

## Health Committee Report 5/08

- **Heritage of DCM Determined.** Dr. Kate Meurs and her cardiology/genetics group at Washington State have published a paper showing the heritage of this dread disease and this has very serious implications for breeders and owners. J Vet Intern Med 2007;21:1016–1020 “A Prospective Genetic Evaluation of Familial Dilated Cardiomyopathy in the Doberman Pinscher.” I have brought a few extra copies for those who want to read it on their own.
- **The heritage is autosomal dominant with (probable) incomplete penetrance.**
  - **Autosomal Dominant:** Dogs carrying only one gene can develop the disease depending on the penetrance.
  - **Incomplete Penetrance** means that the gene has variable expression depending on other genes or environmental factors. (Speculation) Dogs with only one bad gene likely have a smaller chance of dying of cardio or showing heart abnormalities until they are older dogs and they might die of something else first. Dogs with two bad genes may die younger and show more serious heart problems (but if the penetrance is very incomplete even homozygotes (two bad genes) might not show it unless breeders and owners are very vigilant.) However because the gene is DOMINANT, there will likely be SOME detectable signs. Is this why SO many Dobes have hearts that are not normal when compared to other breeds of the same size?
  - **Pattern of Transmission:**
    - **One cardio gene is bred to a clear:** Half the pups will be at risk. The parent and carrier pups will likely not show symptoms until they are old dogs but a few might die younger.
    - **Two cardio genes bred to a clear:** If a homozygote (2 bad genes) is bred to a clear, this parent may die young and show serious symptoms and ALL the pups will be at risk. But they may not die young or show symptoms until they are old dogs. Breeders and owners must be vigilant. Some may be unlucky and die young.
    - **Each parent has one cardio gene:** If two dogs with only one bad gene are bred, 25% of the pups may die young and show serious symptoms young. BUT the parents with only one bad gene may not show symptoms until they are OLD dogs. Owners and breeders must test these parents to see if they are developing heart abnormalities even as old dogs. In this breeding another 25% will have only one bad gene like their parents and YES 25% will be clear. If the pups in this litter are bred once this pattern seems to appear, then it is a matter of ethical concern whether any dog in this litter should be bred even if he/she appears to have a normal phenotype (tests normal). If bred, dogs with a normal phenotype should be bred to other dogs with a long history of longevity and no cardio cases in recent generations. Never forget statistics: Just as breeding two dogs carrying the brown gene could result in a litter of all black pups, the breeding of two dog with only one bad gene might not show the pattern in the paragraph above. But if it does, then all should now be exceedingly cautious. Only breeders that follow all the pups they produce their whole lives have half a chance to work out a reasonable strategy to avoid this tragedy.
  - **Examples of Varying Penetrance.**
    - vWD is a gene with incomplete penetrance and of course it is NOT USUALLY a lethal disease even on homozygotes (2 bad genes) but the similarity is that carriers are intermediate in their level of expression of the gene trait, vWF.
    - Coat Color is a gene with complete penetrance. Brown coat color is a RECESSIVE gene with COMPLETE penetrance. A dog is brown or black and black dogs carrying the brown gene are not an intermediate color--they are black.
    - PHTLV/PHPV is a gene with partial penetrance. Dogs with grade one (normal vision with a small spot) can produce blind puppies and some dogs with undetectable disease can produce blind pups.
- **What causes incomplete penetrance?** Reasonable ideas are nutrition, special supplements to support cardiac health, environment factors, other diseases that compromise the heart's amazing ability to compensate, and other modifier genes that may be very hard to ferret out. We know about some

supplements that have been useful in human cardio and in other breeds. You can bet my dogs are on them their whole lives!

- **Cardio is NOT a "crap shoot"**. It should be apparent it just takes careful records. If a litter has several cases at a young age but with normal parents, the most likely explanation is that this was a breeding between two dogs with only one bad gene. If one of these parents in turn has a parent with a suspicious early death (need necropsy to confirm), then this scenario is even more likely. Look at longevity in pedigrees.
- **How useful would a gene test be?** There are two kinds of tests. One is a test for a gene mutation that is the direct cause of the disease (like vWD) and that is the most useful. The other kind is a marker test. A marker is a DNA sequence that is ASSOCIATED strongly with the disease and is not the disease gene defect itself. Markers may be only partially accurate. Meurs is looking for either a marker or gene mutation but no success so far.

### What can we do?

- **RECORDS RECORDS RECORDS**
  - Breeders need to follow heart health in every dog they breed or use at stud.
  - Breeders need to encourage owners to do likewise and to necropsy any early or unexpected deaths.
  - Breeders need to be honest and forthcoming to puppy inquiries. "There are no clear lines."
  - Breeders must inform owners when a case appears in related dogs. The new drugs improve both longevity and quality of life in dogs affected with the disease.
- **TEST TEST TEST**
  - ECHO and HOLTER: The present recommendations are yearly echo and holter starting at 2 years of age and biannual echo and holters starting at 5 years of age. Should be mandatory for breeding dogs.
  - Yearly HOLTER only: Recognizing that complete testing is very expensive (Thank you Dr. Morris for making it as affordable as possible), many clubs are purchasing their own Holters and members only pay for their analysis.
  - Tests your own Veterinarian can do:
    - BNP blood test
    - Listen for murmurs and take pulse rate and look/listen for misbeats
    - 30 second EKG
- **Puppy Buyers ask breeders for heart testing on parents and longevity information in pedigrees.**
- **Participate in Research**
  - Meurs is/was looking for clear (absolutely normal hearts in dogs over 10 years of age) and also for diagnosed affecteds. I can give you Meurs contact information.
  - O'Grady studies?
- **UDC Database** records cause and age of death when reported to registry and this information can be requested.`
- **CHIC OFA Database** records health test results in several areas.

### Caveats

The study was 8 years with a single pedigree containing 41 dogs. Meurs states: "Although it is possible that different families of Doberman Pinschers with DCM will demonstrate a different mode of inheritance, this would seem unlikely given that the Doberman Pinscher is a pure breed dog with a closed gene pool. Therefore, it is reasonable to assume that most of the affected dogs in this breed would share a pattern of inheritance."