Von Willebrand disease

Von Willebrand disease is a bleeding disorder that slows the blood clotting process, causing prolonged bleeding after an injury. People with this condition often experience easy bruising, long-lasting nosebleeds, and excessive bleeding or oozing following an injury, surgery, or dental work. Mild forms of von Willebrand disease may become apparent only when abnormal bleeding occurs following surgery or a serious injury. Women with this condition typically have heavy or prolonged bleeding during menstruation (menorrhagia), and some may also experience reproductive tract bleeding during pregnancy and childbirth. In severe cases of von Willebrand disease, heavy bleeding occurs after minor trauma or even in the absence of injury (spontaneous bleeding). Symptoms of von Willebrand disease may change over time. Increased age, pregnancy, exercise, and stress may cause bleeding symptoms to become less frequent.

Von Willebrand disease is divided into three types, with type 2 being further divided into four subtypes. Type 1 is the mildest and most common of the three types, accounting for 75 percent of affected individuals. Type 3 is the most severe and rarest form of the condition. The four subtypes of type 2 von Willebrand disease are intermediate in severity. Another form of the disorder, acquired von Willebrand syndrome, is not caused by inherited gene mutations. Acquired von Willebrand syndrome is typically seen along with other disorders, such as diseases that affect bone marrow or immune cell function. This rare form of the condition is characterized by abnormal bleeding into the skin and other soft tissues, usually beginning in adulthood.

Frequency

Von Willebrand disease is estimated to affect 1 in 100 to 10,000 individuals. Because people with mild signs and symptoms may not come to medical attention, it is thought that this condition is underdiagnosed. Most researchers agree that von Willebrand disease is the most common genetic bleeding disorder.

Causes

Mutations in the \( VWF \) gene cause von Willebrand disease. The \( VWF \) gene provides instructions for making a blood clotting protein called von Willebrand factor, which is essential for the formation of blood clots. After an injury, clots protect the body by sealing off damaged blood vessels and preventing further blood loss. Von Willebrand factor acts as a glue to hold blood clots together and prevents the breakdown of other blood clotting proteins. If von Willebrand factor does not function normally or too little of the protein is available, blood clots cannot form properly. Abnormally slow blood clotting causes the prolonged bleeding episodes seen in von Willebrand disease.
The three types of von Willebrand disease are based upon the amount of von Willebrand factor that is produced. Mutations in the \textit{VWF} gene that reduce the amount of von Willebrand factor cause type 1 von Willebrand disease. People with type 1 have varying amounts of von Willebrand factor in their bloodstream. Some people with a mild case of type 1 never experience a prolonged bleeding episode. Mutations that disrupt the function of von Willebrand factor cause the four subtypes of type 2 von Willebrand disease. People with type 2 von Willebrand disease have bleeding episodes of varying severity depending on the extent of von Willebrand factor dysfunction, but the bleeding episodes are typically similar to those seen in type 1. Mutations that result in an abnormally short, nonfunctional von Willebrand factor generally cause type 3 von Willebrand disease. Because there is no functional protein, people with type 3 von Willebrand disease usually have severe bleeding episodes.

\textbf{Inheritance Pattern}

Von Willebrand disease can have different inheritance patterns.

Most cases of type 1 and type 2 von Willebrand disease are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Type 3, some cases of type 2, and a small number of type 1 cases of von Willebrand disease are inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they do not show signs and symptoms of the condition.

\textbf{Other Names for This Condition}

- angiohemophilia
- vascular pseudohemophilia
- von Willebrand disorder
- von Willebrand's factor deficiency

\textbf{Diagnosis & Management}

\textbf{Genetic Testing Information}

- What is genetic testing? 
  /primer/testing/genetictesting
- Genetic Testing Registry: von Willebrand disorder

\textbf{Research Studies from ClinicalTrials.gov}

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22von+Willebrand+disease%22
Other Diagnosis and Management Resources

- GeneReview: von Willebrand Disease
  https://www.ncbi.nlm.nih.gov/books/NBK7014
- MedlinePlus Encyclopedia: von Willebrand Disease
  https://medlineplus.gov/ency/article/000544.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: von Willebrand Disease
  https://medlineplus.gov/ency/article/000544.htm
- Health Topic: Blood Clots
  https://medlineplus.gov/bloodclots.html
- Health Topic: Platelet Disorders
  https://medlineplus.gov/plateletdisorders.html

Genetic and Rare Diseases Information Center

- Von Willebrand disease

Additional NIH Resources

- National Heart Lung and Blood Institute
  https://www.nhlbi.nih.gov/health-topics/bleeding-disorders

Educational Resources

- MalaCards: von willebrand's disease
  https://www.malacards.org/card/von_willebrands_disease
- Merck Manual Consumer Version
- Nemours Foundation
- Orphanet: Von Willebrand disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=903
- St. Jude Children's Research Hospital
- The Centers for Disease Control and Prevention: Bleeding Disorders
  https://www.cdc.gov/ncbddd/hemophilia/
Patient Support and Advocacy Resources

- Canadian Hemophilia Society
  https://www.hemophilia.ca/von-willebrand-disease/

- Hemophilia Federation of America
  https://www.hemophiliafed.org/

- Metabolic Support UK
  https://www.metabolicsupportuk.org/

- National Hemophilia Foundation
  https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Von-Willebrand-Disease

- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/von-willebrand-disease/

- World Federation of Hemophilia
  https://elearning.wfh.org/elearning-centres/vwd/

Clinical Information from GeneReviews

- von Willebrand Disease
  https://www.ncbi.nlm.nih.gov/books/NBK7014

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28von+Willebrand+disease%5BMAJR%5D%29+AND+%28von+Willebrand+disease%5BTI%5D%29%29+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- VON WILLEBRAND DISEASE, TYPE 1
  http://omim.org/entry/193400

- VON WILLEBRAND DISEASE, TYPE 2
  http://omim.org/entry/613554

- VON WILLEBRAND DISEASE, TYPE 3
  http://omim.org/entry/277480

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17701477

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17403089
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18078392

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18315614

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16706266

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18193717

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