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## **Heart Disease Study in the Border Terrier**

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Over the past years there has been a number of Border Terriers with a variety of heart diseases. You may have seen or heard of dogs with ventricular septum defects (VSD), pulmonic stenosis (PS), subaortic stenosis (SAS), and mitral valve dysplasia. All of these defects may lead to exercise intolerance, shortness of breath, and in some cases, premature death. Occasionally a dog may be affected with one of these defects and not show any signs at all. On physical examination, your veterinarian may hear a murmur and may refer you to a cardiac specialist. In these cases, the cardiologist will listen to the heart carefully again, obtain an electrocardiogram (EKG), and an echocardiogram (an ultrasound of the heart). The specialist will then determine the extent of the heart disease and recommend treatment.

While all these types of heart diseases described above have different names, they may have the same underlying genetic cause. We take them all together and call them “conotruncal septum defects” or CTD for short. Dr. Patterson, the father of small animal medical genetics, has been studying the inheritance of CTD in the Keeshond for over 35 years and his research team has found that there appear to be multiple genes involved in causing this defect. Because the disease in the Border Terrier is very similar to that in the Keeshond, we will take the same approach to understanding the mode of inheritance and the genes involved in causing the disease. At this time there is no DNA test for this disease. Therefore, careful clinical evaluation of dogs destined for breeding is most important. Because not all dogs with CTD show clinical signs or have murmurs, an echocardiogram is necessary for a complete evaluation.

For the breeder it is most important to know the mode of inheritance in order to avoid producing affected puppies. Careful analysis of the pedigrees from Keeshonds with CTD indicated that it is a complex genetic disease. To understand complex traits, let us first understand simple autosomal recessive mode of inheritance. For a disease that has autosomal recessive inheritance, an affected dog must have two defective genes in order to show signs of disease. Male and female dogs have an equal chance of being affected, and the parents can be completely normal.

Figure 1 shows the mode of inheritance as an example.

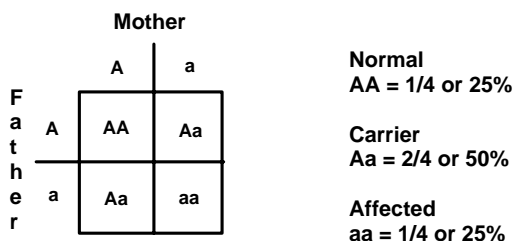
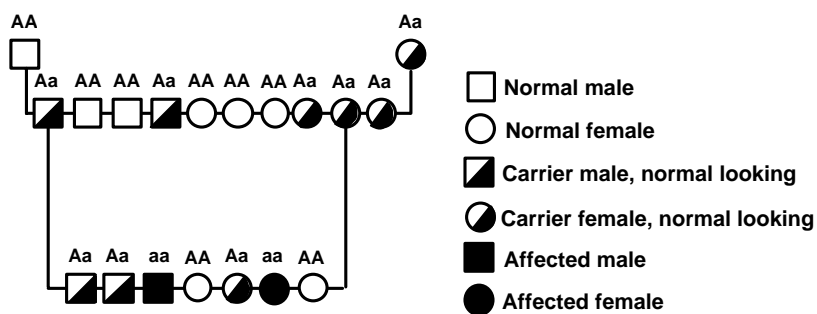


Figure 1 shows a situation where an accidental brother-sister mating occurred. All genes are present in pairs in each individual, except for those genes on the X and Y chromosome. Each parent passes one of its two copies of a gene to an offspring and there is basically a 50:50 chance, which of the genes from each parent gets passed on. In the example above, we will look at only one particular gene. “A” stands for the normal copy of the gene and “a” stands for the defective or mutated copy of the gene. The checkerboard-square demonstrates the possible combinations if both parents were “carriers”. In autosomal recessive traits, carriers (Aa) “carry” the defective gene (a), but they also have a normal one (A), which allows them to be healthy. The checkerboard shows that there is – statistically – a 25% chance of having completely normal offspring, a 50% chance of having carriers, and a 25% chance of having affected dogs. The top of the pedigree above shows the first mating between two unrelated parents, one being a carrier and the other one normal. Remember that both of these parents look normal and do not show signs of disease (i.e. there was no way of knowing the mother was a carrier). If you were to do the “checkerboard” math again, you would see that a mating between AA and Aa would result in 50% AA and 50% Aa offspring. The second breeding in this pedigree was a carrier-brother X carrier-sister mating resulting in normal, carrier, and affected puppies. While the affected pups will be easy to recognize, the carrier and normal dogs cannot be distinguished just by looking at them.

Now imagine you have two different genes involved in the heart disease in the Border Terriers. Each parent has the gene pair Aa and Bb or –as we write it- AaBb. The illustration below shows how you went from 4 different possibilities of offspring to 16!

Figure 2: Two different genes in each parent are examined as they are passed on to the offspring.

	AB	Ab	aB	ab
AB	AABB	AABb	AaBB	AaBb
Ab	AABb	AAbb	AaBb	Aabb
aB	AaBB	AaBb	aaBB	aaBb
ab	AaBb	Aabb	aaBb	aabb

In the case of two genes, let us imagine that **aaBB** and **Aabb** show just one clinical sign, such as PS. However, **aabb** may show the full spectrum of disease, such as a VSD **and** a PS **and** SAS **and** ... . You can imagine what happens when you have three or more genes involved in causing a specific disease. Currently, there is no reasonable way to distinguish carriers from normal dogs, as they look the same. To eliminate CTD from the breeding population, a DNA-based test would be extremely valuable. At this time, the only way to know if potential parents are carriers is by having affected pups born (both parents are automatically carriers) or if a test mating was done by breeding the parent in question to a known carrier. However, this is a very crude method of “genetic testing”. Currently, we are trying to find the genes for CTD and subsequently develop a DNA-based test for the disease. To perform these investigations, we are requesting blood samples from normal and affected dogs to extract DNA. Five – 10 ml of EDTA blood (purple top tube) should be sufficient. The blood may be sent on ice packs or at room temperature, but not frozen. Please include basic pedigree information (parents and possibly grandparents) and remit the signed consent form below. The samples should be sent to the address below. **All information is handled confidentially.** Thank you very much for your participation in this important study that will benefit all Border Terriers!

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**VENIPUNCTURE OWNER INFORMED CONSENT FORM FOR VHUP**

**PRINCIPAL INVESTIGATOR**

*List name(s) of principal investigator(s) and contact number(s).*

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**PURPOSE OF STUDY**

As the owner or duly authorized agent for the owner of “\_\_\_\_\_,” I grant permission to have my dog participate in a clinical study to find *the genes causing heart defects in the Border Terrier.*

**VENIPUNCTURE AUTHORIZATION**

This study requires that 5 - 10 cc of blood be obtained from my pet to make high quality DNA for the marker test that is being developed. The risk involved in drawing blood for this study is minimal. However, my dog may experience mild redness or bruising at the collection site. Additionally, the hair may be clipped in some cases to facilitate visualization of the vein.

The results of this test may not directly benefit my pet, but may provide veterinarians with a better understanding of *the inheritance of heart defects in Border terrier and to eliminate the disease from the breed. A genetic test will also benefit the breed by allowing breeders to make the right breeding decisions once the parents have been tested if they are carriers of these heart defects.* My participation in this study is entirely voluntary and my refusal to participate will not affect my pet’s care in any way.

I understand that any information about my pet, obtained from this study, will be kept confidential. No information by which my pet can be identified will be released or published without my written authorization.

I have been given the opportunity to ask questions and have them answered to my satisfaction. If I have additional questions regarding this particular research study, I may contact the clinician at the telephone number above.

By signing below, I consent to having the described venipuncture procedure(s) performed on my *dog* for the purposes of the study set forth herein.

Date: \_\_\_\_\_

AKC #: \_\_\_\_\_

Pet’s Registered Name: \_\_\_\_\_

Pet’s Call Name: \_\_\_\_\_

Client/Owner/Agent’s Printed Name: \_\_\_\_\_

Client/Owner/Agent’s Signature: \_\_\_\_\_

Clinician’s or Attending Staff Person’s Signature: \_\_\_\_\_

Veterinarian’s Address: \_\_\_\_\_

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