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INHERITED HEART DISEASE: DIAGNOSIS AND SCREENING

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There is increasing evidence that many forms of congenital and acquired heart disease in human beings are of a familial etiology. Given the importance of this etiology for heart disease in human beings, the inbred nature of most purebred domestic animals and the breed specificity of many heart diseases, it is reasonable to consider a familial etiology for common feline and canine heart diseases, particularly those with strong breed predispositions. Unfortunately the mode of inheritance and the specific genetic defect responsible for the majority of cardiac diseases in dogs and cats is not known. In this manuscript we will discuss the more common forms of feline and canine inherited heart disease.

There are important issues in terminology that should be carefully explained to clients to help them understand the difference between inherited and developmental defects. Owners may not realize that the term congenital refers to defects present at the time of birth, generally developmental defects and that these may or may not be inherited. Inherited defects are those that an animal is genetically programmed to develop. These defects may be present at birth (congenital) or may not become apparent until the animal is an adult (adult onset). Not all congenital defects are inherited and vice versa.

GENERAL GUIDE TO THE RULES OF INHERITANCE

X-linked

X-linked traits are almost always recessive and should have the following criteria: more affected males than females, an affected male crossed with a normal (non carrier) female should produce silent carriers, silent carrier females should have a 50:50 chance of passing the trait on to male offspring and affected females are the result of a cross between a silent carrier female and an affected male. This is usually not a frequent occurrence.

Autosomal Recessive.

Autosomal recessive traits should have the following criteria: the disease should appear to "skip" a generation (parents are usually not affected), males and females should be equally affected, the mating of two heterozygotes (silent carriers) should produce affected in a 3:1 ratio and if both parents are affected, all offspring should be affected.

Autosomal Dominant

Autosomal dominant traits should have the following criteria: males and females are equally affected, every affected individual should have at least one affected parent, and all heterozygotes are affected and transmit a mutant gene to half of their offspring.

Mitochondrial Inheritance

Mitochondrial inheritance is an uncommon mode of inheritance. It should meet the following criteria: males and females should be equally affected and since mitochondria appear to only come from the maternal side, affected offspring must have an affected mother.

FELINE HEART DISEASE Congenital Heart Disease

The most commonly reported congenital heart defects in the cat include mitral and tricuspid valve malformations and ventricular septal defects. A strong breed predisposition and familial nature for any of these defects has not been well documented. It may be that the defects prevent the affected cat from reaching the age of reproductive maturity and passing on the trait or it may be that a familial etiology is just not likely.

Acquired Heart Disease

Hypertrophic cardiomyopathy (HCM) is the most common form of acquired heart disease in the cat. Multiple examples of an inherited etiology have been suggested in both mixed breed and pure breed cats. The more commonly documented pure breed cats include the Ragdoll, the Persian, British and American shorthairs and the Maine coon cat. In the Maine Coon cat, an autosomal dominant pattern of inheritance has been documented. Given the adult onset nature of this disease, owners interested in screening their breeding animals cats should be encouraged to have an annual evaluation including both auscultation and echocardiogram (2-D, M-Mode and Doppler) performed by a cardiologist. Cats with heart murmurs should be evaluated for HCM since a murmur may be the first sign of disease. However, many cats have physiologic, flow murmurs without evidence of actual cardiac disease. Thus, a murmur may be fairly sensitive but not specific for this disease. Therefore we recommend that cats with new heart murmurs or gallops have an echocardiogram.

Additionally owners that are breeding cats of breeds that have increased prevalence of the disease or have had a problem with HCM in their line should have echocardiography used as their screening test. Since variability in normal echo values with regard to cat size may exist, we recommend having the echocardiogram performed by a specialist with a strong interest in feline cardiology. It should be remembered that HCM is an adult-onset disease. Some cats develop a severe form of disease as a very young adult (8-12 months). This may be particularly true in some breeds of cats, perhaps Ragdolls. While other cats do not develop the disease until they are very mature adults (8-12 years). Therefore, it is very important to evaluate a cat **every year** to accurately screen.

Since the disease is inherited as an autosomal dominant trait in the Maine coon cat, affected cats should not be bred and all affected cats should eventually show the trait (no silent carriers). We do not know if this information can be extrapolated to other breeds.

CANINE HEART DISEASE Congenital Heart Disease

The most commonly reported congenital heart defects in the dog include the patent ductus arteriosus (PDA), subaortic stenosis and pulmonic stenosis. The PDA has been demonstrated to have a familial origin in the poodle, subaortic stenosis has been demonstrated to be familial in the Newfoundland and pulmonic stenosis has been demonstrated to be familial in the beagle. The mode of inheritance has been difficult to ascertain and in many cases it may be a polygenic defect. Although an inherited nature has not been well documented in many of the other commonly identified predisposed breeds with these defects, caution should be relayed to owners that this may be simply

due to a lack of investigation as opposed to a lack of evidence.

PDA

The PDA is the most common congenital heart defect in the dog. It has an increased prevalence in several breeds, particularly in the toy breeds. A few of the more common breeds include the Maltese, toy and miniature poodle, and Shetland sheepdog. The PDA has been shown to be inherited in the poodle and is likely to be inherited in other breeds. The breeding of affected animals, or unaffected animals with a history of producing affected animals is not recommended.

PULMONIC STENOSIS - Pulmonic valve stenosis (PS) is the third more commonly reported congenital defect in the dog. In this case, it is usually a stenosis or dysplasia of the actual valve, rather than a subvalvular lesion. It is observed most commonly in smaller breed dogs including Fox terriers, miniature schnauzers and West Highland white terriers. The familial nature of this defect is not known, although it has been shown to be inherited in the beagle.

English Bulldogs are also reported to have a high incidence of pulmonic stenosis, however, in most cases the valve area is narrowed because of a coronary anomaly rather than an actual valve abnormality.

SUBVALVULAR AORTIC STENOSIS (SAS) - SAS has been shown to be inherited in the Newfoundland and is likely inherited in other breeds, however, the pattern of inheritance is not well understood. At least in the Newfoundland dog, there is some evidence that breeding two mildly affected dogs to each other can produce more severely affected individuals. This would suggest that breeding any Newfoundland with the defect is not recommended. It is not known if this is true in all breeds and the high prevalence of the defect in some breeds (Boxers) may suggest that removal of all mildly affected dogs from breeding programs may not be wise for the breed overall.

Diagnosis of SAS for screening purposes can be challenging. The classic physical examination finding is a systolic heart murmur at the left base. The heart murmur of SAS can be fairly similar to pulmonic stenosis. Therefore a full evaluation (including an echocardiogram) should be performed in order to really determine the severity of the defect. Although one of the key findings of SAS is the presence of a fibrotic ridge below the aortic valve, this lesion is not evident in many dogs with mild or moderate disease. Therefore the diagnosis of SAS is typically based on a variety of factors including Doppler echocardiographic identification of a significant increase in the left ventricular outflow tract velocity (converted to a pressure gradient by squaring the velocity and multiplying by 4). In all cases, Doppler echocardiography should be performed by an experienced echocardiographer that pays careful attention to parallel alignment of the Doppler signal to blood flow. This is best achieved by evaluation from the subcostal position. In most cases, the severity of SAS is categorized as mild, moderate or severe based on the Doppler determined pressure gradient. Severe is typically diagnosed when the gradient is > than 100 mmHg and moderate > 50 mmHg. Unfortunately the diagnosis of mild disease without the presence of an obvious structural defect is harder because there appears to be some normal variation in aortic outflow velocities. This variation

may be breed dependent and may also vary with sympathetic tone (physiologic murmurs). It is likely that a velocity of less than 1.7 m/s is normal and that a velocity > 2.5 is abnormal, but the interpretation of values in - between are more difficult to interpret. This becomes particularly important and frustrating for the evaluation of dogs with a left basilar heart murmur that are being considered for breeding, because it may not be possible to completely rule-in or rule-out SAS. Generally, since the pattern of inheritance of canine SAS is not well understood affected dogs should not be used for breeding.

ACQUIRED HEART DISEASE

Endocardiosis - The most common forms of acquired heart disease in the dogs are endocardiosis and dilated cardiomyopathy. Although endocardiosis is frequently diagnosed in many breeds of dogs, the Cavalier King Charles spaniel is one of the most commonly reported and is the only breed in which a familial nature has been identified.

Dilated cardiomyopathy - Strong familial tendencies for dilated cardiomyopathy have been observed for the Doberman pinscher, Irish wolfhound, great Dane and boxer. Owners should be advised that since this is an adult onset disease with variability in the age of onset screening tests should be performed annually. In the Doberman pinscher there is evidence that the disease may be inherited as an autosomal dominant trait. Annual echocardiography and ambulatory electrocardiography (Holter monitoring) are believed to be the best predictors of early DCM. Criteria that are believed to be indicators of early disease include a left ventricular diastolic dimension of greater than 4.6 cm and a systolic dimension of 3.8 cm even without evidence of systolic dysfunction. These numbers are based on average sized dogs and may not be valid for very large dogs. Annual Holter monitoring has been recommended to detect Doberman pinschers that may develop ventricular arrhythmias before ventricular dilation and systolic dysfunction. Adult Doberman pinschers with greater than 50 ventricular premature complexes (VPCs) per 24 hours, or couplets or triplets are suspect for the development of DCM.

Occasional cases of familial disease in the Great Dane, Newfoundland and Irish wolfhound have been identified. In the Great Dane, it is most likely an X-linked disease. Sons of affected females are at high risk of developing the disease; daughters of affected fathers are likely to be silent carriers. Sons of affected females are at high risk of developing the disease; daughters of affected fathers are likely to be silent carriers. Since it is adult onset, all dogs should be screened annually with echocardiography. Dogs with atrial fibrillation without other evidence of cardiomyopathy should probably be withheld from until it can be determined if they will develop DCM.

Arrhythmogenic Right Ventricular Cardiomyopathy - Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), a familial, adult onset Boxer disease appears to be inherited as an autosomal dominant trait. Since this disease appears to present as an electrical abnormality, any screening efforts should be based on annual Holter monitoring and possibly, annual echocardiography. This is a familial, adult onset disease that appears to be inherited as an autosomal dominant trait. Since this disease appears to present as an electrical abnormality, any screening efforts should be based on annual Holter monitoring and possibly, annual

echocardiography. As mentioned above, clear criteria for affected status are still being determined and day to day variability of arrhythmias exist, so owners should be encouraged to screen annually rather than put emphasis on a single Holter reading.

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