Glanzmann's Thrombasthenia in Great Pyrenees dogs

A bleeding disorder called Glanzmann's thrombasthenia (GT) was recognized and described in a Great Pyrenees dog in 1996.[1] GT has been recognized for many years in humans and is due to a congenital/inherited glycoprotein receptor defect in platelets. Platelets are small, circulating cytoplasmic fragments that are the first line of defense in stopping the flow of blood from injured blood vessels. An important aspect of platelet function is their ability to stick to each other and plug holes in damaged vessels until blood clotting and tissue repair can occur. The platelets of people and dogs with GT are defective in their ability to stick to each other due to a missing platelet receptor. These individuals are at increased risk for spontaneous hemorrhage and they are also at high risk for excessive hemorrhage as a result of injury or surgery. The type of spontaneous bleeding that occurs with GT includes excessive gingival bleeding during tooth eruption, nose bleeds, and superficial skin bleeds. The receptor missing on GT platelets is encoded by two separate genes; all cases of GT are due to mutations in one of those genes. In early 1999, the two genes encoding for the platelet receptor missing on GT platelets were sequenced in dogs and the molecular basis for the disease was determined in Great Pyrenees dogs.[2] Shortly afterward another distinct mutation was found in the same gene in Otterhounds with GT and most recently the genes were sequenced in horses and two different mutations have been identified as causing GT in horses.[4,5] The findings in animals have been very similar to those described in people with GT; over 50 different mutations have been identified as causing GT in humans.

GT has been identified in Great Pyrenees from Show, Livestock Guardian, and Companion lines and is inherited as an autosomal recessive trait. Carriers of the mutation have no clinical signs and are impossible to identify without either DNA testing or by breeding trials (sires and dams who produce affected puppies are obligate carriers of the mutation). Even dogs who are affected with GT may not be diagnosed properly. Many veterinarians are not aware of this disorder and may provide an incorrect diagnosis. If the disease is not identified properly, the mutation will continue to be propagated. Veterinarians may need help from knowledgeable breeders and owners to understand what GT is and how to diagnose it. It is critically important that Great Pyrenees breeders and owners form a partnership with their veterinarians in understanding and properly identifying this disorder and working together to eliminate the mutation from their breeding lines. Unlike dwarfism, also inherited as an autosomal recessive trait, you can't identify an affected dog from across the street!

With autosomally inherited traits, if a carrier is bred to a dog that is clear of the mutation, statistically 50% of the litter will be carriers (I have seen the actual number of carriers produced from such a mating range from 20 to 80% so 50% is a statistical prediction, not an absolute value). As long as carriers are only bred to clear dogs, there will be no outward evidence that a problem exists; affected puppies will never be produced from such matings. If the population is fairly large and dogs are disseminated fairly widely it will take years before the population becomes saturated enough with carrier dogs that the odds become favorable for two carriers to be mated. If two carriers are bred the litter distribution is predicted to be 25% affected, 50% carrier, and 25% clear. Again this is a statistical prediction, I have personally seen a mating of two carriers produce 4 (40%) affected, 5 (50%) carriers, and 1 (10%) clear. I've also seen the statistics swing the other way where no affected puppies were produced and the litter only had carriers and one normal puppy. Affected puppies are sometimes born dead or die shortly after birth (secondary to trauma) which may explain some of these discrepancies. Some researchers feel that it takes at least a 25% saturation of the population with carriers before the odds become favorable enough for two carriers to mate and produce affected puppies. (This does not count mating of highly related dogs in a fairly small region. In this situation the likelihood of mating two

carriers becomes much higher and affected puppies will be produced much more rapidly, long before there is a 25% prevalence of carriers in the population). Great Pyrenees puppies are often disseminated widely geographically which makes the scenario of widely distributing carriers throughout the population unknowingly more likely.

By using DNA testing, Great Pyrenees dogs carrying the mutation for GT have been identified in Illinois, Indiana, Missouri, Florida, Oklahoma, Minnesota, Alabama, and Mississippi. Affected dogs have been identified in Illinois (1), Missouri (2), Florida (2), and Mississippi (1). One dog in Minnesota was presumed to have GT (based on clinical signs and ruling out other disorders) but the dog was not DNA tested to confirm that it had GT. Forty-four Great Pyrenees dogs have been DNA tested for GT as of March 2007. Of those 44 dogs, six (14%) were affected, 18 (41%) were carriers, and 20 (45%) were clear. The dogs in this group are diverse and include show dogs, livestock guardians, and pets. Dogs range in color from heavily marked (black and white) to blaireau to pure white. Many dogs that are known to come from families in which GT is present have not been tested. Examples of situations I have encountered include:

Florida breeder – Tested 8 dogs on his premises. Two dogs were carriers. One of these dogs was a female that had produced multiple litters and the puppies had been shipped all over the country. When told that this bitch was a carrier his response was that he was no longer using her for breeding (she was too old now) so he did not consider this to be a problem. He made no attempt to contact anyone he had sold puppies to from this bitch. I do not know if these puppies entered the breeding population.

Indiana breeder – A male she had been using for breeding tested as a carrier. The male had sired at least 35 puppies that were scattered throughout the mid-West. She contacted all of the owners of puppies and alerted them to the potential problem. Only one tested their puppy for GT (the puppy tested clear). I do not know what the other 34 puppies were used for or if they became part of the breeding population.

Illinois breeder – Produced an affected puppy that was confirmed with DNA testing. She had all of the litter-mates tested. There were several carriers in the litter which she pulled from the breeding line. She contacted the owner of the sire (obligate carrier since it sired an affected puppy). He refused to speak to me or test any of his dogs or their progeny.

Oklahoma owner – She sent in a sample on her Great Pyrenees for testing. The dog tested as a carrier. She refused to speak with me when she was informed of the results. I do not know if this dog was used widely for breeding purposes although the owner did indicate he had sired at least one litter.

Mississippi owners – Owned two Great Pyrenees puppies. One was affected and one was a carrier for GT. They had purchased the puppies from a traveling circus and did not know where the breeders were. I do not know how many other dogs were bred and sold through this operation.

Alabama owner – Tested 4 puppies for GT. Two were dwarfs. The two dwarfs were carriers for GT. The sire of this litter was unknown. The dam had been abandoned and adopted while pregnant; her source and lineage were not known.

Missouri breeders – Have produced at least 2 affected puppies in the span of one year from two different mating pairs. They have not spoken to me directly in spite of me providing the owner of one of the affected puppies with my phone number and asking for them to have the breeders call me. They have thus far not alerted any of the people they have sold puppies to that there is a potential problem. They told their veterinarian that the

breeding pair that produced the second affected puppy has been used for breeding on at least 7 other occasions. The odds are that 50% of those puppies are carriers. Their locations and uses are not known.

Many Great Pyrenees breeders submit DNA samples from their breeding stock to the AKC. This DNA is used for pedigree verification purposes and is not available for or used for research purposes. Great Pyrenees breeders may have the false impression that the submitted DNA samples will be screened for genetic disorders and they will be alerted if there is a problem. This is not true. The responsibility for testing for inherited genetic disorders lies with the breeders. Great Pyrenees breeders and those who love and care about the breed will ultimately determine the future and health of this breed.

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