SURGERY AND
Von Willebrand Disease

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VON WILLEBRAND – A FATHER OF MEDICINE

Erik von Willebrand was born in Vaasa, Finland, on February 1, 1870, to a district engineer and his wife. After receiving his bachelor's degree, von Willebrand went on to receive his medical degree from the University of Helsinki in 1896. Upon completion of his medical training, the new doctor defended his own thesis about the changes in blood after severe blood loss. During his internship, and a short time as an assistant physician, Dr von Willebrand served as a lecturer in anatomy. After two years as an anatomy professor, he gained his docent in physical therapy and taught microscopical anatomy along with practical exercises. In 1908, he received his docent in internal medicine, and described how the blood changes when one engages in physical exercise, the body undergoes changes due to metabolism or obesity and water exchanges take place within the human body.[1,7]

In 1925, von Willebrand was asked to see a 5-year-old girl, who was from a village on the Aland Islands, a region of Finland. Her family's history included excessive bleeding. Four of her siblings had died at an early age from this unknown condition. As he investigated the family's medical history, he discovered that 23 of the 66 members had bleeding problems, and more women than men were affected by this condition.

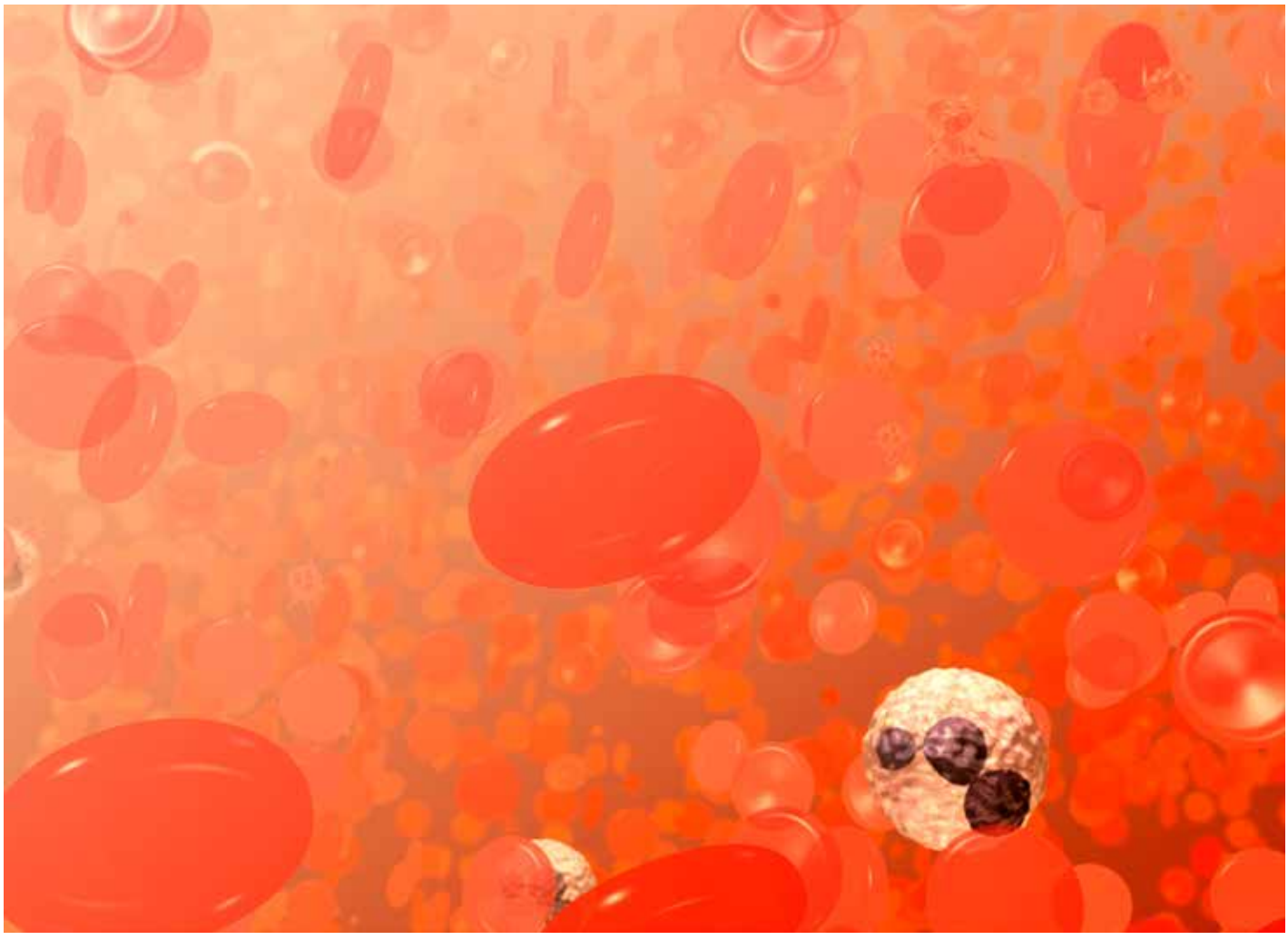
Dr von Willebrand came to the conclusion in 1926 that this was an unknown form of hemophilia and coined it pseudo-hemophilia, of which prolonged bleeding is the prominent sign. It would later be known as von Willebrand disease, or VWD.[1,7]

LEARNING OBJECTIVES

- Learn about the history of von Willebrand disease
- Review the types and subgroups of VWD
- Determine the surgical complications when treating patients with VWD
- Identify which treatment methods help control VWD
- Read about three case studies of VWD patients and the outcomes of each surgery

CASE NUMBER ONE

She was diagnosed with the disease in 2001. She was pregnant with her third child when she was only six months along when she started cramping and bleeding. Her doctor admitted her to the high-risk OB floor at a community hospital. Her water broke two weeks after she was admitted and was rushed in for an emergency C-section. The baby was born weighing 2.2 pounds. He was flown by helicopter to a children's hospital and was admitted to the NICU. Eleven years later he is a healthy boy. His mother continued to bleed after the boy was delivered, so she was given blood transfusions and doctors were finally able to stabilize her. She was released after three days in the hospital. She later began experiencing vaginal bleeding. Her doctor conducted a vaginal exam and concluded her uterus had not properly healed from the birth of her last child. The doctor advised for a total hysterectomy. She was also referred to hematologist because of anemia concerns. At that point, the patient was diagnosed with Von Willebrand type 2A. Her blood levels were so low that her doctor suggested an iron transfusions. Over the next six months, she had several iron transfusions, which worked off and on for a while. After consulting a friend, she was informed that iron was not the recommended treatment for von Willebrand disease and that she should seek a second opinion. The patient saw a doctor at cancer center, and he wanted to try desmopressin. After a few treatments with desmopressin, the patient's von Willebrand seemed to be stabilized. Since that time, she has received regularly scheduled factor VIII injections and continued doses of desmopressin. She remains a fairly healthy lifestyle.[1]



DEFINING VON WILLEBRAND DISEASE

VWD is the most common hereditary coagulation abnormality in humans. It is a quantitative deficiency of von Willebrand factor (VWF), a protein that is required for platelet adhesion. VWF also carries a clotting factor VIII. Factor III is missing protein or doesn't work well in patients that have hemophilia. There are three forms of VWD: inherited, acquired and pseudo or platelet. Hereditary types of this disorder are:

- VWD type 1 – Type 1 is the most common type of this disorder. Out of the people who have VWD, three out of four have type 1.[7]
- VWD type 2 – Type 2 is divided into subtypes: 2A, 2B, 2M and 2N. Various gene mutations cause these various types.[7]
- VWD type 3 – People who have type 3 usually have no von Willebrand factor and low levels of factor VIII. Type 3 is the most serious form of this disease, but is also the rarest.[7]

Signs and symptoms of von Willebrand disease for type 1 and 2 include hard-to-stop nosebleeds, frequent and large bruises, prolonged dental bleeding, heavy or prolonged menstrual bleeding (for women), heavy bleeding after a cut, surgery, blood in one's stools or urine. People who have type 3, may have the symptoms listed above or they may experience severe bleeding for no apparent reason. These episodes can be fatal.

Testing for von Willebrand disease can be complicated because the high percentage of people that have the mild form of the disease, especially if they have little to no signs of this disease. If there is a family history of Von Willebrand disease, then patients will be tested over a period of time and the results of each test will be compared with the previous test. Certain blood tests will show if bleeding times are increasing or if factor VIII is decreasing. There is no single test to diagnose VWD so one's doctor will call for a series of blood tests to occur, including tests to look at the von Willebrand factor antigen, von Willebrand factor ristocetin cofactor activity, factor VIII clotting activity, von Willebrand multimers and a platelet function test.[5]

VON WILLEBRAND TYPES

Von Willebrand disease consists of three types, with type 2 having several different subtypes. The first type of Von Willebrand disease is type 1. This type is autosomal dominate

CASE NUMBER TWO

A 75-year-old man had been diagnosed with type 2N VWD in 2002 on a blood test before surgery. He was administered recombinant FVIII preoperatively and the surgery was uneventful. He has no significant bleeding history except for easy bruising. He had even undergone multiple surgeries prior to his diagnosis and had no complications. He had no family history of excessive bleeding. Prior to his most recent surgery, total knee replacement, he and his doctor agreed on a clotting factor replacement therapy prior to the procedure to reduce the potential of significant blood loss. It was also decided that recombinant FVIII would also be administered preoperatively to control the risks of plasma-derived clotting factors. Thirty minutes after the dose of FVIII was administered, his levels were maintained and the surgery proceeded. The operation was uneventful and the patient had a local wound infection following the procedure, but reported no abnormal or excessive bleeding. Since this patient only had a mild bleeding history, it was determined to give him recombinant FVIII prior to surgery and supplement with further levels as needed through monitoring. His postoperative FVIII levels remained haemostatic with no evidence of bleeding.[3]

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CASE NUMBER THREE

A 57-year-old man with a medical history of hypertension and external hemorrhoids was admitted to a hospital for cerebral infarction of the left anterior cerebral artery. To reduce impaired consciousness, a craniotomy and hematoma evacuation, trapping and external decompression was performed. The patient improved for a short time, but a sacral pressure developed and his condition worsened. Necrotic tissue was debrided from the ulcer at his bedside and each time the bleeding was difficult to stop. Pressure hemostasis was issued, but it quickly worsened the pressure of the ulcer. Due to the uncontrollable bleeding, and a battery of tests, it was determined the patient had von Willebrand disease. A factor VIII dosage was administered daily and his von Willebrand factor improved, allowing for preparation to close the wound. A fasciocutaneous flap including the gluteal perforators were made to close the wound. The decision was made to quickly transfer the patient to a rehab hospital and to discontinue the factor VIII dosage. The flap healed and the man's postoperative stay was uneventful. No excessive bleeding was reported and the patient was transferred to a rehab clinic one month after surgery.[6]

Once it is determined that VWD patients may proceed with the surgery, careful monitoring by the OR team is essential, with blood or platelets ready at all times.

and is the most common appearing in 70% to 80% of the cases.[11] With type 1, patients will have mild to moderately severe bleeding. There also is a partial quantitative deficiency of von Willebrand factor. With type 1, all multimers are present and in same proportion, but reduced. Factor VIII, von Willebrand factor activity and von Willebrand factor antigen can be reduced or around the normal range. Type one von Willebrand disease is the least dangerous, but will require test of the clotting factors prior to any surgery or dental work. If there is a deficiency, then the patient should be treated with desmopressin, and then rechecked for clotting factors.[4]

Blood or platelets need to be ready at all times during surgical procedures on VWD patients

The four subtypes define type 2. Type 2A is also autosomal dominate; it occurs in 10% to 15% of all von Willebrand cases. Patients with type 2A will have moderate to moderately severe bleeding. The platelet to von Willebrand factor interaction is defective along with the absence of hemostatically active von Willebrand factor multimers in plasma. The test results for type 2A will show low von Willebrand factor activity, normal von Willebrand antigen, normal factor VIIII and decreased large multimers on electrophoresis.[1,5,7,9]

In type 3, the most serious of the three types, factor VIII is either in extremely low levels or absent and patients have no von Willebrand factor.

TREATMENT

Treatments for VWD vary depending on which type a person has. Since most cases of VWD are mild, medicines

are generally only used for when surgery or a dental procedures are necessary. Other treatments include increasing the amount of von Willebrand factor and factor released into the bloodstream, preventing the breakdown of blood clots and to control heavy menstrual bleeding. Desmopressin is commonly used and is usually administered by injection or nasal spray. It makes one's body release more von Willebrand factor and factor VIII into the bloodstream. Desmopressin generally works well for type 1 cases and for some type 2 cases. Another treatment used for people who can't take desmopressin or need prolonged treatment, have type 1 VWD that doesn't respond to this hormone or have type 2 or 3, is von Willebrand factor replacement therapy. This treatment involves an infusion of a concentrated amount of von Willebrand factor and factor VIII into one's arm vein. Antifibrinolytic medicines are used prevent the breakdown of blood clots and fibrin glue is sometimes used directly on a wound to control bleeding.[7] There are some various other treatments available for women to help control and reduce heavy menstrual bleeding. Birth control pills can increase the amount of von Willebrand factor and factor VIII in a women's body and a levonorgestrel intrauterine device placed in the uterus can also increase these levels. Aminocaproic acid can reduce bleeding by slowing the breakdown of blood clots.[1,2,7]

Patients with VWD need to be cautious when having surgery or dental procedures performed

SURGERY AND VWD

As with any other patient, a preoperative evaluation will need to be performed, including a detailed medical history that showcases bleeding history. A decision might be made to perform additional testing prior to the surgery, dependent on the patient's medical history. Once it is determined that VWD patients may proceed with the surgery, careful monitoring by the OR team is essential, with blood or platelets ready at all times. With the potential for significant blood loss, specific replacement therapies may be decided on prior to the surgery.[7] As previously stated, most VWD patients with type 1 and 2, respond to desmopressin and no other therapy medicine is needed to control VWD disease during surgery. In other patients, plasma-derived VWF concentrates may be required. In rare cases, other selective therapies may be used for the use of recombinant FVIII, although they are not recommended based on pharmacokinetic data.[3]

Most people diagnosed with VWD live relatively normal lives with few complications. Staying educated about and avoiding over-the-counter medicines that can affect blood clotting and informing others of one's condition, especially doctors and dentists as well as neighbors, coworkers and friends, can help prevent serious risk.[1] If a relative is diagnosed with VWD, then other family members should be tested so that preventative measures can be taken to combat this disease. Pregnancy can be a challenge for women with VWD. These women should look into using an OB/GYN and medical center with a hematologist on staff that specializes in high-risk pregnancies should complications arise.[10] Most women with VWD, however, have successful pregnancies and deliver with few complications.

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