Emergency Care for Patients with von Willebrand Disease

von Willebrand Disease (VWD) is classified by ‘type 1, 2, or 3’. If the type is unknown proceed as if type 1, if bleeding continues consult a hematologist.

Gynecological bleeds (pg. 12)

Immobilizers
p.r.n. for joint bleeds

Abdominal bleeds (pg. 10)

Trauma (pg. 23)
Administer the recommended treatment

Mucous membrane bleeds (pg. 6)
Administer the recommended treatment and anti-fibrinolytics

Ice pack
for soft tissue, muscle, joint bleeds

For VWD type 3: Avoid intra-muscular injections due to the possibility of causing a muscle bleed

Minor cuts / bruises
no treatment

Head Injury (pg. 4)
Always treat immediately with the recommended treatment

Authors and Editors: Susan C. Zappa RN, Lucie Lacasse RN, Rose Jacobson RN, Sherry Purcell RN and Karen Wulff RN
Medical Reviewers: David Lillicrap MD, FRCPC and Marcela Torres MD
# Treatment and Management Guidelines for von Willebrand Disease

<table>
<thead>
<tr>
<th>Type of von Willebrand Disease</th>
<th>Major life-threatening bleeds (ex. - head injury, GI bleeding, severe menorrhagia, etc.)</th>
<th>Other bleeds (ex. - sutures, nosebleed, mouth bleed, dental extractions etc.)</th>
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<tr>
<td>Type 1 or Type 2</td>
<td>Factor concentrate containing both FVIII (8) and von Willebrand factor (eg. Humate P®, Alphanate®, wilate®): 60-80 Ristocetin cofactor units/kg IV or Vonvendi®, recombinant von Willebrand protein 40-60 units/kg</td>
<td>If Patient is known to respond to desmopressin (DDAVP®): Desmopressin 0.3 mcg/kg IV in 50 ml of Normal Saline over 30 minutes or subcutaneously if volume can be given safely. Recommendation: a maximum dose of 20 mcg. Mucosal bleeding - anti-fibrinolytics (pg. 9)</td>
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<tr>
<td>Should not be given to type 2 B patients</td>
<td>Does not contain factor VIII Package insert will instruct as to rate per volume. Note: monoclonal or recombinant factor VIII (8) products do NOT have von Willebrand factor in them and will not stop the bleeding.</td>
<td>For patients who do not respond to desmopressin: Give a factor concentrate containing both FVIII (8) and von Willebrand factor (eg. Humate P®, Alphanate®, Wilate®): 40-60 Ristocetin cofactor units/kg IV or Vonvendi® a recombinant von Willebrand protein 40-60 units/kg IV</td>
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<td>The type 2 VWD known as 'pseudo VWD or VWF platelet type' will only respond to a platelet transfusion - call a hematologist.</td>
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<tr>
<td>Type 3</td>
<td>Factor concentrate containing both FVIII (8) and von Willebrand factor 60-80 Ristocetin cofactor units/kg or Vonvendi® with recombinant factor VIII (contact hematologist for instructions) on doses. Package insert will instruct as to rate per volume. Note: monoclonal or recombinant factor VIII (8) products do NOT have von Willebrand factor in them and will not stop the bleeding.</td>
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<td>Most severe form of VWD.</td>
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If your institution does not have Humate-P®, or Alphanate®, wilate®, or Vonvendi® but does have Koate DVI® available, consult a hematologist for guidelines and instructions.

Per the Medical and Scientific Advisory Council of the National Hemophilia Foundation: Because of the increased risk of HIV and hepatitis A, B, and C transmission, cryoprecipitate should not be used (for the treatment of von Willebrand Disease) except in an emergency situation where one of the above products is not available and delay of treatment would be life or limb threatening.
Hemophilia Treatment Center (HTC) addresses, telephone numbers and other contact information can be found at:  
www.cdc.gov/ncbddd/hemophilia/index.html

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<tr>
<th>Canadian Hemophilia Society</th>
<th>World Federation of Hemophilia</th>
<th>CDC</th>
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<th>National Hemophilia Foundation</th>
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Introduction & von Willebrand Disease Basics

Purpose

This manual contributes to von Willebrand Disease (VWD) care by enhancing the emergency department personnel’s understanding of this disorder and its treatment. The goals of this manual are to:

• promote understanding of the complexities of von Willebrand Disease with an emphasis on rapid treatment for correction of the hemostatic abnormality

• provide a reference for the emergency center staff

• promote a consultative dialogue with the emergency department (ED), treatment center, and patient/family

Early triage and treatment reduce morbidity.

Use

This manual provides a standardized format for evaluation and treatment of VWD emergencies. The content is segmented by systems and complications of VWD. Turn to an area of interest. The illustration on the left page provides information points for quick review. The text on the right page gives further detail of bleeding presentations, their possible complications and treatment. The treatment varies to the type and the severity of VWD. Treatment and management information is provided on the inside cover of the manual as a reference.

It is suggested that the patient’s treatment center or hematologist be consulted for final management of bleeding complications.

To The Attending Medical Staff

This manual is a guide for medical personnel who may be less familiar with VWD treatment. The content consists of guidelines, recommendations and suggestions only. The attending physician has the final responsibility for appropriate diagnosis and treatment.

Definition

von Willebrand Disease is an autosomally-inherited bleeding disorder caused by the quantitative deficiency or dysfunction of von Willebrand factor, a large multimeric glycoprotein. It is non-sex linked. Therefore, it can occur equally in both men and women.

Effects of von Willebrand Disease

von Willebrand factor is essential for platelet-plug formation as an adhesion protein that diverts circulating platelets to the sites of vascular injury, particularly through larger multimers. It also forms a non-covalent complex with coagulation factor VIII in plasma, thereby protecting it from inactivation and clearance.

Even though the primary deficiency or defect in von Willebrand Disease is that of von Willebrand factor, the secondary deficiency of factor FVIII, which is dependent on von Willebrand factor as its naturally occurring plasma carrier and stabilizer, leads to a defect both in platelet-plug formation and in fibrin formation.

Prevalence

The prevalence is as high as 1 to 2 percent in the general population.
Types of von Willebrand Disease

The type of VWD determines the treatment - see inside of the front cover for treatment options. von Willebrand Disease is classified by ‘type 1, 2 or 3’. If the type is unknown, proceed as if type 1. If bleeding continues contact a hematologist.

von Willebrand Disease is classified into three main phenotypes and each have subtypes based on the quantity and quality of the von Willebrand factor (VWF):

- **Type 1**: which accounts for 60 to 80 percent of cases, results from a decreased production of normal von Willebrand factor and factor VIII; typically transmitted as an autosomal dominant trait in the heterozygous state.

- **Type 2**: which accounts for 10 to 30 percent of cases is characterized by qualitative abnormalities of von Willebrand factor and is further divided into subtypes 2A, 2B, 2M and 2N. Inheritance is generally autosomal dominant.

- **Type 3**: Accounts for 1 to 5 percent of cases and is transmitted as an autosomal recessive trait in homozygous or compound heterozygous persons. This severe form of the disease is characterized by a very low or undetectable von Willebrand factor in plasma with a low, usually detectable factor VIII activity. It is in these rare cases of type 3 (1 in 1 million people) that symptoms are more frequent and severe, similar to those cases of severe hemophilia.

Acquired von Willebrand Disease: This is an acquired syndrome that resembles von Willebrand Disease in its clinical manifestation and laboratory patterns. It occurs in rare instances in association with clinical conditions such as lymphoproliferative and autoimmune diseases, hypothyroidism, essential thrombocythemia, cancer, Wilm’s tumor and valvular heart disease.

Bleeding episodes

The hallmark of von Willebrand Disease is mucosal bleeding. Mucous membrane bleeds such as bleeding from the nose, mouth, gastrointestinal tract, genitourinary and vaginal bleeding are the most common. If left untreated, these mucous membrane bleeds can become acute and sometimes life-threatening emergencies. Serious bleeding resulting from untreated trauma and/or post-surgical bleeding can also become life or limb-threatening in these patients.

Serious bleeding sites

The major sites of serious bleeding which threaten life, limb, or function are:

- intracranial
- oropharynx
- vaginal bleeding
- spinal cord
- gastrointestinal
- intra-abdominal
- ocular

Treatment

The mainstay of treatment is the replacement of the deficient/defective protein at the time of bleeding or before invasive procedures are performed. This may require desmopressin (subcutaneous, intranasal, or intravenous) or an infusion of commercial von Willebrand factor/FVIII concentrate such as Humate-P®, Alphanate® and wilate® or VONVENDI® recombinant von Willebrand factor. Specific doses, additional drugs and medical interventions depend upon the type of VWD and the site and severity of bleeding. Please refer to the inside cover of the manual, page ii, for more detailed information on the recommended treatment. Once treatment has been given, emergency diagnostic procedures can begin.

Family

Patients living with VWD or their parents are often knowledgeable about the management of their disorder and their input should be sought and heeded. Interview the family about whether any medication has been administered prior to arriving at the ED; if so, determine when and what dose. Additional treatment may be required, dependent on the time lag and severity of the bleed. Determine the treating hematologist or treatment center, and contact them for assistance and follow-up as needed.
Intracranial hemorrhage (ICH) is a potential for all head injuries.

Administer recommended treatment first*, and then perform diagnostic studies such as CT scan.

If an ICH is diagnosed, the patient should be admitted and the hematologist contacted immediately. If no ICH is diagnosed, the patient may be discharged.

Discharge Instructions

Call the treatment center or the patient’s hematologist for follow-up treatment recommendations*.

Head injury instructions should be given for a two week period (instead of the usual instructions for 24 - 48 hour period).

Report any signs or symptoms of an ICH to the treatment center or the patient’s hematologist.

*Recommended treatment table inside front cover
Intracranial hemorrhage (ICH) is a potential risk for individuals with von Willebrand Disease, and is most commonly associated with injury. The risk of intracranial hemorrhage is increased with the more severe types of VWD. Without early recognition and treatment, death or severe neurologic impairment can occur. Early neurologic symptoms may not always be evident.

**Treatment**

All significant head trauma, with or without hematoma, should be treated promptly with the appropriate treatment* before any diagnostic tests. A hematologist should be contacted.

**Diagnostic imaging**

Obtain an emergency CT scan to rule out ICH after the appropriate treatment has been given. Notify the patient’s hematologist or treatment center as soon as possible.

**Possible admission**

The patient should be admitted to the hospital for observation if he/she has suffered a severe blow to the head or exhibits any neurologic symptoms. Symptoms can include headache with increasing severity, irritability, vomiting, seizures, vision problems, focal neurologic deficits, stiff neck, or changes in level of consciousness. Patients with a past history of ICH are at increased risk of repeated head bleeds.

**Instructions**

If the patient is discharged home, instruct the family to monitor the patient for signs and symptoms of neurologic deterioration and report any abnormalities to the hematologist. Consult the treatment center to arrange for follow-up treatment if the patient is discharged home from the emergency department.

*Recommended treatment table inside front cover
Mucous Membrane Bleeding

A Dental or E.N.T. consult may be needed.

Nose bleeds may respond to other measures. Refer to "Controlling Epistaxis" table on pg. 8.

Mouth bleeds (gum, tooth, frenulum or tongue laceration) may require treatment* and the use of anti-fibrinolytics. If the bleeding is minor, local measures such as topical thrombin (if available) or fibrin glue (Tisseal®) in conjunction with anti-fibrinolytics can be used. Refer to the anti-fibrinolytics on pg. 9.

Assess for anemia if there has been prolonged mucosal bleeding.

Discharge Instructions

Patients should follow-up with their treatment center or hematologist the next day.

Instruct the patient on how to control epistaxis, the use of anti-fibrinolytics, and the importance of a modified diet. Consult the Diet Modifications table on pg. 9 as needed.
Mucous membrane bleeding may require medical care in the emergency department. Treatment may be required for patients who:

- are experiencing profuse and/or prolonged bleeding
- have sustained a known injury to the mouth, tongue, or nose
- have severe swelling in the mouth or throat area
- are experiencing respiratory distress
- have difficulty swallowing or speaking

The patient may not know the reason for the symptom or bleeding. It may have been caused by trauma, infection, or the bleed may be spontaneous. If airway blockage is suspected, prompt treatment* is required prior to any invasive procedures.

**Remember prompt treatment will greatly reduce the bleeding, often preventing serious complications.** The longer the patient waits, the more bleeding takes place. If the bleed is in a closed space, the accumulation of blood will cause surrounding tissue damage, airway obstruction and pain.

**Epistaxis**

Uncontrolled epistaxis may require treatment in conjunction with anti-fibrolytics. Be sure the patient knows how to control and stop the bleeding (see pg. 8) ENT may need to be contacted for localized treatment such as cauterization or other interventions such as packing of the nares.

**Oral Cavity**

Bleeding in the mouth can be hard to control. A frenulum or tongue laceration may respond to topical thrombin or other similar agents. If the bleed continues, the patient will probably need further treatment. A single treatment may temporarily stop the bleeding, but clot lysis from saliva enzymes often results in re-bleeding. Re-bleeding is most commonly seen on days 3-5. An anti-fibrinolytic may be indicated to maintain hemostasis. A modified diet should be started at the same time as treatment (see Diet Modifications pg. 9).

Bleeding may occur with extracted, erupting or exfoliating teeth. It is more common with extracted and exfoliating teeth. A dental consult may be needed to extract the tooth. Treatment* to increase the von Willebrand factor will be necessary prior to extraction. A frenulum or tongue laceration will require treatment*.

**Retropharyngeal**

Retropharyngeal bleeding may occur after prolonged sore throat, cough, or flu. After the recommended treatment*, further observation, X-rays and admission may be required depending upon the specific circumstance.

*Recommended treatment table inside front cover
Controlling Epistaxis
Instruct the patient:

1. To gently blow his/her nose to remove mucus and unstable clots that will interfere with hemostasis.

2. Tilt the head forward so any blood will come out the nares and not down the back of the throat.

3. Apply firm constant pressure to the entire side of the nose that is bleeding for 15 minutes.

4. Release the pressure to see if bleeding has stopped, gently blow out and remove any soft clots.

5. If the bleeding continues, reapply pressure for another five minutes.

6. Recommended treatment* and/or anti-fibrinolytic agents (see next page) may be needed.

7. During active bleeding, NoseBleed QR® powder an over-the-counter preparation can be utilized. The powder needs to be mixed with blood, as per the manufacturer’s directions. The powder will solidify the blood, form a crust and bleeding may stop.

8. During active bleeding, or when the bleeding has stopped, you may spray or apply two drops of oxymetazoline (eg. NeoSynephrine®, Dristan® or Afrin®) nasal spray/drops to the side that was bleeding. These can be used at home PRN for epistaxis.

9. Instruct the patient to use mucosal membrane moisturizer (eg. Aquaphor®, Ayr gel® or normal saline spray) in the nares to keep the membranes soft and moist, and prevent the formation of hard crusts which might crack and restart bleeding. Adequate cool-mist humidification in the home is also helpful.

10. An Ear Nose Throat (ENT) consult may be required for possible cauterization of a vessel.

*Recommended treatment table inside front cover
Anti-Fibrinolytics

Anti-fibrinolytics may be indicated in nasal or oral bleeding. Amicar® and Cyklokapron® are both anti-fibrinolytic agents. Either may be prescribed for mucous membrane bleeding to promote clot stabilization in conjunction with the recommended treatment*. In some cases they may be prescribed independently.

Amicar - epsilon aminocaproic acid  
Recommended dosage:
Child: oral dose 50-100 mg/kg (not to exceed 4 g) every 6 hours for 3 - 10 days  
Adult: oral dose 3-4 g every 6 hours for 3 -10 days  
Supplied: Tablet: 500 mg or 1000 mg per tab  
Syrup: 250 mg per ml  
Injectable: 250 mg /ml available in 20 ml vial  
*Contraindicated if hematuria present

Cyklokapron - tranexamic acid  
Recommended dosage:
Child: oral dose 25 mg/kg every 6- 8 hours for 3 - 10 days  
Adult dose: oral dose 1000 mg-1500 mg tid for 3 - 10 days  
Supplied: Tablet: 500 mg tranexamic acid per tab  
Injectable: 100 mg/ml available in 5 and 10 ml ampules  
*Contraindicated if hematuria present

These medications must be given as ordered to keep blood levels constant. They are not readily available through local pharmacies (they must be ordered). If possible, dispense the amount for 2-3 days from the hospital pharmacy to allow time for the local pharmacy to order. Other options are the family’s home supply, bleeding disorders treatment center or (U.S.) home care companies.

Follow-up care per the treatment center or patient’s hematologist. Topical agents such as topical Thrombin® and Gelfoam® may also be used to help control mucous membrane bleeding.

Diet Modifications

Directions for the patient:

1. Diet should be restricted to soft, cool, or lukewarm foods until the area is fully healed. Suggested foods: flavored gelatin, non-carbonated drinks, sherbet, lukewarm soups (no cream soups), baby foods, blenderized or pureed foods, pasta.

2. Avoid using a straw, chewing gum, and do not smoke. Negative pressure from the sucking action can dislodge the clot and aggravate the bleeding site.

3. Foods to avoid include hard foods like chips, nuts, popcorn, tacos, etc.

4. If Desmopressin (DDAVP®, Octostim®, or Stimate®) has been utilized for treatment, the patient has fluid restrictions for 24 hours.

*Recommended treatment table inside front cover
Nausea and vomiting may indicate intracranial hemorrhage as well as gastrointestinal problems.

**Iliopsoas bleeding**
- flexed hip
- pain on extension
- may be mistaken for appendicitis
- Management: Treatment product* as per hematologist

**Abdominal pain**
Treat immediately* as per hematologist for:
- flank pain
- melena
- vomiting blood
- rectal bleeding

**Hematuria**
- bed rest for 24 hours
- force fluids
- consult the treatment center or the patient’s hematologist
- avoid anti-fibrinolytics

**Discharge Instructions**
- increase fluids
- rest
- no heavy lifting
- report any symptoms such as fever, pain, or increased hematuria, melena, hematemesis
- follow-up with the treatment center or the patient’s hematologist

*Recommended treatment table inside front cover
Initial presentation

Acute abdominal pain in a patient with von Willebrand Disease may have many origins, such as gastrointestinal (GI) tract hematomas (both spontaneous or trauma induced), iliopsoas or retroperitoneal bleeding.

Bleeding may also occur with hemorrhoids or the passage of kidney stones. Notify the treatment center or the patient’s hematologist.

Patients who present to the emergency department with abdominal or flank pain, melena or hematemesis should be triaged for immediate examination and the recommended treatment should be initiated. Once this is done, then diagnostic x-rays, scans and endoscopy procedures can be carried out.

Abdominal trauma and benign events such as forceful coughing or vomiting can precipitate an abdominal bleed. Blood loss can be significant before outward signs and symptoms appear. Infants can have bleeds with gastroenteritis, intussusception or Meckel’s Diverticulum.

A history of lifting heavy objects, weight lifting, falling on a bicycle crossbar or stretching the groin can precipitate abdominal wall, iliopsoas (see pg. 14 and 15), or retroperitoneal bleeding. These types of bleeds can occur more commonly in individuals with type 3 VWD, and are rarely seen in type 1 and type 2 VWD.

Symptoms

Symptoms of abdominal muscle bleeding (rectus, pectorals, latissimus, obliques) are a palpable mass, rigidity, and pain. Concurrent bleeding in the abdominal cavity may be present and go unnoticed for days with a steadily dropping hemoglobin. Rupture of the liver, spleen, or pancreas should be considered when the hemoglobin falls dramatically following trauma.

For nausea and vomiting without an obvious cause, consider that these may be symptoms of intracranial bleeding. Inquire about head injury, mental status changes, and other neurologic signs and symptoms, and consider CT scan of the head.

Genitourinary bleeding

Hematuria is often frightening to the patient but not a serious event. Instruct the patient to remain at bed rest and to increase fluids to 16 oz or 500 ml every hour over the next 24 hours. Protracted hematuria may require treatment.

Anti-fibrinolytics are contraindicated with hematuria. Contact the hematologist.

Scrotal bleeding may occur after trauma, especially in toddlers. Treatment will be required and follow-up with the hematologist or treatment center should be arranged.
Gynecological Bleeding

Assess for signs of anemia
- check hemoglobin
- check ferritin level

Obtain accurate menstrual history
- pad and/or tampon count per hour or per 24 hr time period (include nights)
- frequency of changing protection
- amount of blood on each pad (use a pictorial chart if available)
- presence of clots, size of clots
- number of overflow or flooded pads
- length, regularity of menses
- missed days at school/work due to menses
- need for iron therapy either currently or in the past
- history of medications, hormonal therapy and birth control

For active menorrhagia:
In addition to Humate-P®, Alphanate and wilate® or Desmopressin (DDAVP® or Stimate®/Octostim® as preparation available), start an anti-fibrinolytic (pg. 9).

Consider prescribing birth control therapy or IV Premarin as adjunctive therapy to prevent more bleeding.

Discharge Instructions
- follow-up with the treatment center or the patient’s hematologist (within one week)
- Instruct patient to accurately record bleeding, menstrual history
- Recommend rest, drinking fluids, (careful of amount if taking DDAVP) eating iron rich foods & supplemental iron preparations PRN
Menstrual Bleeding

Prolonged and heavy menstrual bleeding is one of the most common symptoms for females with bleeding disorders.

**Menarche** – a teenage girl with von Willebrand Disease can present to an emergency department at menarche or soon after with a severe, occasionally life-threatening hemorrhage. Appropriate treatment should commence immediately. Major vaginal bleeding requires treatment with a von Willebrand factor concentrate, see page ii. Consultation with an OB-GYN specialist and hematologist at a bleeding disorder treatment center is essential for ongoing follow-up. Oral contraceptives, anti-fibrinolytic treatment and desmopressin (IV, intranasally or subcutaneously) may be recommended on an ongoing basis.

Assess for signs of anemia, as the patient's hemoglobin can drop 2-3 g/ml Hgb, in just a few days, from prolonged menses.

**Menses** - Some women bleed excessively through their menstrual cycle. Others bleed between cycles or continuously through the month. These women may present to the ED with menorrhagia, iron deficiency, anemia, or mittelschmerz due to increased bleeding with ovulation. Obtain an accurate menstrual history and contact the patient’s hematologist for treatment recommendations.

Assess for signs of anemia, as the patient's hemoglobin can drop to 2-3 g/ml Hgb, in just a few days, from prolonged menses.

**Postpartum Bleeding** – During pregnancy, the majority of women with von Willebrand Disease, type 1, will have normal von Willebrand factor and factor VIII levels due to increased estrogen levels. “There are very few published data on the use of desmopressin during pregnancy, but there are some concerns that desmopressin causes uterine contraction with premature labour, intrauterine growth retardation and hyponatremia. For these reasons, it is advisable to be cautious about the use of desmopressin during pregnancy. Once the cord is clamped, desmopressin can be used if necessary. It is also probably reasonable to use desmopressin before a caesarean. Desmopressin is not contraindicated during lactation.”


The von Willebrand factor levels will decrease 24 to 48 hours following delivery, thereby increasing the risk of post-partum bleeding. In the event of a post-partum hemorrhage, treatment* should be initiated immediately to elevate the von Willebrand factor levels. Life-threatening post-partum hemorrhage will require treatment with either a von Willebrand factor/FVIII concentrate (ex. Humate-P®, Alphanate® and wilate®) or the recombinant product Vonvendi®. Adjunctive treatment with intravenous or oral anti-fibrinolytics may be useful (see pg. 9).
Soft Tissue / Muscle / Joint Bleeding

**Neck swelling**: EMERGENCY
- potential airway compromise
Management: Treatment product* as per hematologist

**Soft tissue bleeds and bruising**
- no functional impairment
- tenderness, but no severe pain
Management: No treatment, R.I.C.E.**

**Iliopsoas bleeds**
- flexed hip
- pain / inability to extend the leg on the affected side
Management: Treatment product* as per hematologist

**Thigh/calf/buttock bleed**
- pain with/without swelling
- impaired mobility
- observe for signs and symptoms of compartment syndrome
Management: Treatment product* as per hematologist

**Deltoid / forearm bleed**
- increased swelling and bruising
- observe for symptoms of compartment syndrome
Management: Treatment product* as per hematologist

**Early onset joint bleed**
- tingling - pain
- limited range of motion

**Advanced joint bleed**
- heat - pain
- swelling
Management: Treatment product* as per hematologist. Ice and immobilization for comfort.

**Discharge Instructions**
- **RICE - Rest, Ice, Compression (Ace® wraps), Elevation**
- Crutches - for weight bearing joints and crutch instructions
- Sling or splinting if support is needed (i.e. Aircast® for ankles)
- follow-up with the treatment center or the patient’s hematologist

*Recommended treatment table inside front cover 14
Soft tissue and superficial bleeds

Soft tissue bleeds usually do not require aggressive treatment. Superficial hematomas and bruises respond well to rest, ice and elevation. If the hematoma and bruising continue to increase in size, impairing movement or function, treatment may be required.

Muscle bleeds

Muscle bleeding is usually only associated with trauma in persons with mild von Willebrand Disease.

Persons with the most severe type of von Willebrand Disease, type 3, can experience muscle bleeding spontaneously or with minimal trauma. Any muscle group may be subject to bleeding. Common bleeding sites include the upper arm, forearm, thigh, and calf muscles.

Muscles that exhibit warmth, pain, and swelling should be managed with the recommended treatment. Anti-fibrinolytics may also be helpful.

Consequences of muscle bleeds: Muscle bleeds can result in serious consequences if not treated promptly. Extensive blood loss may occur in large muscle groups. Muscle bleeding can place pressure on nerves and blood vessels and, if untreated, may result in compartment syndrome, leading to permanent disabilities such as foot drop and wrist contracture. It is important that the patient’s hematologist be consulted before any invasive procedures such as a fasciotomy.

Treatment and follow-up care: Occasionally muscle bleeds may require treatment but more often will resolve with conservative treatment such as rest and ice. If compartment syndrome is suspected, appropriate treatment should be initiated and the patient should be admitted with an emergency consult to hematology.

Joint Bleeding

Joint bleeding is uncommon in individuals with type 1 and 2 von Willebrand Disease and is usually associated with trauma. Individuals with type 3 von Willebrand Disease can experience joint bleeding without trauma, and bleeding can occur into any joint space.

The joints most commonly affected are the elbows, knees, and ankles. Less common sites include the shoulders and hips. As repeated bleeding occurs, the synovial tissue thickens and develops even more friable blood vessels. A vicious cycle of bleeding and re-bleeding may set in and the affected joint is referred to as a “target joint.” Eventually, repeated bleeding into joints leads to arthropathy with destruction of cartilage and the eventual erosion of bone. The end result is decreased joint mobility and function. Again, this is very rare in von Willebrand Disease.

Signs and symptoms: Outward signs of joint bleeding include decreased range of motion, swelling, warmth and erythema on and around the joint. The patient may report symptoms of a bubbling or tingling sensation with no physical signs. Later symptoms include a feeling of fullness within the joint and moderate to severe pain as the bleed worsens.

Treatment: Some patients may present for treatment with no other outward signs of bleeding other than decreased range of motion and a complaint of pain or tingling. This is indicative of an early onset joint bleed and is the optimal time to treat. The patient should be infused as quickly as possible with the recommended treatment in order to minimize pain and joint destruction. Extreme pain, swelling, warmth, and immobility are signs and symptoms of an advanced joint bleed which occurs only after blood has filled the joint space.

Initiate treatment before any diagnostic procedures such as x-ray or MRI. In the instance of a dislocated joint, infuse with the recommended treatment before attempting relocation of the joint.

Joint Aspiration: Caution!

The aspiration of joint bleeds in VWD is contraindicated unless discussion takes place between the hematologist and the ER or orthopedic physician.
Desmopressin

Desmopressin is a synthetic form of antidiuretic hormone which causes the release of factor VIII and von Willebrand factor from the endothelial cell storage sites. It can increase the VWF level by as much as three to five fold.

Desmopressin is the preferred treatment for type 1 VWD and certain patients with type 2. The response to desmopressin can vary greatly with each individual. Therefore, prior to use, a desmopressin trial should be done with results reviewed and recorded by a hematologist. If the patient does respond to desmopressin, the full effect is reached 30 to 90 minutes after administration and hemostasis is maintained for approximately 24 hours. If the patient does not respond to desmopressin, hemostasis can be maintained with infusions of factor concentrates, see inside front cover.

Expected side effects: short term facial flushing, increased heart rate, change in blood pressure, red conjunctiva, and headache.

**Dose**

SC/IV: 0.3 mcg/kg/dose. Recommendation: a maximum dose of 20 mcg.

IV ROUTE: Dilute with normal saline (50-100 ml). Infuse over 30-60 minutes. (No less than 30 minutes.) It is recommended to administer the medication with the individual in a supine position.

SC ROUTE: The subcutaneous route is advantageous to minimize drug side effects.

**Supplied**

Ampules: 4 mcg/ml DDAVP®, 15 mcg/ml OCTOSTIM®

**Nasal Spray**

OCTOSTIM® or STIMATE® nasal spray must be brand specific to ensure patient receives the correct dose of DDAVP® that will stop the bleeding. There is no generic for this medication.

150 mcg / 0.1 ml per single spray (OCTOSTIM®, STIMATE®)

Recommended dose for patients over 50 kg: 300 mcg (1 spray per nostril, total of two sprays)

Recommended dose for patients under 50 kg: 150 mcg (1 spray in one nostril, total of one spray)

Unreliable absorption if the intranasal route is compromised. Hematologist should be consulted for treatment guidelines.

**Indications**

Treatment of von Willebrand Disease Type 1 and certain forms of Type 2

**Contraindications**

Hypersensitivity, infants under 3 months, patients suffering from dehydration, history of seizure, coronary artery insufficiency.
Use With Caution

- Elderly
- Patients with von Willebrand Disease Type 2B
- Young children especially under 2 years of age
- Hypertensive cardiovascular disease
- Individuals with low-normal blood pressure

Desmopressin has an antidiuretic effect. Patients should be advised to avoid alcohol and restrict their fluid intake to thirst only for 24 hours after receiving the drug. Infants and children will require careful fluid intake restriction to prevent possible hyponatremia and water intoxication. Accurate intake and output should be recorded on any patients receiving IV fluids.

Adverse Effects

- Cardiovascular: facial flushing, sweating, dizziness, transient hypertension, hypotension, and tachycardia, hyponatremia.
- Gastrointestinal: nausea, vomiting.
- Neurologic: headache, tremor, seizures.
- Local: pain and erythema at injection site or in nasal mucosa if intranasal spray is used.
- Thrombocytopenia: in Type 2B von Willebrand Disease

Topical Preparations

<table>
<thead>
<tr>
<th>Amicar 10% topical solution</th>
<th>Mix 2 ml Amicar (IV preparation 250 mg/ml), and 3 ml sterile water for injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Soak gauze in solution, squeeze out excess and apply to area.</td>
</tr>
<tr>
<td></td>
<td>Discard solution after 24 hours</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tranexamic Acid 5% topical solution</th>
<th>Mix 5 ml Tranexamic acid, use the IV preparation 100mg/ml (5 ml ampule size) and 5 ml sterile water for injection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Soak gauze in solution, squeeze out excess and apply to area.</td>
</tr>
<tr>
<td></td>
<td>Discard solution after 24 hours</td>
</tr>
</tbody>
</table>

Request from Pharmacy

Tranexamic Acid 5% Nasal Gel: To make a 5% Tranexamic Acid Nasal gel, take ten (10) Tranexamic acid 500 mg tablets and crush with a very small amount of 70% alcohol. Measure out 100 grams of Intrasite gel (methylcellulose). Gradually add the Intrasite gel to the crushed tablets/paste. Once mixed put in an ointment jar. Stable for 10 days refrigerated (probably much longer). Apply with Q-tip® or finger once or twice a day.

Topical agents such as topical Thrombin® and Gelfoam® and fibrin glue (Tisseal-R) may also be used to help control mucous membrane bleeding.

Antibiotics and pain medications may also be indicated in the treatment of mucosal bleeds.
Factor Administration

Reconstitute per package insert.

Products containing von Willebrand factor are plasma derived products.

Example for dose calculation

<table>
<thead>
<tr>
<th>Patient’s weight = 50 kilograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Order: 60 ristocetin co-factor units/kg IV</td>
</tr>
<tr>
<td>60 ristocetin co-factor units X 50 kg =</td>
</tr>
<tr>
<td>3,000 ristocetin co-factor units</td>
</tr>
</tbody>
</table>

Mixing instructions and the rate of administration are found on the drug insert.

It is best to follow treatment recommendations that the patient may carry or to consult with the patient’s treatment center.

Dosage

Each bottle of plasma-derived factor concentrate is labeled with the activity expressed in both von Willebrand ristocetin co-factor international units (vWF:RCo I.U.) and factor VIII international units (F VIII I.U.). Vonvendi ® will not have factor VIII units indicated since it does not contain factor VIII.

The dosage to be administered is based on the patient’s body weight in kilograms (kg) and is normally ordered in ristocetin co-factor units (VWF:RCo I.U.). The von Willebrand factor/FVIII concentrate is a plasma-derived factor that has been virally inactivated.

The ENTIRE contents of all the vials reconstituted for an infusion should be used, even if it exceeds the calculated dosage. A larger dose will only prolong the period of normal coagulation. Due to its cost, factor concentrate should never be discarded!

Document the lot number(s), expiration date(s), factor concentrate trade name and total number of units infused. This information can be found on the factor concentrate’s box.

Some patients are instructed to bring unmixed factor concentrate with them to the ED to minimize treatment delay and cost. Many institutions donotcarrythesefactorproductssandincludethisfactoritcouldtakehourstooobtainthem. If you donothavetheseproductsavailablepleaseconsider usingwhat the patient has brought in. Occasionally, patients will bring prepared factor concentrate after unsuccessful home venipuncture attempts. Please assist with venipuncture and allow the patient or family to infuse the prepared factor concentrate, if possible, per your institution's policy.
Other Medications

Routine medications

Patients with VWD can receive routine medications (e.g. pain medications, antibiotics, etc.) that do not interfere with clotting function. Avoid non-steroidal anti-inflammatories (NSAIDS), ASA and any product with aspirin-related ingredients (e.g. Pepto-Bismol®, Excedrin®, Percodan®).

Medications for fever or pain

Acetaminophen can be given for fever or pain. Opioids can be given to control pain experienced by the patient with a bleeding disorder. Avoid giving intramuscular injections of pain medications because of the possibility of causing a muscle bleed.

Routes of administration

Medications which can be given PO, SC, or IV are preferred. If the rabies vaccination series is needed, an experienced hematologist (preferably the patient’s) should be contacted for advice prior to and after the injections in order to prevent internal bleeding.

For any needle stick, pressure for a minimum of 5 minutes afterward will minimize soft tissue or muscle bleeding. Avoid giving intramuscular injections of antibiotics, pain medications, or immunizations because of the possibility of causing a muscle bleed. You can also apply an ice pack for 15 - 20 minutes.

Caution

Some patients with VWD may have liver disease from hepatitis or may have been exposed to HIV. Use caution when prescribing drugs that may cause liver toxicity or could cause potential serious drug interactions.
**Invasive Procedures, Labs, X-rays**

Treatment should never be delayed for laboratory studies to be drawn or completed. Laboratory tests that test for VW are often done at reference laboratories and are not available at most institutions.

### Head injury

First give the recommended treatment*. . .

. . . then perform a CT scan.

### Fracture

First give the recommended treatment*. . .

. . . then obtain x-rays immobilize appropriately.

### Discharge Instructions

Patient should follow-up with the treatment center or hematologist the next day.

Head injury: Discharge with routine post head injury instructions (patient should be assessed for two weeks instead of 48 hours).
In general, patients with VWD who are experiencing an acute bleeding episode may need treatment as well as basic first aid measures. Do not delay treatment to perform testing.

**Laboratory studies**

If the only complaint is an acute joint or muscle bleed, no laboratory studies are necessary. If GI, uterine, or oral cavity bleeding is suspected and has potentially been extensive, a complete blood count may be indicated to determine if the individual is anemic. Treatment should never be delayed for laboratory studies to be drawn or completed.

**X-rays and other radiological studies**

Remember that a swollen joint or extremity can be the result of internal bleeding. X-rays of the joint can be used to document a joint bleed, but only in the very late stages and are generally not useful in detecting early onset bleeds when treatment is optimal. An MRI could be helpful in determining the degree of blood in the joint after treatment has been administered. A CT of the head (see pg. 4) is necessary when dealing with a potential intracranial hemorrhage. Give the maximum recommended treatment before sending the patient to CT scan.

**Fractures**

Give the recommended treatment, then X-ray and set the bone.

**Lacerations and sutures**

Sutures and staples can be used. If the laceration is significant enough to require sutures, the patient should first receive the recommended treatment and then proceed with the procedure. Contact the patient’s hematologist for follow-up treatment instructions. Treatment may not be needed for suture removal and will be determined by the patients hematologist.

**Invasive procedures**

Invasive procedures should be performed as clinically indicated, i.e. lumbar puncture with symptoms of meningitis. However, factor replacement treatment should be given prior to the procedure.

**Arterial sticks and venipunctures**

Do not perform arterial sticks unless no other option is available. If an arterial stick must be done, then the recommended treatment and precautions should be taken before the procedure begins.

Venipuncture may be done at any location; hands are generally excellent and no pre-treatment is necessary. Avoid “digging” for deep veins. Apply pressure for several minutes or until there is no further oozing noted at the venipuncture and IV removal sites.
Many different emergencies / trauma may occur to persons with von Willebrand Disease, just as to others.

- Animal bites
- Burns
- Falls
- Fractures (see pg. 20)

- Motor vehicle accidents
- Gunshot wounds
- Ocular injuries
- Puncture wounds

**Treatment**

For any serious injury, a major dose of a factor VIII product containing von Willebrand factor (e.g., Humate-P®, Alphanate®, wilate® Vonvendi®*) should be infused prior to blood work, CT scan, X-rays or other scans, debriding, sutures, etc. See page ii.

For less serious injuries, other treatment options may suffice and can be considered: local treatment (pg. 8), desmopressin (pg. 16-17), anti-fibrinolytics (pg. 9).
Selected Bibliography


Kasper, Carol K. (2004). Von Willebrand Disease.[Monograph]. Los Angeles, USA::Orthopedic Hospital, [Published by Aventis Behring Foundation for research and advancement of patient care].


**Acknowledgements**

*Authors and editors 2006:*

Susan C. Zappa, RN, CPN, CPON  
Bleeding Disorders Nurse Coordinator  
Cook Children’s Medical Center  
Fort Worth, Texas USA

Lucie Lacasse, RN, BScN  
Hemophilia Nurse Specialist  
The Ottawa Hospital  
Ottawa, Ontario, Canada

Rose Jacobson, RN, Nurse Clinician  
MB Bleeding Disorders Program  
Health Sciences Centre  
Winnipeg, Manitoba, Canada

Sherry L. Purcell, RN  
Nurse Coordinator  
Bleeding Disorders Clinic  
Kingston General Hospital  
Kingston, Ontario, Canada

Karen Wulff, RN  
Nurse Coordinator  
The Louisiana Center for  
Bleeding and Clotting Disorders  
Tulane University School of Medicine  
New Orleans, Louisiana USA

**Reviewers 2006:**

David Lillicrap, MD, FRCPC  
Director, Kingston/Belleville  
Regional Hemophilia Program  
Professor, Department of  
Pathology and Molecular Medicine  
Canada Research Chair in Molecular Hemostasis  
Kingston, Ontario, Canada

Marcela Torres, MD  
Pediatric Hematology and Oncology  
Director of Hematology  
Cook Children’s Medical Center  
Fort Worth, Texas USA

Clare Cecchini  
Program Development Coordinator  
Canadian Hemophilia Society  
Montreal, Quebec, Canada

Jim Munn, RN, MS  
Program Coordinator  
University of Michigan  
Hemophilia and Coagulation Disorders Program  
Ann Arbor, Michigan USA

Annette Smith  
VWD Type 1  
New Mexico, USA

Canadian consumer  
VWD Type 3  
Toronto, Ontario, Canada
Acknowledgements

Reviewers 2018

Susan C. Zappa, RN-BC, CPN- Editor
susan.zappa@sbcglobal.net
Cook Children’s Medical Center- retired

Susan Geraghty, RN, MBA
University of Colorado Hemophilia and Thrombosis
Center-retired

Chris Guelcher, Hemostasis RN-BC, MS, PPCNP-BC
Lead Advanced Practice Provider
Center for Cancer and Blood Disorders
Children’s National Health System

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