997;48:525-542.

Treatment With vWF Concentrates

- Intravenous factor with von Willebrand factor and factor 8 in them (Humate-P or Alphanate)
- vWF concentrates are used for
 - Severe bleeding episodes and major surgeries in patients with type 1 vWD
 - Most bleeding episodes and surgery in type 2B and type 3 vWD
 - Bleeding in any patient with vWD who does not respond well to DDAVP (Stimate or intravenous DDAVP)

Treatment With vWF Concentrates (cont)

- vWF concentrates contain both vWF and FVIII
- Blood product-obtained from screened, pooled human plasma –
 - Treated to inactivate and remove viruses
- Administered intravenously over several minutes
- Costly

Psychosocial Issues: Adolescent Young Women

In addition to the other psychosocial issues experienced by others with vWD, young women have unique issues including:

- Embarrassment- Managing heavy menses and the feeling that "everyone knows"
- Stigma -Related to use of oral contraceptives to control menses

Psychosocial Issues: Adolescent Women (cont)

- Isolation- Feeling they are the only one dealing with disorder
- Intimacy & Dating- Developmental tasks faced during adolescence are challenged by dealing with issues related to disclosing medical condition
- Concerns about Future Health -Teens begin to think about future health, specifically pregnancy and childbirth

Sports and Activities

- Regular exercise is encouraged to maintain strong muscles and joints
- Avoid high-contact sports such as football, hockey, and wrestling (Type 3)
- Recommended sports include biking, swimming, golf, tennis, baseball, and softball

Recommendations for Patients

- Have regular check-ups at your HTC
- Avoid the frequent use of aspirin and ibuprofen medications (can effect platelet function)
- Call your doctor before any planned surgeries, excessive dental work or other procedures that may cause bleeding

School Challenges

- Infusions
- Emergency care
- Liability
- Independence from family
- Relating to peers
- Early recognition and referral

Strategies in School

1. Plan for Emergency Care
2. Early treatment of bleeds
3. "Home treatment" at school
 - Home health nursing for routine infusions
 - Self-infusion at school
4. Keeping medications at school

Strategies in School

- Accountability vs. accommodation
 - Reducing risk: Changing classes
 - Home bound instruction
 - Books at home
 - BUT, kids will be kids....
- Sports and school
 - Individualized approach
 - Type of sport, when actively bleeding or recovering, on menstrual cycle
 - Playground
- Communication!

Summary

- vWD is the most common inherited bleeding disorder
- It affects men and women equally
- Diagnosis requires detailed personal and family history and blood tests
- Symptoms are usually mild
- Bleeding sites generally involve mucous membrane tissue

Summary

- In VWD, you either have low levels of a certain protein in your blood or the protein doesn't work the way it should. There are three major types of VWD: type 1, type 2, and type 3.
- The signs and symptoms of VWD depend on the type and severity of the disease. Many people have such mild symptoms that don't know they have the disease.
- VWD is almost always inherited. Parents pass the gene for the disease on to their children.

Summary

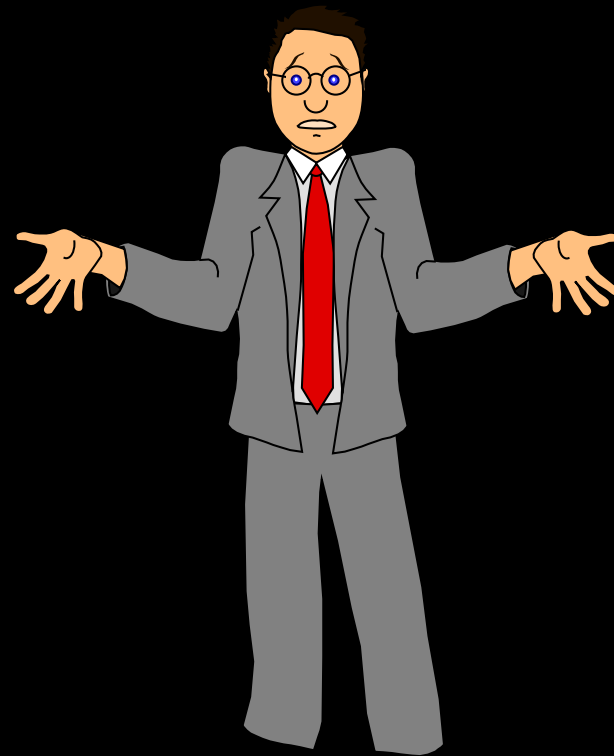
- Women with VWD also may be treated with oral contraceptives, intrauterine devices, or a procedure that destroys the lining of the uterus, thus reducing menstrual blood loss.
- Preventing bleeding and staying healthy are important for people with VWD.
 - Avoid over-the-counter medicines that can affect blood clotting;
 - Always check with your doctor before taking any medicines
 - Wear a medical ID bracelet if you have a serious form of VWD
 - Alert people like your dentist, pharmacist, employee health nurse, gym trainer, and sports coach of your condition.

Summary

- Treatments for VWD include medicines and therapies to replace or increase the amount of von Willebrand factor in your blood, prevent the breakdown of clots, and control heavy menstrual bleeding in women
- If your child has VWD that's severe enough to pose a significant risk of bleeding, anyone who is responsible for him or her should be told about the condition. This will help them handle the situation if your child has an injury.
- VWD can't be cured, but it can be treated. With the right treatment, people who have VWD can lead normal, active lives.

Who can help with this family?

HELP!!



Hemophilia Treatment Center Team Members

- Patient / Family
- Hematologist
- Nurse
- Social Worker
- Physical Therapist
- Orthopedist
- Primary Care
- Infectious Disease
- Genetics
- Pharmacy
- Dental
- Hepatology
- OB/GYN

Role of Hemophilia Treatment Centers

- State-of-the-art medical treatment for persons with hemophilia through the life span
- Education
- Research
- Outreach
- Model of comprehensive care for chronic disease

Community Support for Students with Bleeding Disorders: The United VA Chapter of the National Hemophilia Foundation



Resources:

Family Assistance Program
Lyman Fisher Scholarship Fund
Facts N' Factors Newsletter

Programs/Events:

Annual Meeting
Camp Youngblood at Camp Holiday Trails
First Step New Parent Program
Hemophilia Federation's Dads in Action Program
Other Special Events

Fundraising:

Annual Golf Tournament – Fall 2009
Annual Wine Tasting and Raffle Event – Spring 2009
Annual Youngblood 5k Race – 9
Other Special Events