Scientist Seeks Genetic Cause of Hip Dysplasia

Congenital hip dysplasia has been called the No. 1 genetic health problem in dogs today. Congenital hip dysplasia (CHD) is an inherited joint laxity disease that by most accounts is polygenic. This means expression of the disease appears to be controlled or affected by more than one gene. Because of this, work on a genetic test for CHD has been challenging.

One of the foremost investigators of congenital hip dysplasia is George J. Brewer, a physician and professor emeritus of human genetics and internal medicine at the University of Michigan Medical School. His authority on genetically linked canine diseases has earned him research grants from the American Kennel Club Canine Health Foundation and the Orthopedic Foundation for Animals. Brewer also is the chief scientist for VetGen, a commercial veterinary genetic diagnostic company.

Earlier estimates that a genetic test for hip dysplasia would be available by now were based upon the possibility of using linkage tests to develop one. Linkage tests involve looking for similar diseases or patterns of inheritance in which the genetic cause is known. A scientist then can develop a list of candidate genes and study them one at a time to see if they are linked and thus responsible for the disease.

"At first we had some 12 candidate genes, but they didn't provide the data to support them as a factor in CHD," Brewer says. "Right now we've identified six more candidate genes, and we have one in particular that is showing some moderate promise."

Once the genetics of CHD is determined, developing a test for that genetic abnormality presents its own set of difficulties. Since CHD is considered to be polygenic, the question of what the test will entail and how good it will be remains to determined.

"The nature of a test depends on the genetic cause," Brewer says. "For example, in Labs it may turn out there is indeed one primary gene responsible for the greatest penetration of CHD through generations of dogs. Perhaps several other genes also are involved but to a much lesser extent. The test would likely then be developed around the gene that is primarily involved."

Another possibility, Brewer says, is that Labrador Retrievers may have one primary gene that causes CHD, but another breed has a different primary gene responsible for the disease, and both may have lesser-involved genes. Such a scenario could result in different tests for different breeds.

"Or, maybe we're talking about three genes—two that are responsible for CHD and one that is less involved," Brewer says. "That, too, would be a different testing method, because it would mean we would have to run two tests. Obviously, we will develop a test based upon whatever genetic data we have indicating which gene or genes produce the most significant amount of risk for CHD."

If it turns out that CHD is caused by 10 genes, each contributing 10 percent to the overall expression of the disease, developing a sound test would become very challenging. "I don't think that's the case," Brewer says. "Other studies indicate we are only dealing with two to four genes."

To add further optimism, Brewer points out that there are reliable tests available that offer some help with supposedly polygenic diseases. "In humans, we have tests for hypercholesteremia, which has been classified as a polygenic disease. In purebred dogs, where the genetic makeup involves a smaller number of genes, potentially we also can develop a successful test once the disease genes are known."

Despite its apparent complexity, the genetic riddle for CHD could take a turn for the better, as has similar work with other inherited diseases. For example, Brewer and VetGen scientists, in collaboration with the University of Michigan and Michigan State University, discovered a mutation that causes a complex bleeding disorder known as Type I von Willebrand's Disease or VWD.

"Initially the work done on VWD showed it to have a very complex genetic cause," Brewer says. "There were all kinds of theories about its inheritance, and a number of other factors played into that thinking including a blood assay that 'wandered' (meaning it was not accurate and reliable). The thyroid also affected the tests.

"After we sequenced the genes, all the theories fell apart. We now know Type I VWD is caused by a simple autosomal recessive gene. We can test for it very easily. The same thing could happen with CHD in Labrador retrievers and other breeds. It all depends upon the data we obtain in the near future."

Breeders Should Know Labradors' Ancestry

Given all we currently know about the Labrador retriever, its genes, the incidence of congenital hip dysplasia (CHD), and the lack of a test for the disease, the best advice for breeders is not to breed dogs with hip dysplasia in their pedigree.

"Avoid breeding dogs whose ancestry includes individuals with CHD if at all possible," says George J. Brewer, M.D., a leading researcher of genetically linked canine diseases. "It's the same advice we've told breeders forever."

Brewer says he prefers to see a pedigree free of CHD for at least four generations to statistically decrease the likelihood of CHD in the future. "The closer generations to the prospective mating are the most important of course, but I would minimize the number of CHD affected dogs back through four generations, to the extent possible."

Brewer emphasizes that the more data a breeder has, the better off they are. "Dogs that have been certified for normal hips are higher on my list (of good ancestors or prospective mates)."