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Chronic Valve Disease and Left Atrial Splitting in the Dog [Dissertation]

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Appendix 6 has been archived separately from this dissertation. These articles can be found as follows:

6.1 Clinico-Pathologic Conference: Pulmonic Stenosis and Patent Foramen Ovale in a Dog
6.2 Clinico-Pathologic Conference: Chronic Nephritis in a Bull
6.3 Persistent Left Cranial Vena Cava in Dogs: Angiocardiography, Significance, and Coexisting Anomalies
6.4 Endocardial Splitting of the Left Atrium in Dogs with Hemorrhage and Hemopericardium
6.5 Chronic Valvular Fibrosis (see Additional Files below)
6.6 Spontaneous Arrhythmias and Conduction Disturbances in Domestic Animals
6.7 Selective Angiography and Angiocardiography in Dogs with Acquired Cardiovascular Disease [links to publisher record]
6.8 Selective Angiography and Angiocardiography in Dogs with Congenital Cardiovascular Disease [links to publisher record]
6.9 Surgical Treatment of Congenital Cardiovascular Diseases

Chronic Valve Disease and Left Atrial Splitting in the Dog [Dissertation]

Abstract
Age, sex, and breed evaluations of 392 dogs with chronic valve disease (CVD) from a survey of 4,831 dogs revealed a predominance of CVD in purebred male dogs. Male Cocker Spaniels were most frequently affected.

A questionnaire survey concerning aspects of medical history, environment, behavior, and survival was made 3-5 years after initial clinical examinations on 471 dogs. This study revealed no marked differences between dogs with CVD and dogs with no heart disease, except that dogs with CVD more often had signs of congestive heart failure.

Endocardial and endomyocardial splitting of the left atrium occurred in 30 dogs with CVD; primarily in males of the Dachshund and Cocker Spaniel breeds. Left atrial perforation in several of the cases caused hemopericardium or acquired atrial septal defects which could be diagnosed by clinical means. The cause of splitting was considered to be left atrial dilatation with left atrial degeneration playing primarily a permissive role. Lipid deposition in the endocardium and ruptured chordae tendineae was found in preliminary frozen section studies. A method of postmortem cardiotomy was developed which permitted recognition of spontaneously ruptured cordae tendineae were frequently found in dogs with severe chronic valve disease with or without left atrial splitting.

The Dachshund, Cocker Spaniel, and Beagle breeds in varying order constituted the three most common breeds with CVD, left atrial splitting or the intervertebral disc syndrome. This finding was suggestive of an underlying connective tissue disorder predominant in those breeds which have been classified by others as belonging to a "chondrodystrophoid" group.

Radiographic studies of dogs with left atrial enlargement revealed a characteristic bulge in the dorsoventral cardiac silhouette caused by dilatation of the left atrial appendage. This was most apparent in dogs with left atrial splitting.

Clinical and pathological studies on 60 "hyperimmune" dogs from which blood was withdrawn by cardiocentesis for immune serum production revealed serious heart disease in nearly all dogs. This was considered the results of weekly cardiocentesis for periods up to three years rather than the results of repeated vaccinations during this time.

Disciplines
Cardiology | Medicine and Health Sciences | Veterinary Medicine

Comments
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6.9 Surgical Treatment of Congenital Cardiovascular Diseases

6.10 Cardiac Tamponade During Catheterization of a Dog with Congenital Heart Disease

6.11 Aortic Embolism in Cats: Prevalence, Surgical Treatment and Electrocardiography

6.12 Patent Ductus Arteriosus Surgery in Dogs Weighing 490 to 3200 Grams

6.13 Experimental Studies on Ectopic Atrial Rhythms in Dogs

Chronic Valve Disease and Left Atrial Splitting in the Dog*

by

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** Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania toward the requirements for the degree of Master of Medical Science (M.Sc. (Med.)) for graduate work in cardiology.

D.K. Detweiler

Sponsor: D.K. Detweiler

This thesis was written for the sake
and at the expense of my family;
I dedicate it to God, Marolyn,
Scott, Mike, Maureen and Danny.

ACKNOWLEDGEMENTS

The author wishes to express his appreciation to Drs. D.K. Detweiler, D.F. Patterson, K. Hubben, and R.P. Botts, and to Mrs. Joyce Bradley for making available data they had accumulated from a survey of 5,000 dogs, an additional evaluation of which constitutes part of this thesis; to Miss Sue Wallenius for her assistance in the questionnaire survey; to Dr. R.P. Botts for his assistance in examining the group of dogs used for immune serum production; to Drs. D. Cohen and D. Abt for their suggestions regarding epidemiologic portions of this thesis; to Drs. A. Kelly and H. Luginbühl for the assistance they gave in aspects of pathology and photography; to other staff members in the Comparative Cardiovascular Studies Unit for their work on some of the cases presented in this thesis; and to many others in the University of Pennsylvania School of Veterinary Medicine, whose cooperation directly or indirectly made possible the completion of this thesis.

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PREFACE

For the sake of continuity in reading the manuscript portion of this thesis, all tables, illustrations, and example case histories have been removed from the results section and grouped into various appendices. The first number for each table or figure in the text indicates the appropriate appendix, and the decimal identifies its position therein: Table 2.4 refers to Appendix II, table 4; Figure 3.12 refers to Appendix III, figure 12.

Reprints of published articles are included in the last appendix to illustrate various types of papers which were written in forms intended for publication.

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* Previously published with permission in papers included in Appendix VI. Thesis illustrations were obtained from reprints to reduce photographic costs.

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Reprints and Abstracts

1. Clinico-Pathologic Conference: Pulmonic Stenosis and Patent Foramen Ovale in a Dog. 1961

2. Clinico-Pathologic Conference: Chronic Nephritis in a Bull. 1961

3. Persistent Left Cranial Vena Cava in Dogs: Angiocardiography, Significance, and Co-existing Anomalies. 1963

4. Endocardial Splitting of the Left Atrium in Dogs with Hemorrhage and Hemopericardium. 1964

5. Chronic Valvular Fibrosis. 1964

6. Spontaneous Arrhythmias and Conduction Disturbances in Domestic Animals. 1965

7. Selective Angiography and Angiocardiography in Dogs with Acquired Cardiovascular Disease. 1965

8. Selective Angiography and Angiocardiography in Dogs with Congenital Cardiovascular Disease. 1965

9. Surgical Treatment of Congenital Cardiovascular Diseases. 1966

10. Cardiac Tamponade During Catheterization of a Dog with Congenital Heart Disease. 1966

11. Aortic Embolism in Cats: Prevalence, Surgical Treatment, and Electrocardiography. 1966

12. Patent Ductus Arteriosus Surgery in Dogs Weighing 490 - 3200 Grams. 1966

13. Experimental Studies on Ectopic Atrial Rhythms in Dogs. 1966

INTRODUCTION

Chronic valve disease (CVD) in dogs is a diagnostic term used in a specific sense for diffuse or nodular thickening of the heart valves due to chronic fibrosis (Fig. 3.4). It involves mainly the mitral valve either alone or in combination with the tricuspid valve. It is the most frequent canine heart lesion and occurs more commonly in middle aged and older dogs. The cause of this change is unknown although aging must have some etiologic or pathogenetic effect. The line of distinction between slight valve opacification compatible with normal aging and pathologic thickening and distortion is not clear. Degeneration and rupture of chordae tendineae are often found in advanced stages of chronic valve disease; however, shortening and fusion of chordae tendineae and fusion of valve commissures almost never occur.

The pathophysiologic effect of chronic valve disease alone or in combination with ruptured chordae tendineae or ventricular dilatation is the development of atrioventricular valve insufficiency. Mitral or tricuspid stenosis almost never occurs. Valvular insufficiency often leads to left heart enlargement, arrhythmias, and congestive heart failure in combination with myocardial disease.

Previous studies of chronic valve disease in dogs have emphasized clinical diagnosis, pathologic description, clinicopathologic correlations, prevalence of disease, frequency of valve involvement, and hemodynamic effects. Various etiologic factors have been proposed. These include chronic inflammation, hyperimmune mechanisms, previous bacterial endocarditis, degenerative valve sclerosis, and others.

To obtain more information about chronic valve disease which might be helpful in clarifying its etiology, epidemiologic studies were carried

out. These included a retrospective evaluation of the age, sex, and breed distribution of 392 dogs with chronic valve disease out of a hospital clinic population sample of 4,831 dogs. A 3 to 5 year post-examination survey was also made by means of mailed questionnaires to the owners of 1,390 dogs; and a preliminary comparative breed study was made of dogs with one of three chronic diseases apparently involving connective tissue.

In the course of clinical examinations of approximately 2,000 dogs and pathologic examinations of about 400 (mostly preselected) canine hearts, 30 cases of endocardial or endomyocardial splitting of the left atrium were detected in dogs with mitral insufficiency. These dogs had in common severe chronic mitral valve disease with usually one or more broken chordae tendineae, marked left atrial enlargement, and endocardial degeneration. In 9 of the animals, a split perforated the left atrial wall and resulted in hemopericardium. In 4 others, spontaneous acquired atrial septal defects occurred. Twenty-six of the dogs (86 %) were males and breed predilections were noted.

Although endocardial degeneration was consistently present in these dogs, the main cause of splitting was considered to be left atrial dilatation. Degenerative changes in the endocardium were considered more important in determining the locations of the splits. This tentative conclusion was based upon the additional necropsy finding of left atrial splitting in a few young dogs with patent ductus arteriosus and a dilated left atrium. Left atrial splitting apparently does not occur in man even though greater degrees of

left atrial enlargement exist over longer periods of time.

A report of the clinical and radiographic features of hemopericardium in 7 out of the first 22 dogs with left atrial splitting has been published including preliminary pathologic obeservations. Eight additional dogs with left atrial splitting have been observed and more extensive pathologic studies have been made.

Since the clinical aspects of left atrial splitting have not been described by others in the literature, illustrations of the clinical syndromes observed and related gross pathologic findings are included as a part of this thesis. The radiographic and angiocardiographic features of left atrial enlargement in dogs will also be presented.

Because hyperimmunity has been proposed as a possible factor in the development of chronic valve disease, clinical and pathologic studies were made on 60 dogs used for commercial "hyperimmune" antiserum production. This study proved to be of no value in assessing the role of hyperimmunity because of the pathologic effects of direct cardiac punctures with a 13 gauge needle once a week for periods up to 3 years. However, the auscultatory and electrocardiographic changes associated with 10 to 200 punctures of the heart merit reporting.

LITERATURE REVIEW

A. Chronic valve disease

The normal histology of the cardiac valves in dogs and the gross and histologic features of chronic valve disease have been described by several authors; they have been reviewed recently (6 ,26 ,33 , 52,).

Frater and Ellis (19) reported on the gross anatomy of the mitral valve in the dog and compared their findings in this species with observations in man and several other animals emphasizing aspects of surgical importance.

Epidemiologic studies have established that chronic valve disease is the most common acquired cardiovascular lesion in dogs; increases in frequency with age; and affects primarily the atrioventricular valves (especially the mitral valve). Involvement of the aortic or pulmonic valves occurs much less commonly. In a screening survey of 4,831 dogs in a veterinary clinic, reliable evidence of cardiovascular disease was found in 545 animals (11.3 %). Seventy-two percent of the latter dogs had clinical or postmortem evidence of chronic valve disease. These and other findings in this survey have been published in detail in several articles which are cited in a recent paper summarizing the results (15). Using similar clinical criteria, Pensinger (44) found the same frequency of chronic valve disease (73 %) in 142 dogs with reliable evidence of heart disease.

Bretschneider (6) evaluated necropsy records on 3,245 dogs. He found reports of valvular endocarditis in 688 animals. Chronic valve disease ("endocarditis chronica fibrosa") constituted the most common type of lesion observed; it was present in 573 (83.3 %) of the dogs

with some type of valvular endocarditis and in 17.7 % of all the dogs necropsied. The frequencies of valve involvement (all forms of endocarditis included) were as follows: mitral alone, 57.3 %; mitral and tricuspid, 26.6 %; tricuspid alone, 7.5 %; aortic alone, 2.1 %; pulmonic alone, 0.4 %; other combinations of valves, 6.1 %.

Bretschneider also examined histologically the mitral and tricuspid valves of 103 dogs diagnosed at necropsy as having chronic valve disease. He found that blood vessels almost always extended nearly to the free edge of the valves and regarded "endocarditis chronica fibrosa" as a consequence of serous endocarditis.

Hubben, Patterson, and Botts (24) found valve hematocysts in 1.7 % of 1293 dogs examined postmortem. They considered these to be ectatic dilatations of blood vessels but did not find any relationship between the occurrence of telangiectasis and chronic valve disease.

Harper (22) studied heart valves in man, rabbits, and dogs. He concluded that dog valves normally are vascularized in contrast to man and rabbits whose valves are largely non-vascular.

Von Racknitz (45) investigated the occurrence of blood vessels in normal and fibrosed canine heart valves. This article is cited by title only, because I have been unable to obtain or locate a copy or abstract as of this date.

Angrist and co-workers in recent years have studied canine valves as well as human and rat valves by a variety of techniques including routine histologic stains, enzyme digestion methods and electron

microscopy. They refer to chronic valve disease in dogs as "billowing sail" distortion and consider the sclerotic valve changes in both the dog and man as a degenerative process associated with aging which occurs earlier in some individuals. They regard the process of arteriosclerosis as similar if not identical to the sclerotic change occurring in valves. References to specific aspects of these studies have been summarized recently by Angrist (3).

Jubb and Kennedy (27) prefer the term "endocardiosis" to describe the thickened valves commonly seen in old dogs; they found no evidence of inflammatory changes.

Stünzi (52) also emphasized the noninflammatory nature of chronic valve disease. He tabulated necropsy material over a one-year period and reported "endocarditis valvularis fibrosa", mainly of the atrioventricular valves, in 86 out of 789 dogs (11 %). Because inflammatory changes were absent, bacterial cultures were always negative, and degenerative changes were usually seen, he considered chronic valve disease to be a dystrophic process for the most part.

Jones and Zook (26) reviewed necropsy findings on 404 dogs and reported 139 cases of chronic valve disease. The percentage of affected animals increased linearly with age.

Das and Tashjian (11) observed chronic valve disease in 42 % of 550 dogs at necropsy. The frequency in dogs 0-1 year of age was 3 %; it increased in nearly linear fashion to 70 % in dogs 14 years of age and older. Forty-five percent of males were affected and 38 % of females had the disease. No age and sex adjusted prevalence ratios were given; thus, the significance of possible sex and breed predispositions could

not be evaluated. Because the disease was not confined to aged animals, the authors did not consider it a disease of senile degeneration. They regarded chronic mitral valve fibrosis as "secondary to some primary cardiac pathology".

Andre (2) suggested that chronic valve disease might be the result of increased cardiac work and cardiac dilatation rather than the cause of either. He cited as evidence the work of Lillehei et al. (30) who found valvular endocarditis in dogs in which an arteriovenous fistula had been created.

Munich (41) examined 100 dog hearts with endocardial lesions at necropsy. Although he noted a sex difference (61 males, and 39 females), he regarded this as not significant because he thought more male dogs came to necropsy than females (data not given). He classified the lesions in 92 of the dogs as "endocarditis valvularis chronica nodosa" and considered previous endocarditis as the cause. Primarily the mitral valve alone or in combination with the tricuspid valve was involved. Most of the dogs were over 6 years of age.

Shouse and Meier (50) found "acute vegetative endocarditis" in 40 out of about 600 dogs and cats at necropsy. The number of dogs affected was 27 but the number of dogs examined was not given. The involvement of the cardiac valves in descending order of frequency was mitral, aortic and tricuspid. Based upon the overall frequency of acute vegetative endocarditis (in dogs and cats) in their material (6.6 %), the authors suggested that chronic valve disease in dogs might represent the healed phase of this process.

Lundh (33) reviewed necropsy reports on 11,574 dogs and tabulated 67 cases (0.58 %) with fibrinous endocarditis. He considered this term analogous to that of acute vegetative endocarditis used by Shouse and Meier (50) and found the same order of valve involvement as in their series; i.e., mitral, aortic, and tricuspid. In neither series were the pulmonic valves found to be affected. Lundh demonstrated a predisposition for fibrinous endocarditis in the German Shepherd breed but found no evidence for a sex predisposition. He used the term "fibrous valvular endocarditis" for dogs with chronic valve disease and cited the pattern of valve involvement (mitral and tricuspid primarily) as evidence against this being usually the result of previous fibrinous endocarditis.

Miller, Pick, and Katz (37) were able to produce a degree of endomyocardial fibroelastosis in dogs by ligating the major lymphatics leading from the heart. They also noted opacification of mitral valve leaflets. In a subsequent article (38), they reported an increased size and number of thin-walled vessels in the mitral valve which they regarded as dilated lymphatics as a consequence of experimentally impaired cardiac lymphatic drainage. They suggested a possible association between chronic valve disease and spontaneous lymphatic obstruction. Later (39) they revised their statements in this regard and considered unlikely the possibility of such a relationship. They did find, however, that chronic lymphatic obstruction made dogs more susceptible to bacterial endocarditis. More recently (28), they found dilated lymphatics in two human patients with endocardial fibroelastosis; they emphasized lymphatic obstruction as a likely cause of this disease.

Symbas et al. (54) interrupted the cardiac lymphatics in dogs and demonstrated valve thickening consisting of edema and moderate to marked basophilic mesenchymal changes within 16-40 days.

Johnson and Blake (25) also studied valve lymphatics in man, dogs, and pigs. They suggested that dilated lymphatics may be the result of fibrosis and thickening of the valves; however, they also suggested a possible role of the lymphatics in the spread of inflammation throughout the valves in cases of rheumatic fever or bacterial endocarditis.

B. Aging

All reports of chronic valve disease in dogs have indicated an increasing frequency associated with aging. Although a complete search of the literature was not made for all cardiovascular aspects of aging, several references in this regard were found.

Nakao et al. (42) reported the results of an electron microscopic study of the aging process in the rat heart valve. They emphasized changes in structure and orientation of collagen and elastic fibers. This was a detailed report of work in progress mentioned by Angrist (3) in a paper on aging heart valves and a unitary pathological hypothesis for sclerosis.

McMillan and Lev reported on aging changes in the heart in a series of papers including one on the endocardium (35), and one on the valves (36). Aging changes in the aortic and mitral valves were also reported recently by Sell and Scully (49).

Lapin and Yakovleva, in a book on comparative pathology in monkeys (29), reported a systematic investigation of the valve structure in 39 monkeys of different ages in order to determine the changes associated with aging and form a basis for evaluating pathological changes in other monkeys.

Moretti (40) found differences in mucopolysaccharide compositon in a comparison of heart valves in calves and adult cattle. Changes in mitral valve mucopolysaccharides in man associated with aging were reported recently by Trnavsky et al. (55).

Visscher and Henschel (56) studied the relation of age and other factors in the occurrence of subendothelial hemorrhage in canine hearts following the injection of pitressin or epinephrine. They noted that the mitral valve appeared to be a predilection site for subendothelial hemorrhage and they found the incidence in dogs over 5 years of age to be over three times as great as in animals under 3 years of age.

Sokoloff et al. (51) studied mitral valve chordae tendineae in 200 nonrheumatic human hearts and 50 bovine hearts. Since the authors did not find evidence of posterior leaflet chordae tendineae sclerosis, they used the average length of posterior leaflet chordae as a reference and compared to this the diameter of the largest chorda of the anterior leaflet. On this basis, they found 11 instances of thicker than normal anterior leaflet chordae and distinguished two types; one in which the chordae had a normal structural pattern, and the other in which acquired, sclerotic thickening was present. Both types involved secondary (central) chordae tendineae, and the authors regarded mechanical factors as the probable cause of the changes.

C. Left atrial splitting

Stünzi and Teuscher (53) reviewed causes of cardiac rupture in various species of animals. In the dog, they reported the left atrium as the most common site of rupture, particularly in animals with chronic mitral insufficiency. They mentioned seeing more cases in Dachshunds and

considered atrial myocardial disease as the cause of rupture.

Buchanan and Kelly (7) reported the clinical and radiographic features of hemopericardium due to left atrial hemorrhage in 7 out of a series of 22 dogs with endocardial and endomyocardial splitting of the left atrium.

Das and Tashjian (11) and Pensinger (44) also reported seeing occasional instances of left atrial "tears" in dogs with mitral insufficiency.

Jubb and Kennedy (27) reviewed the causes of mural endocarditis in dogs. They recognized a form of endocardial ulceration in the left atrium associated with intimal changes in certain arteries (mucoarteritis) as described by McGill et al. (34) in dogs with induced renal failure. Jubb and Kennedy considered the instances of left atrial hemorrhage and hemopericardium which they observed in dogs, to be a result of endocardial ulceration associated with uremia.

MATERIALS AND METHODS

A. Epidemiology

1. Survey of 4,831 dogs (Appendix I)

Studies were made of the age, sex, and breed distributions of 392 dogs with chronic valve disease. These dogs were detected in a cardiovascular screening survey of 4,831 dogs at the University of Pennsylvania School of Veterinary Medicine Hospital and Clinic (14). An additional 169 dogs were examined in this survey (total 5,000), but were excluded from tabulation because they had been referred to the clinic as heart disease patients.

All dogs except emergency cases presented to the clinic from January 1958 to July 1960, were given a brief cardiovascular examination consisting of auscultation, palpation of the precordium, palpation of the femoral arteries, and a single lead electrocardiogram. When possible, animals with definite or possible heart disease were studied further by recording a 10 lead electrocardiogram and by thoracic radiography. Selected cases were studied further by phonocardiography, cardiac catheterization, and angiocardiography. Post mortem examinations were performed when permitted on all animals which died during the period of the survey. More detailed descriptions of examination methods, diagnostic criteria for specific diseases, and results other than those in this thesis have been published previously (15).

The diagnosis of chronic valve disease was based upon clinical signs alone in 212 dogs and post mortem evidence in 180 dogs. A clinical diagnosis of chronic valve disease was made in dogs which had at least a grade 3 (out of 5) holosystolic murmur in either the mitral (left 5th or 6th intercostal space near sternum) or tricuspid

(right 4th intercostal space near costochondral junction) precordial areas and no evidence of anemia or infection. It was also made in a few cases when grade 2 systolic murmurs were heard in the same areas in dogs which had radiographic evidence of left or right heart enlargement.

2. Questionnaire (Appendix II)

Additional data on 471 dogs with definite, possible or no heart disease were obtained 3-5 years after initial cardiovascular examinations in the 5,000 dog survey (including referred cases). This information was derived from mailed questionnaires concerning medical history, survival time, cause of death, environmental history, and behavioral patterns. Cover letters, questionnaires, and self-addressed return envelopes were sent to the owners of 1,390 dogs in 4 groups. Group A: dogs examined clinically and at necropsy in the 5,000 dog survey. Group B: dogs examined only clinically which had reliable signs of heart disease and were alive, lost to study, or dead but not necropsied. Group C: dogs examined clinically which had signs of possible heart disease. Group D: similar sized sample of dogs 5 years of age and older with no clinical evidence of heart disease.

Evaluation of the initial questionnaire format was made when 50 completed forms were returned and tabulated. A few points of omission or potential misinterpretation by the questioner or questionee were identified and corrected in preparing a final format. This consisted of providing a list of common canine diseases in the medical history section of the final format rather than just asking

what illnesses the dog had had. Common signs of congestive heart failure were also added in the final version. In addition, it appeared necessary to ask specifically if dogs had died spontaneously or had been euthanatized.

Of the total questionnaires tabulated, 55 (11.7%) were of the initial format and 416 (88.3%) were of the final version. Where these differed, tabulations were based upon the final format. Questionnaires on 115 dogs with reliable evidence of chronic valve disease were used for group comparison with 110 dogs over 5 years of age with no clinical evidence of heart disease. In 33 of the 115 dogs in the chronic valve disease group, post mortem examinations had been performed which confirmed the clinical diagnosis.

All returned questionnaires were interpreted and tabulated by one person, and the data were punched by case number on Termatrex* characteristic cards. A photosensitive automatic counter* was used to determine the number of case entries on each card and those remaining with selected overlays. Comparisons were made between total males and females for each characteristic as well as male and female subgroupings of dogs with no heart disease and dogs with chronic valve disease.

The number of positive answers for each item in the questionnaire was converted to a group percentage for ease in making comparisons. Certain questions almost always elicited either a "yes" or "no" response. In these instances, "yes" and "no" answers were tabulated separately and the percentage of positive answers was obtained by dividing the number

*Jonker Corp., Gaithersburg, Maryland

of "yes" responses by the total number of "yes" and "no" answers. The denominator in each instance represented approximately 95% of the total dogs.

Some "yes or no" type questions were frequently answered by a check mark which, based upon the overall patterns of response, consistently indicated an affirmative reply and was tabulated as such. In these cases, the absence of a check mark was not tabulated since it could mean either a negative reply or no response. The percent positive answers for questions of this type were obtained by dividing the number of positive responses by the number of dogs in each group.

The percent of positive answers for individual items in multiple choice type questions with two or more suggested responses was obtained by dividing the number of positive responses for each multiple choice item by the total responses to the stem question. This denominator was usually 2-10% larger than the total number of dogs because more than one response was sometimes selected in answering the stem question.

Survival data were based upon average ages at initial cardiovascular examinations and were subdivided according to live or dead status at the time of the questionnaire and also by cause of death, i.e., whether died spontaneously or were euthanatized. The interpreted causes of spontaneous death or indications for euthanasia were based upon the owner's descriptions or statements accordingly and were listed as possible or probable congestive heart failure; other cause; or no cause given.

3. Split left atrium (Appendix III)

Left atrial splitting was confirmed or detected at necropsy in 30 dogs with chronic valve disease from 1961 to 1966. The Dachshund and Cocker Spaniel breeds accounted for most of the cases. The only other purebred dogs encountered in this series were Poodles and one Beagle. A predominance of males (86 %) was noted. The significance of these apparent breed and sex predilections was tested by comparison with the breed and sex distribution of dogs of similar age in the Veterinary Clinic population.

A similar breed distribution study of chronic valve disease was made based upon data obtained in the survey of 4,831 dogs in 1958-1960. For this purpose, the breed and sex distribution of dogs with chronic valve disease, 5 years of age and older, was compared with that of the clinic population of the same age and during the same period (1958-60). The disease and clinic population comparison was made using dogs 5 years of age and older, because this subgroup included 93 % of the dogs with chronic valve disease and lessened the effect of differences in the average ages of each breed at the time of examination.

Because clinical experience suggested similar breed predilections, the sex and breed distributions of dogs with left atrial splitting were also compared with those of dogs diagnosed as having the intervertebral disc syndrome (cervical or thoracolumbar intervertebral disc protrusion, herniation, loss of joint space or calcification with signs of neck or back pain, and paresis or paralysis). Data on dogs with the latter syndrome were obtained from hospital records entered into the Termatrex data coding and retrieval system from July 1963 to December 1965.

MATERIALS AND METHODS

B. Clinical and Pathologic Studies

1. Dogs with left atrial splitting

Clinical examinations including auscultation, palpation, electrocardiography, and radiography were performed at least once in 25 out of 30 dogs with chronic valve disease, left atrial dilatation, and endocardial or endomyocardial splitting at necropsy.

The clinical and radiographic features of dogs with left atrial splitting and hemopericardium were compared with the clinical and radiographic features of dogs with other causes of hemopericardium to develop criteria for differential diagnosis in dogs with sanguineous pericardial effusion.

The histories and clinical findings in 3 dogs with acquired atrial septal defects at necropsy were reviewed and led to a correct clinical diagnosis of the same condition in another dog which was examined 20 times over a period of 20 months prior to necropsy. Clinical studies done on this animal included repeated blood analyses, many electrocardiograms and radiographs, two cardiac catheterizations for pressure and oxygen determinations, and one series each of lateral and dorsoventral angiocardiograms.

2. Radiography and angiocardiography of left atrial enlargement

An undiagnosed prominence was observed in the left craniolateral segment of the cardiac silhouette in dorsoventral radiographs of several dogs with clinically severe mitral insufficiency or patent ductus arteriosus. To determine if this prominence was usually caused by a dilated left atrial appendage, studies were made by oblique radiography or angiocardiography, and surgical or necropsy examinations.

3. Hyperimmune dogs

Acute valvulitis has been induced by injections of antigen into appropriately immunized animals (57). In similar fashion, dogs used by drug companies for immune serum production are repeatedly inoculated with antigens to maintain high serum antibody titers. To investigate the role of antigen-antibody reactions in the genesis of chronic valve disease, studies were made of a group of these dogs to determine the types and prevalence of heart disease. A screening examination consisting of auscultation, palpation, and electrocardiography was carried out on 60 large, mature dogs used for canine "hyperimmune" antiserum production for an average of 1.5 years by a commercial drug company.*

When obtained, all dogs were inoculated weekly with attenuated live Distemper and Hepatitis vaccines, and a killed Leptospirosis vaccine. One month after isolation and initial vaccination, the dogs were entered into the group used for serum production. High antibody titers were maintained with subsequent biweekly or monthly vaccinations. Blood was withdrawn once a week by one and sometimes 2 or 3 direct cardiac punctures with a 13 gauge needle in the lower right 5-8th intercostal spaces.

The hearts of 22 dogs which died at a later date were received by mail and examined grossly. Microscopic studies were not done because the hearts were submitted for examination in a semi-frozen state and the condition of each specimen was unacceptable for histology.

* Lederle Laboratories, American Cyanamid Co., Pearl River, New York.

RESULTS

A. Epidemiology

1. Material from a survey of 4,831 dogs (Appendix I)

The previously published age, sex, and breed distribution of 4,831 dogs specifically examined to determine the presence of cardiovascular disease in a veterinary hospital clinic population is reproduced here with permission for reference purposes (Table 1.1). The prevalence ratio of chronic valve disease (CVD) in this population was 81/1000 based on clinical diagnoses plus post mortem findings on 284 of the dogs (15).

Further evaluation of the age, sex, and breed distribution of 392 dogs with chronic valve disease detected in the above survey yielded the following results:

1. The Cocker Spaniel breed had the highest prevalence ratio of CVD (Table 1.2)
2. The disease was more common in males than in females (Table 1.3).
3. CVD increased in frequency with age, ranging from 2/1000 in female dogs under one year of age to 417/1000 in male dogs 13 years of age and older. In each age group, the prevalence ratio in males was higher than in females (Table 1.4).
4. In each age group, the prevalence ratio of CVD was greater in male Cocker Spaniels than in other dogs (Table 1.5).
5. The frequency of CVD was greater in purebred than in mongrel dogs (Table 1.6).
6. When Cocker Spaniels were excluded, the frequency of chronic valve disease in purebreds was not significantly greater than in mongrel dogs ($P > .10$) unless subdivided by sex: Male purebreds, excluding Cocker Spaniels, still had a higher frequency of CVD than male mongrel dogs (Table 1.7).

7. The high prevalence of CVD in Cocker Spaniels resulted from a particularly high frequency in males of this breed; however, female Cocker Spaniels had a higher rate of CVD than other females (Table 1.8).

8. The high prevalence ratio of CVD in male Cocker Spaniels corresponded well with published data on the high frequency of congestive heart failure in male Cocker Spaniels (Table 1.9) (15).

9. The mitral valve was most commonly involved either alone or in combination with the tricuspid valve in 230 hearts examined at necropsy (Table 1.10).

2. Questionnaire (Appendix II)

Cover letters, questionnaires and self addressed return envelopes were sent by first class mail to the owners of 1,390 dogs initially examined between January 1958 and July 1960 (examples shown in Appendix II). This total included approximately equal numbers of dogs diagnosed as having definite, possible or no heart disease. The majority of the questionnaires were mailed in August, 1963 with some mailed in July and September of 1963. Because of insufficient address, change of address or other reasons indicated by the postal service, 219 envelopes were returned unopened. Of the remaining 1,171 questionnaires which apparently reached the addressee, 492 were returned as requested for an actual response of 42 %. The return rate for dogs with reliable signs of heart disease was 48 % and that for dogs with no evidence of heart disease was 40 %. A total of 21 questionnaires including some from each group were eliminated before tabulation because they were incomplete, the identity or age of the animal was questionable or the dogs were under 5 years of age and were rejected from the no heart disease control group by definition (5 years of age or older).

The results of 471 tabulated questionnaires are presented in tables 2.1-2.9 according to various categories:

Tables 2.1 + 2.2: Medical history

Table 2.3 : Environment

Tables 2.4 + 2.5: Individual behavioral characteristics

Table 2.6 : Aggressive behavior patterns

Table 2.7 : Nervous behavior patterns

Table 2.8 : Percent survival and cause of death

Table 2.9 : Survival time

Tables 2.6, 2.7 and 2.9 include the data on the control group of dogs which had no evidence of heart disease when examined at five years of age and older (N = 110) and dogs with reliable evidence of chronic valve disease (N = 115). All other tables include the responses for all the dogs (N = 471) in addition to the above subgroups.

The data are expressed as the percent of dogs in each group for which positive (affirmative) responses were given for the indicated characteristic. At the top of each of 10 columns are the numbers of dogs upon which the percentages were based. Also at the top of the first 6 columns are the average group ages at the time of initial examination.

	Groups	Number of dogs
Column 1:	Male dogs with no heart disease	55
" 2:	Male dogs with chronic valve disease	75
" 3:	All male dogs tabulated*	265
Column 4:	Female dogs with no heart disease	55
" 5:	Female dogs with chronic valve disease	40
" 6:	All female dogs tabulated*	206
Column 7:	Total dogs with no heart disease	110
" 8:	Total dogs with chronic valve disease	115
" 9:	Sex adjusted values for Col. 8	115
" 10:	Sex adjusted values for all dogs*	471

* Includes dogs with no heart disease, chronic valve disease, other heart disease and possible heart disease.

The average age of dogs in the no heart disease group (N = 110) was 9.0 years (range 5-15 years). There were equal numbers of males and females without preselection of mailed questionnaires for this purpose. Although these dogs did not have evidence of heart disease, they could not be called a group of normal dogs since most of them had been brought to the veterinary clinic because of some type of illness.

The average age of dogs in the chronic valve disease group (N = 115) was 10.8 years (range 2-18 years). Ten of them had been referred to the clinic initially because of heart disease. There were 75 males and 40 females; therefore, disease specific (non-adjusted) as well as sex adjusted determinations were made. An adjustment for sex was considered necessary to make meaningful comparisons of a few characteristics where sex differences were quite marked. For example, the percentage of spayed females was about 7 times that of castrated males. Although the sex differences in other characteristics were less obvious, the 1:1 sex adjusted values for all percentages in the chronic valve disease group were considered more reliable than unadjusted percentages for comparison with the no heart disease group where the sex ratio was 1:1 without adjustment.

The average age at the time of initial examination of all the dogs tabulated (N = 471) was 8.8 years (range 6 months - 18 years). This group included approximately equal numbers of dogs with definite heart disease, possible heart disease and no heart disease.

The number of dogs in some of the groups in Table 2.2 was less than in the other tables because of the change in questionnaire format. The questions in Table 2.2 were not asked in the initial format; therefore, these group percentages were based upon the final format tabulations.

Comparisons were made between dogs with no heart disease (No HD) and chronic valve disease (CVD), and between male and female dogs. Statistical significance was ascribed to differences in which the probability of their occurrence due to chance was less than 5 %.

Medical history (Tables 2.1 and 2.2)

More female dogs (49.3 % of the total) were castrated than were male dogs (6.3 %); $P < .001$. When males and females were combined, a significantly greater percentage of dogs with No HD had been castrated than dogs with CVD (Columns 7 and 8); $P < .02$. This difference became slightly less than significant when adjustment for sex was made to take into consideration the fact that there were more males than females in the CVD group (comparison of columns 7 and 9). If this trend was present in samples of twice the size of the above subgroups, the difference in castration percentages would be significant.

No differences were found between sex or disease groupings with regard to at least one distemper or rabies vaccination. The number of vaccinations which individual animals had received was not tabulated because many owners did not provide a record of this. Tabulation of hepatitis and leptospirosis vaccinations was not made because many owners did not know what vaccines had been given other than distemper and rabies.

With regard to reproduction, the owners often did not indicate the number of times female dogs had had a litter of puppies. Tabulation was limited therefore, to whether or not a bitch had whelped at least one litter of pups. This was true of about 35 % of female dogs regardless of grouping.

The question whether or not dogs had been hit by a car originated from postmortem observations in a few dogs killed in this manner. A band of hemorrhage was sometimes found in the contact surfaces of the mitral valve at the usual site of chronic valvular fibrosis in other dogs. Tabulation of answers was again restricted because owners often failed to indicate the number of times this event occurred. The values in Table 2.1 indicate the percentage of dogs which had been hit at least once by a car (20.4 % of all dogs). The frequency of this event in males (24.2 %) was significantly greater than in females (16.5 %); $P < .05$, and probably was related to the greater tendency of males to chase cars. This is discussed later in a section on behavior (Table 2.4). The null hypothesis (no relationship between CVD and being hit by a car) was accepted because of the absence of a significant difference between the frequency of this event in No HD and CVD dogs.

No difference was found between No HD and CVD dogs with regard to changes in body weight or physical condition at the time of the survey or at death; however, a sex difference was noted. Female dogs (33.0 %) gained weight with greater frequency than male dogs (20.5 %) following initial heart examinations; $P < .001$. At the time of survey or death, female dogs were considered overweight by their owners (33.9 %) more often than were male dogs (17.0 %); $P < .001$. More male dogs (23.1 %) were considered "thin" than were female dogs (15.3 %); $P < .05$.

Signs of possible or probable congestive heart failure were reported much more common in dogs with CVD (44.6 %) than in dogs with No HD (8.2 %); $P < .001$. This obvious difference was anticipated since CVD was the most common lesion found in dogs with congestive heart failure in the clinic

population sample from which both groups of animals were selected. No difference between males and females was observed.

Signs of heart disease were slightly more common in relatives of dogs with CVD than in No HD dogs; the difference, however, was not significant.

The percentages of dogs having signs of common medical problems are presented in Table 2.2. No significant differences were found between dogs with No HD and CVD (columns 7 and 9), other than individual signs often seen in dogs with left sided congestive heart failure (coughing and dyspnea).

Tumors (any abnormal growth whether benign or malignant) were reported more frequently in dogs with No HD than with CVD. Although not quite significant in this case, a difference in this direction could be anticipated since both tumors and heart disease occur more commonly in older animals. These constitute common reasons why owners bring older dogs in for medical attention. If dogs with the most common type of heart disease (CVD) are segregated and compared to other old dogs without heart disease brought to a veterinary hospital, a higher percentage of tumors in the latter group is not surprising. The percentage of tumors in female dogs (48.6 %) was greater than in male dogs (30.0 %); $P < .001$. The chief reason for this was a higher prevalence of mammary tumors in females.

Comments on other differences between various subgroups (columns 1 to 6 of Table 2.2) are not considered worthwhile because the number of dogs in each of the subgroups is small, age differences exist, and the positive as well as the negative diagnosis of noncardiac problems was based upon the owner's ability to recall.

If the above limitations are equally applicable to the replies of owners of dogs with No HD and dogs with CVD, no meaningful difference was found with regard to those aspects of medical history which were evaluated by means of this questionnaire.

Environmental comparisons (Table 2.3)

No environmental differences were found between dogs with No HD and dogs with CVD. In a comparison between all males and all females, it was noted that males were used for hunting purposes more often than females; $P < .02$.

Behavior (Tables 2.4-2.7)

Individual behavioral characteristics are listed in Tables 2.4 and 2.5. No differences were found between dogs with No HD and dogs with CVD except for one characteristic of questionable significance. Dogs with No HD (54.5 %) barked at familiar people more often than did dogs with CVD (40.1 %); $P < .05$. This feature was suggestive of a possible difference in temperament between dogs with No HD and dogs with CVD; therefore, certain questions were grouped in an effort to develop an "aggresive index" and a "nervous index" for more meaningful comparisons.

Six questions were selected from Tables 2.4 and 2.5 for which positive answers were considered compatible with an aggressive tendency (Table 2.6). Data tabulations were then reviewed to obtain the number of dogs for which affirmative responses were given for any of the six questions selected. Of the dogs with No HD, 37.3 % had positive replies for at least three of the six items (aggressive index of 0.5). This was not significantly different than the sex adjusted value of 33.9 % obtained for dogs with CVD. A distinct difference was noted between males and

females: 45.9 % of the combined male dogs had an 0.5 aggressive index, whereas only 25.2 % of the female dogs had a similar index. Because of this difference, sex adjusted values were used in the preceding group comparisons.

A similar procedure was used to evaluate nervous behavior patterns. For this purpose, five items were selected from Tables 2.4 and 2.5 which seemed to reflect nervous tendencies (Table 2.7). Of the dogs with No HD, 22.7 % had positive replies for at least three of the five items (nervous index 0.6). This was not significantly different from the CVD group in which the sex adjusted percentage was 17.2 %. A nervous index of 0.6 was found in 22.6 % of the combined males and in 17.3 % of the females.

On the basis of comparisons of individual and grouped behavioral characteristics, a trend can be said to exist for dogs with chronic valve disease to be less aggressive and less nervous than dogs with no heart disease. Whether this tenuous observation should be relegated to a cause or effect status is open to speculation.

Survival (Table 2.8)

Classical epidemiologic methods for presenting survival data in human patients were not considered appropriate in this study because the majority of dogs which died were killed by euthanasia. Of the total dead dogs tabulated (331 dogs), euthanasia had been performed in nearly 60 %. In most instances this was done because of illness and perhaps in the majority of the dogs, spontaneous death would have occurred within a matter of days or weeks. In a substantial number, however, euthanasia was performed for economic and other reasons when it was probable that the animals might have survived for periods of months or years with treatment.

An additional problem in evaluating these data stems from the fact that necropsy examinations were seldom performed. Consequently, the tabulated cause of death or indication for euthanasia was based usually upon the owners' opinion and recollection and is therefore open to an undesirable degree of speculation. Because of all the preceding limitations, data on survival, death, and age are presented in a summary form which seems reasonable and sufficient for the intended purpose and accuracy.

At the time of follow-up survey (an average of 4 years after initial examination), a greater number of dogs with No HD (38.2 %) were still alive than were dogs with CVD (13.0 %). This difference was not surprising since the average age of dogs in the CVD group at the time of initial examination was 10.8 years in contrast to 9.0 years in the former group. No significant sex differences were noted.

Spontaneous deaths were reported in 19.1 % of the dogs with No HD in contrast to 50.7 % of those with CVD; euthanasia was performed in 75.0 % and 44.4 % respectively. The cause of death or reason for euthanasia was tabulated as possible or probable congestive heart failure in 2.9 % of the dogs with No HD and 36.6 % of the dogs with CVD based upon the owner's remarks (see example questionnaire in Appendix II, section on medical history, questions 8 and 10).

Survival (Table 2.9)

Comparison of the percentage of 4-year survivors was considered insufficient for assessing the effect of CVD on the life span of dogs because there were age differences at the time of initial examination and a greater percentage of dogs with No HD were killed by euthanasia than were dogs with CVD. In order to obtain a more adequate evaluation, the No HD dogs and CVD dogs were subdivided according to live or dead status at the time of the questionnaire survey; and the dead dogs were further

divided according to the manner of death; i.e., death by euthanasia or spontaneous death. Comparisons were then made between the various subgroups with respect to age at initial examination, number of years survived, and age at death or time of survey.

As expected, the average age at initial examination was least in those dogs which were still alive at the time of the survey (7.7 years in dogs with No HD and 9.3 years in dogs with CVD at the time of initial examination). The average number of years survived in these groups (4.3 and 3.9 years respectively) was obtained by subtracting the date of initial examination from the date the owners completed the questionnaire or, in the few instances where this was not indicated, from the date the return envelope was postmarked.

With regard to those which died, there was no appreciable difference in survival time between dogs with No HD and dogs with CVD (1.5 and 1.4 years respectively). As a result of the similar periods of survival, the average age at death of the No HD group (11.3 years) was less than that of the CVD group (12.5 years). The younger age at death in the No HD group might be explained by the fact that a greater number of the dogs in this group were killed by euthanasia than in the CVD group. There is reason to doubt this explanation, however, because the ages at death of dogs killed by euthanasia in both groups (No HD, 11.6 years; CVD, 12.7 years) were greater than the average ages at death of those which died spontaneously (11.1 and 12.3 years respectively).

On the basis of the population samples selected and the results presented in Table 2.9, the conclusion was reached that dogs with chronic valve disease do not die spontaneously or by euthanasia at an earlier age than dogs with illnesses other than clinically detectable heart disease, for which middle aged and older dogs are brought to a veterinary hospital.

3. Epidemiology of left atrial splitting (Appendix III-A)

The age, sex, and breed distributions of 30 dogs with spontaneous left atrial splitting are presented in Table 3.1. There were 10 Mongrels, 9 Dachshunds, 8 Cocker Spaniels, 2 Poodles, and 1 Beagle. The marked predominance of males in these 30 dogs (86%) was significantly different than the male to female ratio (1:1) of a similarly aged clinic population sample ($P < .001$; Table 3.2).

The breed distribution of dogs with left atrial splitting also differed from the clinic population sample ($P < .001$; Table 3.3). This difference resulted chiefly from the predominance of Dachshunds and Cocker Spaniels in the 30 dogs observed with left atrial splitting. The number of Dachshunds observed (9) was six times the calculated number expected (1.5) based upon the breed distribution of the clinic population sample. The number of Cocker Spaniels observed (8) was three times the number expected (2.5). Differences between the observed and expected numbers of Mongrels, Poodles and Beagles were not significant.

The breed distribution of 365 dogs with chronic valve disease in another clinic population sample also differed from the expected distribution ($P < .01$; Table 3.4). The chief reason for this difference was a moderate predominance of chronic valve disease in Cocker Spaniels, Beagles, and Dachshunds - in that order. A moderate predominance of males was also observed ($P < .01$; Table 3.4).

The breed distribution of 236 dogs with the intervertebral disc syndrome differed greatly from the expected distribution ($P < .001$; Table 3.5a). The chief reason for this difference was a marked predominance of the disease in Dachshunds (accounting for over half of the cases). The disease was also observed more frequently than expected in Beagles and Cocker

Spaniels. Although significant without adjustment, the higher frequency in Beagles and Cocker Spaniels was more apparent after excluding the Dachshund breed and recalculating the data (Table 3.5b). The sex ratio was normal with or without the exclusion of Dachshunds.

Summaries of the relative breed frequencies of dogs with left atrial splitting, chronic valve disease or the intervertebral disc syndrome are presented in Table 3.6 along with the relative sex predominance. Breeds are listed in the order of decreasing frequency of disease. The breed with the highest frequency of disease is listed first in each column. Dachshunds, Cocker Spaniels and Beagles in various order account for the first three places in each column.

The Poodle breed occupies the fourth position in each column for different reasons. In the first column (left atrial splitting), Poodles are listed fourth because they were the only other purebreds in which the condition was observed. The number observed, however, was the same as the number that would be expected if the disease was distributed evenly throughout the clinic population.

Poodles are listed fourth in the columns pertaining to the frequency of occurrence of chronic valve disease and the intervertebral disc syndrome because they held this position among the eight most common breeds examined. Other purebreds less commonly brought to the veterinary clinic for examination were tabulated as a group. Among these, based upon small numbers, Chihuahuas appeared to have chronic valve disease more frequently than Poodles; and Pekingese, Chihuahuas, and Basset Hounds appeared to have the intervertebral disc syndrome more often than Poodles.

B. Clinical and Pathological Studies

1. Left Atrial Splitting (Appendix III)

From a clinical and pathological standpoint, dogs with mitral insufficiency and left atrial splitting can be conveniently placed into one of 3 diagnostic categories: 1) Hemopericardium or 2) acquired atrial septal defect resulting from a perforating left atrial split; and 3) nonperforating left atrial splits (Table 3.1).

The clinical diagnosis of a perforated left atrium with hemopericardium or atrial septal defect can be substantiated by antemortem methods, whereas nonperforating left atrial splits only have been confirmed at necropsy thus far. Both clinical and pathological studies have been made on most of the dogs in each of these categories. Selected case examples are presented in sections C to F of Appendix III.

Broken chordae tendineae were occasionally found at necropsy in some of the dogs which had chronic valve disease with or without left atrial splitting examined early in the course of this investigation. Because of the necropsy method, however, it was not always possible to determine if the chordae tendineae had ruptured prior to death or had been inadvertently cut at the time of postmortem cardiotomy.

The customary cardiotomy methods used for postmortem examination of the heart at this institution consisted of opening the cardiac chambers and vessels in the sequence and direction of normal blood flow. This method ordinarily results in the transection of one or more chordae tendineae, particularly of the mitral valve, before the entire valve apparatus can be inspected.

To overcome this problem, various cardiotomy methods were devised and evaluated in a number of experimental animals. One of those which

proved satisfactory is described in section B of Appendix III. All of the hearts illustrated in sections C to F were examined using this method and all were found to have non-iatrogenic ruptured chordae tendineae.

HEMOPERICARDIUM (Appendix III-C)

Hemopericardium caused by left atrial splitting occurred in 9 dogs (Table 3.1). Illustrations of gross pathological findings in two dogs representative of this group are presented in Appendix III-C along with a reprint of a paper on the clinical and radiographic aspects of this syndrome.

One series of photographs are of the heart and lungs of a male Cocker Spaniel with left atrial splitting and hemopericardium before and after removal of the pericardial sac (Fig. 3.1). Evidence of pericardial effusion and pulmonary edema had been seen in radiographs made 36 hours prior to death. At necropsy, pulmonary edema was present and the pericardium was thicker than normal. A large unattached blood clot was present within the pericardial sac in addition to approximately 200 cc. of nonclotted blood. The left atrium was very dilated and the wall was translucent in some areas. A specific site from which intrapericardial hemorrhage had occurred was not apparent in the nondistended condition of the atrium at necropsy. The total volume of intrapericardial hemorrhage was estimated to be 300 cc.

In experimental dogs of similar body weight, intrapericardial injections of more than 100 cc. of fluid cause signs of acute cardiac tamponade and death (18). Because of thickening of the pericardial wall and the estimated volume of hemopericardium, it was concluded that some degree

of chronic or subacute hemopericardium had been present in the case described.

Several thrombus covered endomyocardial splits were observed in the left atrium of this dog. In addition, a fibrosed, deep split was present dorsal to the largest thrombus covered lesion (Fig. 3.2).

Postmortem examination of another dog with hemopericardium revealed a 2 mm. x 1 mm. perforation in the dorsocaudal left atrial epicardium (Fig. 3.3). A blood clot weighing 73 grams and an estimated 50-100 cc. of sanguineous fluid were present in the pericardial sac. The dog had shown no clinical signs of heart disease prior to sudden death. No radiographs had been made.

The epicardial perforation communicated with a relatively small (1 cm. long) endomyocardial split at the junction of the left atrial appendage and the main body of the left atrium (Fig. 3.4). A parallel, nonperforating split was located 1 cm. medial to the one which perforated. Just ventral and perpendicular to both of these splits was a larger, fibrosed split. The location of all 3 splits was just dorsal to a region of jet impact lesions in the left atrial endocardium. Typical, severe, chronic mitral valve disease was present with the commonly observed ruptured primary chordae tendineae of the anterior leaflet.

As can be seen in the preceding illustrations, the location, number, size, and age of the splits in the left atrium of dogs with hemopericardium were variable. One dog with hemopericardium (not mentioned previously) had only two well fibrosed, apparently healed splits in the left atrium. Some dogs with extreme splitting and separation of the endocardium and underlying myocardium did not have hemopericardium.

Although the endocardial and endomyocardial splits were large in some of the dogs with hemopericardium, the epicardial perforations were small and were only identified in 3 of the dogs. The largest of these (2 mm.) was found in the dog with the smallest endocardial lesions in the group (Fig. 3.4). In the other 2 cases, the epicardial perforations were about 1 mm. in diameter.

The clinical and radiographic features of the first 7 dogs observed with left atrial splitting and hemopericardium have been reported previously. To avoid unnecessary duplication, a reprint of this article is included in Appendix III-C. A table summarizing the differential diagnostic features of hemopericardium caused by left atrial splitting and two other diseases in dogs is presented in this reprint. All of the first 7 dogs with this syndrome were males and this was mentioned in the table as a useful diagnostic point. However, one of two dogs examined subsequently with this syndrome was a female. In other respects, this published account of left atrial splitting resulting in hemopericardium in the dog is still considered accurate.

ACQUIRED ATRIAL SEPTAL DEFECT (Appendix III-D)

An atrial septal defect caused by left atrial splitting was observed in 4 male dogs (Table 3.1). The pathological evidence for calling these defects acquired consisted of three features: an endomyocardial split was present; the septal defects had sharp irregular edges; an anatomically closed foramen ovale was distinguishable.

A large endomyocardial split was present in each case in the caudal wall of the left atrium where splits were most commonly located in 26 other dogs of similar age, sex and breeds. In the dogs with acquired atrial septal defects, however, the endocardial and subendocardial separation extended medially across part or all of the interatrial septum. Where the split crossed the usually thin, slightly translucent portion of the fossa ovalis, an atrial septal defect was present measuring 0.5 to 1.0 cm. in diameter (Fig. 3.8). The edge of the defect was sharp and somewhat irregular, with different degrees of retraction of various tissue layers (Figures 3.8 and 3.9). In all cases, anatomic closure of the foramen ovale was complete and the free edge of the embryonic septum primum could be distinguished where it was joined by fibrous tissue to the septum secundum. This area was always one to two centimeters anterior to the acquired defect in the septum primum.

A review of the clinical findings in the first three dogs with acquired atrial septal defect, diagnosed at necropsy, revealed several features in common. The dogs had been alert and active but had persistent, severe ascites which could not be eliminated or significantly diminished by extensive medical therapy over a period of weeks or months. Coughing or dyspnea had been noted occasionally in two of the dogs, but the owners of all three were mainly concerned because of the ascites.

Grade 4-5 (out of 5) intensity holosystolic murmurs were heard in the mitral and tricuspid valve areas. Marked generalized cardiac enlargement was noted in radiographs of each dog and in one instance an incorrect diagnosis of pericardial effusion was made. Wide, notched P-waves, consistent with left atrial enlargement, were present in electrocardiograms of two of the dogs. The other had high amplitude peaked P-waves suggestive of right atrial enlargement.

Similar clinical signs became apparent during the course of repeated examinations of another dog with an initial diagnosis of mitral insufficiency and moderate left atrial enlargement (Fig. 3.5 and Table 3.7). Ascites began to develop in this dog 18 months after signs of left sided congestive heart failure (coughing and dyspnea) were first noted. When ascites developed, the left heart failure signs became much less apparent. Ascites progressively increased in subsequent months to a marked degree in spite of medical therapy. Radiographically the right atrium and right ventricle increased in size disproportionately more than the left atrium and ventricle (Figures 3.5 and 3.6).

A tentative diagnosis of acquired atrial septal defect was made and cardiac catheterization was performed. This study confirmed the presence of an atrial septal defect (Table 3.8). Angiocardiograms made at the time of a second catheterization also revealed a left-to-right shunt within the heart. However, it could not be determined from these whether the shunt occurred at the atrial or ventricular level (Fig. 3.7). Necropsy examination confirmed the presence of an acquired atrial septal defect as a result of left atrial splitting (Figures 3.8 and 3.9).

A more detailed discussion of the clinical course of this dog and the results of many examinations are presented in Appendix III-D.

NONPERFORATING LEFT ATRIAL SPLITS (Appendix III-E)

Nonperforating endocardial and endomyocardial splits in the left atrium were observed at necropsy in 17 dogs (Table 3.1). Although suspected clinically in some of the dogs, the diagnosis was not confirmed antemortem. The clinical signs consistently exhibited by these dogs were those of severe mitral insufficiency with acute left heart failure and fulminating pulmonary edema. Radiographic evidence of a markedly dilated left atrium was almost always present. Electrocardiograms in most of the dogs had evidence of left atrial enlargement (wide, notched P-waves) and/or atrial myocardial disease (atrial premature beats, paroxysmal atrial tachycardia, or atrial fibrillation). When coupled with the accumulating knowledge of age, sex, and breed predilections, a clinical diagnosis of left atrial splitting was made in some of the dogs examined later in this series. Although confirmed at necropsy in most of the dogs in which it was suspected, all of the clinical signs associated with left atrial splitting have been observed in dogs which did not have this lesion at necropsy.

With present knowledge, a clinical diagnosis of a nonperforating left atrial split might be substantiated by means of angiocardiography. Filling defects in the left atrium might have been observed in two of the dogs which had thrombi of 1-2 cm. diameter attached to splits in the left atrium. Irregularities in the caudal left atrial wall also may have been observed in angiocardiograms of the dogs with deeper splits. Angiocardiography was not performed in any of the dogs in this group.

At necropsy, evidence of a nonperforating left atrial split was often noted before the left atrium was opened. A band of subepicardial hemorrhage was usually visible in areas where deep endomyocardial separations were present (Fig. 3.10). The number as well as the size of left atrial

splits was variable. One of the largest (1 x 6 cm.) was found in a dog which did not have hemopericardium or an acquired atrial septal defect (Fig. 3.11). This dog was known to have mitral insufficiency for at least 5 years; it died at 8 years of age from acute pulmonary edema. An old healed endocardial split was also found at necropsy. A more detailed case history on this dog is presented in Appendix III-E.

ENDOCARDIAL DEGENERATION WITH LIPID DEPOSITION (Appendix III-F)

Endocardial degeneration with lipid deposition is listed as a separate category of left atrial splitting at this time because an adequate evaluation of this aspect has not been completed. A summary of the clinical history of the dog in which sudanophilic material was first observed is presented in Appendix III-F.

This dog had severe chronic valve disease, ruptured chordae tendineae, and several nonperforating splits of the left atrium (Fig. 3.12). Significant amounts of sudanophilic material were found in the endocardium of the left atrium adjacent to the endomyocardial splits as well as in other areas (Fig. 3.13).

Several primary chordae tendineae of the anterior mitral leaflet were ruptured resulting in loss of support for most of the leaflet (Fig. 3.14). The initial frozen section studies which were made on this dog were done to evaluate intact, but yellowish chordae tendineae segments adjacent to those which were ruptured. These studies revealed large amounts of sudanophilic material in areas of degenerated collagen fibers (Fig. 3.15).

Studies performed thus far on material from three other dogs with left atrial splitting also have revealed the presence of varying amounts of endocardial lipid. Since atherosclerosis is uncommon in dogs, the endocardial lipid deposition in these cases was considered an important finding and additional studies are in progress to compare and contrast the endocardial changes with those of vascular atherosclerosis in man.

B. Clinical and Pathological Studies

2. Radiology of left atrial enlargement (Appendix IV).

Single as well as serial radiographic examinations of dogs with mitral insufficiency led to improved criteria for recognizing left atrial enlargement. A prominence in the left-cranial segment of the cardiac silhouette in dorsoventral radiographs was previously considered a result of left ventricular hypertrophy or dilatation. However, selective angiocardiography in dogs with mitral insufficiency consistently revealed the left atrial appendage as the cause of such a prominence. This finding also was substantiated by surgical or postmortem observations in these and other dogs in which a similar prominence was observed in dorsoventral radiographs.

Tracings made from a dorsoventral angiocardiogram of a normal dog show that the left atrium ordinarily does not contribute to the cardiac silhouette in this projection (Fig. 4.1).

Lateral angiocardiograms illustrating the size and locations of the cardiac chambers and great vessels in a normal dog are presented in Figure 4.2. In lateral radiographs of normal dogs, cranial and caudal waists are present at the base of the heart. These are caused by the confluence of the narrowed cardiac silhouette with the mediastinal structures cranially and the pulmonary veins caudally.

A left ventricular injection lateral angiocardiogram in a dog with chronic valve disease illustrates the regurgitant flow associated with mitral insufficiency (Fig. 4.3). The effect of moderate left atrial dilatation upon the cardiac silhouette in this projection can also be seen. Left atrial enlargement is mainly responsible for straightening of the

caudal border of the heart (loss of the caudal waist) (see also Fig. 4.5b). It also causes dorsal displacement of the cardiac silhouette toward the vertebral column. This is manifested in survey radiographs by dorsal deviation of the trachea and, in particular, of the left mainstem bronchus. In addition to apparent compression of the left mainstem bronchus, left atrial enlargement often causes divergence of the two mainstem bronchi resulting in a characteristic "forking" appearance (see also Fig. 4.7d).

A lateral radiograph of a dog with mitral insufficiency, marked left atrial enlargement and a nonperforating left atrial split at necropsy illustrates extreme displacement of the cardiac silhouette in a dorsal and caudal direction (Fig. 4.4a). In a dorsoventral radiograph of this dog, a large prominence can be seen in the left craniolateral segment of the cardiac silhouette (Fig. 4.4b). This was caused by marked dilatation of the left atrial appendage. The right atrium in this dog also was quite large at necropsy. The right craniolateral prominence in the dorsoventral radiograph was probably caused by right atrial enlargement in combination with right atrial displacement by the extremely dilated left atrium.

Dilatation of the left ventricle and mitral annulus without severe valvular disease may also be associated with significant mitral insufficiency (Fig. 4.5a). Extreme enlargement of the left atrium in dogs with mitral insufficiency of this type has been observed. In a lateral angiocardiogram of one of these dogs, the left atrial appendage was enlarged to such a degree that it was displaced cranially and ventrally over the main pulmonary artery and right ventricular outflow tract (Fig. 4.5b).

Left atrial appendage injection angiocardiograms were made in another dog with marked cardiac enlargement and mitral insufficiency

without severe valvular disease (Fig. 4.6). In the lateral projection, the left atrial appendage did not extend cranially and ventrally as far as in the previous illustration. In dorsoventral angiocardiograms, however, the appendage was visualized as the cause of a large prominence in the cardiac silhouette on the left side.

The latter two dogs had the greatest degrees of left atrial enlargement that have been observed in the author's experience. Both were young animals and neither had evidence of left atrial splitting at necropsy.

Thoracic radiographs were made on 8 occasions over a 6.8 year period in a dog with mitral insufficiency, first diagnosed at two years of age. Initially, the cardiac silhouette was within normal limits (Fig. 4.7a). Four years later, evidence of mild left atrial enlargement was present in addition to a general increase in the size of the cardiac silhouette (Fig. 4.7b). Over the next 2 years, the left atrium in particular continued to increase in size to a marked degree, causing loss of the caudal waist and elevation of the trachea. Increased pulmonary vascular markings were also present (Fig. 4.7c). Seven months later, atrial fibrillation was present and a striking increase in the overall size of the cardiac silhouette was seen in the thoracic radiographs (Fig. 4.7d). At this time, a divergence of the mainstem bronchi caused by elevation of the left bronchus was noted. Pulmonary edema was also present.

Dorsoventral radiographs made at the time of each of the preceding lateral radiographs also illustrate progressive generalized cardiac enlargement (Fig. 4.8). The left craniolateral border of the cardiac silhouette in the region of the left atrial appendage extended almost to the left thoracic wall before the stage of marked generalized cardiac enlargement and congestive heart failure occurred (Fig. 4.8c).

Five months prior to the radiograph illustrated in Fig. 4.8c, dorsoventral and slightly oblique dorsoventral radiographs of varying degree were made to see if improved visualization of an enlarged left atrial appendage could be obtained without significantly distorting the remainder of the cardiac silhouette (Fig. 4.9). The positioning which seemed most satisfactory is described as follows: The dog was placed in sternal recumbency and the spine was shifted approximately one inch to the left of what appeared to be perfect dorsoventral positioning. The primary x-ray beam was directed one inch to the right of the vertebral column and the radiographic exposure was made (Fig. 4.9b). Similar radiographic positioning has been used in other dogs with mitral insufficiency and left atrial enlargement. Usually, improved visualization of a dilated left atrial appendage was obtained.

In the dog whose serial radiographs are presented in Figs. 4.7 to 4.9, a diagnosis of left atrial splitting was considered likely in view of the long-standing mitral insufficiency and the development of marked left atrial enlargement, atrial arrhythmias and congestive heart failure. The owner declined further clinical examinations of the dog because it became dyspneic when transported in a car. Necropsy permission was refused when it died one week after the radiographs in Figures 4.7d and 4.8d were made. Since a necropsy was not performed, the dog was not included in the series of animals with left atrial splitting.

The clinical course of the sire of this dog was similar and necropsy revealed multiple endomyocardial splits in the left atrium with lipid deposition in mitral chordae tendineae and in the left atrial endocardium (Figs. 3.12 to 3.15).

A tracing of the original film used for Fig. 3.7d (dorsoventral angiocardiogram of a dog with left atrial splitting) shows the relationship of a dilated left atrium and the cardiac silhouette (Fig. 4.10). The left atrium comprised almost half of the cardiac silhouette; the appendage caused a left lateral prominence.

Patent ductus arteriosus is the only other lesion in dogs in which extreme left atrial enlargement has been observed. In dorsoventral radiographs of these dogs, a prominence in the left lateral cardiac silhouette also has been noted (Fig. 4.11). The prominence usually was situated more cranially than in dogs with mitral insufficiency; thus, distinction could not always be made between the presence of a dilated left atrial appendage and an enlarged main pulmonary artery. Left ventricular hypertrophy and dilatation is often present to a greater degree in dogs with patent ductus arteriosus and left atrial enlargement than in dogs with mitral insufficiency. This may account for the more cranial displacement of the left atrial appendage in dogs with patent ductus arteriosus.

In the dog with patent ductus arteriosus whose radiograph is presented in Fig. 4.11, the left atrial appendage was found to be markedly dilated when the ductus was divided at surgery.

Based upon angiocardiographic and surgical or postmortem observations in dogs with aortic stenosis, patent ductus arteriosus, persistent right aortic arch, dirofilariasis-induced pulmonary hypertension, pulmonic stenosis and mitral insufficiency, a useful guide for interpreting left-sided prominences in the dorsoventral cardiac silhouette of dogs has been developed using clockface analogy. With the animal's left side to the viewer's right, the cause and location of unusual prominences are as follows: aortic arch, 12 to 1 o'clock; main pulmonary artery, 1 to 2; left atrial appendage, 2 to 3; left ventricle, 3 to 6.

B. Clinical and pathological studies

3. Hyperimmune dogs (Appendix V)

Sixty dogs used for immune serum production were examined by auscultation, palpation and electrocardiography to determine the prevalence and types of heart disease. All had been vaccinated repeatedly for three months to three years and blood had been obtained from them each week by cardiocentesis with a 13 gauge needle via the right precordium. Each dog was tattooed with a number from 1 to 60 at the time of examination.

Nothing abnormal was detected by auscultation or electrocardiography in 9 dogs. The auscultatory findings are listed in Table 5.1 in columns indicating the period of time the dogs (identified by tattoo numbers) had been used for serum production. Abnormal heart sounds, murmurs or rhythms were heard in 44 dogs. The most common findings were: systolic murmurs in the mitral area (25 dogs), systolic murmurs in the aortic area (13 dogs), and diastolic murmurs in the aortic area (10 dogs). A regular bradycardia was noted in 7 dogs, all of which had evidence of complete atrioventricular block in electrocardiograms.

Electrocardiographic findings are listed in Table 5.2 along with an estimate of the number of cardiac punctures each dog had received. The latter was based upon the average period of time animals in each group had been used for serum production. Abnormal electrocardiograms were recorded in 40 dogs. The most common finding was a prolonged QRS complex with an apparent ventricular activation sequence in 16 dogs resembling that seen in dogs with experimental right bundle branch block. This was present in 13 of 40 dogs used for serum production for 1 to 2.5 years. A QRS pattern resembling left bundle branch block was found in 2 other

dogs in this group. Complete atrioventricular block (probably bilateral bundle branch block) was present in 5 of 8 dogs used for serum production for 3 years. Examples of the arrhythmias and conduction defects recorded in this investigation are presented in Figures 5.1 to 5.9.

Dog # 11 was obtained for further cardiovascular studies. When initially examined, grade one (out of five) intensity early systolic murmurs were heard in the mitral and aortic areas in addition to a grade two decrescendo diastolic murmur in the aortic area (Table 5.1). Sinus rhythm and right bundle branch block were present in an electrocardiogram (Table 5.2 and Fig. 5.7).

Clinical examinations and electrocardiograms were subsequently made at approximately one month intervals for one year and then less frequently. Six months after the animal was obtained, an isolated electrocardiogram revealed, in addition to the previous findings, paroxysmal ventricular tachycardia (Fig. 5.10). This subsided spontaneously, although occasional ventricular premature beats were often detected in later examinations.

The diastolic murmur of aortic insufficiency remained unchanged but the systolic murmur in the mitral area gradually increased to a grade three intensity over a two-year period. A change in its character was also noted: initially it was a soft, blowing murmur; later, it became harsh with a high pitched musical component in the first one-third of systole.

Aortic injection lateral angiocardiograms made 4 years after the animal was obtained provided evidence of both aortic insufficiency and mitral insufficiency (Fig. 5.11). The murmur of aortic insufficiency was difficult to record in this dog; however, evidence of its presence

was obtained in a phonocardiogram made one year after the angiocardiograms (Fig. 512). A systolic murmur in the aortic area, splitting of the second heart sound and right bundle branch block were also recorded in the simultaneous phonocardiogram and electrocardiogram.

Gross postmortem examinations were made on the hearts of 22 dogs which died within six months following clinical study. Included in this group were the hearts of 6 of the 8 dogs which had been used for serum production for 3 years. Five of these 6 dogs in addition to 4 others were found to have ascites at necropsy. One of the three-year dogs with ascites and seven others without ascites died from massive hemorrhage into the pericardial or pleural cavities.

Pericardial adhesions and large areas of myocardial fibrosis up to 5 cm. in diameter were found in the right ventricular free wall extending from epicardium to endocardium. The interventricular septum and left ventricular papillary muscles were also severely scarred. Puncture wounds were commonly found in one or more of the cardiac valves and intimal lacerations in the ascending aorta were often seen. The lesions in the valves resulting from cardiac punctures appeared as round foci of fibrosis 2-3 mm. in diameter with a perforated or thin, translucent center (Fig. 5.13). Histologic examinations were not possible because of autolytic changes and the effects of freezing prior to shipment of the specimens.

The only conclusion that could be made based upon the clinical and pathological findings in this group of 60 "hyperimmunized" dogs was that, as would be expected, puncturing a dog's heart 10-200 times with a 13 gauge needle causes heart disease. Allergic hypersensitivity associated with repeated vaccinations may or may not play a role in the genesis of chronic valvular fibrosis.

DISCUSSION

This section deals with general considerations of the various topics included in this thesis. Aspects of discussion which pertain to specific tables or illustrations are included as comments in the preceding section.

Chronic valve disease and the genesis of mitral insufficiency

Most of the epidemiologic data in the first two portions of this thesis were based upon a clinical diagnosis of chronic valve disease. For this reason, a review of the clinicopathologic manifestations of this condition is in order. CVD in dogs affects primarily the mitral valve either alone or in combination with the tricuspid valve (Table 1.10 and references 6 ,26 ,27 ,32 ,33 ,41 ,). When functionally significant, CVD is associated with valvular insufficiency. Because tricuspid involvement is less frequent and usually less severe, attention is focused upon the mitral valve in the following discussion. Unless indicated otherwise, the same statements apply to the tricuspid valve with appropriate changes in nomenclature.

A systolic murmur of at least grade 3 (out of 5) intensity in the mitral precordial area (left 5th or 6th intercostal space near the sternum) in the absence of anemia or signs of infection is sufficient evidence for a clinical diagnosis of chronic mitral valve disease and correlates well with necropsy findings (15). However, pathologic findings do not always reveal which of four anatomic abnormalities usually found in the mitral valve apparatus is primarily responsible for mitral insufficiency (a pathophysiologic diagnosis).

A normal mitral valve apparatus can be defined as a basically bicuspid valve structure consisting of leaflets and their supporting

elements. The leaflets must be intact, pliable and separate except near the annulus, and they must have a greater combined surface area than a normal sized left atrioventricular orifice. The leaflets are attached to functional papillary muscles by intact, pliable, primary and secondary chordae tendineae of sufficient length and number to allow leaflet apposition but prevent leaflet reflexion into the atrium during ventricular systole.

This definition was derived partly in retrospect based upon observed causes of mitral insufficiency in dogs and man. These include: (1) congenital or acquired clefts or perforations in valve leaflets; (2) thickened, firm or nodular leaflets which prevent perfect apposition of contact surfaces; (3) retracted, fibrotic or hypoplastic leaflets which cannot occlude a normal sized orifice; (4) greatly dilated orifice which cannot be occluded by normal leaflets; (5) shortened chordae tendineae which prevent apposition of leaflets; (6) ruptured chordae tendineae or papillary muscles which allow reflexion of leaflets into the atrium; (7) distortion of valve edges by tumors, blood cysts, or vegetations of bacterial endocarditis.

In dogs with chronic valve disease, several of the above causes of insufficiency can often be demonstrated. The leaflets are thickened, often nodular and somewhat retracted; the left atrioventricular orifice is usually dilated; and ruptured chordae tendineae are sometimes found. These changes correspond to items 2, 3, 4, and 6 in the above list.

Previous reports have cited nodularity of the mitral valve as the chief cause of insufficiency in dogs, presumably by preventing perfect coaptation of opposing contact surfaces of the valve leaflets (32).

Although this may be of importance at some initial stage, there are reasons for questioning its significance in severe mitral insufficiency.

Nodularity of the mitral valve, when present, generally is found along the contact surface of all leaflets of the mitral valve tissue. It is most obvious at the points of insertion of the chordae tendineae except in the posterior commissural region where nodular thickening is greatest between the insertions of the chordae tendineae. Thickening of the anterior mitral leaflet is usually greater than of the posterior leaflet. Tricuspid valve thickening is usually greatest in the septal leaflet with less severe changes in the cranial leaflet and least in the caudolateral leaflet. This differs from one report of the order of involvement in man in which chronic thickening of the cranial (anterior) leaflet of the tricuspid valve was observed more commonly (35).

Because of the widespread nature of nodular thickening of the mitral valve, one would expect jet impact lesions to be present in a variety of locations in the left atrial endocardium as a result of trauma from regurgitant streams in different directions. This is not the case, however, based upon surgical and postmortem observations. Direct cardiac palpation via thoracotomy in several dogs with mitral insufficiency consistently revealed a systolic thrill localized to the caudal wall of the left atrium. This correlated well with necropsy findings in these and most other dogs with CVD. Left atrial jet impact lesions were usually found only in the caudal left atrial wall. Jet lesions in the right atrium have seldom been observed.

An additional reason for questioning the role of nodularity is that the nodules are not usually rounded. Instead, convexities and concavities

along the sides and free edges of the leaflet tissue appear to match up well in an interdigitating fashion with adjacent and opposing valve tissue. In necropsy specimens, reduction of the valve annulus by slight, external cardiac compression while the ventricles are filled with water makes the affected valves competent as long as no major chordae tendineae are ruptured. On this basis, it would seem that annular dilatation and/or retraction of the leaflets are of greater importance than valve nodularity in the genesis of severe mitral insufficiency in dogs with CVD.

Ruptured chordae tendineae

The role of ruptured chordae tendineae in dogs with CVD has not been fully clarified. When present, they are an obvious cause of valvular insufficiency. What is yet undetermined is the frequency of their presence in a large number of dogs with CVD and the stage of the disease at which rupture occurs.

In the period since methods of postmortem cardiotomy were developed which permitted their recognition with certainty, ruptured chordae tendineae have been consistently observed in dogs with severe chronic valve disease and clinical signs of congestive heart failure. In the past, an absence of chordae tendineae involvement has been cited as a feature distinguishing CVD in dogs from chronic rheumatic valvular disease in man (14,44).

The most commonly ruptured chordae tendineae have been primary ones supporting the free edge of the anterior mitral valve leaflet. When these were detected, they corresponded well with the location of jet impact lesions observed in the caudal wall of the left atrium and occasionally on the atrial surface of the opposing posterior mitral leaflet. A regurgitant stream of blood coming from the left ventricle through the unsupported

valve area would be directed over the opposing valve leaflet and toward the caudal wall of the left atrium.

Occasionally, primary chordae tendineae were intact and ruptured secondary chordae tendineae were found. In one instance, the unsupported central portion of the valve bulged dorsally above the remainder of the leaflet forming a small aneurysm. Single, ruptured chordae tendineae of the tricuspid valve have occasionally been observed but less often than multiple ruptures of mitral chordae tendineae.

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leaflet is usually directed toward the atrium and is often rigid. In these cases, a thick, fibrous ridge is often present on the ventricular surface of the leaflet, extending from side to side between the remaining supporting secondary chordae tendineae (see posterior mitral leaflet in figure 3.4 and the anterior leaflet in figure 3.11). This finding suggests that a lack of support of the free edge existed for some period of time sufficient for fibrosis to take place in response to altered stress and hemodynamic factors in this region.

Ruptured primary chordae tendineae were found in all of the dogs with CVD and left atrial splitting illustrated in Appendix III, as well as in several of the other cases. Although some of the ruptures may have occurred just prior to death, evidence was found which supports the contention that at least some of the ruptured chordae tendineae had been present for some time and were of major importance as contributing factors to the existence of mitral insufficiency. It is possible that additional chordae tendineae ruptures may have caused a sudden increase in the severity of mitral insufficiency resulting in an acute increase in left atrial size. This might have been responsible for left atrial splitting just prior to death, evidenced by relative lack of organization of a superimposed thrombus in some cases.

Epidemiology of chronic valve disease

Studies of the age, sex, and breed distributions of 392 dogs with CVD in a clinic population sample of 4,831 dogs revealed that the disease was not uniformily distributed in relation to any of these factors. With regard to age, CVD was seldom diagnosed in dogs less than 5 years old; beyond this age, a linear increase in frequency was observed in successive age groups (Table 1.4). In each age group, the prevalence ratio in males was 32-35 % greater than in females.

Since prevalence ratios are the result of a relationship between the incidence and duration of disease ($P \approx ID$), a discussion of the latter factors is in order. The duration of CVD as well as any other chronic disease in dogs is difficult to assess with precision because more dogs are apparently killed by euthanasia than allowed to die spontaneously. Respective percentages of 59 % (euthanasia) and 34 % (spontaneous) were obtained for dogs which had died at the time of a follow-up survey of 471 dogs examined clinically (Table 2.8). Since the average age at death of dogs in which euthanasia was performed was slightly greater than the average age of those which died spontaneously (Table 2.9), it was concluded that euthanasia was not performed in most cases much in advance of the time when spontaneous death might have occurred. This conclusion was supported by clinical experience as well.

In this study, the age at death of dogs without detectable heart disease was less than that of the dogs with CVD. It is unlikely that this would have been true if the control group had been derived from the dog population at large rather than from those which had been brought to a veterinary clinic for some reason.

With the preceding limitations in mind, the average age at death of dogs with chronic valve disease (12.5 years) was not much different than the average life span of all dogs (5). This generalization does not hold for dogs with clinical evidence of chronic valve disease at a relatively early age (5 years or less). In the few animals in this category for which follow-up information was obtained, congestive heart failure usually occurred before the animals reached 10 years of age.

Based upon personal clinical observations and the follow-up data obtained in the survey of 471 dogs, no fundamental disagreement has been found with a previously published profile of chronic valve disease in dogs: "Valvular fibrosis appears to begin during the first third of life, frequently producing mitral and sometimes tricuspid insufficiency during the middle years. The degree of valvular malformation caused is evidently fairly well tolerated in many individuals which reach 9 to 12 years of age or older. It is probable that some form of myocardial disease ordinarily supervenes in those animals with atrioventricular valvular fibrosis and mitral insufficiency which subsequently develop congestive heart failure." (15).

If the assumption is made that chronic valve disease, by itself, ordinarily does not cause death of an animal, and clinical recognition becomes possible starting at approximately 5 years of age, an annual incidence of about 4 % in females and 5.3 % in males can be derived from data in the survey of 4,831 dogs. These values are probably too low for the older age groups, however, because congestive heart failure subsequently occurred more frequently in dogs with CVD than in dogs with no evidence of heart disease at the time of initial examination, and was the reason for spontaneous death or euthanasia in a substantial number

of dogs with CVD (Table 2.8). For this reason, it is likely that annual incidence values in the range of 6-10 % would be more accurate in older dogs to take into account the effect of congestive heart failure in removing some dogs with CVD from the population.

Sex

Chronic valve disease occurred more frequently in males (92.9/1000) than in females (67.7/1000) on an age and sex adjusted basis (Table 1.3). Although this difference was statistically significant, it was not a great difference. Consequently, whatever accounts for the moderate male predominance must be considered a minor contributing factor rather than a primary etiologic factor.

It is possible that a greater sex difference would have been obtained if varying degrees of valvular disease could have been taken into account. Although data were not available to assess this factor directly, indirect evidence that CVD may be generally more severe in males was obtained from the sex distribution of dogs with left atrial splitting. Marked male predominance (26 out of 30 dogs) was noted in a tabulation of the dogs with this condition, all of which also had severe chronic valve disease (Table 3.2). In the case of left atrial splitting, the magnitude of the sex difference was such that a male influence might be considered a major contributory factor.

Breed

Chronic valve disease was found more commonly in purebred dogs than in mongrel dogs (Table 1.6). The Cocker Spaniel breed had the highest prevalence ratio, owing to an unusual predominance in males of this breed (Table 1.2). Since the average age of all male Cocker Spaniels examined was among the highest of the dogs surveyed, this was considered a possible

explanation of the higher prevalence observed in view of the fact that the frequency of CVD in all dogs increased with age.

Against this explanation were the results of age specific comparisons between male Cocker Spaniels and other dogs (Table 1.5). These comparisons revealed that male Cocker Spaniels had prevalence ratios of CVD higher than other dogs in each age group.

Because of the higher frequency of CVD in male Cocker Spaniels, comparisons of purebreds versus mongrels, and males versus females were made with the Cocker Spaniel breed excluded. The prevalence of CVD in purebreds other than Cocker Spaniels was not significantly greater than in mongrels unless subdivided by sex: male purebreds other than Cocker Spaniels had more CVD than male mongrels (Table 1.7).

Comparison of age and sex adjusted prevalence ratios, with Cocker Spaniels excluded, revealed that male dogs still had a higher frequency of CVD than female dogs (Table 1.8). This difference would have been even greater if mongrel dogs (constituting about 1/3 of the 4,831 dogs examined) were excluded. Mongrel dogs did not exhibit any difference between the frequency of CVD in males and females (Table 1.2).

On the basis of the preceding sex and breed data, the conclusion was reached that the etiology or pathogenesis of chronic valve disease is influenced in some degree by an unexplained sex factor which may be operating independently but most likely is related to a genetic predisposition in view of the observed male predominance in purebreds and not in mongrels.

The high prevalence ratio of CVD in male Cocker Spaniels in the present study provides an explanation at least in part for the previously reported observation of a high prevalence ratio of congestive

heart failure in males of this breed based upon data from the same survey (15). The prevalence ratios of congestive heart failure in Table 1.9 are slightly higher than in the previously published tables because all causes of congestive heart failure are included; i.e., congenital heart disease, heartbase tumors, and heartworms in addition to chronic valve disease and/or chronic myocardial disease.

The evidence that chronic valve disease is in part determined by genetic predisposition is less strong than that for congenital heart disease. However, additional support for such a factor may be found in the fact that, occasionally, CVD was found in closely related animals. In most instances, however, these animals were beyond middle age and were in age groups where CVD is detectable in 20-30 % of all dogs; thus, interpretation of a genetic influence on this basis is hazardous.

Other tenuous evidence which might be considered support for a genetic influence was obtained in the questionnaire survey of 471 dogs. Positive responses to a question regarding signs of heart disease in relatives were given for 2.7 % of the dogs with no heart disease and 6.4 % of the dogs with CVD. This difference was not statistically significant and even if it were, a question would still exist regarding the role of increased awareness and suspicion on the part of owners of dogs with heart disease. Known cases of congenital heart disease were not included in this study.

With regard to congenital heart disease, the presence of similar lesions in closely related dogs and the predominance of certain lesions in certain breeds coupled with successful breeding experiments support the conclusion that genetic factors are operative in some dogs with congenital heart disease (43). Similar results also have been obtained in

inbred strains of laboratory animals (13).

Fewer studies have been made regarding genetic predispositions for acquired cardiovascular lesions. The most thorough investigation of this type has been performed in inbred strains of pigeons which have a high incidence of atherosclerosis (8). Environmental stress factors also have been shown to produce vascular and valvular changes in animals (1,4,46).

With regard to chronic valve disease, no important differences from control dogs were found in comparisons of environmental and behavioral characteristics based upon a questionnaire survey (Appendix II). Aspects of medical history evaluated in this survey revealed an expected significant difference in the frequency of congestive heart failure signs. Other differences were observed but these could only be classified as trends because of smallness of numbers.

The difference in the percentages of castrated dogs with CVD and those with no heart disease was significant on a disease specific basis but not quite significant when sex adjusted values were compared (Table 2.1). The observed trend of a lower castration percentage in male dogs with CVD would be consistent with the observation of a higher frequency of CVD in males and the resultant hypothesis that male hormones directly or indirectly play a contributory role in the genesis of CVD. If the alternative hypothesis is considered; i.e., female hormones exert some protective effect against CVD, one would anticipate a higher castration percentage in females with CVD than in females without CVD. The observed results in this regard were opposite those anticipated; thus, the alternative hypothesis was rejected.

Left atrial splitting

Left atrial splitting primarily because of endocardial degeneration and atrial dilatation appears to be a lesion peculiar to dogs. Reports of atrial rupture in human patients have incriminated myocarditis (31) or myocardial infarction (9). No reports of left atrial splitting in man as a result of dilatation have been found and experienced investigators of human cardiovascular disease have denied seeing left atrial lesions of this type (12,17).

Left atrial splitting in dogs with chronic valve disease and mitral insufficiency has been observed by others. Brief mention of "left atrial rupture", especially in Dachshunds, was made in an article on cardiovascular pathology written in Switzerland (53). The proportion of Dachshunds as a breed in that country may be greater than in the United States and the number of cases of atrial splitting observed was not given; consequently, the significance of the apparent breed predominance could not be ascertained from the report. The authors regarded left atrial myocardial disease as the underlying cause of splitting.

Left atrial mural endocarditis has also been observed occasionally in dogs with spontaneous nephritis and uremia; instances of atrial rupture have been ascribed to this process (27). Similar nonbacterial left atrial endocarditis has been produced in dogs on a high fat diet prior to experimentally induced renal insufficiency (34). The lesions were considered part of a syndrome of mucoarteritis which can be produced in this manner in dogs and affects primarily large elastic arteries and the left atrial endocardium. Endocardial degeneration with left atrial splitting in dogs in the present report did not appear to

be caused by the same mechanism. None of the dogs had clinical or laboratory evidence of uremia and necropsy examinations revealed no more than mild degrees of chronic interstitial nephritis in a few of the dogs. Changes in the left atrium did not resemble those described in dogs with experimentally induced mucoarteritis.

Gross and preliminary histologic studies of 0.5-6 cm. long splits with superimposed thrombus formation in the left atria of dogs suggest that this process may be a large scale representation of minute cracks (100-1,000 micra in length) found in coronary arteries of man. Plaque fissures in thrombosed segments of atherosclerotic coronary arteries were observed in 20 consecutive human patients with fatal coronary thrombosis (10). In each case, the thrombus could be traced to one or more fissures in atherosclerotic plaques. No cracks were found in serial section studies of atherosclerotic coronary arteries in 16 other patients who died of causes other than coronary thrombosis. The author concluded that a "sudden break in the brittle lining of atherosclerotic coronary arteries represents a major factor in the causation of human coronary thrombosis."

Preliminary histologic studies in dogs with left atrial splitting suggest that endocardial degeneration is the main anatomic factor involved in addition to atrial dilatation. The endocardium is generally thickened; swollen collagen fibers are often present; and elastic fibers are often mineralized, distorted and ruptured. Although varying amounts of lipid staining material have been found in the endocardium of dogs studied by frozen section technique thus far, in no case has the degree of endocardial "atherosclerosis" approached that reported in coronary arteries and aortas of human patients. In view of the rarity of

atherosclerosis in dogs, however, the amount of lipid material in the endocardium of these dogs was unusual and is being investigated further.

Atrial splits varied in depth from superficial endocardial separations to full thickness fissures with dissecting hemorrhage into the myocardium and occasionally into the pericardial sac. These have been termed respectively endocardial or endomyocardial splits.

Myocardial fibers were often separated by varying degrees of hemorrhage and stages of thrombosis. Occasionally, sequestered myocardial fibers appeared to be undergoing necrosis; however, these changes were considered secondary to dissecting hemorrhage. Healing by fibrosis of even deep splits into the myocardium was observed.

Although foci of apparently primary atrial myocardial necrosis and fibrosis were sometimes demonstrable, the changes were not of sufficient degree to explain the widespread endocardial splitting which was usually present. Much greater degrees of atrial myocardial disease with almost complete replacement by fibrous tissue have been reported in human patients with extreme left atrial dilatation and an apparently intact endocardium (16).

Illustrations and more complete discriptions of the histologic findings in dogs with left atrial splitting are not included in this thesis, because these studies are still in progress.

At the present time, left atrial splitting in dogs is believed to be related to a disease process primarily affecting connective tissue elements in the subendocardium. Whether this is primarily a change in ground substance, or collagen and elastic fibers has not been determined.

Also undetermined is the relationship this process has with chronic valve disease. The atrial endocardial change could be just secondary to

atrial dilatation, or it may be a result of an etiologic factor similar to that causing chronic valve disease. Epidemiologic studies indicate definite sex and breed predispositions for left atrial splitting which are an extension of the trends noted in dogs with chronic valve disease. However, the data do not permit conclusions to be made regarding the primary or secondary nature of the atrial endocardial disease found in dogs with left atrial splitting. In either event, it appears that left atrial dilatation is the main cause of splitting with endocardial disease playing a permissive role and determining the location of the splits.

Endocardial trauma by regurgitant jet streams in mitral insufficiency probably is in part responsible for endocardial disease; however, the occurrence of splits in the atrial appendage and in other areas where jet impact lesions are not seen, makes it necessary to consider dilatation a more important factor.

Insufficient coronary blood flow cannot be ruled out as a contributing element even though organic arterial obstruction has rarely been observed. Three reasons for this viewpoint are as follows: Increased oxygen requirements occur because of the increased atrial work associated with mitral insufficiency. The coronary blood supply, however, may be diminished in advanced states of congestive heart failure because of low cardiac output. The third factor to consider is the potential effect of elevated mean left atrial pressure in mitral insufficiency and congestive heart failure. This, in combination with atrial dilatation, thinning of the atrial wall, and pericardial restriction may be sufficient to cause functional impairment of coronary blood flow in the absence of organic obstruction.

All of the preceding considerations obtain in human patients with mitral insufficiency and relatively much greater left atrial enlargement; however, no reports of left atrial splitting were found. The conclusion was reached, therefore, that the presence or absence of some factor in the left atrial endocardium of dogs permits endocardial and endomyocardial splitting to occur before the atrium reaches a relative size comparable to that seen in some human patients.

That this factor may be genetically determined at least in part was suggested by the occurrence of atrial splitting predominantly in males of the Dachshund and Cocker Spaniel breeds. Experimental studies to clarify this aspect would be formidable because of the difficulty of clinical diagnosis and the age at which the condition becomes apparent. The youngest animals with left atrial splitting at necropsy were 8 years old (4 of the 9 Dachshunds and the single Beagle observed). The average age of all the dogs was 10.8 years. This time element makes it impractical to perform controlled breeding experiments and also makes it difficult to trace relatives of affected dogs. In addition, many dogs which might be genetically predisposed to the condition could die for various other reasons before reaching the age where the condition would be manifested.

The most practical approach to investigate a genetic influence would be to examine related animals clinically and at necropsy. In one instance where this was possible, provocative but inconclusive results were obtained. Dog # 15 in Table 3.1, a male Cocker Spaniel with left atrial splitting at 11 years of age, lived most of its life in Conneticut. A male offspring of this dog (Fig. 4.7-4.9) was raised in Pennsylvania and had clinical evidence of chronic valve disease at 2 years of age.

It died in congestive heart failure at 9 years of age with clinical, electrocardiographic, and radiographic signs similar to those of its sire and other dogs with nonperforating left atrial splits. Unfortunately, necropsy was not permitted.

Epidemiologic comparisons

The Dachshund, Cocker Spaniel and Beagle breeds in differing orders of frequency were the most common breeds represented in dogs with chronic valve disease, left atrial splitting, and the intervertebral disc syndrome.

Others reporting on the age, sex, and breed distribution of dogs with the disc syndrome obtained similar results and included the Pekingese breed as one also predisposed to the condition (20). The breeds particularly affected were considered to have characteristics of chondrodystrophy as a common denominator which caused investigators to classify them as a chondrodystrophoid group (21). From a body conformation standpoint, the Dachshund breed exhibits the greatest degree of chondrodystrophy; i.e., short extremities in proportion to the size of the head and trunk.

Dystrophic changes in the nucleus pulposus of the intervertebral disc in this group of dogs appeared to result in disc degeneration at an earlier age and to a greater degree than in other breeds of dogs (23). Other conclusions were also made: disc prolapse presupposes disc degeneration; disc degeneration occurs in the spinal column much more frequently than the number of prolapses; local disc prolapse is caused by mechanical factors; disc degeneration occurring in multiple areas is a definite systemic disease; the tendency of discs to become diseased probably can be explained by a predisposition to chondrodystrophy (20).

The epidemiologic similarities between aspects of left atrial splitting and the intervertebral disc syndrome were striking; the only exception was that a male predominance obtained in the former condition and no sex difference was noted in the latter. Based upon pathologic studies thus far, the word "endocardium" could be substituted, in essence, for the word "intervertebral disc" in the conclusions in the preceding paragraph and result in essentially correct statements concerning endocardial degeneration and left atrial splitting. It may be significant that a previous episode of intervertebral disc syndrome was mentioned in case histories of two of the Dachshunds with left atrial splitting. These episodes had not occurred during the period when tabulations were made for the intervertebral disc syndrome, and these two cases were not included in Table 3.5a.

With present information, it seems reasonable to suggest the possibility that a "chondrodystrophic" process similar to that found in dogs with the intervertebral disc syndrome may be an underlying factor in dogs with left atrial splitting. Chronic valve disease might also be related by considering the possibility that moderate male predominance in dogs with CVD could be reflected as a marked male predominance in dogs with left atrial splitting. This presupposes that the degree as well as the frequency of valvular disease is greater in males. Such was the case in dogs with left atrial splitting; however, it has not been studied in other dogs with CVD.

On the basis of epidemiologic evidence, and not inconsistent with reported pathologic findings, chronic valve disease, left atrial splitting, and the intervertebral disc syndrome may all be related to a

specific degenerative process of connective tissue which occurs earlier and is more common or more severe in dogs of the chondrodystrophoid type.

The clinical signs in dogs with left atrial splitting varied with the location and depth of the splits. It was convenient to divide the 30 cases into three groups: Group I, 9 dogs with hemopericardium; Group II, 4 dogs with acquired atrial septal defect; Group III, 17 dogs with nonperforating atrial splits.

All of the 25 dogs examined clinically had loud murmurs of mitral insufficiency and radiographic evidence of moderate to marked left atrial enlargement. Some of the dogs with hemopericardium died abruptly with acute cardiac tamponade; however, a surprising number survived several days after diagnosis by radiography and pericardiocentesis. In most of these cases, signs of left heart failure predominated although some had ascites and hepatomegaly. The dogs with acquired septal defects had predominant signs of right heart failure with intractable ascites for several weeks or months. An antemortem diagnosis in one case was confirmed by cardiac catheterization. Dogs with nonperforating left atrial splits generally were presented in acute left heart failure with fulminating pulmonary edema. Although left atrial thrombi of various sizes were present in all the dogs with recent splits, no clinical or necropsy evidence of embolization was observed.

Radiography

Since dilatation appeared to be the common factor in dogs with left atrial splitting, a section of this thesis was devoted to the radiographic and angiocardiographic appearance of left atrial enlargement. Others reporting on cardiac radiography in dogs have not mentioned the

characteristic appearance of a dilated left atrial appendage in the dorsoventral cardiac silhouette of dogs with or without left atrial splitting. The changes observed in lateral radiographs have been reported by others (47).

In lateral radiographs, left atrial enlargement caused a dorsal displacement of the terminal trachea and the left mainstem bronchus. A caudal displacement of the cardiac silhouette was also observed in the region where the base of the heart is normally narrowed. The atrial displacement in this area, in combination with dilatation of the mitral annulus, caused straightening of the caudal border of the cardiac silhouette.

In dorsoventral radiographs, the appendage of a markedly dilated left atrium caused a leftward and slightly cranial bulge in the cardiac silhouette in the region of 2-3 o'clock using clockface analogy with the dog's left to the viewer's right. This prominence was made more visible in some cases by slightly oblique dorsoventral positioning. To accomplish this, the dog's thoracic spine was shifted to the left of the midline.

In some instances in survey dorsoventral radiographs, it was possible to demonstrate a double border in the right caudal region of the cardiac silhouette resulting from near superimposition of the right ventricle and left atrial wall as described by others (48). However, this finding was less frequent than that of a bulge produced by a dilated left atrial appendage.

A bulge in the cardiac silhouette caused by an enlarged left atrial appendage also has been observed in dogs with patent ductus arteriosus, marked cardiac enlargement and congestive heart failure. In two of these cases in which the ductus was divided at surgery, systolic murmurs of

mitral insufficiency were detected postoperatively. The cause and effect relationship of left heart enlargement and mitral insufficiency in these cases was not clear. One of the dogs developed atrial fibrillation 3 months after surgery and congestive heart failure recurred.

Dogs used for immune serum production

The study of dogs used for immune serum production did not provide any useful information regarding the role of antigen-antibody reaction in the genesis of chronic valve disease. It did confirm, however, that cardiocentesis is not an innocuous procedure. Clinical evidence of heart disease was present in 75 %, 80 %, 93 % and 100 % of 4 groups of dogs in which the average numbers of cardiac punctures in each dog were 20, 50, 100, and 150 respectively. If pathologic studies had been performed on the additional dogs in each group which had died before clinical studies were made, it is likely that the percentage of dogs with heart disease in the first three groups would have been higher.

The most common electrocardiographic abnormalities were those of delayed ventricular depolarization time (31 of 60 dogs). The fact that cardiac punctures were generally made via the right precordium probably is sufficient to explain the large number of dogs with QRS patterns resembling right bundle branch block (16 dogs). One of the technicians stated that surviving dogs usually were not kept on the bleeding program more than 3 years, because the area of scarring of the heart became so large and was so hard that it was difficult to insert a needle into the heart for bleeding.

Even though the conditions under which bleeding of the dogs was performed were less than ideal, and the bleeding was done by technical personnel, it is unlikely that a skilled cardiologist under ideal conditions

could puncture the heart with a 13 gauge needle once a week for periods up to 3 years without also causing significant heart disease. Although repeated cardiac punctures for diagnostic studies in man were rarely done in the past and isolated punctures are seldom performed today, the present study supports the contention of many investigators that significant cardiac damage can be caused by cardiocentesis and therefore, the procedure should be avoided if at all possible.

SUMMARY

Age, sex, and breed evaluations of 392 dogs with chronic valve disease (CVD) from a survey of 4,831 dogs revealed a predominance of CVD in purebred male dogs. Male Cocker Spaniels were most frequently affected.

A questionnaire survey concerning aspects of medical history, environment, behavior, and survival was made 3-5 years after initial clinical examinations on 471 dogs. This study revealed no marked differences between dogs with CVD and dogs with no heart disease, except that dogs with CVD more often had signs of congestive heart failure.

Endocardial and endomyocardial splitting of the left atrium occurred in 30 dogs with CVD; primarily in males of the Dachshund and Cocker Spaniel breeds. Left atrial perforation in several of the cases caused hemopericardium or acquired atrial septal defects which could be diagnosed by clinical means. The cause of splitting was considered to be left atrial dilatation with left atrial endocardial degeneration playing primarily a permissive role. Lipid deposition in the endocardium and ruptured chordae tendineae was found in preliminary frozen section studies. A method of postmortem cardiotomy was developed which permitted recognition of spontaneously ruptured cordae tendineae with certainty. Ruptured mitral chordae tendineae were frequently found in dogs with severe chronic valve disease with or without left atrial splitting.

The Dachshund, Cocker Spaniel, and Beagle breeds in varying order constituted the three most common breeds with CVD, left atrial splitting or the intervertebral disc syndrome. This finding was suggestive of an underlying connective tissue disorder predominant in those breeds which have been classified by others as belonging to a "chondrodystrophoid" group.

Radiographic studies of dogs with left atrial enlargement revealed a characteristic bulge in the dorsoventral cardiac silhouette caused by dilatation of the left atrial appendage. This was most apparent in dogs with left atrial splitting.

Clinical and pathological studies on 60 "hyperimmune" dogs from which blood was withdrawn by cardiocentesis for immune serum production revealed serious heart disease in nearly all dogs. This was considered the results of weekly cardiocentesis for periods up to three years rather than the results of repeated vaccinations during this time.

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