

Von Willebrand's Disease in the Bernese Mountain Dog
February, 2001

There has been considerable discussion about von Willebrand's Disease (vWD) in Berners over the last two years. Very recent developments now give Berner owners and breeders the opportunity to evaluate their dogs and with prudent breeding practices eliminate this disease from our breed. VetGen has recently developed a DNA test for vWD in Berners. This test is identical to the test for Doberman Pinschers.

A great deal of thanks goes to Cindy Stauch for serving as the vital liaison between VetGen and dog owners. We also need to thank VetGen for doing this study on 30-50 dogs free of charge to determine if vWD in Berners has a mutation that is already known in another breed. The owners of the dogs that submitted samples to VetGen need to be thanked. We as a breed fancy should be mindful of how lucky we are. If vWD in Berners was not due to one of the known mutations it would have cost us literally hundreds of thousands of dollars to find the mutation. There are already a few breeds that are not so lucky.

A little background is in order. There are three types of vWD, based on DNA mutations, so far found in dogs. Type I is autosomal recessive and the one seen in Doberman Pinschers as well as Manchester Terriers, Poodles, and Pembroke Welsh Corgis. It is a relatively mild disease with infrequent spontaneous bleeds and will be discussed in more detail. Type II is found in German Shorthaired and Wirehaired Pointers. Type III is a mutation that stops production of the von Willebrand's Factor (vWF) completely. This type is seen in Scottish Terriers and Shetland Sheepdogs and is severe, often resulting in spontaneous bleeds and death in puppyhood for affected dogs. Of note is that the mutation for these two breeds is different in the Type III disease but both result in no vWF production. This is important because the test for Scottish Terriers won't work on Shetland Sheepdogs.

Much of the remainder of the discussion is based on information known in Doberman Pinschers. Because the mutations are the same in Berners, and some other breeds, we can assume much of the information will be true for Berners. The type I mutation is what is known as a splice mutation, that is, the gene product (vWF) is abnormal/inactive 90-95% of the time but normal 5-10% of the time even in the presence of two mutated genes. How this occurs is beyond the scope of this article and probably not completely understood by those who do this work full-time. This same mutation is the cause of some cases of vWD in humans.

Clotting factors, of which there are several, are consumed when there is a need for blood clotting such as injury or surgery. In vWD there is a limited amount of vWF (von Willebrand's Factor) which is replenished slowly during blood clotting. If the bleeding is more rapid than vWF can be generated then a dog will not clot normally and will have excessive bleeding when the vWF is exhausted. The lower the assay for vWF is, the more likely the individual is to bleed with any given event.

In Doberman Pinschers a vWF assay of 36% is usually adequate to prevent excessive bleeding. Levels of 10-20% may be adequate to prevent excessive bleeding for mild events such as a neuter. Major events, such as trauma followed by major surgery, may exhaust the vWF in animals that have higher assays including some carriers.

Affected dogs will have both mutated genes in their DNA. They will have between 5 and 20% vWF levels on assay and this level will vary over time within the same dog and will vary greatly between dogs even those that are related. They do not commonly bleed spontaneously but are at great risk to bleed due to injury or surgery. It is not rare for an affected dog to have minor surgery, such as a neuter, or trauma and to not bleed excessively.

Carriers have one normal gene and one mutated gene. They will have vWF assays of 30-100%. This level will vary over time with any given dog and vary greatly between dogs. Carriers rarely bleed except at times of great stress to their clotting system.

Normals have two normal genes. Interestingly, their vWF assays will vary from 50-100%. It should be noted that in the event of a prolonged stress to the clotting system, such as very long surgery or a bleeding ulcer, normal dogs and humans would exhaust their vWF and other clotting factors so that they have a prolonged bleeding time. This is treated with transfusion of platelets and clotting factors. This in no way implies they have vWD or hemophilia but is a normal result of a prolonged bleeding episode.

Since this is an autosomal recessive disease, for which we now have a test, and the carrier frequency is relatively low, we have the potential to eliminate this disease from our breed with prudent breeding practices. The carrier frequency is the percentage of all dogs within a breed that carry the gene. Because the number of Berners tested to date is small the carrier frequency is not accurately known but is probably less than 20%.

Breeding two affected dogs will always result in all offspring being affected. Breeding an affected dog to a carrier will result in 50% affected and 50% carriers in the offspring. Breeding an affected dog to a normal will result in 100% carriers in the offspring. Breeding two carriers will result in 25% affected, 50% carriers and 25% normal offspring. Breeding a carrier to a normal will result in 50% carriers and 50% normal offspring. These percentages are based on Mendelian ratios for autosomal recessive genes. They will be accurate for large populations or many litters. Results for individual litters will likely vary from these percentages to a substantial degree.

If your goal is to eliminate the disease (affected) state then you will never want to breed an affected to another affected or a carrier. A strong case can also be made to never breed two carriers since 25% of their offspring will be affected. This assumes that the two individuals are shining examples of the breed and their only health/conformation problems are vWD. When you take into account other breeding issues there will likely be times when two carriers may be crossed. Attempting to eliminate the carrier state would be considerably more difficult and severely limit the size of the breeding gene pool and likely exacerbate other health problems in our relatively small breed.

It should be stressed that vWD is only one part of the breeding decision-making process and not the only part. Breeding affected dogs should be absolutely minimized but breeding carriers may be necessary to maintain the size of the gene pool and not exacerbate other health problems in the breed. Now that we have a DNA test for carrier status of vWD, we do not need to overreact to the resulting information and can, instead act in an informed and responsible manner in our breeding decisions.

These types of breeding decisions are currently being faced by Doberman Pinscher breeders. In that breed the carrier frequency is 50% and close to 25% of Dobermans are affected with this disease. Their attempt to rid the breed of the disease is a much more difficult task than ours is because less than a third of their dogs are normals. Even though it is a much more common breed than Berners the number of Doberman Pinschers normal for vWD is very small.

The test itself is quite simple and involves cheek swabs only, no blood. The test costs \$140 per dog, a large discount is offered for "clinics" or groups of 25 or more and only needs to be done once in a dog's life. Results are available in two weeks and reveal whether a tested dog is affected, a carrier or normal. Since this is a DNA-based test, you can obtain a cheek swab at any age to test your offspring. This test is much more accurate and specific than the vWF assay and is the test of choice for breeding decisions or testing offspring. It is available from VetGen 800/483-8436.

The vWF assay, while no longer useful for diagnosing a dog's vWD status, can have some uses. If a known affected or carrier needs surgery, knowledge of the vWF levels can help with surgical timing and preparation, as an example. It provides specific information about the vWF that the DNA test does not.

It is recommended that all dogs with an abnormal vWF assay be tested to determine their vWD carrier status. In keeping with the conservative and prudent breeding practices of our fancy, it is recommended that all animals utilized for breeding also be tested. The Berner-Garde is making preparations to include these test results in its database. As fanciers of this breed, we should consider ourselves quite lucky that this test became available at essentially no cost to the fancy and that our problem is not as large as that seen in other breeds. Hopefully we will be able to eliminate von Willebrand's Disease completely from this breed in the near future. This is the first DNA test available for this breed and we need to utilize it wisely.