DILATED CARDIOMYOPATHY IN SALUKIS
I. What Is a Normal Saluki Heart ?
II. Dilated Cardiomyopathy

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I. LITERATURE REVIEW AND JUSTIFICATION

There has been much debate regarding the importance and types of cardiac disease found in the Saluki. Several congenital heart defects have been reported including patent ductus arteriosus, tricuspid valve dysplasia, pulmonic stenosis, and mitral valve insufficiency (1) . Although some dogs had clinical signs of congestive heart failure, the most common clinical sign was simply the presence of a heart murmur. This study also found that the incidence of heart murmurs in a group of related Salukis was quite high.

Recently, some Salukis have been diagnosed with dilated cardiomyopathy (DCM), a disease that produces heart enlargement and decreased pumping ability of the ventricles. Heart muscle that has decreased pumping ability is said to have a "systolic dysfunction" or "decreased contractility". Since the ventricles can't pump as efficiently as normal, the heart attempts to compensate both by enlarging and increasing the heart rate. The weakened ventricles are also prone to the development of ventricular rhythm disturbances (abnormal heart beats coming from the ventricles).

The clinical signs of a weakened pump are twofold - 1) the lack of adequate blood flow causes weakness, lethargy, and cold feet and ears, 2) the blood that the left heart fails to pump causes an increase in pressure in the veins of the lung leading to fluid weeping out into the lung tissue (pulmonary edema). This causes an increase in respiratory rate and trouble breathing. Failure of the right heart causes a pressure increase in the veins of the liver allowing fluid to weep into the abdomen (ascites, which we see as an increase in abdominal girth). Ventricular rhythm disturbances may cause clinical signs of weakness, fainting, or sudden death.

The diagnosis of DCM is by ultrasound examination of the heart (echocardiography). The typical echocardiographic findings are: 1) decreased pump function as measured by % delta D (Figure 1), 2) dilation of all four heart chambers, and 3) leaking of the mitral and tricuspid valves assessed by Doppler echocardiography. Since dilation of the heart is a non-specific cardiac compensatory mechanism, it is important to realize that 1) dilation occurs with many types of heart disease including valvar insufficiency, some types of congenital heart disease, and DCM, 2) a cardiac physical examination and echocardiogram including a Doppler study must be done to distinguish these diseases from each other and 3) if the disease is mild, even these tests cannot always distinguish valvar insufficiency from DCM. Chest x-rays are used in DCM to detect fluid buildup in the lungs. Heart rhythm disturbances are detected with an electrocardiogram (EKG). If heart enlargement is marked, this might also be detected on an EKG.

In order to interpret echocardiograms and EKGs, they must be compared to normal values, preferably from the same breed. To date, most of the normal echocardiographic data in dogs has been done in mixed breed populations, or Doberman Pinschers (2,3,4). No normal echocardiographic data base exists for the Saluki. The EKG of normal Greyhounds has been described (5), but has not been studied in the Saluki.

Dilated cardiomyopathy in man is a syndrome that has over 75 specific causes. However, often the cause is elusive despite sophisticated testing including heart muscle biopsy (6). A list of possible causes in man is shown in Table 1. The causal factors in dogs are thought to be as vast, but most are not documented due both to cost factors and the invasive nature of some types of testing (heart muscle biopsy). However, defects in carnitine metabolism have been documented in heart muscle biopsies of Boxers (7) and some Doberman Pinschers (8) with DCM. Some dogs with low carnitine in heart muscle also had either low plasma or urine carnitine levels, but the heart muscle carnitine was the most specific. Supplementation with L-carnitine produced clinical and ultrasound improvement in some dogs (7). Heart muscle carnitine levels are decreased in some people with DCM, but the significance of this finding is presently unknown (6). There is speculation that carnitine deficiency may be a non-specific result (and not a cause) of heart muscle injury (8).

A few Salukis with DCM have had heart muscle biopsies and have been shown to have low heart muscle carnitine concentrations (9). One author has stated that L-carnitine supplementation in Salukis will eliminate heart murmurs (10). At this point, all possible causal factors of DCM in Salukis need to be considered and investigated thoroughly before making conclusions. A critical part of this type of investigation is examination of fresh heart muscle from Salukis with DCM.

One potential factor affecting heart muscle function is thyroid hormone. The relationship of hypothyroidism to DCM has been debated but not well defined in veterinary medicine. (11). In man, severe longstanding hypothyroidism may be associated with decreased ventricular pump function and occasionally with heart failure (12).

II. PRELIMINARY STUDY

We have done physical examinations, electrocardiograms, and echocardiograms in 51 Salukis, including some follow-up studies. 18 of the 51 (34 %) had systolic heart murmurs. Most of the dogs, including most with heart murmurs were asymptomatic. Preliminary findings are summarized below.

A. Dogs without Heart Murmurs

The EKGs of these dogs were different from normals established for most other breeds. They were similar to the EKGs reported for normal Greyhounds (5). The preliminary findings from the echocardiograms indicate that the % delta D may be lower and the aortic diameter larger than in previously reported normals (2,3). The low % delta D in asymptomatic dogs is similar to O'Grady's findings in asymptomatic Dobermans (4).

B. Dogs with Heart Murmurs

Many dogs with grade I-II/VI systolic murmurs had minimal or no changes on echocardiogram and Doppler study. However, it must be stressed that soft murmurs are not always benign, and that these dogs could still develop DCM later in life. Dogs with grade III/VI or louder murmurs frequently had evidence of a leaky mitral valve by Doppler echocardiography. Some of these dogs also had left ventricular enlargement by echocardiography when compared to normals established in mixed breed populations. One dog had congenital tricuspid valve dysplasia.

C. Dogs with Heart Rhythm Disturbances, with or without Heart Murmurs

Some dogs in each group had ventricular rhythm disturbances, although the frequency of the disturbance varied both between dogs and within the same dogs on different dates. This illustrates the point that routine EKGs are not adequate if one wants to determine the "average" number of disturbances over time. To better determine how dangerous the disturbances are, a 24 hour EKG should be done. The 24 hour EKG (also called a "Holter EKG") records the dog's EKG on tape over 24 hours, and a computer analyzes the number and type of disturbances that occur. The results are used to determine the initial frequency. Follow-up Holter EKGs are done to assess the effects of any treatment.

D. Other Studies & Samples Collected

Two asymptomatic dogs with soft heart murmurs and mildly leaking mitral valves were supplemented with L-carnitine (2 grams given orally twice daily) to evaluate its effect on their murmurs. After 4.5 months, their echocardiograms and murmurs were unchanged. Two asymptomatic dogs with dilated ventricles and poor ventricular pump function have been supplemented with L-carnitine at the same dosage, and are awaiting follow-up echocardiograms.

Five dogs that either died or were euthanized after being studied had a gross autopsy, and samples were collected for histopathology. Histopathology has not been done due to lack of funds. Samples were quickly frozen and saved for carnitine analysis when possible (Enclosure 1). One dog with decreased % delta D, left ventricular enlargement and a leaky mitral valve had low heart muscle carnitine levels at autopsy. Other carnitine samples are pending funding.

Fifty one dogs have had baseline thyroid blood samples drawn. Analysis of these samples is pending funding.

III. PROPOSED STUDY, June 1992-June 1993

A. Dogs without Heart Murmurs

Thirty new dogs will have physical examinations, EKGs, echocardiograms with Doppler studies. If these studies are "normal", they will also have samples collected for thyroid testing, and urine and plasma carnitine. These dogs will be monitored for development of signs of cardiac disease by contacting owners. Any previously studied dog that had a low % delta D will have repeat echocardiograms done at intervals dictated by the severity of the decrease.

B. Dogs with Heart Murmurs

These dogs will have follow-up echocardiograms done at intervals dictated by the severity of heart enlargement (if present), the loudness of the murmur, or the onset of any clinical signs of heart disease.

C. Dogs with Rhythm Disturbances

These dogs will have 24 hour (Holter) EKGs done to better determine the frequency and significance of rhythm disturbances.

D. Dogs with Dilated Cardiomyopathy

Any dogs diagnosed by physical examination, echocardiography with Doppler study and EKG will have urine carnitine measured before any treatment. They will be treated with standard therapy +/- L-carnitine. A complete autopsy including heart muscle carnitine (if obtainable) will be done if the dog dies or is euthanized.

E. Reporting of Data

All data will be statistically evaluated and reported in peer-reviewed journals. For purposes of reporting, dogs will be identified by a research code only. All data on individual animals will be confidential, and reported to the owner of the dog in writing.

IV. FUTURE STUDY

It is anticipated that the study of 1) the incidence of DCM in Salukis, 2) the cutoff point for normality of % delta D in Salukis and 3) the cause of DCM in Salukis will take several years to elucidate. This parallels what has been found to date in the Doberman Pinscher (8,13) a breed predisposed to DCM. We hope to expand our data base in the future to follow any dogs with marginal echocardiograms to see if they develop DCM, or if perhaps the normal values for Saluki echocardiograms are truly different from those in mixed breed populations. Finding the cause/causes of DCM in the Saluki may prove to be a long and arduous task. To accomplish this, the initial step is to identify and study as many Salukis as possible with this disease. As more dogs with DCM are identified, and our normal data base is completed, our emphasis will shift toward exploring the possible causes of DCM.

Table 1 - Important Causes of Cardiomyopathy and Myocarditis (6)

1. Inflammatory
   - a. Infective
     - Viral
     - Rickettsial
     - Bacterial
     - Mycobacterial
     - Spirochetal
     - Fungal
     - Parasitic
   - b. Noninfective
     - Collagen diseases
     - Granulomatous
     - Kawasaki

2. Metabolic
   - a. Nutritional
     - Thiamine
     - Kwashiorkor
     - Pellagra
     - Scurvy
     - Hypervitaminosis D
     - Obesity
     - Selenium deficiency
     - Carnitine deficiency
   - b. Endocrine
     - Acromegaly
     - Thyrotoxicosis
     - Myxedema
     - Uremia
     - Cushing's disease
     - Pheochromocytoma
     - Diabetes mellitus
   - c. Altered metabolism
     - Gout
     - Oxalosis
     - Porphyria
   - d. Electrolyte imbalance

3. Toxic
   - a. Cobalt
   - b. Alcohol
   - c. Bleomycin
   - d. Adriamycin
   - e. Phenothiazines & antidepressants
   - f. Antimony compounds
   - g. Carbon monoxide
   - h. Lead
   - i. Emetine & dehydroemetine
   - j. Chloroquinine
   - k. Lithium
   - l. Cyclophosphamide
   - m. Hydrocarbons
   - n. Catecholamines
   - o. Phosphorus
   - p. Mercury
   - q. Insect stings
   - r. Snake bites
   - s. Paracetamol
   - t. Reserpine
   - u. Corticosteroids
   - v. Cocaine
   - w. Methysergide

4. Infiltrative
   - a. Amyloidosis
   - b. Hemochromatosis
   - c. Neoplastic
   - d. Glycogen storage disorders
   - e. Sarcoidosis
   - f. Mucopolysaccaridosis
   - g. Fabry disease
   - h. Whipple disease
   - i. Gaucher disease
   - j. Sphingolipidosis

5. Fibroplastic
   - a. Endomyocardial fibrosis
   - b. Endocardial fibroelastosis
   - c. Loeffler's fibroplastic endocarditis
   - d. Carcinoid

6. Hematological
   - a. Sickle cell anemia
   - b. Polycythemia vera
   - c. Thrombotic thrombocytopenic purpura
   - d. Leukemia

7. Hypersensitivity
   - a. Methyldopa
   - b. Penicillin
   - c. Sulfonamides
   - d. Tetracycline
   - e. Phenindione
   - f. Phenylbutazone
   - g. Antituberculous drugs
   - h. Giant cell myocarditis
   - i. Cardiac transplant rejection

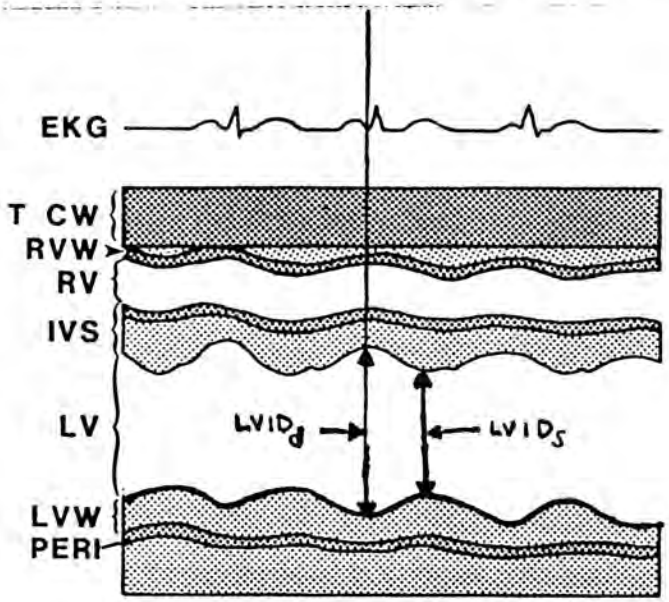
8. Genetic
   - a. Hypertrophic cardiomyopathy
   - b. Neuromuscular

9. Miscellaneous acquired
   - a. Postpartum cardiomyopathy
   - b. Obesity

10. Idiopathic
    - a. Idiopathic dilated cardiomyopathy
    - b. Idiopathic restrictive cardiomyopathy
    - c. Idiopathic hypertrophic cardiomyopathy
    - d. Idiopathic right ventricular cardiomyopathy

11. Physical agents
    - a. Heat stroke
    - b. Hypothermia
    - c. Radiation
    - d. Tachycardia

Figure 1. Schematic of an M-Mode Echocardiogram Showing % Delta D Calculation



$$\% \text{ Delta D} = \frac{\text{LVIDd} - \text{LVIDs}}{\text{LVIDd}} \times 100$$

LVIDd - left ventricular internal diameter in diastole (relaxed phase), LVIDs - left ventricular internal diameter in systole (muscle contraction phase), EKG - electrocardiogram, T - transducer, CW - chest wall, RVW - right ventricular wall, RV - right ventricle, IVS - interventricular septum, LV - left ventricle, LVW - left ventricular wall, PERI - pericardium

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