Animal Models of Primary Myocardial Diseases

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Feline and canine cardiomyopathies (primary myocardial diseases) were reviewed and divided into three groups based on the clinical, hemodynamic, angiocardio- graphic, and pathologic findings: (1) feline and canine hypertrophic cardiomyopathy, (2) feline and canine congestive (dilated) cardiomyopathy, and (3) feline restrictive cardiomyopathy. All three groups consisted predominantly of mature adult male cats and dogs. Cardiomyopathy in the hamster and turkey was also reviewed. The most common presenting signs were dyspnea and/or thromboembolism in the cat, systolic murmurs with gallop rhythms on auscultation, cardiomegal with (groups 1 and 3) or without (group 2) pulmonary edema, abnormal electrocardiograms, elevated left ventricular end-diastolic pressures, and angiocardio- graphic evidence of mitral regurgitation with left ventricular concentric hypertrophy (group 1), left ventricular dilatation (group 2), or midventricular stenosis (group 3). Some cats in groups 1 and 3 also had evidence of left ventricular outflow obstruction. The principal pathologic findings in all of the cats and dogs were left atrial dilation, hypertrophy, increased septal:left ventricular free wall thickness ratio with disorganization of cardiac muscle cells (group 1); dilatation of the four chambers with degeneration of cardiac muscle cells (group 2); and extensive endocardial fibrosis and adhesion of the left ventricle (group 3). Aortic thromboembolism was commonly observed in the cats of all three groups. These clinical and pathologic findings indicate that cardiomyopathy in the cat or dog is similar to the three forms of cardiomyopathy in humans (hypertrophic, congestive, and restrictive).

Primary myocardial disease (cardiomyopathy) is the term applied to an abnormality in the heart muscle of unknown or obscure etiology. Three major types of cardiomyopathy are recognized in the human patient [1-3]: (1) hypertrophic (with or without obstruction), (2) congestive (dilated), and (3) restrictive. Primary myocardial disease (cardiomyopathy, hypertrophic, congestive, or both) has recently been reported in the hamster [4-6], turkey [7-9], cat [10-18], and dog [19-22].

This report reviews the clinical, hemodynamic, angiocardio- graphic, and pathologic findings of spontaneous hypertrophic and congestive cardiomyopathy in the cat, dog, hamster, and turkey, and spontaneous restrictive cardiomyopathy in the cat.

FELINE HYPERTROPHIC CARDIOMYOPATHY

Age, Sex, and Breed

Cats with hypertrophic cardiomyopathy ranged in age from eight months to 16 years (mean, 6.5 years). Seventy-five percent were male [13,14,16-18]. There was a higher incidence of hypertrophic cardiomyopathy in the Persian cat than in other breeds [18].
Clinical Findings

Dyspnea was the most common clinical sign, occurring in 70 percent [16,17,18,23] and thromboembolism was the second most common sign, occurring in 48 percent of the cats [16–18]. The aortic bifurcation was the most common site for thromboemboli. Aortic thromboembolism was manifested by acute onset of posterior paralysis, absence of femoral pulses, and coldness of the extremities. The nonspecific sign of anorexia was found in 34 percent of the cats [23].

Physical examination revealed systolic murmurs in all cats, most commonly a low intensity systolic murmur (Fig. 1). The systolic murmurs were sometimes short in duration, and were most prominent during midsystole. A fourth heart sound was recorded in 78 percent [12,13,14,16,18], and a third heart sound in 20 percent of the cats.

Electrocardiographic abnormalities were observed in 68 percent of the cats with hypertrophic cardiomyopathy. Prolongation of both the P wave and QRS interval in lead II beyond 0.04 seconds was the most common finding. Conduction disturbances and rhythm disturbances, including premature ventricular contraction and atrial fibrillation, were recorded in 30 percent of the cats (Fig. 2) [14,16,18].

FIG. 1. Heart sound tracing from a five-year-old male domestic short-haired cat with hypertrophic cardiomyopathy (paper speed = 100 mm/sec). Note systolic murmur (I) and gallop rhythm.

FIG. 2. Electrocardiogram illustrating rhythm disturbances in feline hypertrophic cardiomyopathy. (A) Normal sinus rhythm in a control cat. Heart rate = 200 beats/min. (B) Atrial tachycardia. Heart rate = 260 beats/min. Note increased amplitude and width of QRS complexes. (C) Second degree atrioventricular block with ventricular escape beats. P waves are noted by arrows. (D) Atrial fibrillation. (E) Bigeminal rhythm; every alternate beat is a ventricular premature beat. (F) Ventricular tachycardia based on subsequent studies.
Thoracic radiography revealed gross cardiomegaly in all cats. The dorsoventral projection aided most in the detection of left atrial enlargement. The enlarged right ventricle and enlarged left atrium projected slightly beyond the normal heart silhouette, giving the appearance of a valentine-shaped heart (Fig. 3) [13,14,16,18].

Pulmonary edema, a sign of left-sided heart failure, was identified by a generalized or partial fluffy density of the alveolar type in 58 percent of the cats. Pleural effusion, a sign of right-sided heart failure, was observed in 20 percent.

**FIG. 3.** Dorsoventral thoracic radiograph of a two-year-old male Persian cat with hypertrophic cardiomyopathy. Enlargement of the right atrium and ventricle (open arrows) and left atrium (solid arrows) gives the appearance of a "valentine-shaped" heart.

Hemodynamic studies indicated that the mean systolic pressures remained within normal limits (85 to 135 mm Hg), but the range was greater than normal (90 to 160 mm Hg; mean, 125 mm Hg) in the cats with hypertrophic cardiomyopathy [13,16,18]. The end-diastolic pressure was consistently high in all cats (mean, 30 mm Hg), being more than six times the normal pressure of 4.5 mm Hg (Fig. 4). Left ventricular pressure tracings often revealed a prominent transmitted wave and an elevated end-diastolic pressure [13,16,18].

Angiocardiographic studies showed a smaller than normal left ventricular end-systolic volume and muscular hypertrophy around the body of the ventricle (Fig. 5). Encroachment by a greatly hypertrophied ventricular septum on the outflow tract of the left ventricular cavity was found in some cats. Angiocardiograms showed evidence of radiolucent filling defects in the left ventricle caused by hypertrophied papillary muscles. Mitral insufficiency was present in all cats, and thromboemboli were frequently seen [13,16,18,23].

**Gross Anatomic Finding**

Affected cats had ventricular septal hypertrophy, with the ventricular septal thickness ranging from 6 to 12 mm (mean, 8.8 mm) and the posterobasal left ventricular wall thickness ranging from 6 to 11 mm (mean, 8.1 mm). The septal:free wall thickness ratio ranged from 0.9 to 1.6 (19 cats had ratios of 1.1), with a mean thickness ratio of $1.06 \pm 0.18$, which is greater than that in cats with normal hearts.
FIG. 4. Left ventricular pressure tracings (paper speed = 100 mm/sec; tracings have been retouched). (A) Normal tracing from a control cat. The end diastolic pressure (EDP) is less than 5 mm Hg. (B) Tracing from an eight-year-old male domestic short-haired cat with acute dyspnea. Systolic pressure is normal, but the EDP is increased to 40 mm Hg with a prominent a wave.

FIG. 5. Left ventriculogram of an eight-year-old male domestic short-haired cat with hypertrophic cardiomyopathy. Shows early systole, one second after injection of contrast medium. The chamber is very irregular with prominent filling defect (arrows) caused by the hypertrophied and fibrosed papillary muscles.

(0.93 ± 0.09; \( P < 0.05 \)) [23]. Enlargement and hypertrophy of the left atrium were consistently seen. There was hypertrophy of the left ventricular free wall, papillary muscles, and ventricular septum, with encroachment on the left ventricular cavity (Fig. 6).

Absolute heart weight (6.3 ± 0.6 gm/kg) in the cats with hypertrophic cardiomyopathy was significantly increased over that in normal cats (4.0 ± 0.3 gm/kg; \( P < 0.001 \)) [23]. Aortic thromboembolism was found in 51 percent; ball thrombus was found in the left atrium of 2 percent of the cats [15,23].

Histologic Findings

The cardiac muscle cells were enlarged and had large, rectangular, hyperchromatic nuclei [15]. In 56 percent of the cats with hypertrophic cardiomyopathy, and in all of the normal control cats studied, the cardiac muscle cells in the ventricular septum
FIG. 6. Heart from a seven-year-old male domestic short-haired cat with hypertrophic cardiomyopathy. The ventricular septum (11 mm) was thicker than that portion of the left ventricular free wall (9 mm) directly behind the dorsal mitral leaflet. Fibrous plaque is evident on the left ventricular outflow tract (arrow).

were in normal parallel alignment. However, in the ventricular septum of 44 percent of the affected cats, there were foci of cardiac muscle cells arranged perpendicularly or obliquely to each other (Fig. 7). In 31 percent of the cats, these areas of disorganized cardiac muscle cells occupied a significant amount (≥5 percent) of the total area of myocardium that was viewed in longitudinal section [23].

The cardiac muscle cells in the left ventricular free wall of 88 percent of the cats were normally arranged [23]. The remaining 12 percent has a septal:free wall thickness ratio range of 1.1 to 1.6 with a mean thickness ratio of 1.38 ± 0.19. Marked disorganization of cardiac muscle cells was present in the anterolateral and left posterior ventricular free walls of the combined tissue sections, similar in extent to that present in the ventricular septum. This pattern of distribution of myocardial disorganization is characteristic of human patients with hypertrophic cardiomyopathy who do not have obstruction of left ventricular outflow [24].

FIG. 7. Histologic sections of ventricular septal myocardium from Fig. 6. Cardiac muscle cells are arranged obliquely and perpendicularly to each other. (H&E, × 100).
FELINE CONGESTIVE CARDIOMYOPATHY

Age, Sex, and Breed

Cats with dilated cardiomyopathy ranged in age from three to 16 years (mean, 7.5 years). The distribution by sex indicated a predominance of male cats. There was no breed predilection [16,18].

Clinical Findings

Dyspnea was recorded in 60 percent of the cats with congestive cardiomyopathy [17,18]. Aortic thromboembolism was found in 25 percent and anorexia in 30 percent of the cats. Physical examination revealed that 30 percent had systolic murmurs, and a fourth heart sound was recorded in 47 percent (Fig. 8).

Electrocardiographic abnormalities were observed in 53 percent of the cats. Prolongation of both the P wave and QRS interval in lead II was found in 25 percent; ventricular premature contractions were recorded in 30 percent [17,18].

Thoracic radiography revealed gross cardiomegaly with general enlargement of all chambers (Fig. 9) in all affected cats. Pulmonary edema was seldom found; however, pleural effusion, considered a sign of right-sided heart failure, was observed in 74 percent of the cats [17,18].

Hemodynamic studies indicated that the mean systolic pressure (94 mm Hg) was within normal limits. The left ventricular pressure tracings revealed an elevation of end-diastolic pressure (Fig. 10), with elevation of both the peak-systolic and diastolic pressure tracings [16,17,18].

Angiocardiographic studies revealed end-diastolic volumes that were greater than normal, but the thickness of the left ventricular wall was normal (Fig. 11). Mitral insufficiency was observed in all cats.

Gross Anatomic Findings

In the cats with congestive cardiomyopathy, the heart was enlarged and globular due to extreme dilatation of the ventricles (Fig. 12) and atria [15,16,17,18,23]. The papillary muscles and trabeculae in the ventricles were flattened and atrophied. Heart
weights of the affected cats (5.4 ± 1.0 gm/kg) were greater than those in cats with normal hearts (4.0 ± 0.3 mg/kg; \( P < 0.001 \)). Ventricular septal thickness ranged from 3 to 6 mm (mean, 4.0 mm) and posterobasal left ventricular wall thickness ranged from 4 to 6 mm (mean, 4.5 mm) [23]. The septal left ventricular free wall ratio (0.9 ± 0.1) did not differ from that in cats with normal hearts (0.9 ± 0.1) [23]. Aortic thromboembolism was found in 30 percent of the affected cats.

**Histologic Findings**

The muscle cells appeared thinner than normal and were separated by edematous, extracellular ground substance or connective tissue (Fig. 13). Areas of wavy muscle
FIG. 11. Left ventriculogram of a five-year-old male domestic short-haired cat. Left atrial enlargement is seen because of mitral insufficiency. The left ventricle is severely dilated.

FIG. 12. Heart from a six-year-old male domestic short-haired cat with congestive cardiomyopathy. Note dilatation of all four chambers.

FIG. 13. Histologic section of the left ventricular free wall from Fig. 12, showing elongated and thin myofibers. (H&E, × 100).
fibers were seen in the myocardium. In other areas, the muscle fibers showed various changes, from coagulation, granulation, and vacuolation of sarcoplasm to myocytolysis [10,11,15,17,23].

**FELINE RESTRICTIVE CARDIOMYOPATHY**

Cats with restrictive cardiomyopathy ranged in age from one to 11 years (mean, 6.8 years). The distribution by sex indicated a predominance of male cats [23]. There was no breed predilection.

*Clinical Findings*

Dyspnea was the most common clinical sign, observed in 62 percent of the cats. Thromboemboli and anorexia were found in 25 percent and 31 percent of the cats, respectively [23].

Physical examination revealed that 25 percent had systolic murmurs; a fourth heart sound was recorded in 18 percent.

Electrocardiographic abnormalities observed in the cats with restrictive cardiomyopathy were similar to those recorded in the cats with hypertrophic cardiomyopathy. Conduction and rhythm disturbances including premature ventricular contractions and atrial fibrillation were recorded in 31 percent.

Valentine-shaped hearts were observed in all cats on examination of thoracic radiographs, and pleural effusion was observed in 18 percent. The mean systolic pressure remained within normal limits, but the range was greater than that of normal cats. A midventricular systolic gradient (Fig. 14) was recorded in some of the affected cats.

Angiocardiographic studies revealed extensive endocardial fibrosis causing midventricular stenosis, or irregular filling defects in the left ventricular cavity with dilatation of the apical portion of the cavity (Fig. 15) [13,15,18,23].

*Gross Anatomic Findings*

The ventricular septal thickness ranged from 6 to 12 mm (mean, 8.2 mm), and the posterobasal left ventricular wall thickness ranged from 5 to 10 mm (mean, 8.2 mm). The mean septal:free wall thickness ratio was 1.0 ± 0.18. Heart weights in the cats

![FIG. 14. Tracing from a 13-year-old male Persian cat with restrictive cardiomyopathy. A catheter was moved through the narrow midventricular chamber from the apex of the left ventricle to the aortic valve. It recorded a change in systolic pressure from 160 to 100 mm Hg. No further pressure gradients were recorded when the catheter was withdrawn to a portion above the aortic valve.](image)
with restrictive cardiomyopathy (6.4 ± 1.2 mg/kg) were greater than those in cats with normal hearts (4.0 ± 0.3 gm/kg; \( P < 0.001 \)) [23]. There was extreme dilatation of the left atrium, right ventricle, and right atrium; the left ventricle was moderately enlarged or of normal size. Left atrial enlargement was extreme to the point that the chamber appeared much larger than the left ventricle. Severe endocardial thickening (Fig. 16) was frequently observed in the left ventricular outflow tract, papillary muscles, inflow tract, lateral wall, and chordae tendineae. The thickened endocardium sometimes ended abruptly in the outflow tract. Severe focal or diffuse endocardial fibrosis caused adhesion of the papillary muscles, thickening and shortening of the mitral leaflets, and fusion and shortening of the chordae tendineae, and occasionally resulted in adhesion of the entire endocardium and a significantly diminished left ventricular cavity. Mural thrombus was superimposed in 18 percent of the cats [15,23]. Aortic thromboembolism was found in 43 percent, and ball thrombus was found in the left atrium of 12 percent [15,23].

**Histologic Findings**

The endocardium was extremely thickened by the presence of hyalin and fibrous and granulation tissue (Fig. 17)[15,23]. There was a layer of mixed hyaline tissue and collagenous fibers on the surface. Underneath this there was a layer of loose, cellular

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**FIG. 15.** Left ventriculogram in early diastole of a seven-year-old male domestic short-haired cat with restrictive cardiomyopathy. Left ventricular hypertrophy and marked endocardial fibrosis have produced an irregular left ventricular cavity. Mitral insufficiency is indicated by a large opacified left atrium.

**FIG. 16.** Left side of the heart from a 3½-year-old male Siamese cat with restrictive cardiomyopathy. Note extreme endocardial fibrosis of inflow tract and trabecular zone, fusion of chordae tendineae and papillary muscles, and enlargement and hypertrophy of the atrium.
fibrous tissue. Granulation tissue comprising histiocytes, lymphocytes, and plasma cells was seen in the adjacent myocardium. Chondroid metaplasia was occasionally seen in the hyaline and collagenous tissue [15,23]. The atrioventricular Purkinje cells were interrupted by or mixed with collagenous fibers. Hypertrophy of the muscle cells and interstitial fibroplasia were frequently detected in the myocardium. Examination of the intramural coronary arteries revealed proliferation of the intimal smooth muscle, and hypertrophy and disorganization of the media with loss or absence of the internal elastic membrane and luminal narrowing. In 18 percent of the cats with restrictive cardiomyopathy, focal disorganization of cardiac muscle cells was observed in the ventricular septum. In 12 percent, these areas of disorganized cardiac muscle cells composed a significant amount (≥ 5 percent) of the total area of myocardium that was viewed in longitudinal section.

CANINE HYPERTROPHIC CARDIOMYOPATHY

Age, Sex, and Breed

The ages of the dogs with hypertrophic cardiomyopathy ranged from one to 13 years (mean, six years) [22]. The distribution by sex indicated a predominance of males. There was a higher incidence of hypertrophic cardiomyopathy in the German Shepherd dog than in other breeds [22].

Clinical Findings

Forty percent of the affected dogs had congestive heart failure one week to one year prior to death [22]. In half of these dogs, cardiac decompensation was mild and was manifested by coughing, mild dyspnea, and radiographic evidence of pulmonary venous congestion. In the other half, cardiac failure was marked, as evidenced by severe dyspnea and radiographic evidence of cardiomegaly, hepatomegaly, and pleural or pericardial effusion. All but one of the dogs with heart failure died unexpectedly while under anesthesia during surgery; the remaining dog was euthanatized at the request of the owner. Sixty percent of the dogs with hypertrophic

FIG. 17. Histologic section of the ventricular myocardium from Fig. 15 exhibiting extremely thickened endocardium caused by presence of dense collagenous fibers, and hyalinized and chondroid tissue. (H&E, × 100).
cardiomyopathy had no evidence of cardiac disease prior to death; 50 percent died unexpectedly, including 20 percent that died during operations for noncardiac abnormalities. One dog died of causes apparently unrelated to heart disease.

Electrocardiograms were performed on 50 percent of the dogs with hypertrophic cardiomyopathy, which revealed that 30 percent had complete heart block (Fig. 18); 10 percent had a history of syncope and died during implantation of a pacemaker; 20 percent also showed evidence of bifascicular block with left axis deviation and right ventricular conduction delay (Fig. 19); and in 10 percent the condition was noted just prior to death on a cardiac monitor during surgery for a urologic problem. Of the remaining 20 percent having electrocardiograms, 10 percent showed first degree atrioventricular block (PR interval = 0.16 seconds; normal, 0.13 seconds), and the other 10 percent were normal [22].

Radiography was not performed on the dogs with hypertrophic cardiomyopathy; neither were catheterization or angiocardiographic studies done.
**Gross Anatomic Findings**

Heart weights in the affected dogs (9.6 ± 0.3 gm/kg) were significantly greater than those in dogs with normal hearts (6.6 ± 0.3 gm/kg; P < 0.001). The ventricular septal thickness ranged from 13 to 22 mm (mean, 18.8 mm) and posterobasal left ventricular wall thickness ranged from 10 to 19 mm (mean, 14.8 mm) (Fig. 20) [22]. The mean septal:free wall thickness ratio (1.3 ± 0.04) was significantly greater than that in dogs with normal hearts (1.0 ± 0.01; P < 0.001) [22]. In 20 percent of the dogs, a fibrous endocardial plaque was present on the ventricular septum in the left ventricular outflow tract adjacent to the anterior mitral leaflet. In another 20 percent, a more diffuse fibrous tissue formation was present on the ventricular septum. The left ventricular cavity was moderately or severely reduced in size in all dogs, and the left atrium was moderately dilated in 20 percent [22]. The cardiac values in all dogs were normal.

**Histologic Findings**

In 80 percent of the dogs with hypertrophic cardiomyopathy, the cardiac muscle cells in the ventricular septum were hypertrophied in normal parallel alignment [22]. In the ventricular septum of the remaining 20 percent, foci were present in which cardiac muscle cells were arranged perpendicularly or obliquely to each other (Fig. 21). These areas of disorganized cardiac muscle cells occupied a significant amount (≥ 5 percent) of the total area of myocardium that was viewed in longitudinal section. In 10 percent of the dogs, the septal:free wall thickness ratio was 1.3; marked disorganization of cardiac muscle cells was present in the anterior and posterior left ventricular free walls [22].

**CANINE CONGESTIVE CARDIOMYOPATHY**

**Age, Sex, and Breed**

Dogs with congestive cardiomyopathy ranged in age from two to nine (mean, 4.9 years) [21]. The distribution by sex indicated a predominance of males. Only dogs of large breeds were affected, including Great Dane, Doberman Pinscher, German Shepherd dog, Irish Wolfhound, Standard Poodle, and St. Bernard [19,20,21].

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**FIG. 20.** Heart of a nine-year-old Airedale Terrier showing disproportionate thickening (17 mm) of the ventricular septum (VS) with respect to the left ventricular free wall (12 mm) (LV). Fibrous plaque is evident on the left ventricular outflow tract (arrow); RV = right ventricular wall. With permission from [22].
Clinical Findings

A majority of the dogs with congestive cardiomyopathy presented with varying degrees of right and left heart failure. The predominant clinical signs reported by the owners were weight loss, general disability, weakness, and abdominal enlargement over a period of from two to four weeks [19-21]. Other signs included coughing, dyspnea, and ascites. A rapid, irregular heart rate was clearly palpated over the left caudal sternal border in most cases. Systolic murmurs of low to moderate intensity were heard over the mitral valve area at auscultation. A diastolic gallop sound was frequently heard and was usually loud and consistent in frequency [21].

Rapid and irregular heart rates were confirmed by electrocardiography, which also revealed wide QRS complexes. Normal sinus P waves were absent (Fig. 22) [21],

![FIG. 21. Histologic section of ventricular septal myocardium from Fig. 18. Area of cardiac muscle cell disorganization. (H&E, × 100).](image)

![FIG. 22. Conversion of atrial fibrillation to normal sinus rhythm in a dog with congestive cardiomyopathy. (A) Electrocardiogram from a dog in atrial fibrillation with a ventricular rate of 200 beats/min. The rate is rapid and irregular with absence of P waves. (B) The ventricular rate is reduced with cardiac glycoside. (C) A normal sinus rhythm with a heart rate of 160 beats/min is the result after electrical cardioversion at 250 watt-sec. Lead II, paper speed = 50 mm/sec. Standard amplitude of 10 mm/mv for strip C and one-half the amplitude for strips A and B.](image)
which is consistent with atrial fibrillation and left ventricular hypertrophy. Ninety percent of the dogs had atrial fibrillation [22]; some had single or multiple ventricular premature complexes.

Thoracic radiography revealed moderate to severe enlargement of all cardiac chambers, and signs of either right- or left-sided heart failure: diffuse pulmonary congestion or edema, pleural effusion and ascites, and a wide, elevated caudal vena cava [22].

The results of cardiac catheterization indicated poor myocardial contractility with elevation of the left ventricular and right ventricular end-diastolic pressure (Fig. 23). Measurement of the left ventricular volume parameters showed a moderate increase in the end-diastolic volume, an ejection of 0.42, and a reduced net stroke work compared with normal dogs with volume overload. Angiography showed gross enlargement of the cardiac chambers with resultant secondary mitral and tricuspid insufficiency.

**Gross Anatomic Findings**

Heart weights in the dogs with congestive cardiomyopathy (11.5 ± 2.4 gm/kg) were significantly greater than those in dogs with normal hearts (6.6 ± 0.3 gm/kg; P < 0.001). The hearts were rounded due to the extreme dilatation of the ventricles (Fig. 24). The vessels on the epicardial surfaces were tortuous and dilated. The left ventricular wall (range, 8 to 19 mm; mean, 12.9 mm) and septal (range, 8 to 17 mm; mean, 11.0 mm) thicknesses were thinner than normal. The mean septal:free wall thickness ratio in the dogs with congestive cardiomyopathy (0.85 ± 0.08) did not differ from that in dogs with normal hearts. The endocardial surfaces were opaque, and the papillary muscles and trabeculae in the ventricles were flattened and atrophied. The circumferences of the mitral and tricuspid valves were greater than normal, but the leaflets and chordae tendineae of the atrioventricular valves were normal. Excessive amounts of abdominal and thoracic effusion (500–2500 ml) and pericardial effusion (25–250 ml) were seen in all dogs [21].

**Histologic Findings**

In all dogs with congestive cardiomyopathy, the thin, wavy cardiac muscle cells were separated by edematous fluid or fine connective tissue. In some areas, the
cardiac muscle cells were characterized by various degrees of degeneration from coagulation, granulation, or vacuolization or sarcoplasm to myocytolysis (Fig. 25) [22].

CARDIOMYOPATHY IN HAMSTERS

Clinical Findings

Golden Syrian hamsters with cardiomyopathy have a lifespan of about 146 days, or approximately one-third the normal life expectancy of normal hamsters of the same breed [4]. Affected hamsters were characterized by retarded growth and were smaller in size and lighter in weight than normal hamsters during the first half of their lives. However, the hamsters with heart failure and fluid retention were often significantly heavier than normal during the second half of their lives [4].

Clinical signs including hypernea, cyanosis, generalized edema, abnormal electrocardiograms with distinct alteration within the QRS complex, and degeneration and

FIG. 24. The heart from a three-year-old male St. Bernard showing dilated ventricles.

FIG. 25. Histologic section of the left ventricle from a four-year-old male Great Dane with congestive cardiomyopathy, showing thin and elongated muscle fibers separated by edematous ground substance. (H&E, × 100).
weakness of the skeletal muscles were observed in the terminal stage of the disease. Death usually occurred a few weeks after these signs were noted [4-6].

Pathologic Findings

There were no detectable anatomic changes in the heart during the early stage of the disease. Ventricular hypertrophy and myocardial degeneration were detected in the affected hamsters at approximately 60 days of age. Hypertrophy, gradually replaced by dilatation of the cardiac chambers and newly formed thrombi attached to the atrium and auricle, was observed at approximately 80 days of age. Extreme dilatation of the cardiac chambers with organized thrombi in the atrium and auricle, pleural effusion, pulmonary edema, and hepatic congestion were observed in the diseased hamsters after 100 days of age [4-6].

The earliest histologic abnormality of the myocardium observed was focal vacuolization and lysis of the sarcoplasm of the muscle cells, and hypertrophy of the adjacent muscle fibers, in the absence of cellular infiltration. As this process progressed, myocytolytic changes became more pronounced and diffuse, and the disintegrated muscle cells were replaced by fibrous connective tissue. In the advanced state, myocytolytic lesions and extensive fibrosis were observed throughout the ventricular free wall, auricle, and interventricular septum. Infiltration of histiocytes and fibroblasts was occasionally observed in and around the lesions [4-6].

Cardiomyopathy in hamsters is transmitted by an autosomal recessive gene, and the disease is phenotypically expressed in 100 percent of the hamsters in affected lines [4,5]. The myopathic lines are available today (Bio 14.6, 40.54, 82.62, and 53.58; TELACO, Bar Harbor, ME).

CARDIOMYOPATHY IN TURKEYS

Round heart disease (cardiomyopathy) of unknown etiology occurred spontaneously in commercial turkeys [7,8,9]. Clinical signs included intolerance to exercise, the presence of cardiac murmurs, and electrocardiographic abnormalities [7,9]. Hemodynamic data from the affected turkeys indicated low-normal cardiac output, increased pulmonary arterial wedge, elevated pulmonary pressure, increased right atrial pressure, and low systemic arterial pressure [9]. Anatomic features of the disease included left ventricular hypertrophy and, later, dilatation with focal or diffuse endocardial fibrosis. Histologic findings consisted of focal areas of myocardial necrosis, infiltration of mononuclear cells, and fibrosis [8]. Electron microscopy revealed myocardial necrosis in the turkey embryos, and these lesions became more severe in the poults at four weeks of age [8]. Focal or diffuse endocardial fibrosis was evident in the ventricular outflow tract of the dilated heart [7-9].

DISCUSSION

Feline and canine cardiomyopathies occur in mature male cats or dogs [18,21,-23]. The most common clinical features are: acute onset of dyspnea and/or feline aortic thromboembolism; systolic murmur with a gallop rhythm; cardiomegaly with (hypertrophic or restrictive cardiomyopathy) or without (congestive cardiomyopathy) pulmonary edema; abnormal electrocardiogram; elevated left ventricular end-diastolic pressure; and angiocardiographic evidence of mitral regurgitation with left ventricular concentric hypertrophy (hypertrophic cardiomyopathy), left ventricular dilatation (congestive cardiomyopathy), or left ventricular stenosis or irregular filling defects (restrictive cardiomyopathy [13,14,16,18]. These clinical electrocardio-
graphic, hemodynamic, and angiocardiographic findings of feline [12-14,16-18] or canine cardiomyopathies [22] are similar to those of human patients with hypertrophic, congestive, or restrictive cardiomyopathy [25,26].

The consistently elevated end-diastolic pressures recorded in all cats, together with the thick, hypertrophied ventricular walls, indicated a loss of ventricular compliance during diastole [13,18]. A marked concentric hypertrophy of the left ventricle and decreased end-systolic volume have also been found in valvular aortic stenosis and hypertrophic cardiomyopathy in man [25,26]. In cardiomyopathy in both cat and man, greater pressure is needed to fill the left ventricle, as it is less compliant than normal, causing resistance to left ventricular filling. Tachycardia produced by stress or exercise shortens diastolic filling time and further limits diastolic filling. Cardiac output falls because the tachycardia is not sufficient to compensate for the drop in stroke volume caused by poor filling [13,18]. Pulmonary congestion and edema with dyspnea result from mitral regurgitation. In hamsters, hypertrophic cardiomyopathy may progress to congestive cardiomyopathy [4,27], but in cats, most with hypertrophic cardiomyopathy appear to die before congestive cardiomyopathy is reached. It has been suggested that each human patient with this syndrome is subject to individual variation, and this may also be true for the cat [26,28].

Angiography in cats with hypertrophic cardiomyopathy showed gross hypertrophy and distortion of the left ventricular cavity [13,16,18], similar to that of the nonobstructive variety of hypertrophic cardiomyopathy in man [29–31]. The cats with restrictive cardiomyopathy had angiographic evidence of midventricular stenosis, and midventricular systolic pressure gradients [13,18] that resembled those seen in restrictive cardiomyopathy in man. The cats with congestive cardiomyopathy had end-diastolic volumes that were greater than normal with a normal thickness of left ventricular free wall [13,16,18]. All of these findings are similar to those of human patients with congestive cardiomyopathy [32].

The principal pathologic findings in the cats and dogs with hypertrophic cardiomyopathy were ventricular septal and ventricular free wall hypertrophy, left atrial dilatation and hypertrophy, and disproportionate septal thickening [11,13,15,18,22–23]. The mean septal:free wall thickness ratios in the dogs and cats with hypertrophic cardiomyopathy were significantly greater than those of dogs and cats with normal hearts or with acquired or congenital disease. Septal:free wall thickness ratios in 80 percent of the dogs and in 46 percent of the cats exceeded the greatest ratio observed in the control animals (i.e., 1.1) [15,22,23]. Hence, our data suggest that a septal:free wall thickness ratio of 1.1 may be more appropriate than ≥ 1.3 [31,33] as a diagnostic criterion for disproportionate septal thickening (and, therefore, hypertrophic cardiomyopathy) in dogs and cats.

Forty-four percent of the cats [15,18,23] and 20 percent of the dogs [22] with hypertrophic cardiomyopathy showed disorganization of cardiac muscle cells in the ventricular septum, characteristic of hypertrophic cardiomyopathy in humans [24,31,34,35]. In these cats and dogs, the area of myocardium involved by disorganized cardiac cells was significant [15,22,23]. This degree of involvement is typical of patients with hypertrophic cardiomyopathy and is distinctly uncommon in patients with concentric cardiac hypertrophy due to other forms of heart disease [24]. In 12 percent of the cats with a septal:free wall thickness ratio of 1.38 ± 0.19, and in 10 percent of the dogs with a septal:free wall thickness ratio of 1.3, marked disorganization of cardiac muscle cells was present in the anterolateral and posterior left ventricular free walls [22], similar in extent to that present in the ventricular septum. This pattern of distribution of myocardial disorganization [22] is characteristic of
human patients with hypertrophic cardiomyopathy who do not have obstruction to left ventricular outflow [24].

The main cardiac lesions in the cats [15,17,18,23] and dogs [21] with congestive cardiomyopathy included dilatation of the four cardiac chambers, and elongated and degenerated muscle cells with interstitial edema and fibrosis, similar to those found in human patients with congestive cardiomyopathy [2,29].

The major pathologic findings in the cats [15,23] with restrictive cardiomyopathy included extreme dilatation of the left atrium, extensive endocardial and myocardial fibrosis, and hypertrophy of cardiac muscle cells, and were similar but not identical to those in human patients with restrictive (obliterative) cardiomyopathy [36–38]. In 18 percent of the cats with restrictive cardiomyopathy, classified previously as hypertrophic cardiomyopathy [10,11,15–18,23], with a septal:free wall thickness ratio of 1.2, focal disorganization of cardiac muscle cells was observed in the ventricular septum. In 12 percent, these areas of disorganized cardiac muscle cells occupied a significant amount of the total area of the myocardium that was viewed in longitudinal section. These cats (18 percent) might be primarily affected by hypertrophic cardiomyopathy with characteristic disorganization of cardiac muscle cells, superimposed by lesions of restrictive cardiomyopathy.

In turkeys with cardiomyopathy, focal myocardial necrosis, infiltration of mononuclear cells, myocardial fibrosis, and endocardial fibroplasia [7–9] are lesions similar to those found in cats [11,23] and humans [2,36,37] with endocarditis and restrictive cardiomyopathy. The etiology of restrictive cardiomyopathy in the turkey is unknown. Virus-like particles resembling the C-type particles have been found in the myocardium of the affected poults [8], but a causal relationship of these to the disease has not been established.

Aortic thromboembolism was observed in 41 percent of the cats with primary myocardial disease [10,11,23]; all cats with aseptic thromboembolism have cardiomyopathies [11,13]. Intracardiac fibrin-platelet thrombi are common in human patients with cardiomyopathies [2,29,36,37] and in cats with restrictive cardiomyopathy [15,23]. Atrial and auricular thrombi are often observed in hamsters [4] and in cats [11,23] with cardiomyopathies. The pathogenesis of thromboembolism is unclear; however, it is possible that the hemodynamic effects of feline cardiomyopathies contribute to the formation of thromboemboli [11,13]. Hemostasis is the supposed cause of left atrial thrombus in mitral stenosis in man [39]. Extremely dilated atria and auricles with ball thrombi were found in the cats [11,13] and hamsters [4] with cardiomyopathies. Sluggish circulation was observed on angiocardiography in the cats [13], particularly in the affected chamber, a likely site for thrombus formation. Endocardial inflammation and subsequent fibrosis in man, cats, and probably turkeys with endocarditis or restrictive cardiomyopathy provoke platelet aggregation and precipitate thrombus formation in the intracardiac chambers.

On the basis of comparative pathology, spontaneous feline hypertrophic, congestive, and restrictive cardiomyopathies, and canine hypertrophic and congestive cardiomyopathies, as well as cardiomyopathies in hamsters and turkeys, present new and important models to the experimental pathologist and cardiovascular investigator. Our laboratory is continuing to explore the natural history of these diseases.

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