Von Willebrand Disease is a Genetic Disorder

Von Willebrand Disease (VWD) is a common genetic disorder affecting up to 1-2 percent of the general population. VWD is caused by a variety of changes, also called alterations or mutations, in the Von Willebrand Factor gene which interfere with the normal production of the Von Willebrand Factor protein needed for our blood to clot properly.

Genes contain all of the information our bodies need, such as the code needed to produce the clotting factor proteins. Genes are located on our chromosomes, which are in each of our cells. We inherit a set of chromosomes from each of our parents, and therefore have a pair of each — two copies of chromosome #1, two copies of chromosome #2, etc.

Types and Subtypes of Von Willebrand Disease

Many different changes can occur in the Von Willebrand Factor gene and they do not all have the same effect on the gene’s function. VWD is divided into types which are determined by the overall abnormality of the Von Willebrand Factor. Type 1 and type 3 are caused by a decrease in the amount of Von Willebrand Factor produced by the body. Type 2 is caused by alterations which interfere with the structure and/or function of the protein. Type 2 is further divided into subtypes including 2A, 2B, 2M, 2N, etc.

Type 1 is the most common form and accounts for 70-80% of individuals with VWD. Type 2 is estimated to account for about 15-20% of individuals with VWD. In the state of Indiana, compared to other parts of the country, there is a relatively higher number of individuals with type 2M and 2B. Type 3 is the most severe and the least common type.

Inheritance of Type 1 Von Willebrand Disease

» VWD type 1 is inherited in an autosomal dominant pattern with variable expression and incomplete penetrance. This means:

» Type 1 affects males and females equally.

» Individuals with VWD type 1 have one Von Willebrand Factor gene which is altered and one which functions normally — called heterozygous.

» Children born to individuals with VWD type 1 each have a 50% chance of inheriting the VWD gene and being affected with VWD type 1.

» Individuals within families and among different families who have VWD type 1 can experience a variety of symptoms and with different degrees of severity — called variable expression.

» Some individuals with the altered Von Willebrand Factor gene may not have VWD, having normal laboratory evaluations and no bleeding symptoms — called incomplete penetrance. These individuals can still pass VWD on to their children.

» See the IHTC’s informational sheet “Type 1 Von Willebrand Disease” for additional information, such as symptoms and treatment.
Inheritance of Type 2 Von Willebrand Disease

Type 2 Von Willebrand disease is usually inherited in an autosomal dominant pattern with variable expression; however, it has high penetrance within families. This means:

» Individuals who have the altered Von Willebrand Factor gene will have Von Willebrand Disease.

» There can be differences in the symptoms family members’ experience.

» Most subtypes of VWD type 2 have autosomal dominant inheritance, and an individual has a 50% chance to pass it on to each of his or her children, either a son or daughter.

» VWD type 2N and rare cases of other type 2 subtypes are inherited in an autosomal recessive pattern in which both parents carry an altered Von Willebrand Factor gene, sometimes of different types of VWD. This pattern of inheritance is more complex. If you have one of these type 2 subtypes, please contact the IHTC’s genetic counselor to discuss inheritance further.

Inheritance of Type 3 Von Willebrand Disease

Von Willebrand disease type 3 occurs when an individual has an alteration in both copies of their Von Willebrand gene, preventing the production of Von Willebrand Factor protein. In this case, each of the individual’s parents has one altered copy of the Von Willebrand Factor gene; the parents may or may not have previously been diagnosed with VWD. When both parents pass on an altered VWF gene to their child and the child does not receive a normal functioning copy of the gene, they have Von Willebrand disease type 3. This is called autosomal recessive inheritance.

What Families Should Know

» Individuals with Von Willebrand disease and their parents should make family members aware of this diagnosis.

» Family members should be informed of their chance of having the bleeding disorder, available testing, and who to contact for additional information.

» Individuals with a family history of type 1 Von Willebrand disease can be at risk for abnormal bleeding despite never having experienced previous symptoms. Some individuals with VWD have a milder form of the disease for which they do not require treatment until they experience a stressful event such as surgery or trauma.

» It is recommended that all first degree relatives (immediate family members) of an individual with Von Willebrand disease have testing performed for VWD. In addition, family members who have experienced abnormal bleeding symptoms should also be tested.

Tell your family and contact the IHTC to discuss recommendations for you and your family members.

You may contact the IHTC’s genetic counselor at 317-871-0000 or toll-free 1-877-256-8837 for additional information including:

» Who should consider testing and additional information based on your personal and family history

» Referral to a center in your area for evaluation if you are a family member living outside of Indiana

» Discussion of additional details regarding the type of VWD in your family, and any additional questions you and your family may have