The Diagnosis & Management of von Willebrand Disease

Wednesday, April 6
7:00-8:45 a.m.
Hilton Orlando—Orange Ballroom FG

Supported by an unrestricted educational grant from Octapharma USA
The Diagnosis & Management of von Willebrand Disease

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04-S. The Diagnosis & Management of Von Willebrand Disease
Hilton Orlando – Orange Ballroom FG
Pharmacist, Pharmacy Technician and Nurse Continuing Education Contact Hours: 1.5
ACPE Pharmacist and Pharmacy Technician Program #: 207-999-11-220-L01-P&T
Knowledge-Based Learning Activity

Education Overview:
As the most common inherited bleeding disorder in humans, von Willebrand Disease (VWD) affects one to two percent of the general population or approximately three million people in the United States. The severity of VWD is highly variable, from severe cases in which the tendency for excessive bleeding is obvious and treatment essential, to mild cases which often go undiagnosed until a traumatic event or surgery occurs. Home infusion nurses and pharmacists are uniquely positioned to assist patients and families in managing this bleeding disorder in the home. Expertise in treatment options is essential to achieving optimal patient outcomes of therapy. This program will provide a comprehensive overview of the genetic inheritance and pathophysiology of VWD, the signs and symptoms of the disorder, diagnostic testing, current treatment options and considerations for their delivery in the home setting. Strategies will be reviewed for maximizing patient quality of life through pharmacologic intervention.

Faculty: Hetty A. Lima, RPh, FASHP, Vice President, Specialty Infusion Services, Diplomat Specialty Pharmacy, Highlands Ranch, CO

Hetty Lima is the Vice President of Specialty Infusion Services for Diplomat Specialty Pharmacy, the nation’s largest privately held specialty pharmacy. An accomplished health care executive with over 27 years of home infusion/specialty pharmacy experience, Lima has held executive-level health care positions at specialty pharmacy provider corporations such as Baxter Healthcare, CVS/Caremark’s Specialty Pharmacy division, and Coram’s Hemophilia Services division. A graduate of the University of Rhode Island, Lima is also the past President of the American Society of Health-System Pharmacists (ASHP) Section of Home Care Practitioners. She has lectured at national pharmacy and nursing meetings and has published extensively on the clinical and practical aspects of home infusion and specialty pharmacy. Her work has appeared in numerous pharmacy and nursing journals and pharmaceutical texts. No strangers to von Willebrand disease, Lima and her family all have VWD. She and her son Benjamin have Type 1 moderately severe VWD, her husband Peter has mild Type 1, and her youngest son, Nik has severe Type 3 VWD.

Pharmacist and Nurse Education Objectives:
1. Compare the pathophysiology of von Willebrand Disease (VWD) to the normal clotting cascade.
2. Describe the types of Von Willebrand disease and their prevalence.
3. List treatment options and goals of each therapy when used for VWD.

Pharmacy Technician Education Objectives:
1. Review the changes in the clotting cascade for patients with von Willebrand Disease (VWD).
2. Describe the types of Von Willebrand disease and their prevalence.
3. List treatment options and goals of each therapy when used for VWD.
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Learning Assessment Questions:

1. Within the U.S., approximately how many people have von Willebrand disease?
   a. 3,000
   b. 3 million
   c. 30 million
   d. 1,000

2. Individuals with Type 2 VWD have:
   a. A qualitative defect of VWF
   b. A quantitative deficiency of VWF
   c. Both A & D
   d. VWF that is structurally dysfunctional

3. Which statement regarding hemorrhagic tendency in VWD is true?
   a. It can be mild (e.g., nosebleeds, easy bruising)
   b. It can be severe and life-threatening, similar to that seen in individuals with hemophilia
   c. It can vary depending on the Type and severity of VWD
   d. All of the above

4. Which statement is true regarding the diagnosis of von Willebrand disease (VWD)?
   a. Diagnostic testing must often be repeated in order for an accurate diagnosis to be made
   b. Diagnosis may be inaccurate and influenced by many factors
   c. Diagnosis is confirmed by a series of complex tests that must be performed by specialized laboratories
   d. All of the above

5. The treatment of choice for patients with mild to moderate forms of Type 1 VWD is:
   a. Vasopressin
   b. Cryoprecipitate
   c. DDAVP (high concentration)
   d. Intravenous clotting factors containing Willebrand factor complex

6. All of the FDA-approved intravenous clotting factors used in the treatment of VWD may be used interchangeably when patients with VWD undergo surgery.
   a. True
   b. False

7. Antifibrinolytics can be used for women with von Willebrand disease who have severe menorrhagia.
   a. True
   b. False

8. Individuals with bleeding disorders such as hemophilia and von Willebrand disease are advised to seek treatment from a federally funded hemophilia treatment center (HTC)
   a. True
   b. False

9. All of the commercially available intravenous FVIII / VWF clotting factors contain the exactly same amount of von Willebrand clotting factor (VWF)
   a. True
   b. False

Answers can be found on the last page of this booklet.
Top 5 Things to Know for CE:

- Make sure your BADGE IS SCANNED each time you enter a session, to record your attendance.
- Carry the Evaluation Packet you received on registration with you to EVERY session. If you’re not applying for CE, we still want to hear from you! Your opinions about our conference are very valuable.
- Pharmacists, Pharmacy Technicians and Nurses need to track their hours on the Statement of Continuing Education Certificate form as they go.
- FOR CE: At your last session, total the hours and sign both pages of your Statement of Continuing Education Certificate form. Keep the PINK copies for your records.
- Place the YELLOW and WHITE copies in your Evaluation packet.
- Make sure an evaluation form from each session you attended is completed and in your Evaluation packet (forgot to pick up an evaluation form at a session? Extras are available in an accordion file near the registration desk).
- Put your name and unique member ID number (six digit number on the bottom of your badge) on the outside of the packet, seal it, and drop it in the drop boxes in the NHIA registration area at the convention center.

Disclosures

- Hetty Lima is a consultant member of the US Nurse Advisory Board for Octapharma, this continuing education activity’s commercial sponsor.
- Hetty Lima does not discuss off-label drug usage in this article.
- Hetty Lima briefly discusses the investigational use of recombinant VWF products in the drug pipeline but does not mention brand or generic names, or the company performing the investigation.
- The conflict of interest was resolved by peer review of slide content.
Von Willebrand Disease

- The most common congenital bleeding disorder has a prevalence of 1-2% of the general population

- Caused by a defect in the concentration, function, and or structure of the von Willebrand factor (VWF) and presents with varying clinical manifestations
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Von Willebrand Disease

• First reported in 1926 by Dr. Eirik von Willebrand in Finland, Aland Islands
• VWD affects men and women equally & affects people of all backgrounds
• Caused by a lack of or defect in the von Willebrand factor (VWF)

Genogram of the Original Family

Von Willebrand, EA. Finska Lakaresällskapets Handl. 1926;67:7-112.
Von Willebrand Factor (VWF)

- Large, multimeric blood protein that initiates the first step in the coagulation process
- Variable clinical manifestations
- Stored in the endothelial cells and platelets
- Promotes adhesion of platelets to the sites of vascular injury via interaction with platelet glycoprotein Ib (GPIb)
- Carrier protein for factor VIII (FVIII)

The Blood Clotting Process

<table>
<thead>
<tr>
<th>Normal Bleeding Starts</th>
<th>Hemophilia Bleeding Starts</th>
<th>VWD Bleeding Starts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Blood vessels contract</td>
<td>Blood vessels contract</td>
</tr>
<tr>
<td></td>
<td>Platelet plug forms</td>
<td>incomplete platelet plug; bleeding continues</td>
</tr>
<tr>
<td>Step 2</td>
<td>Blood vessels contract</td>
<td>Blood vessels contract</td>
</tr>
<tr>
<td></td>
<td>Platelet plug forms</td>
<td>incomplete platelet plug; bleeding continues</td>
</tr>
<tr>
<td>Step 3</td>
<td>Fibre clot forms; bleeding stops</td>
<td>incomplete or delayed fibrin clot; bleeding continues</td>
</tr>
</tbody>
</table>
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Clinical Manifestations of VWD

- Characterized by variable mucosal bleeding particularly in the mouth, nose, throat, GI tract, and skin surfaces.
- Five hallmark signs of bleeding associated with VWD:
  1. Easy bruising with indurations
  2. Menorrhagia
  3. Frequent or prolonged nosebleeds (epistaxis)
  4. Prolonged bleeding following injury, childbirth, and surgery
  5. Prolonged bleeding/mucous membrane bleeding during dental work

VWF Multimers

- Inherited coagulation disorder
- Abnormality/deficiency of blood protein
- Easy bruising and excessive mucosal bleeding

Large multimers

Small multimers

Types of VWF multimer patterns
VWD: Inheritance & Prevalence

Diagnosing VWD
• Based on symptoms and family history
  – Easy bruising
  – Stop / Start bleeding from cuts
  – Epistaxis (nosebleeds)
  – Menorrhagia (increased menstrual bleeding)
  – Abnormal bleeding
• Severe
  – More frequent bleeding
  – Symptoms may be life threatening

Diagnosing VWD: Initial Evaluation
• Initial screening for a bleeding disorder starts with obtaining a detailed personal and family history
• Guidelines published by the U.S. Department of Health and Human Services, National Heart, Lung, and Blood Institute (NHBLI), and National Institutes of Health offer a detailed algorithm and questionnaire
VWD: Initial Diagnostic Evaluation

- Detailed personal and family history is key
- Screening laboratory values are often normal
  - Platelet count
  - Prothrombin time (PT)*
  - Activated partial thromboplastin time (aPTT)*
- Bleeding time (BT) is an insensitive screening tool for type 1 disease
- Platelet function analyzer (PFA)
* Screens for coagulation factors that lead to the fibrin clot

The Hematologic Focused History

- Easy bruising, petechiae
- Nose/gum/mouth bleeding
- Menorrhagia/bleeding post childbirth
- Surgical (including dental) bleeding
- Increased bleeding with lacerations
- Hemarthrosis (joint hemorrhage)/muscle bleeding
- Gastrointestinal/gastric ulcer bleeding
- Severe, life-threatening bleeds

VWD: Primary Laboratory Screening Tests

- Complete blood count (CBC): especially, hemoglobin
- Platelet count
- Bleeding time (BT)
- Prothrombin time (PT): evaluates plasma clotting factors I, II, V, VII and X
  - VWD does not involve any of these clotting factors
- Partial thromboplastin time (aPTT): evaluates clotting factors I, II, VIII, IX, X, XI and XII. Only VIII is involved
Standard Laboratory Tests for VWD

<table>
<thead>
<tr>
<th>TEST</th>
<th>PURPOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII Clotting Activity (FVIII:C)</td>
<td>Measures the functional activity of Factor VIII. Normal ranges are 50-150 IU/dl</td>
</tr>
<tr>
<td>VWF Antigen (VWF:Ag)</td>
<td>An immunooassay protein quantification that measures the total amount VWF. Normal ranges are 50 to 200 µg/dl</td>
</tr>
<tr>
<td>von Willebrand Ristocetin CoFactor and/or (VWF:RCO and/ or VWF:CB)</td>
<td>Measures the aggregation of normal platelets in the presence of ristocetin, thus, measuring the functional activity of VWF; Normal ranges are 50 to 200 µg/dl</td>
</tr>
<tr>
<td>von Willebrand Factor [VWF] Multimer Analysis</td>
<td>Measures the quantity and molecular structure of the VWF molecule and Analysis of the VWF multimers is necessary to ensure an accurate classification of the disease</td>
</tr>
<tr>
<td>Ristocetin-Induced Platelet Aggregation (RIPA)</td>
<td>Measures the sensitivity of VWF relative to Ristocetin. Useful in distinguishing Type 3A from 2A VWD</td>
</tr>
</tbody>
</table>

VWD Classification

- **Type 1** - most common and mildest form
  - Affects approximately 70-80% of cases
  - Due to a quantitative defect of VWF
  - VWF is normal but levels are reduced to 20-50% of normal values, causing a wide range of severities can be seen
  - Generally inherited as an autosomal dominant trait with incomplete penetrance

- **Type 2 VWD** - involves a qualitative defect in the VWF and affects 15-20% of patients with VWD.
  - Patients produce normal levels of VWF; however, the VWF is structurally and functionally dysfunctional.
  - There are four distinctive subgroups of type 2 VWD
### Type 2 VWD Classification

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2A</td>
<td>accounts for ~75% of cases of Type 2 VWD. VWF-dependent platelet adhesion is decreased because patients do not have a sufficient quantity of high molecular weight multimers.</td>
</tr>
<tr>
<td>Type 2B</td>
<td>Patients lack medium to high VWF multimers. The increase in platelet aggregation leads to mild to moderate thrombocytopenia</td>
</tr>
<tr>
<td>Type 2M</td>
<td>Autosomal dominant pattern but is not very common. Similar to Type 2B, but with decreased platelet-function and absence of high-molecular weight multimers, results in a reduced binding of VWF multimers with platelets</td>
</tr>
<tr>
<td>Type 2N</td>
<td>Inherited as an autosomal recessive gene that causes mutations that inactivate the binding site of VWF to Factor VIII. Similar to mild hemophilia A with a reduced half-life of factor VIII by approximately 5-20% of normal</td>
</tr>
</tbody>
</table>

### Type 3 VWD

- Rarest and most severe form of VWD
- Inherited as a recessive trait with the individual receiving one defective gene from the mother and the father.
- Incidence: 1-3: 1,000,000
- Caused by a reduced or complete absence of VWF
- Higher prevalence in geographic areas where consanguineous marriages are frequent
Individuals can develop VWD later in life due to the formation of antibodies that attack and destroy the VWF. Acquired VWD is caused by antibodies that attack and destroy VWF. Usually seen in individuals with autoimmune disorders:
- Lupus
- Kidney failure
- Rheumatoid arthritis
- Certain cancers
- Drug-induced VWD
  - Valproic acid
  - Ciprofloxacin

### VWD Laboratory Values

<table>
<thead>
<tr>
<th>VWD Type</th>
<th>VWF:Ag</th>
<th>VWF:RCo</th>
<th>FVIII:C</th>
<th>Diagnostic Key</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>Family, personal history</td>
</tr>
<tr>
<td>2A</td>
<td></td>
<td>♦</td>
<td>♦</td>
<td>Absence of high molecular weight multimers</td>
</tr>
<tr>
<td>2B</td>
<td>♦</td>
<td></td>
<td>♦</td>
<td>LD RIPA/thrombocytopenia</td>
</tr>
<tr>
<td>2M</td>
<td>♦ or ♦</td>
<td>♦</td>
<td>♦</td>
<td>Normal multimers absent LD RIPA</td>
</tr>
<tr>
<td>2N</td>
<td>♦ or ♦</td>
<td>♦</td>
<td>♦</td>
<td>PUPH like mild hemophilia</td>
</tr>
<tr>
<td>3</td>
<td>♦ or ♦ or Absent</td>
<td>♦ or ♦ or Absent</td>
<td>1 – 3%</td>
<td>Very severe or absent deficiencies</td>
</tr>
</tbody>
</table>
Lab Test Variability

- VWD is highly variable, repeated laboratory testing is often needed to confirm diagnosis.
- Additionally, there is a high degree of lab test variability that may cause false negatives.
- Levels of VWF fluctuate

VWF Levels Fluctuate With:

- Stress and anxiety
- Exercise
- Pregnancy
- Estrogen therapy
- Cold temperatures
- Systemic inflammation
- Infection
- ABO blood
- Certain foods

Food & Drugs Affecting Platelets

- These can also mask the diagnosis of VWD and may include (but are not limited to):
  - Aspirin
  - NSAIDs
  - Guaifenesin
  - Quinine
  - Penicillin
  - Fish high in omega-3 fatty acids
  - Vitamin E
  - Herbs such as ginkgo biloba, ginseng, and echinacea.
VWD Case Study # 1

- Female diagnosed at age 40 with type 1 moderate to severe VWD
- Lifelong history of menorrhagia, anemia and easy bruising
- Positive maternal familial history for the above (mother, maternal grandmother)
- Three miscarriages
- Postpartum hemorrhage

Case Study # 2 - NL

- Diagnosed with severe type 3 VWD at age 8
- Normal circumcision
- Lifelong history of easy bruising and excessive bleeding, particularly, tongue and mouth bleeds
- Took Nik to pediatricians in three different states "nothing abnormal in his labs"

Case Study # Patient 2 - NL

<table>
<thead>
<tr>
<th></th>
<th>Patient Value</th>
<th>Lab Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>aPTT</td>
<td>45 sec's</td>
<td>26-38 seconds</td>
</tr>
<tr>
<td>F VIII</td>
<td>30</td>
<td>50-200 µ</td>
</tr>
<tr>
<td>VWF:AG</td>
<td>8</td>
<td>35-157 µ</td>
</tr>
<tr>
<td>VWF RCoF</td>
<td>&lt;10</td>
<td>45-200 µ</td>
</tr>
<tr>
<td>VWF Multimers</td>
<td>None</td>
<td>Level too low to interpret</td>
</tr>
<tr>
<td>Bleeding Time</td>
<td>30+ mins.</td>
<td>3.5 - 6.5 mins</td>
</tr>
</tbody>
</table>
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Case Study Family Genogram

RCF 36
VWF 34
M = Normal
FVIII 91
type A

RCF 41
VWF 26
M = normal
FVIII 50
BT = 13 mins

RCF <3
VWF <3
M = Absent
FVIII 16
BT = 3D+ mins

RCF 22
VWF 18
M = Normal
FVIII 38
BT = 3 mins

RCF 22
VWF 18
M = Normal
FVIII 38
BT = 3 mins
type A
type 1 Moderate-Severe

HAL 2

BKL 2

PBL 1

RCF 36
VWF 34
M = Normal
FVIII 91
type A

RCF 41
VWF 26
M = normal
FVIII 50
BT = 13 mins

RCF <3
VWF <3
M = Absent
FVIII 16
BT = 3D+ mins

RCF 22
VWF 18
M = Normal
FVIII 38
BT = 3 mins
type A
type 1 Moderate-Severe

HAL 2

BKL 2

PBL 1

FVIII 91
type A

FVIII 50

FVIII 38

FVIII 38

FVIII 16

Normal

Mild

Moderate

Moderate-Severe

Mild

Type 1

Type 1

Type 1

Type O

Type 3 - Severe
Diagnosis Confirmed

- Their youngest son NL (Case Study 2) was prescribed intravenous clotting factor containing VWF.
- The family was taught to perform peripheral 'self-infusion' of clotting factor at home.
- Medications were delivered to their home by a national specialty pharmacy.
- Oral aminocaproic acid syrup was also prescribed for the boys and maintained at home to treat mouth bleeds or prior to any dental procedures.

VWD Treatment Goals

1. Increase the plasma concentration of VWF by stimulating the release of endogenous VWF from storage sites within blood vessel endothelium through the use of desmopressin.
2. Replace VWF by intravenous infusions of plasma-derived, virally inactivated VWF concentrates.

VWD Treatment Goals – cont’ed

3. Promote hemostasis and wound healing without significantly altering the plasma concentration of VWF via the use of adjunctive agents.
Treatment Options: Mild VWD

Specific Therapies Include:
1. Desmopressin acetate (DDAVP) – synthetic derivative of vasopressin
   • Parenteral – intravenous (IV) or subcutaneous (SQ)
   • Intranasal (high concentration)
2. Antifibrinolytics
3. Adjunctive therapies
4. Plasma-derived FVIII products containing high concentrations of VWF

Desmopressin Acetate (DDAVP)

• Synthetic derivative of the antidiuretic hormone vasopressin
• DDAVP causes the release of VWF and factor VIII from storage sites within the endothelium of the blood vessels.
• Indicated for Type 1 VWD and mild hemophilia A; some Type 2A, but is not indicated for Types 2 and Type 3 VWD
• A test dose of DDAVP is usually given in a controlled medical setting (during a non-bleeding state) in order to determine patient response

Desmopressin Acetate: Indications

• Generally used as treatment for spontaneous or trauma-induced injuries in patients with mild to moderate VWD, mild hemophilia A; not indicated in type 2A and 3
• Frequently used to treat:
  – Mucosal bleeding
  – Menorrhagia
  – Minor surgical procedures after documenting patient response
### Desmopressin Acetate (DDAVP)

- Requires initial test dose administered under controlled medical conditions
- Dosage forms:
  - IV: 0.3 mcg/kg in 25 – 50 ml NS over 30 minutes
  - Intranasal spray (use Stimate®, highly concentrated not DDAVP)
    - Ped’s: < 50 kg – 150 mcg (1 puff)
    - Adults: > 50 kg – 300 mcg (1 puff each nostril)
- Duration: every 12-24 hours for 2-3 days

### Desmopressin Acetate (DDAVP)

- CAUTION - - - Highly concentrated (1.5 mg/ml) intranasal spray (Stimate®).
- Do not dispense generic DDAVP spray; much weaker concentration (0.1 mg/ml), and is indicated for diabetes insipidus

### VWF/FVIII Factor Concentrates

- Indicated for individuals with:
  - Type 2A, 2B, and 3 or
  - Those patients where desmopressin is not effective or is contraindicated including individuals with Type 1 VWD prior to surgery or injury.
- Factor concentrates work by raising the patient’s plasma levels of VWF and factor VIII
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Dosing Factor Concentrates

- Unlike factor products for hemophilia which are dosed by international units (IU) vials of factor concentrate are labeled with the activity expressed in both:
  - von Willebrand ristocetin co-factor international units (vWF:RCo I.U.)
  - Factor VIII international units (F VIII IU)
- Not a direct 1:1 concentration

VWF-FVIII Containing Concentrates

- Use in VWD patients that do not respond to DDAVP or when desmopressin acetate is contraindicated
- Contain VWF - FVIII:C
  - Increases plasma VWF levels
  - Indicated for types 2A, 2B and 3
- Slow intravenous (IV) push or infusion
- Alphanate®: Maximal infusion rate 4 mL/ min
- Alphanate®: Infusion rate not to exceed 10 mL/minute
- wilate®: 2 – 4 mL/min

VWF-FVIII:C Key Product Characteristics

- All currently available VWF - FVIII:C products are plasma-derived and pathogen-inactivated (heat or solvent detergent treated)
- Cryoprecipitate is not recommended, as it is not pathogen-inactivated
- Humate-P®:
  - 2 - 4 RCoF IU per 1 FVIII IU
  - Lower diluent volume
- Alphanate®: 0.5-1° RCo IU per 1 FVIII IU
- wilate®: 1 RCo IU per 1 FVIII IU
- Use for surgical indications varies by product review package insert
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Dosing Factor Concentrates

- Dose will vary by patient’s weight and type of hemorrhagic incident.
- Goal is to achieve a level of 100 IU/dL of VWF:RCo and for ~first 3 days of treatment a nadir of 50 IU/dL of VWF:RCo

\[ \text{RCoF Dose (IU)} = \frac{\text{Body Weight (kg)} \times \% \text{ Target increase in VWF plasma level}}{1.5 \text{ Recovery Rate}} \]

Dosing VWF/FVIII Concentrates

\[ \text{IU RCoF Dose} = \frac{\text{Body Weight (kg)} \times \% \text{ Target Increase}}{1.5 \text{ Recovery Rate}} \]

(expected in vivo recovery rate)

**Patient A – Type 1 VWD**
- Pt’s baseline level of VWF = 15
- Weight in kg = 50 kg
- Target level of VWF = 60

\[ 50 \text{ kg} \times 45 \text{ (\% increase)} = 1,500 \text{ IU RCoF} \]

\[ 1.5 \text{ Recovery Rate} \]

**Patient B – Type 3 VWD**
- Pt’s baseline level of VWF = 0
- Weight in kg = 50 kg
- Target level of VWF = 80

\[ 50 \text{ kg} \times 80 \text{ (\% increase)} = 2,667 \text{ IU RCoF} \]

\[ 1.5 \text{ Recovery Rate} \]
### Dosing FVIII:VWF in VWD Patients

<table>
<thead>
<tr>
<th>Type of Bleeding</th>
<th>Dose (IU/kg)</th>
<th># of Infusions</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Surgery</td>
<td>40-60 QD</td>
<td>&gt;50 IU/dL</td>
<td>Maintain VIII:C until healing is complete*</td>
</tr>
<tr>
<td>Minor Surgery</td>
<td>30-50 QD or QOD</td>
<td>VIII:C&gt;30 IU/dL</td>
<td>until healing is complete*</td>
</tr>
<tr>
<td>Dental Extractions</td>
<td>20-30 Single</td>
<td>VIII:C&gt;30 IU/dL for at least 12 hours</td>
<td></td>
</tr>
<tr>
<td>Spontaneous Bleeding Episodes</td>
<td>20-30 Single</td>
<td>VIII:C&gt;30 IU/dL</td>
<td></td>
</tr>
</tbody>
</table>

*Depending on type of surgery

### Antifibrinolytics

- **Aminocaproic Acid (Amicar®):** Available as 500 mg tablets and a 250mg/ml liquid
- **IV:** 50 to 100 mg/kg
- **Orally:** Every 6 to 12 hours followed by maintenance doses of 100 mg/kg every 6 hours for 3 – 7 days, maximum of 6 gm/dose

### Tranexamic Acid (Cyklokapron®)

- Intravenous dosage form is available in a concentration of 100mg/ml.
- Prior to teeth extractions, the dosage is 10 mg per kg of body weight three to four times daily for 2 to 8 days.
- Dosages and frequency of administration must be adjusted in patients with moderate to severe impaired renal function
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Tranexamic acid (Lysteda™)

- Approved November 2009
- Indicated for the treatment of cyclic heavy menstrual bleeding or menorrhagia.
- Menorrhagia is oftentimes a chief complaint in women with von Willebrand disease
- Sustained release tablet that allows for less frequent dosing than the standard dose formulation

Adjunctive Therapies

- Oral contraceptive agents (OCAs) - control menorrhagia
  - OCAs help regulate and reduce the duration of menstrual bleeding
- Progesterone IUD
- Topical hemostatic agents applied to exposed bleeding sites are an adjunctive treatment for VWD
- Nosebleeds: Nosebleed QR™, UrgentQR™
  - Ay™ nasal gel
  - Topical phenylphrine (NeoSynephrine®)
  - Gel pink

VWD Treatment Summary

- Mucosal bleeds: antifibrinolytics + desmopressin acetate or IV VWF concentrate
- Menorrhagia: desmopressin acetate, antifibrinolytics, birth-control pill, VWF concentrates
- Prophylaxis: consider with VWF concentrates
  - Severe epistaxis, mouth bleeds
  - Severe menorrhagia
  - Target joint bleeding
- Surgery: follow VWF:RCo and FVIII levels for 7–10 days
  - VWF important for the first few days
Specialty Pharmacy/HIT Providers

- Homecare services included provision of factor and related ancillary supplies, as well as education and teaching materials for her prescribed therapies, IV access and disease process
- Educate patients to become self-sufficient in the management of VWD and proficient with peripheral IV access for factor replacement therapy

Effective Management

- Management of VWD is a life-long effort that requires comprehensive care from skilled clinicians
- Specialty pharmacy/home infusion providers are uniquely positioned to train & educate families with VWD importance of self-infusion and compliance to medication regimens
The Diagnosis & Management of von Willebrand Disease

NOTES
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Answers:
1. B
2. C
3. D
4. D
5. C
6. B
7. A
8. A
9. B
SHAPING OUR HORIZON

Maximizing 20 Years of Achievement to Craft a Future of Possibilities