Chapter 36

Cardiovascular Disease

Philip Roudebush
Bruce W. Keene

"Give neither advice nor salt, until you are asked for it."
English Proverb

CLINICAL IMPORTANCE

Cardiovascular disease and congestive heart failure (CHF) are common conditions in dogs and cats. The types and prevalence of heart disease in dogs in the United States were characterized more than 40 years ago in a survey of 5,000 dogs at the University of Pennsylvania (Detweiler and Patterson, 1965). Eleven percent of dogs had reliable signs of heart disease and another 9% had possible heart disease. Congenital heart disease has been recognized in 0.56 to 0.85% of dogs and 0.2% of cats (Detweiler and Patterson, 1965; Harpster and Zook, 1987; Buchanan, 1992). These results predominantly reflect the prevalence of congenital disease in the necropsy populations of referral institutions, and may significantly underestimate the prevalence of heart diseases in the general pet population.

The overall prevalence of heart disease appears to be similar today, but comparable epidemiologic data for acquired heart disease in the U.S. are not available (Buchanan, 1992). A clinical review in Italy found heart disease in 11% of 7,148 dogs (Fioretti et al, 1988). One informal survey identified heart problems as the third leading cause of nonaccidental death of dogs (MAF, 1991). The results of a more recent informal survey of veterinary clinics performed by a pharmaceutical company also suggest that the prevalence of cardiovascular disease among dogs has probably not changed dramatically from these earlier estimates.[a]

Chronic mitral valvular disease (endocardiosis) is by far the most common acquired cardiac abnormality in dogs, affecting more than one-third of patients over 10 years of age (Buchanan, 1992, 1977). The tricuspid valve is also frequently involved (in approximately 30% of cases), but disease of the tricuspid valve is usually less severe. Chronic valvular disease occurs with relatively greater frequency in small dogs, especially poodles, miniature schnauzers, Chihuahuas, cocker spaniels, fox terriers, Boston terriers, dachshunds, Pekingese, miniature pinschers and whippets (Buchanan, 1977; Thrusfield et al, 1985). Mitral valvular disease has been identified in more than 50% of cavalier King Charles spaniels in the United Kingdom, Sweden and the U.S. (Darke, 1995; Beardrow and Buchanan, 1993). Acquired valvular disease in cats is rare.

Since 1987, the prevalence of dilated (congestive) cardiomyopathy in cats has decreased markedly following the discovery that taurine deficiency was the principal cause (Pion et al, 1987, 1989), and the subsequent supplementation of most commercial feline foods with taurine. One study documented that the prevalence of dilated cardiomyopathy as a cause of myocardial failure in cats decreased from 28% in 1986 to only 6% in 1989, whereas the occurrence of hypertrophic cardiomyopathy did not change (Skiles et al, 1990). Referral institutions continue to observe several individual cases of dilated cardiomyopathy in cats each year, only a few of which are now associated with taurine deficiency. Hypertrophic and restrictive cardiomyopathies are now the most common causes of myocardial failure in cats.

Various types of myocardial disease that were not recognized 40 years ago are now seen relatively commonly in dogs (Buchanan, 1992). Large-breed dogs, especially males, are predisposed to dilated cardiomyopathy. Doberman pinscher dogs are particularly susceptible. Hypertrophic cardiomyopathy occurs rarely in dogs. Arrhythmogenic right ventricular cardiomyopathy is common among boxer dogs (Meurs and Spier, 2009).

Pulmonary vascular disease with secondary cor pulmonale is most commonly associated with *Dirofilaria immitis* infection (heartworm disease). The prevalence of this disease is high in endemic areas in those dogs that do not receive appropriate preventive medication. Pulmonary hypertension unrelated to heartworm disease appears to be more common than previously believed and the frequency of diagnosis has increased because of heightened awareness about the condition (Henik, 2009) and the more widespread application of Doppler echocardiography. Pulmonary thromboembolism is most commonly associated with renal disease, hyperadrenocorticism, corticosteroid therapy, neoplasia, nephrotic syndrome, pancreatitis and immune-mediated hemolytic anemia. Primary systemic vascular disease is uncommon, but atherosclerosis and aortic or coronary thrombosis are occasionally recognized, particularly in dogs with hypothyroidism and elevated serum cholesterol concentrations. Secondary aortic thromboembolism in cats may occur with any of the forms of cardiomyopathy and is the most frequently acquired feline vascular abnormality.

Systemic hypertension in dogs and cats appears to be more common than studies indicated 40 years ago (Brown et al, 2007). Because blood pressure measurement in dogs and cats is technically challenging compared to measurement in people, and because of the prominent "white coat effect" in animals (elevations in measured blood pressure associated with the stress of the clinical visit) the actual prevalence of systemic hypertension in dogs and cats is still unknown. Spontaneous essential hypertension occurs in dogs, but hypertension most commonly develops secondary to chronic kidney disease in dogs and cats, hyperadrenocorticism in dogs and hyperthyroidism in cats (Littman and Drobatz, 1995). The demographic characteristics of dogs and cats at risk for the diseases that predispose to systemic hypertension overlap with those of dogs and cats with acquired heart disease. Although hypertensive dogs and cats may present at any age, most often they are middle-aged to geriatric (mean age: dogs nine years; cats 15 years, Littman and Drobatz, 1995). The strength of the peripheral pulses does not help detect systemic hypertension; absolute blood pressure numbers need to be determined. Retinal hemorrhages and detachments are common end-organ changes in patients with moderate to severe hypertension. These ocular signs are often the first evidence of hypertensive disease, which suggests that a fundic examination should be included in the routine evaluation of all dogs and cats. Other clinical signs of hypertension are most often related to the underlying disease that causes systemic hypertension.

The effects of long-term or severe systemic hypertension may cause significant heart disease (e.g. left ventricular concentric hypertrophy), and hypertension may complicate the treatment of chronic mitral valvular disease in dogs by worsening valvular regurgitation. It makes good clinical sense to screen dogs and cats with significant heart disease for the presence of systemic hypertension (by repeated blood pressure measurements), and also makes sense to search for underlying heart disease in patients with known hypertension, especially those exhibiting clinical signs that may be referable to heart disease.

The most frequently encountered problems associated with cardiovascular disease that require nutritional modification are fluid retention states associated with chronic CHF, primary or secondary hypertension, obesity, cachexia and myocardial diseases related to a specific nutrient deficiency (taurine- and carnitine-associated cardiomyopathy and electrolyte disorders that may predispose to cardiac dysrhythmias.

PATIENT ASSESSMENT

History and Physical Examination

Heart failure is a condition characterized by inadequate cardiac output and insufficient delivery of nutrients relative to tissue metabolic needs. Heart failure is not a specific disease, but a clinical syndrome caused by a variety of structural and functional disorders of the heart or great vessels. Clinical manifestations of heart failure are due to reduced cardiac output (weakness, exercise intolerance, syncope), pulmonary congestion (dyspnea, orthopnea, cough, abnormal breath sounds with crackles and wheezes), systemic fluid retention (jugular venous distention, hepatomegaly, ascites, pleural effusion) or a combination of these conditions.

In general, the clinical manifestations of heart failure are similar irrespective of the underlying cause, although the onset may vary. Occasionally, for example, heart failure may occur abruptly and lead to acute pulmonary edema (e.g., ruptured mitral valve chorda tendineae). Diagnosis of this fulminant form of heart failure is based on the history and overt, acute clinical signs. In many instances, however, heart failure becomes evident gradually; a long asymptomatic period (years) following the diagnosis of chronic valvular heart disease based on the presence of the typical murmur of mitral valve insufficiency is typical–this period may be followed by the onset of mild clinical signs that worsen gradually, or by the sudden onset of severe pulmonary edema. Most of the clinical signs used as the basis for diagnosing chronic heart failure may also occur as a result of other conditions.

Validity of a clinical diagnosis of heart failure in human patients was studied in a primary health care setting (Remes et al, 1991). One-third of human patients who were initially diagnosed with heart failure were subsequently found to have other conditions that caused their clinical problems. Obesity and pulmonary diseases were the most important conditions leading to false-positive diagnoses of heart failure in this population of human patients. Obesity and chronic bronchitis often occur in dogs and cats with heart disease and cause clinical manifestations similar to those of heart failure, thereby complicating the

diagnosis. As an example, a small-breed dog may be admitted with moderate obesity, cough, tachypnea, exercise intolerance, abnormal breath sounds with crackles and a holosystolic murmur loudest over the mitral valve. It is important that this patient be evaluated thoroughly to determine whether the cause of the clinical signs is: 1) chronic bronchitis, 2) early heart failure, 3) obesity or 4) a combination of these conditions.

Human patients with heart disease and failure are categorized according to functional and structural schemes. The functional scheme is based on the clinical signs and symptoms evident at rest and during exercise (New York Heart Association functional classes). Members of the International Small Animal Cardiac Health Council popularized a functional classification scheme that is applicable to veterinary patients (**Table 36-1**) (ISACHC, 1994). Although patients with heart disease may follow an orderly progression though a functional classification, animals may change classifications in both directions–e.g., from Class III or IV to Class II or III following therapy, or from Class I to Class III or IV following a salty meal.

In 2001, the American College of Cardiology (ACC) and the American Heart Association (AHA) developed a staging scheme for heart failure patients emphasizing the progressive nature of the diseases that cause heart failure. This scheme has been adapted as follows for veterinary use (Keene and Bonagura, 2009):

- Stage A–patients at high risk for the development of heart failure, but without currently apparent structural heart abnormalities (e.g., cavalier King Charles spaniels, boxers, Doberman pinschers and other animals belonging to breeds, families or demographic groups known to be predisposed to heart disease).
- Stage B–patients with a structural heart abnormality, but without past or current symptoms of heart failure (e.g., patients with an asymptomatic murmur of mitral regurgitation).
- Stage C–patients with a structural abnormality and current or previous clinical signs of heart failure (this stage includes all patients that have experienced clinical signs of heart failure, and they stay in this stage despite resolution of their clinical signs with standard therapy).
- Stage D–patients with clinical signs of heart failure that have become refractory to standard treatment (defined practically as standard doses of furosemide, angiotensin-converting enzyme [ACE] inhibitor and pimobendan).

The ACC/AHA staging system emphasizes that progressive structural abnormalities of the heart underlie the pathogenesis of heart failure. This scheme is meant to encourage a program of client education and heart failure management that supports early screening for heart disease and provides a loosely defined plan for therapeutic intensification, including nutritional intervention, as heart disease progresses. This staging system further departs from functional classifications in that while a patient can still progress suddenly from Stage B to Stage C (or D, for example, if a previously asymptomatic dog with chronic valvular heart disease experiences a ruptured mitral valvular chorda tendineae), that path cannot be traveled in reverse.

Table 36-1. Functional classes of heart failure.*

Class I. The asymptomatic patient
Heart disease is detectable (cardiac murmur, dysrhythmia), but the patient is not overtly affected and does not demonstrate clinical signs of heart failure.
a. Heart disease is detectable but no signs of compensation are evident, such as volume or pressure overload ventricular hypertrophy.
b. Heart disease is detectable in conjunction with radiographic or echocardiographic evidence of compensation, such as volume or pressure overload ventricular hypertrophy.

Class II. Mild to moderate heart failure
Clinical signs of heart failure are evident at rest or with mild exercise and adversely affect the quality of life. Typical clinical signs include exercise intolerance, cough, tachypnea, mild respiratory distress and mild to moderate ascites. Hypoperfusion at rest is generally not present.

Class III. Advanced heart failure
Clinical signs of CHF are immediately evident. These clinical signs include respiratory distress (dyspnea), marked ascites, profound exercise intolerance and hypoperfusion at rest. In the most severe cases, the patient is moribund and suffers from cardiogenic shock.

*Adapted from International Small Animal Cardiac Health Council. In: Recommendations for the Diagnosis of Heart Disease and the Treatment of Heart Failure in Small Animals. Academy of Veterinary Cardiology, 1994.

The ACC/AHA scheme provides a framework for thinking about heart disease that is more analogous to the clinical approach to cancer, i.e., the identification of patients who are known to be at risk for cancer and who might benefit from more intensive screening to identify disease at an early stage (Stage A); the identification and treatment of patients with in-situ disease (Stage B); and the identification and treatment of patients with established (Stage C) or widespread (Stage D) disease. As our knowledge of the pathophysiology of heart disease and the progression of heart disease to heart failure expands, there is hope that early pharmacologic and/or nutritional intervention (often possible before the onset of clinical signs in heart disease) might significantly affect the eventual course of disease and survival in an individual patient. Currently, however, there are essentially no well-defined, effective therapies that prevent or delay the onset of heart disease or failure in either dogs or cats.

In assessing the nutritional status of patients with cardiovascular disease, overall body condition is the most important indicator of nutritional status and it appears to be an important, independent prognostic indicator. As will be discussed later, obesity causes cardiovascular changes that can complicate the management of cardiovascular disease, but in dogs and cats, significant weight loss is a far more common problem after the onset of heart failure. Although treatment of obesity is occasionally necessary in the management of patients with significant cardiovascular disease, it is relatively uncommon that clinically significant obesity coexists with life-threatening cardiovascular disease in dogs and cats. Cachexia is a syndrome of severe wasting seen clinically in a variety of diseases, especially chronic heart failure, cancer and acquired immunodeficiency syndrome. Cachexia is an additional risk factor in people with heart failure; loss of lean

body mass is a negative predictor of survival (Freeman and Roubenoff, 1994). Systems for accurately assessing and scoring body condition are available for dogs and cats (Chapter 1). The body condition of dogs and cats with cardiovascular disease should be followed closely as part of reassessment.

Laboratory and Other Clinical Information

Measurement of Systemic Blood Pressure

Hypertension is often defined as that blood pressure two standard deviations above the mean for the population (Littman and Drobatz, 1995). Most investigators agree that the systemic systolic/diastolic blood pressure in awake, untrained dogs and cats normally should not exceed 180/100 millimeters of mercury (mm Hg), with values up to 200/110 mm Hg considered borderline or mild hypertension (Littman and Drobatz, 1995), especially in cats.

Direct blood pressure measurement is obtained by inserting a needle or catheter into an artery. The needle or catheter is connected to a pressure transducer and the result displayed on an oscilloscope/recording device. Anxiety and pain may falsely elevate the blood pressure of awake, restrained or uncooperative patients when measured by direct techniques.

Indirect blood pressure measurement is noninvasive and obtained with a cuff constricting a peripheral artery (leg or tail). An ultrasonic, oscillometric or photoplethysmographic transducer distal to the cuff is used to detect blood flow or arterial wall motion (Hansen, 1995). Blood pressure values obtained by direct and indirect methods generally correlate well, but indirect methods may produce values less than those obtained simultaneously by direct methods. In general, blood pressure measurements obtained routinely during hospital visits are reasonable estimates of a dog's true blood pressure (Remillard et al, 1991). Uncooperative, anxious patients may have elevated blood pressure measurements in the hospital setting that do not reflect normal values. A review of blood pressure measurements describes these techniques (Hansen, 1995). Comprehensive, current guidelines for the diagnosis and management of hypertension have recently been published (Brown et al, 2007).

Screening for Concomitant Disease

Cardiovascular disease is frequently associated with or exacerbated by underlying chronic renal disease in dogs and cats. All patients with cardiovascular disease should be screened for concomitant renal disease. This is best accomplished with a urinalysis and a serum biochemistry profile, which includes urea nitrogen, creatinine, electrolyte, calcium and phosphorus concentrations.

Hyperthyroidism in cats is a risk factor for secondary thyrotoxic cardiomyopathy and systemic hypertension. Cats over the age of seven years with evidence of cardiovascular disease should be screened for hyperthyroidism (Chapter 29).

Measuring and Interpreting Tissue Nutrients and Hormones

ELECTROLYTES AND MAGNESIUM

Serum electrolyte and magnesium concentrations are important factors to assess in patients with cardiovascular disease. Abnormalities in electrolyte and magnesium homeostasis can cause or contribute to the progression or severity of cardiac dysrhythmias, and decreased myocardial contractility associated with severe electrolyte abnormalities may cause profound heart muscle weakness. Electrolyte and magnesium abnormalities can also potentiate adverse effects from cardiac glycosides and other cardiac drugs. Unfortunately, the precise diagnosis of potassium and magnesium depletion can be difficult to make because these are primarily intracellular constituents. Normal serum potassium and magnesium concentrations can occur in the presence of total body depletion of these elements; therefore, serum potassium and magnesium concentrations do not always reflect total body stores.

TAURINE

Plasma and whole blood taurine concentrations are routinely measured to evaluate the taurine status of cats and dogs. Most early experimental and clinical studies used plasma taurine concentration to define taurine status. Values for plasma taurine of less than 20 to 30 nmol/ml (μmol/l) have been associated with deficiency in clinical studies involving client-owned cats (Pion et al, 1987; Sisson et al, 1991) and dogs (Kramer et al, 1995).

Studies involving laboratory cats have shown that plasma, but not whole blood taurine concentrations are affected by meals and food deprivation (Trautwein and Hayes, 1991; Pion et al, 1991). Therefore, whole blood taurine concentration is a more reliable index of taurine status in cats. In general, the whole blood taurine pool is remarkably stable and declines only during prolonged depletion, whereas plasma taurine concentrations fluctuate acutely depending on availability in food. Cats with whole blood taurine concentrations consistently less than 150 nmol/ml should be considered taurine deficient (Pion et al, 1989, 1991). Whole blood taurine concentrations have also been adopted by the Association of American Feed Control Officials (AAFCO) as part of its feeding protocols for cats. To successfully complete an AAFCO feeding protocol, no individual cat, kitten or queen can have a whole blood taurine concentration less than 200 nmol/ml (AAFCO, 2008).

Assessment of urinary taurine excretion has also been advocated as an alternative to measuring plasma or whole blood taurine concentrations (Glass et al, 1992). Urinary taurine excretion may provide vital information in the experimental setting for proper formulation of feline foods, but this assessment is probably not a practical technique for use with client-owned cats.

In North America, several laboratories routinely perform plasma and whole blood taurine assays. These laboratories are most easily accessed through regional veterinary reference laboratories that perform routine diagnostic services.

CARNITINE

Many investigators have reported blood and tissue carnitine concentrations in animals. The lowest levels are usually found in serum; in contrast, heart and skeletal muscle contain very high levels of carnitine, which underscores its importance in these tissues. Normal canine and feline values are similar for

total, free and esterified carnitine concentrations in plasma based on measurements from a small number of healthy dogs and cats fed a standard dry commercial food (Jacobs et al, 1990, 1990a; Keene, 1992; Shelton, 1995). Total carnitine concentrations in plasma are influenced by intake of carnitine in food. Plasma concentrations will be elevated in animals that eat foods high in carnitine (e.g., raw meat or moist foods high in skeletal muscle content). To measure carnitine concentration, approximately 1 ml of heparinized plasma should be immediately separated, frozen and submitted to an appropriate laboratory.[b]

Carnitine concentrations can also be measured in cardiac muscle, skeletal muscle and liver (Jacobs et al, 1990, 1990a; Keene, 1992; Shelton, 1995). Cardiac tissue is obtained by using a modified transvenous endomyocardial biopsy technique (Keene et al, 1990). Skeletal muscle and liver tissue are obtained using standard biopsy techniques. Tissue specimens are blotted dry, immediately frozen in liquid nitrogen and stored at –70°C (–94°F) until the carnitine concentration is measured at an appropriate laboratory.[b] Tissues for carnitine assay should not be placed in formalin. Dogs with confirmed lipid storage myopathy should have plasma and tissue carnitine assays performed in the hope of identifying a potentially treatable cause of an otherwise difficult to manage disease (Shelton, 1995).[c]

BLOOD CONSTITUENTS ASSOCIATED WITH NEUROHUMORAL ACTIVATION

It is well established that activity of several neurohumoral systems is increased in many patients with chronic CHF. Elevated levels of renin, angiotensin, aldosterone and arginine vasopressin (AVP; antidiuretic hormone [ADH]) occur in both spontaneous and experimental canine models of CHF (Watkins et al, 1976; Riegger and Liebau, 1982; Riegger et al, 1988; Maher et al, 1989; Villarreal et al, 1990; Himura et al, 1994). Increased concentrations of renin, aldosterone, norepinephrine and brain or atrial natriuretic peptide or atrial natriuretic factor (BNP, ANP or ANF) occur in dogs with spontaneous heart disease and failure (Knowlen et al, 1983; Ware et al, 1990; Takemura et al, 1991; Vollmar et al, 1991; Buoro et al, 1992; Haggstrom et al, 1994; Pederson et al, 1995). Aldosterone, norepinephrine and ANP concentrations also increase with the severity of heart failure (Knowlen et al, 1983; Ware et al, 1990; Haggstrom et al, 1994). Aldosterone concentrations may offer some prognostic information about the severity of heart failure (Knowlen et al, 1983). Measurement of n-terminal BNP or troponin-I (a calcium regulatory protein that leaks from myocytes in many heart diseases) in the serum of dogs or cats shows significant promise as a means of identifying patients with either clinical or subclinical heart disease; however, the optimal application of these techniques awaits the availability of a reliable point-of-care test with proven positive predictive value in a variety of clinical settings (Prosek et al, 2007; Oyama et al, 2007). Norepinephrine, angiotensin, ANP and AVP analyses are only available through research laboratories. Plasma renin activity and aldosterone measurements are available through several reference laboratories.

Risk Factors

Risk factors for causing or complicating cardiovascular disease include breed, gender, obesity, renal disease, drug therapy, endocrinopathies and heartworm infection. Breed and gender appear to be the most important risk factors for cardiovascular disease in dogs. A number of breeds are at increased risk for several different congenital cardiovascular malformations, including patent ductus arteriosus, portacaval shunts, aortic stenosis, pulmonic stenosis, ventricular septal defects, tricuspid dysplasia and persistent aortic arch and related vascular abnormalities. Estimated relative risks (odds ratios) are listed elsewhere by breed for many of these congenital abnormalities (Buchanan, 1992). Chronic valvular heart disease occurs with relatively greater frequency in small dogs, whereas large dogs, especially males, are predisposed to dilated cardiomyopathy. Certain canine breeds also have characteristic cardiac dysrhythmias that may occur with or without significant cardiomegaly or signs of CHF. Finally, an increased risk of pericardial effusion is noted in golden retrievers, Labrador retrievers, German shepherd dogs, German shorthaired pointers and Akitas (Buchanan, 1992).

Obesity occurs frequently in dogs and cats with cardiovascular disease. Obesity not only produces clinical signs that mimic those of early heart failure (i.e., exercise intolerance, tachypnea, weakness), but also causes cardiovascular changes that can exacerbate underlying cardiovascular disease.

Chronic progressive kidney disease and failure often occur in dogs and cats with cardiovascular disease, especially in older patients. Cardiac disease often exacerbates underlying renal disease because a large proportion of the cardiac output is normally destined for the kidneys. Renal disease influences the types and dosages of medications that are used to treat patients with cardiovascular disease. Chronic kidney disease is also a risk factor for secondary hypertension in dogs and cats.

Therapy for CHF often includes: 1) diuretics and salt restriction to reduce preload and venous congestion, 2) pimobendan to increase contractility and dilate veins and arteries to increase contractility and decrease preload and afterload and 3) ACE inhibitors, which also act as arterial and venous dilators to reduce venous congestion, preload and afterload, but more importantly appear to have long-term survival benefits from inhibiting the activity of the renin-angiotensin-aldosterone (RAA) system. Dehydration, systemic hypotension, renal insufficiency, electrolyte abnormalities, acid-base disturbances, arrhythmias and loss of appetite are all potential complications of combined pharmacologic and nutritional therapy for patients with CHF.

Hyperthyroidism is a risk factor for hypertrophic cardiomyopathy and secondary hypertension in older cats. Hyperadrenocorticism is a risk factor for pulmonary thromboembolism. Heartworm infection is a risk factor for pulmonary vascular disease, cor pulmonale, right-sided CHF and pulmonary thromboembolism.

Table 36-2. Compensatory mechanisms in heart failure.

Autonomic nervous system
Heart
Increased heart rate
Increased myocardial contractile stimulation
Peripheral circulation
Arterial vasoconstriction (increased afterload)
Venous vasoconstriction (increased preload)
Kidney (renin-angiotensin-aldosterone)
Arterial vasoconstriction (increased afterload)
Venous vasoconstriction (increased preload)
Sodium, chloride and water retention (increased preload and afterload)
Increased myocardial contractile stimulation
Endothelin 1 (increased preload and afterload)
Arginine vasopressin (increased preload and afterload)
Atrial natriuretic peptide (decreased afterload)
Prostaglandins
Frank-Starling law of the heart
Increased end-diastolic fiber length, volume and pressure (increased preload)
Hypertrophy
Peripheral oxygen delivery
Redistribution of cardiac output
Altered oxygen-hemoglobin dissociation
Increased oxygen extraction by tissues
Anaerobic metabolism

Etiopathogenesis

Compensatory Mechanisms in Heart Failure

The first priority of the cardiovascular system is to provide oxygen and nutrients to critical organs such as the brain, kidneys and heart. The next priority is to supply nutrients to all other tissues; a final priority is to maintain normal venous pressure. In heart failure, these cardiovascular priorities are often lost in reverse order. The body will sacrifice normal venous pressure to provide nutrients to tissues. Increased venous pressure values above normal often result in clinical signs of CHF. The first and second cardiovascular priorities are maintained through compensatory responses from several neurohumoral mechanisms (**Table 36-2**), including the sympathetic nervous system, AVP secretion and the RAA system (Schlant and Sonnenblick, 1994; Kubo, 1990; Knight, 1995). In some animals, these compensatory changes ultimately result in: 1) sodium and water retention, 2) expanded extracellular fluid volume, 3) increased venous filling pressure and 4) clinical signs of cough, dyspnea, orthopnea, tachypnea, hepatomegaly and ascites.

SYMPATHETIC NERVOUS SYSTEM

The entire myocardium and peripheral vascular system are supplied with sympathetic nerve terminals. When cardiac output falls, the sympathetic nervous system coordinates increases in heart rate, strength of cardiac contraction and selective peripheral vascular vasoconstriction to restore hemodynamic equilibrium. Increased sympathetic discharge causes: 1) vasoconstriction of arterial resistance vessels with increased cardiac afterload, 2) increased renal neural traffic, which stimulates renin release and thus activation of the RAA system, 3) direct stimulation of renal sodium and water reabsorption and 4) splanchnic venoconstriction with central translocation of blood volume and increased cardiac preload (**Figure 36-1**). Sympathetic stimulation also causes the nonosmotic release of AVP. Diminished circulatory perfusion of arterial baroreceptors appears to activate simultaneously the three major vasoconstrictor systems: 1) the sympathetic nervous system, 2) the RAA system and 3) the nonosmotic release of AVP.

Generalized neurohumoral excitation occurs with impaired parasympathetic control of heart rate (Floras, 1993). The pathophysiologic implications of parasympathetic withdrawal in patients with heart failure have not been fully investigated.

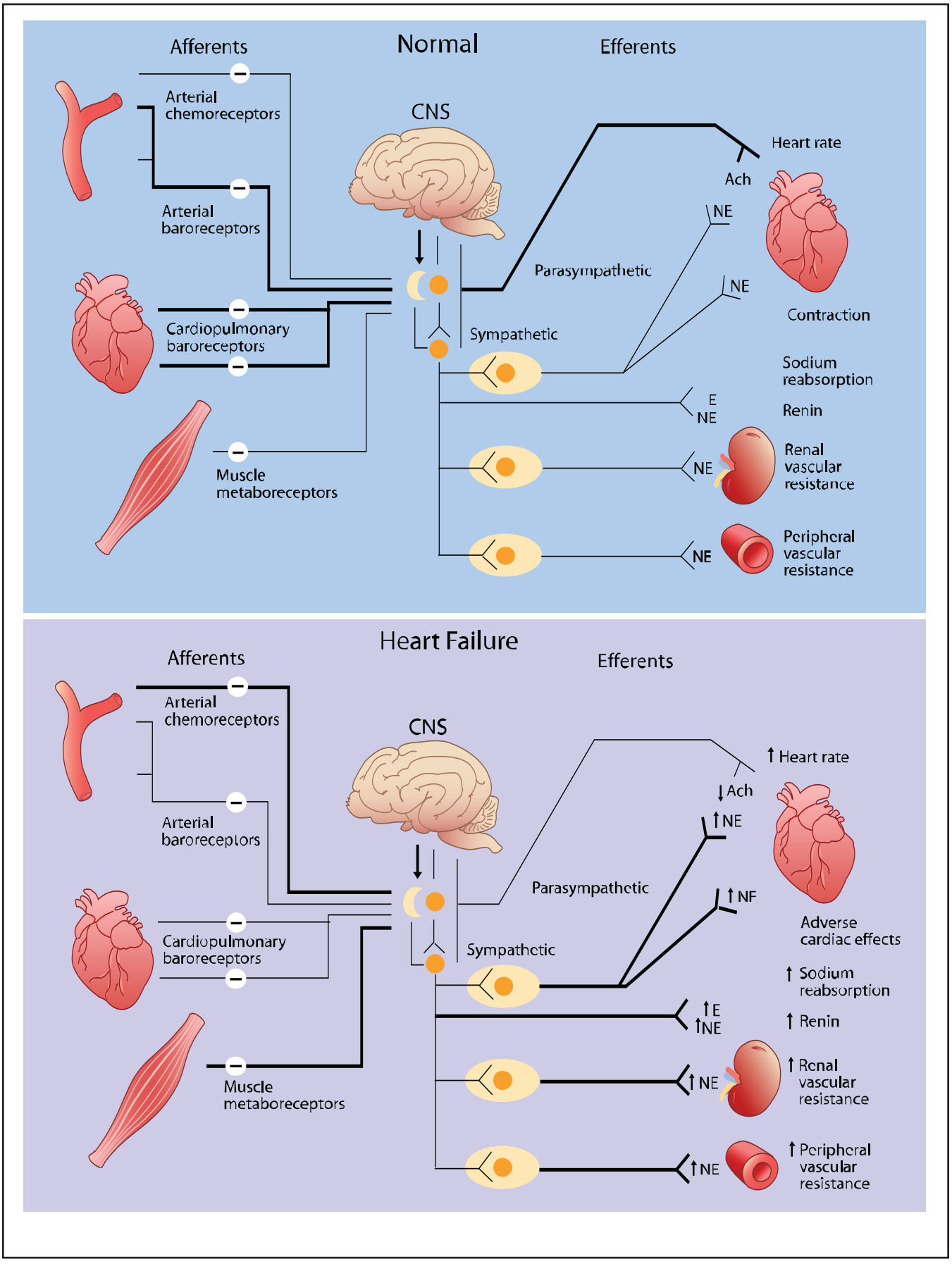
Excessive sympathetic drive to the periphery can exacerbate the hemodynamic derangements of heart failure by increasing preload and afterload. Sympathetic activation occurs in dogs with spontaneous heart failure (Ware et al, 1990). Compared with clinically normal dogs, dogs with heart failure due to chronic mitral valvular disease or dilated cardiomyopathy have increased plasma norepinephrine concentrations that correlate positively with the clinical severity of disease (Ware et al, 1990). Dogs with the most severe degree of heart failure have mean norepinephrine concentrations significantly greater than those of dogs with all other functional classes of heart failure.

RENAL-ADRENAL-PITUITARY INTERACTIONS

In normal hearts and in those patients affected with mild disease, sympathoadrenal stimulation is the primary mechanism for adjusting to transient increases in workload (Schlant and Sonnenblick, 1994). However, as cardiovascular disease progresses, it imposes chronic, sustained changes in hemodynamics that require more stable, long-term adaptations. In this regard, the kidney plays a pivotal role in expanding blood volume and facilitating ventricular filling (increased preload).

Blood volume expansion results from renal conservation of sodium, chloride and water brought about by a combination of intrarenal hemodynamic alterations and neurohumoral stimulation. A decrease in cardiac output and blood pressure decreases renal perfusion pressure, which triggers renin release from the adjacent juxtaglomerular cells. Renin release is also stimulated by a decrease in the amount of sodium and chloride delivered to the distal renal tubules and by direct adrenergic stimulation of the juxtaglomerular cells. (See Sympathetic Nervous System above.) Renin acts on the circulating substrate angiotensinogen to produce angiotensin I. This relatively inactive decapeptide is converted by a peptidase enzyme, ACE, to the octapeptide angiotensin II.

Figure 36-1. (Opposite) Mechanisms for generalized sympathetic activation and parasympathetic withdrawal in heart failure. Normally (top figure), inhibitory input from arterial and cardiopulmonary receptors is high and heart rate is controlled by parasympathetic input (heavy lines). With progressing heart failure (bottom figure), sympathetic activity increases with resulting increases in vascular resistance, heart rate and adverse cardiac effects (heavy lines). Key: Ach = acetylcholine, E = epinephrine, NE = norepinephrine, CNS = central nervous system. (Adapted from Floras JS. Journal of the American College of Cardiology 1993; 22 [Suppl. A]: 72A-84A.)


Normal
Afferents
Efferents
Arterial chemoreceptors
Arterial baroreceptors
Cardiopulmonary baroreceptors
Muscle metaboreceptors
CNS
Parasympathetic
Sympathetic
Heart rate
Ach
NE
NE
Contraction
Sodium reabsorption
E
NE
Renin
NE
Renal vascular resistance
NE
Peripheral vascular resistance
Heart Failure
Afferents
Efferents
Arterial chemoreceptors
Arterial baroreceptors
Cardiopulmonary baroreceptors
Muscle metaboreceptors
CNS
Parasympathetic
Sympathetic
↑ Heart rate
↓ Ach
↑ NE
↑ NE
Adverse cardiac effects
↑ Sodium reabsorption
↑ Renin
↑ E
↑ NE
↑ NE
↑ Renal vascular resistance
↑ NE
↑ Peripheral vascular resistance

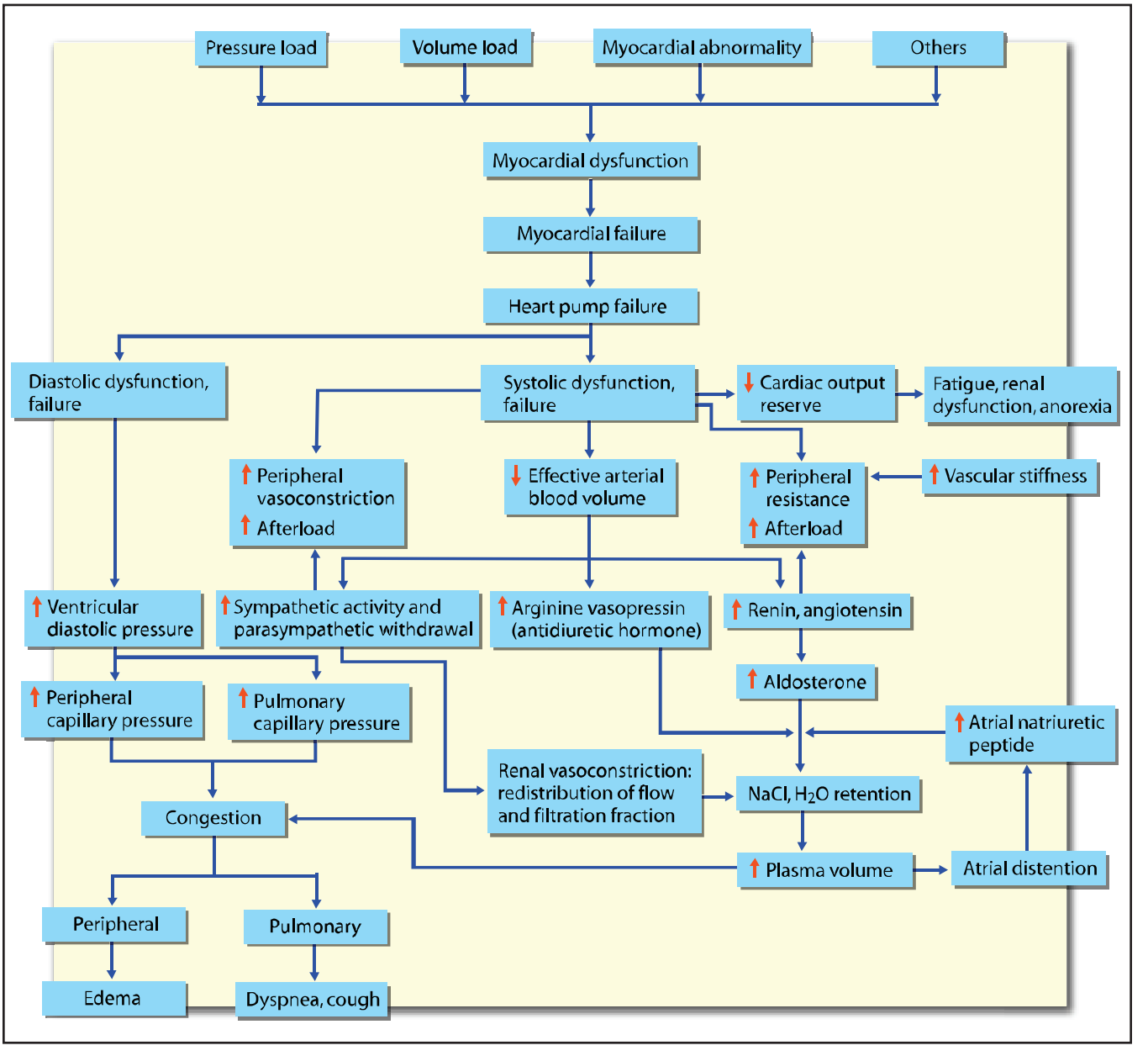


Figure 36-2. Schema of the sequence of events in heart failure. An increased load or myocardial abnormality leads to myocardial failure and eventually to heart failure. This results in increased sympathetic activity, increased levels of renin-angiotensin-aldosterone, pulmonary and peripheral congestion and edema and decreased cardiac output reserve. (Adapted from Schlant RC, Sonnenblick EH. Pathophysiology of heart failure. In: Schlant RC, Alexander RW, eds. The Heart, 8th ed. New York, NY: McGraw-Hill, 1994; 525.)

Angiotensin II counters a decline in effective arterial blood volume by serving as a potent constrictor of veins and arteries, and as a regulator of sodium-potassium homeostasis. Venoconstriction facilitates the return of blood to the heart and increases cardiac preload. Arteriolar vasoconstriction helps maintain systemic blood pressure. Angiotensin II also plays an important role in maintaining blood pressure and volume by stimulating secretion of aldosterone from the adrenal cortex. Aldosterone promotes reabsorption of sodium and chloride, and thus water, from the distal renal tubules and collecting ducts. The effects of aldosterone on sodium excretion may be less important than the direct intrarenal actions of angiotensin II. Studies in dogs support the theory that the intrarenal action of angiotensin II increases sodium and water retention (Hall and Brands, 1992). Angiotensin II also stimulates thirst, which facilitates expansion of blood and interstitial fluid volume. Blood levels of aldosterone tend to parallel those of renin and angiotensin II (Riegger and Liebau, 1982). If effective blood volume is restored, the stimulus for RAA secretion is withdrawn. However, if cardiovascular disease is severe, these hormones continue to stimulate the kidneys and tissue edema ensues or worsens (**Figures 36-2** and **36-3**).

In addition to the RAA system, a locally active paracrine renin-angiotensin system may exist in a number of tissues, par-

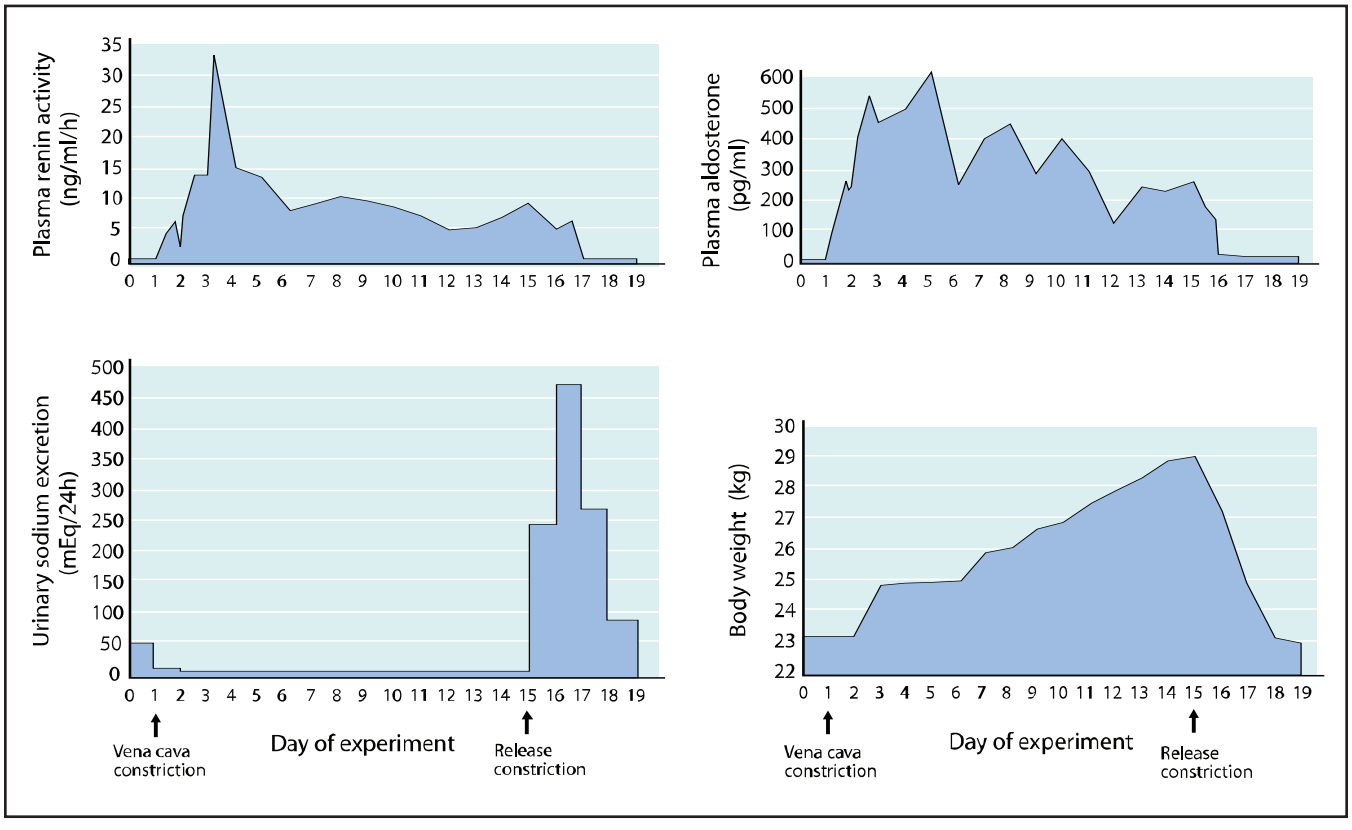


Figure 36-3. The response of a dog to thoracic vena cava constriction and the development of moderate to severe CHF. The first arrow indicates when vena cava constriction was applied. Note the persistent elevation in plasma renin activity (PRA) and plasma aldosterone (PA) concentration with a subsequent decrease in urinary sodium excretion and increase in body weight. The second arrow denotes when vena cava constriction was released. Note the rapid decrease in PRA and PA concentration with marked excretion of excess sodium in the urine and decrease in body weight. (Adapted from Watkins L, et al. Journal of Clinical Investigation 1976; 57: 1606-1617.)

ticularly those associated with cardiovascular homeostasis (MacFadyen, 1993; Straeter-Knowlen et al, 1995). ACE activity, renin substrate and renin-like enzymatic activity have been found in a number of sites including vascular, cardiac, renal, brain and adrenal tissues. Tissue renin-angiotensin activity may contribute to the pathophysiology of heart failure, but this is a topic of considerable debate (Hall and Brands, 1992). Further studies are needed to elucidate the role of extrarenal renin in the development and progression of heart failure.

AVP is secreted by the posterior lobe of the pituitary gland in response to nonosmotic stimuli. (See Sympathetic Nervous System above.) AVP is a potent vasoconstrictor and increases thirst and permeability of cortical and medullary collecting tubules, which allows reabsorption of free water. AVP secretion does not play a major role in the pathogenesis of edema. However, inappropriate AVP secretion probably plays a role in the pathogenesis of the hyponatremia associated with CHF.

Elevated levels of renin, angiotensin, aldosterone and AVP occur in experimental models of CHF in dogs (Watkins et al, 1976; Riegger and Liebau, 1982; Riegger et al, 1988; Maher et al, 1989; Villarreal et al, 1990; Himura et al, 1994). Plasma renin activity and aldosterone concentrations are also increased in dogs with spontaneous heart disease and failure (Knowlen et al, 1983; Buoro et al, 1992; Pederson et al, 1995). As disease in human patients progresses from early asymptomatic (heart disease but no heart failure) or mildly symptomatic left ventricular dysfunction to symptomatic heart failure, neuroendocrine mechanisms are progressively activated (Francis et al, 1990). The point at which significant neuroendocrine activation occurs in dogs and cats with spontaneous heart disease and failure has not been well documented.

CARDIORENAL INTERACTIONS

The volume expansion induced by activation of the RAA system is helpful to a point, after which deleterious clinical signs of pulmonary and peripheral edema begin to develop. ANP, primarily of atrial origin, counteracts these effects. An increase in transmural pressure (atrial distention or stretch) causes release of ANP, which triggers natriuresis and vasodilatation. ANP acts directly on the kidneys to: 1) cause diuresis through increased sodium and chloride excretion, 2) promote vasodilatation and 3) suppress aldosterone secretion and plasma renin activity. The last effect is presumably a result of the increase in sodium and chloride delivery to the distal tubules and macula densa. Studies have demonstrated a significant natriuretic and diuretic response using physiologic levels of ANP in normal dogs and dogs with experimental heart failure (Riegger and Liebau, 1982; Scriven and Burnett, 1985; Zimmerman et al, 1987). The renin-inhibiting effects of ANP may be dependent on the degree of activation of the RAA sys-

Table 36-3. Cardiovascular and neurohumoral adaptations that occur during the transition from lean to obese body condition.

Increased perfusion requirements of expanding adipose tissue
Elevated cardiac output
Abnormal left ventricular function
Variable blood pressure response (normotensive to hypertensive)
Increased retention of sodium and water by the kidney with subsequent increase in plasma volume
Increased plasma aldosterone and norepinephrine concentrations
Increased left atrial pressure
Increased heart rate
Exercise intolerance

tem (Kivlighn et al, 1990).

Although ANP is unable to normalize hemodynamics and natriuresis, it appears to provide an important modulating effect on the pathogenesis of CHF. Elevated ANP concentrations occur in dogs with spontaneous heart failure; furthermore, ANP concentration increases with increasing severity of heart failure (Takemura et al, 1991; Vollmar et al, 1991; Haggstrom et al, 1994).

CHF-ASSOCIATED HYPONATREMIA

Although the precise pathogenesis of CHF-associated hyponatremia remains controversial, the important factors can be divided into two categories (Oster et al, 1994). First, the increase in plasma angiotensin II concentration promotes thirst resulting in greater water intake. Second, renal diluting ability is impaired because the delivery of glomerular filtrate to the distal renal tubules is decreased (resulting from a reduced glomerular filtration rate and enhanced reabsorption proximally) and the plasma levels of AVP are increased. Both of these abnormalities might be mediated in part by angiotensin II. The osmotically inappropriate increase in plasma AVP concentration may be caused by a downward resetting of the osmostat because of a reduction in the effective blood volume (Oster et al, 1994). Aggressive use of diuretics may also contribute to the pathogenesis of hyponatremia in some patients.

CHF-associated hyponatremia is an important marker of poor prognosis in people with heart failure; it is seen almost exclusively in decompensated patients (Lee and Packer, 1986). People with heart failure and hyponatremia seem to have decreased renal blood flow, higher serum urea nitrogen concentrations, lower blood pressure and higher plasma renin activity (Oster et al, 1994; Lee and Packer, 1986). Anecdotal reports also suggest that hyponatremic patients in CHF have a poorer prognosis.

Obesity

Obesity has potentially profound cardiovascular consequences. From a cardiovascular perspective, obesity is a disease of blood volume expansion with: 1) elevated cardiac output, 2) increased plasma and extracellular fluid volume, 3) increased neurohumoral activation, 4) reduced urinary sodium and water excretion, 5) increased heart rate, 6) abnormal systolic and diastolic ventricular function, 7) exercise intolerance and 8) variable blood pressure response (**Table 36-3**) (Alexander, 1986; Crandall and DiGirolamo, 1990).

Obese people have increased plasma volume, cardiac output and plasma insulin, aldosterone and norepinephrine concentrations when compared with age-matched nonobese individuals (Rocchini et al, 1989). These changes occur whether the individuals eat high- or low-salt foods. Increases in blood pressure, heart rate, cardiac output, left atrial pressure and extracellular fluid volume also occur in dogs with experimentally induced obesity (Hall et al, 1993; Mizelle et al, 1994). Blood pressure always increases with increasing weight in dogs, regardless of the initial blood pressure.

The tendency toward blood volume expansion and neurohumoral activation in obese animals parallels the compensatory changes that often occur in patients with cardiac disease. Obesity, therefore, may have profound adverse effects in patients with concomitant cardiovascular disease.

Body weight and blood pressure correlate strongly in people. Hypertension occurs more often in obese individuals than in nonobese individuals (Alexander, 1986). The increase in blood pressure may be due to the combined effects of hyperinsulinemia, hyperaldosteronemia and increased sympathetic nervous system activity that characteristically occur in obesity (Rocchini et al, 1989). Hyperinsulinemia and blood pressure elevation also occur in dogs that have become rapidly obese (Rocchini et al, 1987). Hyperinsulinemia markedly reduces urinary sodium excretion (antinatriuresis) with resultant sodium and water retention (Hall et al, 1990, 1990a; Brands et al, 1991), possibly contributing to blood pressure changes. However, hyperinsulinemia for up to 28 days at levels comparable to those found in obese hypertensive people does not elevate mean arterial pressure in dogs with reduced renal mass even when sodium intake is high (Hall et al, 1990). This finding suggests that chronic hyperinsulinemia per se cannot account for obesity-associated hypertension. Further studies are needed to elucidate the pathophysiology of blood pressure responses and hypertension in obese patients.

Cachexia

Cachexia is a syndrome of weight loss (defined generally as unintentional loss of more than 10% body weight), lean tissue wasting and anorexia seen clinically in a variety of diseases, including chronic heart failure. The loss of lean body mass seen in cachexia is caused by a mismatch between food intake and nutritional requirements, resulting in negative nitrogen and energy balances (Freeman and Roubenoff, 1994). These imbalances may be due to inadequate intake, excessive losses or altered metabolism (**Figure 36-4**).

In patients with heart failure, anorexia may be due to the clinical signs of heart failure itself (dyspnea, fatigue), the presence of concomitant disease (nausea associated with renal failure), use of drugs that cause nausea (e.g., toxic doses of cardiac glycosides), the presence of elevated levels of inflammatory cytokines or sudden nutritional changes. The rate of loss of lean body mass with cardiac cachexia exceeds that attributable to anorexia alone, and reflects in part the excessive caloric expenditures of the increased work of respiration and elevated heart

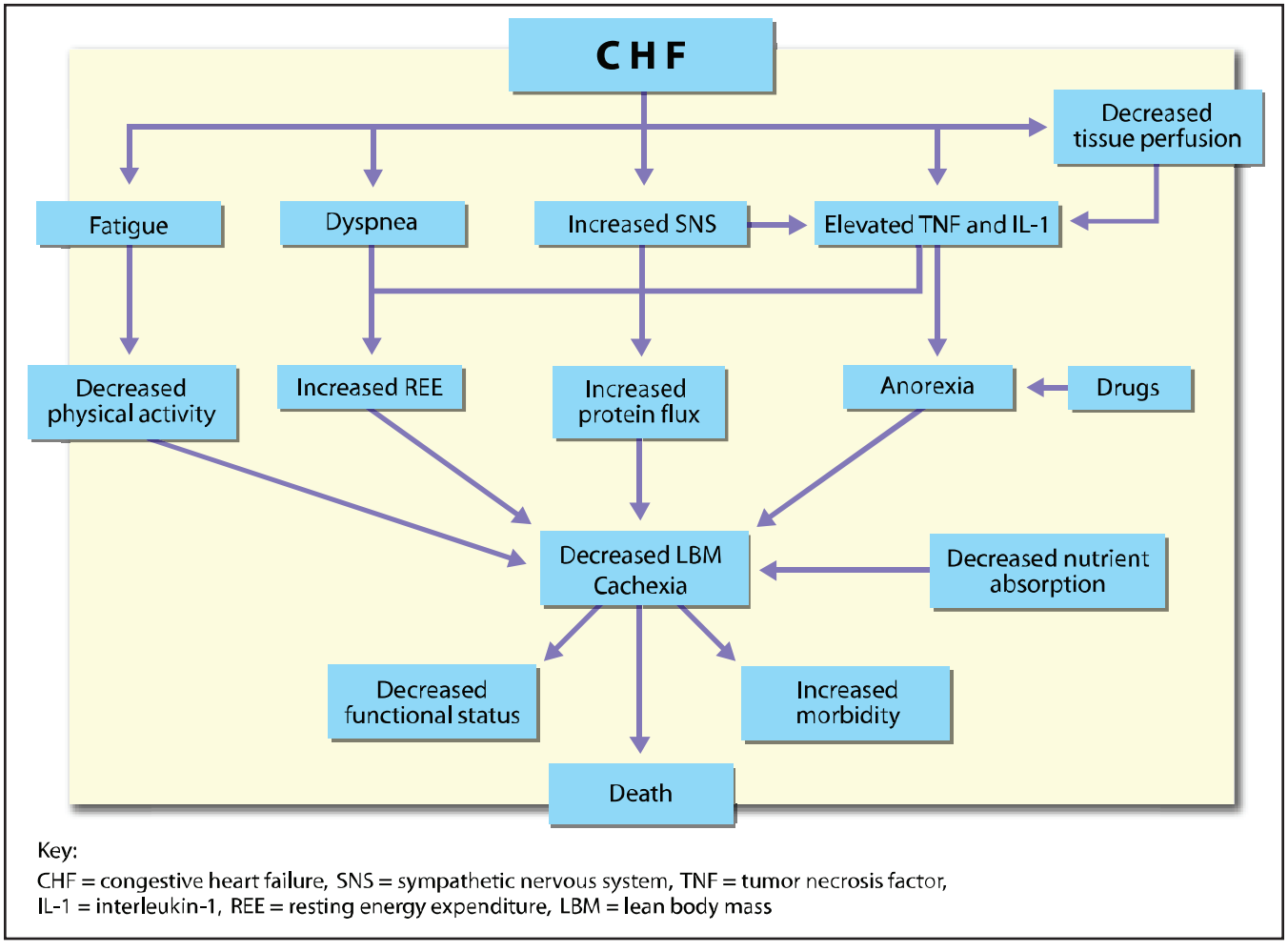


Figure 36-4. The cascade of factors in CHF that contributes to loss of lean body mass and cardiac cachexia. (Adapted from Freeman LM, Roubenoff R. Nutrition Reviews 1994; 52: 340-347.)

rate and in part, more complex metabolic issues. With simple starvation, most weight loss is loss of fat mass, whereas lean tissue is relatively spared, at least early on. Cachexia involves depletion of lean body mass. Physical inactivity may also contribute to loss of lean body mass because exercise is routinely restricted in patients with moderate to severe heart failure.

Altered metabolism appears to play a role in the pathogenesis of cachexia (**Figure 36-4**). Resting energy expenditure is elevated in some people with heart failure (Riley et al, 1991), and may be caused by increased ventilatory effort, sympathetic nervous system activity and concentrations of certain cytokines, specifically tumor necrosis factor (TNF, cachectin) and interleukin-1 (IL-1). Elevated serum TNF concentrations occur in people, dogs and cats with CHF (Levine et al, 1990; Freeman et al, 1994; Meurs et al, 1995). Both TNF and IL-1 cause cachexia by suppressing food intake and altering metabolism (Le and Vilcek, 1987; Oliff, 1988; Tracey et al, 1988, 1988a; Schollmeier, 1990). TNF suppresses the expression of several genes that encode for essential lipogenic enzymes, including lipoprotein lipase, and promotes the breakdown of adipose tissue and skeletal muscle (Le and Vilcek, 1987; Oliff, 1988; Tracey et al, 1988, 1988a; Schollmeier, 1990). TNF may also change the normal metabolic adaptation that accompanies caloric restriction and thus contribute to the nutritional imbalances observed in cachectic patients (Oliff, 1988).

As heart failure worsens, tissue perfusion and renal blood flow decline progressively. The kidneys release renin and prostaglandins, particularly prostaglandin E2, into the circulation in response to decreased renal blood flow. Prostaglandin E2 stimulates production of TNF from monocytes in vitro (Levine et al, 1990). Further studies are needed to confirm whether this pathogenic mechanism occurs in animals with cardiac cachexia and to explore the interaction of TNF with IL-1 and other cytokines.

Relationship of Taurine Deficiency to Myocardial Disease

Taurine is an essential amino acid in cats. Cats have a limited ability to synthesize taurine from cysteine and methionine because their tissues contain low concentrations of cysteine dioxygenase and cysteine sulfinate acid decarboxylase, key enzymes in the synthesis of taurine. Cats must also use taurine exclusively for conjugation of bile acids, which contributes to an obligatory loss of taurine. The decreased ability to synthesize

taurine and the continuous obligatory losses predispose cats to taurine deficiency when they eat foods with low taurine concentrations.

The association of feline dilated cardiomyopathy with low plasma concentrations of taurine was first reported in 1987 (Pion et al, 1987). This observation was subsequently confirmed by large studies in North America and Europe (Sisson et al, 1991). Treatment with oral taurine supplements significantly improved clinical signs, restored myocardial function and improved survival of cats with dilated cardiomyopathy. Since 1987, supplementation of most commercial cat foods with taurine has resulted in a marked decline in the number of feline dilated cardiomyopathy cases. Several controlled experiments support the clinical studies. Myocardial taurine concentrations are reduced and left ventricular dilatation and myocardial dysfunction occur in cats fed foods low in taurine (Pion et al, 1992, 1992a; Fox and Sturman, 1992). However, idiopathic dilated cardiomyopathy is occasionally diagnosed in cats that show no evidence of taurine deficiency, and the condition does not improve with taurine supplementation (Sisson et al, 1991).

Dilated cardiomyopathy has also been associated with plasma taurine deficiency and low myocardial taurine concentrations in captive foxes (Moise et al, 1991) and a small number of dogs (Kramer et al, 1995; Kittleson et al, 1997; Pion et al, 1998). A retrospective study was conducted to determine dietary taurine concentrations in dogs with dilated cardiomyopathy and compare clinical outcomes (Freeman et al, 2001). Taurine concentrations were low in blood samples from 20 of 37 dogs with dilated cardiomyopathy but there was no correlation between dietary and circulating taurine concentrations. Other studies have confirmed that there is no clear and constant association between diet and taurine status in dogs with dilated cardiomyopathy (Vollmar and Biourge, 2004).

The mechanism of heart failure in taurine-deficient cats and dogs is poorly understood. Taurine may function in osmoregulation, calcium modulation and inactivation of free radicals (Pion et al, 1998). Other unidentified factors may be involved in the development of myocardial failure in patients with taurine deficiency. Many cats fed taurine-deficient foods for prolonged periods fail to develop clinical myocardial dysfunction. Dilated cardiomyopathy and heart failure may result from an inciting or contributing factor or factors in combination with taurine deficiency (Fox and Sturman, 1992).

Several studies have demonstrated an association between taurine and potassium balance in cats (Dow et al, 1992). Inadequate potassium intake may be sufficient to induce significant taurine depletion and cardiovascular disease in healthy cats (Dow et al, 1992). Female cats with dilated cardiomyopathy have significantly lower plasma taurine concentrations than do similarly affected male cats (Fox et al, 1994). This finding suggests that male cats are more prone to developing taurine-dependent dilated cardiomyopathy than are female cats, or they are more prone to developing clinical signs associated with cardiac decompensation at higher plasma taurine concentrations (Fox et al, 1994).

Relationship of L-Carnitine Deficiency to Myocardial Disease

L-carnitine is a small, water-soluble, vitamin-like quaternary amine found in high concentrations in mammalian heart and skeletal muscle. In dogs, L-carnitine is synthesized from the amino acids lysine and methionine, primarily in the liver. A poorly understood transport mechanism concentrates L-carnitine in cardiac and skeletal myocytes.

Although the heart uses various metabolic substrates to maintain the constant energy supply needed to sustain effective contraction and relaxation, it is well established that long-chain fatty acids are quantitatively the most important. Carnitine is a critical component of the mitochondrial membrane enzymes that transport activated fatty acids in the form of acyl-carnitine esters across the mitochondrial membranes to the matrix, where β-oxidation and subsequent high-energy phosphate generation occur (**Figure 36-5**). In addition to its role in fatty acid transport, free L-carnitine serves as a mitochondrial detoxifying agent by accepting (or "scavenging") acyl groups and other potentially toxic metabolites and transporting them out of the mitochondria as carnitine esters (Pion et al, 1998).

A subset of dogs with dilated cardiomyopathy apparently suffers from myopathic L-carnitine deficiency and may respond to L-carnitine supplementation (Keene, 1992; Pion et al, 1998). Plasma L-carnitine deficiency appears to be a specific but insensitive marker for myocardial L-carnitine deficiency in dogs with dilated cardiomyopathy (Keene, 1992; Pion et al, 1998); unfortunately, dogs with myocardial L-carnitine deficiency do not always have low plasma L-carnitine concentrations. Most dogs in which myocardial L-carnitine deficiency has been associated with dilated cardiomyopathy fall into the classification of myopathic L-carnitine deficiency (i.e., decreased myocardial L-carnitine concentrations in the presence of normal or elevated plasma L-carnitine concentrations). Many of these dogs may suffer from a membrane transport defect that prevents adequate amounts of L-carnitine from moving into the myocardium from the plasma at plasma L-carnitine concentrations found in dogs fed most commercial foods. Systemic L-carnitine deficiency (decreased plasma and myocardial L-carnitine concentrations) accounts for approximately 20% of the cases.

Hypertension

Regulation of systemic blood pressure involves complex relationships between central and peripheral nervous, renal, endocrine and vascular systems (Littman and Drobatz, 1995). Most people with hypertension have essential hypertension, which means their hypertension occurs without a discernible organic cause (primary or idiopathic hypertension). Hypertension secondary to an identifiable underlying cause is more common in dogs and cats.

The kidneys ultimately provide long-term control of blood pressure because they are able to excrete sodium and water (Guyton, 1981). This control is accomplished by manipulating the determinants of systemic blood pressure: cardiac output and total peripheral resistance (BP = CO x TPR). Cardiac output is

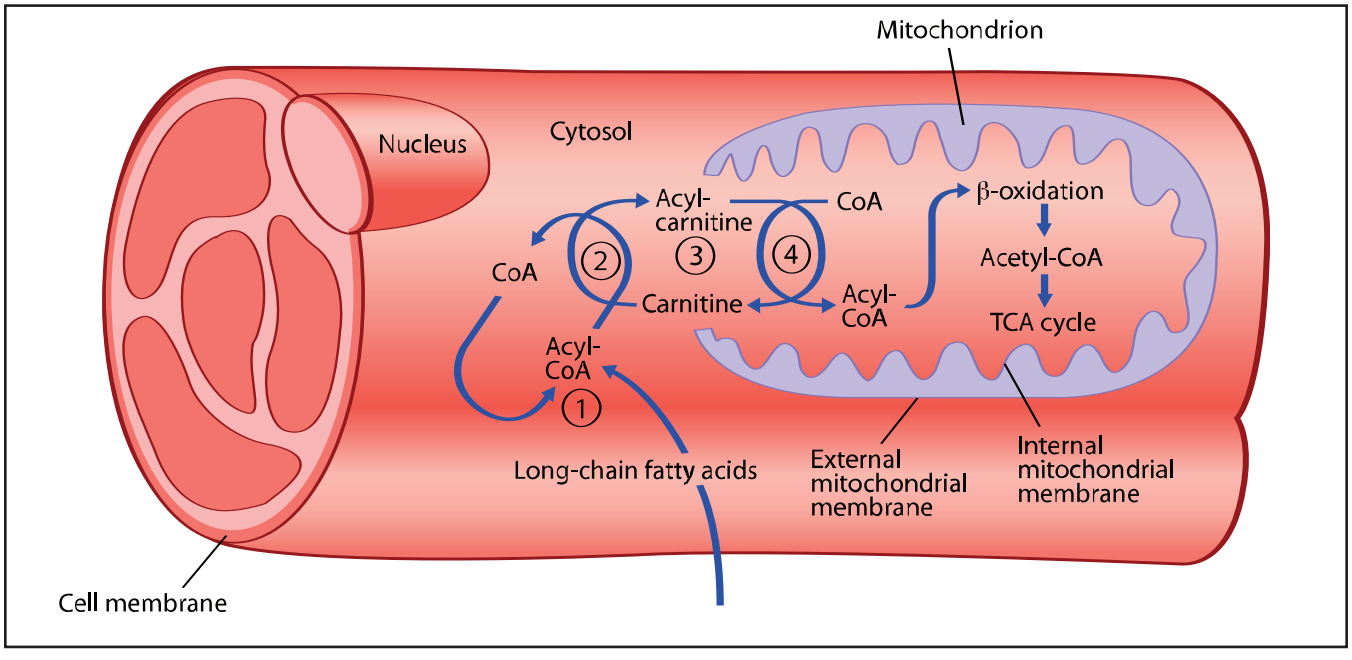


Figure 36-5. L-carnitine is essential for aerobic mitochondrial energy production and assists in the transit of energy (ATP) into the cytoplasm, where it provides the fuel for cellular functions. After entry into the cell, fatty acids are activated to form acyl-CoA (1). The acyl-CoA can then be transported into the mitochondrion as acyl-carnitine (2) via a carnitine-dependent shuttle (3). Acyl-carnitine then undergoes beta-oxidation to acetyl-CoA on the inner mitochondrial membrane (4) for entry into the TCA cycle and production of ATP. Secondarily, L-carnitine is involved in processes that prevent accumulation of toxic metabolites inside the mitochondrion. (Adapted from Neu H. Kleintierpraxis; 40: 197-220.)

related to heart rate and stroke volume (CO = HR x SV). Diseases associated with hypertension that increase heart rate include: 1) hyperthyroidism, 2) anemia, 3) hyperviscosity, 4) polycythemia and 5) pheochromocytoma. Increased stroke volume may occur during hypervolemic states, but is usually due to increased retention of sodium, chloride and water. Renal failure, hyperadrenocorticism and hyperaldosteronism may cause increased total body sodium, chloride and water.

Activation of the RAA pathway may elevate blood pressure by increasing stroke volume and total peripheral resistance. Angiotensin II is a potent vasoconstrictor, and angiotensin II and aldosterone stimulate renal sodium and chloride retention. Increased arteriolar tone, sensitivity to circulating vasopressors and levels of circulating catecholamines and decreased arteriolar elasticity may also increase total peripheral resistance.

Common causes of secondary hypertension include: 1) chronic progressive renal disease in dogs and cats (glomerulonephritis, amyloidosis, chronic interstitial nephritis, pyelonephritis and polycystic renal disease), 2) hyperadrenocorticism in dogs and 3) hyperthyroidism in cats. The "target organs" or end organs or systems that appear most sensitive to increased blood pressure include the eyes, kidneys, cardiovascular system and cerebrovascular system (Littman and Drobatz, 1995). Clinical signs related to end-organ damage are usually the reason an animal with hypertension is brought to a veterinarian for examination.

Pleural Effusion

Hydrostatic and oncotic forces (Starling's forces) are balanced within the pleurae and pleural space. Hydrostatic and oncotic pressures within the systemic circulation, pulmonary circulation and intrapleural space favor transudation of pleural fluid from the parietal pleura (pleura covering the inner chest wall) into the pleural space with subsequent absorption of the fluid into the visceral pleura's vasculature (Bauer and Woodfield, 1995). The result is a continuous flow of fluid through the pleural space. This delicate balance can be disrupted by any disorder that alters oncotic pressure, systemic or pulmonary capillary pressure, lymphatic compliance, capillary permeability or effective pleural surface area.

Biventricular CHF with systemic and pulmonary venous hypertension is a primary cause of pleural effusion. However, other causes of pleural effusion can masquerade as heart failure and may occur in patients with known heart disease, especially older dogs and cats. Other common causes of pleural effusion include diseases that increase capillary permeability and alter the normal flow and absorption of pleural fluid (e.g., primary intrathoracic or metastatic malignancy, pleural space infection, traumatic diaphragmatic hernia with incarceration of abdominal viscera).

Chylothorax is the accumulation of intestinal lymph (chyle) in the pleural space. This milky fluid has a high concentration of chylomicrons and triglycerides (the triglyceride concentration usually exceeds 100 mg/dl) and is low in cholesterol (the triglyceride-cholesterol ratio is greater than 1) (Fossum et al, 1986). The etiology of chylothorax is poorly understood, but has been associated with: 1) traumatic leakage, 2) diaphragmatic hernia, 3) lymphosarcoma, 4) cranial mediastinal masses, 5) pulmonary neoplasia, 6) dirofilariasis, 7) congenital abnormalities of the thoracic duct and 8) CHF. Experimental and clini-

Table 36-4. Key nutritional factors for foods for dogs and cats with cardiovascular disease.*

Factors	Recommended levels
Sodium	Dogs: Class Ia = 0.15 to 0.25%** Class Ib, II and III = 0.08 to 0.15% Cats: 0.07 to 0.30%
Chloride	Dogs: Class Ia = 1.5 x sodium levels** Class Ib, II and III = 1.5 x sodium levels Cats: 1.5 x sodium levels
Taurine	Dogs: ≥0.1% Cats: ≥0.3%
L-Carnitine	Dogs: ≥0.02%
Phosphorus	Dogs: 0.2 to 0.7% Cats: 0.3 to 0.7%
Potassium	Dogs: ≥0.4% Cats: ≥0.52%
Magnesium	Dogs: ≥0.06% Cats: ≥0.04%

*All values are expressed on a dry matter basis.
**Also appropriate in Class Ib, II and III patients when ACE inhibitors are used, especially when used in combination with diuretics.

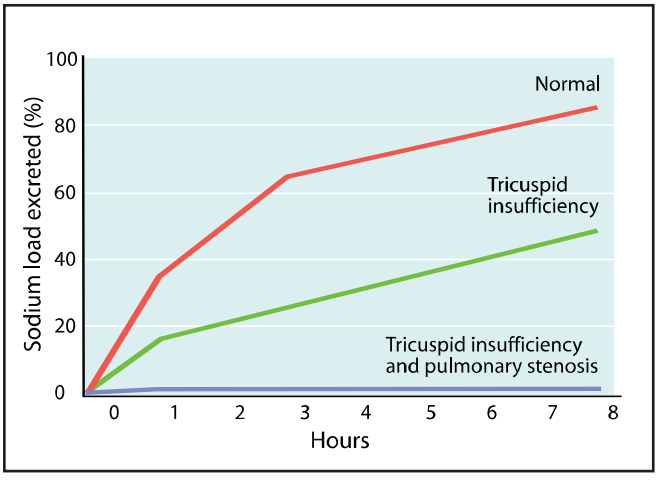


Figure 36-6. The cumulative excretion of sodium after a sodium load in a normal dog (top curve), the same dog with tricuspid insufficiency (middle curve) and the same dog with combined tricuspid insufficiency and pulmonary stenosis with the development of CHF (bottom curve). The inability of the dog to excrete excess sodium is the result of compensatory mechanisms that occur with advanced heart disease. (Adapted from Barger AC, et al. American Journal of Physiology 1955; 180: 249-260.)

cal evidence suggests that cranial mediastinal lymphangiectasia in cats is produced by either a functional or mechanical obstruction to thoracic duct flow. Obstruction of blood flow to the heart via the cranial vena cava, increased lymph flow from biventricular heart failure, elevated central venous pressure and direct duct obstruction may also contribute to lymphangiectasia and chyle accumulation in the pleural space (Smeak and Kerpsack, 1995).

Removal of large volumes of chyle via thoracentesis or chest drains may cause dehydration, electrolyte imbalances and protein-calorie malnutrition. A balance must be established between adequately evacuating the pleural space to prevent respiratory distress and meeting the animal's nutritional, fluid and electrolyte needs.

Key Nutritional Factors

The key nutritional factors for dogs and cats with cardiovascular disease are listed in **Table 36-4** and described in more detail below.

Sodium and Chloride

Because CHF is associated with retention of sodium, chloride and water, these nutrients are of primary importance in patients with cardiovascular disease. Within a few hours of ingesting high levels of sodium, normal dogs and cats easily excrete the excess in their urine. Early in the course of cardiac disease, patients may lose this ability to excrete excess sodium because of compensatory mechanisms described previously. In one experimental model, creation of valvular insufficiency in a dog reduced the excretion of excess sodium by almost 50% (**Figure 36-6**) (Barger et al, 1955). As heart disease worsens and CHF ensues, the ability to excrete excess sodium is severely depressed (**Figure 36-6**).

In the past, retention of sodium was primarily implicated in the pathogenesis of CHF and some forms of hypertension. A number of studies have examined the interaction of sodium with other ions, including chloride. The full expression of sodium chloride-sensitive hypertension in people depends on the concomitant administration of both sodium and chloride (Kurtz et al, 1987; Boegehold and Kotchen, 1989; Luft et al, 1990). In experimental models of sodium chloride-sensitive hypertension in rodents and in clinical studies with small numbers of hypertensive people, blood pressure or volume was not increased by a high sodium intake provided with anions other than chloride, and high chloride intake without sodium affected blood pressure less than the intake of sodium chloride (**Figure 36-7**) (Kurtz et al, 1987; Boegehold and Kotchen, 1989; Kotchen et al, 1981). The failure of nonchloride sodium salts to produce hypertension or hypervolemia may be related to their failure to expand plasma volume; renin release occurs in response to renal tubular chloride concentration (Boegehold and Kotchen, 1989; Luft et al, 1990; Kotchen et al, 1981, 1987). Chloride may also act as a direct renal vasoconstrictor (Boegehold and Kotchen, 1989). These findings suggest that both sodium and chloride are nutrients of concern in patients with hypertension and heart disease.

The minimum recommended allowance for sodium and chloride in foods for adult dogs is 0.08 and 0.12% dry matter (DM), respectively (NRC, 2006); for foods for cats it is 0.068 for sodium and 0.096% for chloride DM (NRC, 2006). In general, sodium levels for foods for cardiovascular disease should be restricted to 0.08 to 0.25% DM for dogs and 0.07 to 0.3% DM for cats. Recommended chloride levels are typically 1.5 times sodium levels. Avoiding excess sodium chloride in cat foods is more difficult than in dog foods because ingredients used to meet the higher protein requirement of cats also contain sodium and chloride and thus increase the sodium chloride content of cat food.

Specific evidence is not available to support the idea that foods low in sodium chloride fed to dogs in the early stages of heart disease will delay disease progression. However, a prudent recommendation for these patients is to begin avoiding excess sodium chloride early in the disease process. Thus, at the first sign of heart disease without cardiac dilatation (Class Ia), foods with levels of sodium and chloride in the upper part of the recommended range (0.15 to 0.25% DM sodium) should be introduced. Cardiac dilatation implies abnormal sodium chloride handling and intravascular volume expansion and, thus, dilatation is a prelude to venous congestion. When cardiac dilatation becomes evident on radiographs or echocardiograms (Class Ib), then foods that are even more sodium chloride restricted (sodium = 0.08 to 0.15% DM) are advised (Roudebush et al, 1994; Rush et al, 2000). As might be expected, moderate to severe cardiac dilatation, congestion or both conditions (Class II or III) also require foods with sodium chloride levels in the lower end of the range.

Water can be a potential source of sodium and chloride. Distilled water or water with less than 150 ppm sodium should be considered for patients with advanced CHF in whom more strictly limited sodium intake is desirable.

Taurine

Taurine can be important in dogs and cats with myocardial failure. The mechanism of heart failure in taurine-deficient cats and dogs is not well understood. Taurine may function in inactivation of free radicals, osmoregulation and calcium modulation (Pion et al, 1998). Taurine also has direct effects on contractile proteins and is a natural antagonist to angiotensin II (Lake, 1993; Gentile et al, 1994). Other unidentified factors may be involved in the development of myocardial failure in patients with taurine deficiency. Dilated cardiomyopathy and heart failure may result from an inciting or contributing factor, or factors, in combination with taurine deficiency (Fox and Sturman, 1992). For example, studies have demonstrated an association between taurine and potassium balance in cats (Dow et al, 1992). Inadequate potassium intake may be sufficient to induce significant taurine depletion and cardiovascular disease in healthy cats (Dow et al, 1992).

Because taurine is an essential amino acid in cats, there is a minimum recommended allowance for taurine in highly digestible purified foods for healthy adult cats, which is 0.04% DM; the minimum recommended allowances for dry expanded and moist foods for adult cats are 0.10 and 0.17% DM, respectively (NRC, 2006). Taurine content of foods for cats with cardiovascular disease should probably contain at least 0.3% DM. Levels of taurine typically recommended for supplementation of feline cardiovascular patients (250 to 500 mg taurine/day) (Pion et al, 1989) provide approximately twice that much. There are no reports of acute or chronic toxicity related to feeding large quantities of free taurine to cats. In one study, foods containing up to 1.0% DM taurine were fed for up to three years and no adverse effects were noted (Sturman and Messing, 1992). The safe upper limit of taurine in foods for kittens is more than 0.89% DM (NRC, 2006).

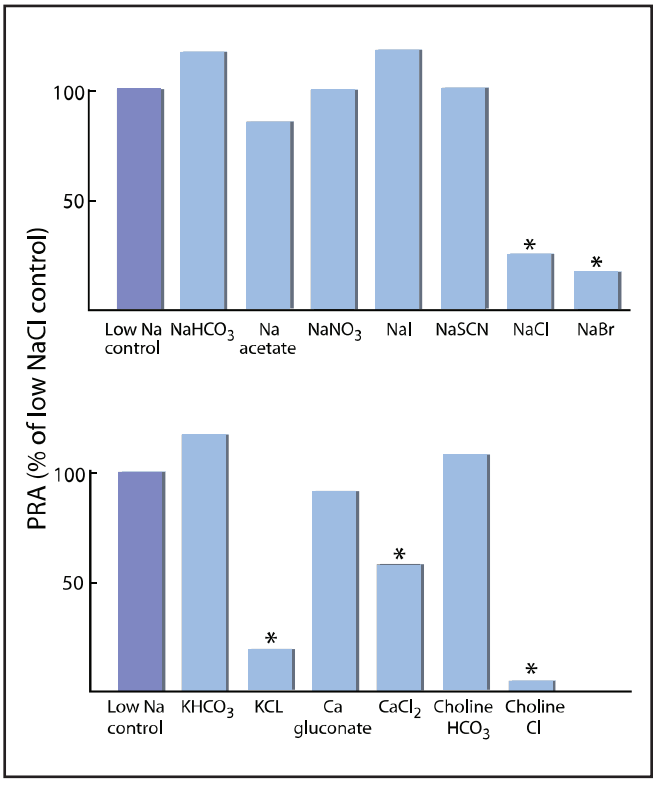


Figure 36-7. Effect of nutritional loading with different sodium and chloride salts on plasma renin activity (PRA) in sodium chloride-deprived rats. Bars marked with * are significantly different ($p < 0.05$) compared with the low-sodium control. These data suggest that chloride is an important determinant of renin secretion by the kidneys. (Adapted from Kotchen TA, et al. Journal of Laboratory Clinical Medicine 1987; 110: 533-539.)

Taurine is not an essential amino acid for dogs. However, dilated cardiomyopathy has been associated with plasma taurine deficiency and low myocardial taurine concentrations in captive foxes and a small number of dogs (Moise et al, 1991; Kramer et al, 1995; Kittleson et al, 1997; Pion et al, 1998; Freeman et al, 2001). In dogs, the association between taurine deficiency and dilated cardiomyopathy is strongest in American cocker spaniels and golden retrievers (Kramer et al, 1995; Kittleson et al, 1997, 1991; Pion et al, 1998). An association between taurine deficiency and dilated cardiomyopathy has also been shown in Newfoundlands, Labrador retrievers, Dalmatians, English bulldogs, Portuguese water dogs and Irish wolfhounds (Sanderson, 2006; Vollmar and Biourge, 2004). Even if plasma and whole blood taurine levels are normal in canine dilated cardiomyopathy patients, additional taurine may still be beneficial. Thus, it is reasonable that foods for dogs with cardiovascular disease contain added taurine. Because dogs can synthesize taurine, the level for foods for canine patients can be lower than for cats. The recommendation for taurine in foods for canine cardiovascular disease patients is at least 0.1% DM. This is somewhat lower than would be supplied by the typical recommendation for taurine supplementation of foods for dogs with dilated cardiomyopathy (500 to 1,000 mg taurine/day) (Pion et al, 1998). In dogs, as in cats, taurine is safe. No reports

could be found on acute or chronic toxicity related to feeding large quantities of taurine to dogs and no safe upper limit has been established (NRC, 2006).

L-Carnitine

L-carnitine deficiency has been associated with dilated cardiomyopathy in dogs. Carnitine is important to cardiac muscle function because it is a critical component of the mitochondrial membrane enzymes that transport activated fatty acids in the form of acyl-carnitine esters across the mitochondrial membranes to the matrix, where β-oxidation and subsequent high-energy phosphate generation occur. Also, free L-carnitine serves as a mitochondrial detoxifying agent by scavenging acyl groups and other potentially toxic metabolites and transporting them out of the mitochondria as carnitine esters (Pion et al, 1998).

A subset of dogs with dilated cardiomyopathy apparently suffers from myopathic L-carnitine deficiency and may respond to L-carnitine supplementation (Keene, 1992; Pion et al, 1998). Plasma L-carnitine deficiency appears to be a specific but insensitive marker for myocardial L-carnitine deficiency in dogs with dilated cardiomyopathy (Keene, 1992; Pion et al, 1998). Thus, dogs with myocardial L-carnitine deficiency do not always have low plasma L-carnitine concentrations. Most dogs in which myocardial L-carnitine deficiency has been associated with dilated cardiomyopathy fall into the classification of myopathic L-carnitine deficiency (i.e., decreased myocardial L-carnitine concentrations in the presence of normal or elevated plasma L-carnitine concentrations). Many of these patients suffer from a membrane transport defect that prevents adequate amounts of L-carnitine from moving into the myocardium from the plasma at plasma L-carnitine concentrations found in dogs fed most commercial foods. Systemic L-carnitine deficiency (decreased plasma and myocardial L-carnitine concentrations) accounts for approximately 20% of the cases.

Most authors recommend supplementing canine dilated cardiomyopathy patients with 50- to 100-mg L-carnitine/kg body weight three times daily. One report suggests that in dogs with systemic carnitine deficiency, a much lower dose generated a better response than the effective dose for myopathic cardiomyopathy (Sanderson, 2006). Even if carnitine deficiency was not the cause of cardiomyopathy in a heart disease patient, supplementing dogs with carnitine does no harm and may be beneficial. Because carnitine is expensive, foods for canine patients with cardiovascular disease do not contain the higher levels recommended for supplementation. Foods for heart disease patients should provide at least 0.02% DM. For a point of reference, this inclusion level provides approximately 1/20th of the amount that would be achieved by supplementing at 50- to 100-mg carnitine/kg body weight.

Phosphorus

Phosphorus is a nutrient of concern in patients with concurrent chronic kidney disease (Chapter 37). To avoid excess phosphorus in patients with concurrent chronic kidney disease, restrict phosphorus to 0.2 to 0.7% DM in dogs and 0.3 to 0.7% DM in cats.

Potassium and Magnesium

Potassium and magnesium metabolism is a concern in patients with cardiovascular disease. Hypokalemia, hyperkalemia and hypomagnesemia, are potential complications of drug therapy in patients with cardiovascular disease. Abnormalities in potassium or magnesium homeostasis can: 1) cause cardiac dysrhythmias, 2) decrease myocardial contractility, 3) produce profound muscle weakness and 4) potentiate adverse effects from cardiac glycosides and other cardiac drugs.

Foods for dogs and cats with CHF should contain at least the amounts of potassium and magnesium recommended for adult maintenance (0.4 and 0.52% DM potassium, respectively, and 0.06 and 0.04% DM magnesium) (NRC, 2006). If abnormalities in these electrolytes occur, supplementation or switching to a different food may be necessary.

Other Nutritional Factors

Protein

The protein requirements of patients with cardiac cachexia have not been investigated and it is unknown how the metabolic changes associated with cachexia affect overall nutrient requirements. Many patients with cachexia have concomitant disease, such as chronic kidney disease, which affects nutrient requirements. Profound anorexia enhances protein-energy malnutrition in patients with cachexia. Patients with cachexia should be encouraged to eat a complete and balanced food that contains adequate calories and adequate high-quality protein.

Omega-3 Fatty Acids

The cytokines TNF and IL-1 have been implicated as pathogenic mediators in cardiac cachexia. Fish oil, which is high in omega-3 (n-3) fatty acids, alters cytokine production. Preliminary results suggest that fish-oil-mediated alterations in cytokine production may benefit dogs with CHF (Freeman et al, 1995). Circulating TNF and IL-1 concentrations decreased significantly in a group of dogs with CHF secondary to idiopathic dilated cardiomyopathy when they were treated with fish oil supplements. Dogs receiving fish oil tended to be judged as less cachectic when compared with those in the placebo group. Ventricular function also improved significantly in the group treated with fish oil when compared with dogs receiving a placebo. These findings suggest that heart failure patients with cachexia may benefit from the alterations of cytokine production brought about by omega-3 fatty acid supplementation or other methods.

Parenteral administration of omega-3 fatty acids (α-linolenic acid, eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA]) was shown to prevent sudden cardiac death in an experimental model of myocardial infarction in dogs (Billman et al, 1999; Leaf et al, 2005). Omega-3 fatty acids appear to electrically stabilize heart cells through modulation of the fast voltage-dependent $Na(^{+})$ currents and the L-type $Ca(2^{+})$ channels in a manner that makes the heart cells resistant to dysrhythmias (Leaf et al, 2005a). Clinical studies have also confirmed that fish oil as a source of long-chain omega-3 fatty acids will reduce the frequency of ventricular arrhythmia in

boxer dogs with arrhythmogenic right ventricular cardiomyopathy (Smith et al, 2007). These data suggest that fish oil supplementation may be useful to help reduce cardiac arrhythmias in dogs. Further studies are needed to determine optimal dose and duration of treatment.

FEEDING PLAN

Assess and Select the Food

The food for patients with cardiovascular disease should be evaluated for all the key nutritional factors mentioned in **Table 36-4**. **Tables 36-5** and **36-6** list key nutritional factor content of selected veterinary therapeutic and other commercial foods marketed for dogs and cats with cardiovascular disease, respectively, and compares them to the recommended levels. Key nutritional factor amounts for foods not listed in these tables must be obtained by contacting the manufacturer or consulting published product information. The levels of the key nutritional factors for regular commercial dog and cat foods typically are considerably outside the recommendations for patients with cardiovascular disease. Some commercial foods greatly exceed the minimum recommended allowance for sodium chloride (Roudebush et al, 2000). Nutrient sources other than commercial pet foods should be investigated. Water quality varies considerably, even within the same community. Water can be a significant source of sodium, chloride and other minerals. Veterinarians should be familiar with the mineral levels in their local water supply. Water samples can be submitted to state or other government laboratories for analysis; municipal water companies can be contacted or private companies that market water conditioning systems can be asked about mineral levels in local water supplies. Distilled water or water with less than 150 ppm sodium is recommended for patients with advanced heart disease and failure (Morris et al, 1976).

Other sources of nutrients include commercial treats and snacks for pets, and human foods offered as snacks or part of the pet's food. Processed human foods are often high in sodium (**Table 36-7**). Some commercial rawhide chews do not contain excessive levels of sodium (Morris and Ettinger, 1995). **Table 36-8** lists selected commercial low sodium canine treats.

Although there is currently little or no evidence that proves foods low in sodium chloride delay disease progression in the initial stages of heart disease in dogs, a prudent recommendation is to begin avoiding excess sodium chloride early in the disease process. Thus, at the first sign of heart disease without cardiac dilatation (Class Ia), foods with levels of sodium in the upper part of the recommended range (0.15 to 0.25% DM) should be introduced. Early intervention may help the patient accept foods if more restricted sodium chloride levels are necessary later, and reminds the owners to remain vigilant for signs of disease progression. Furthermore, avoiding excessive amounts of sodium chloride early in heart disease has not been shown to be harmful.

When cardiac dilatation becomes evident on radiographs or echocardiograms (Class Ib), then sodium chloride-restricted foods are appropriate (Roudebush et al, 1994; Rush et al, 2000). Cardiac dilatation implies abnormal sodium chloride handling and intravascular volume expansion, and it is a prelude to venous congestion. The presence of moderate to severe cardiac dilatation, congestion or both conditions (Class II or III) indicates that foods lower in sodium chloride are appropriate. Many veterinary cardiologists prescribe foods with levels of sodium in the upper part of the recommended range (0.15 to 0.25% DM) when ACE inhibitors are used, especially when used in combination with diuretics. **Table 36-9** outlines the daily sodium intake of a 15-kg dog and a 4-kg cat fed different foods, including grocery, specialty and veterinary therapeutic foods. Normal dogs and cats are able to eliminate the excess levels of sodium found in many commercial foods, but patients with heart disease and failure have an impaired ability to handle these sodium levels. There is often concern about the palatability of low-salt foods compared to that of a patient's current food. Low-salt foods can be even more palatable than maintenance foods with higher salt content (**Box 36-1**). However, a few patients might not eat low-salt foods. A common mistake is to insist that an owner feed only a salt-restricted food even if caloric intake is inadequate. Although avoiding excess sodium chloride is important in CHF patients, offering only a salt-restricted food should not be imposed to the detriment of overall nutrient intake. Changing to a different commercial food or homemade food may be a more beneficial solution in some patients. Appetite may be cyclical in patients with advanced heart failure, both in respect to overall appetite and food preferences. A dedicated owner is often required and a trial-and-error approach should be used with different foods and feeding methods.

Low-salt foods may also be of value in the management of respiratory diseases (**Box 36-2**). Another criterion for selecting a food that may become increasingly important in the future is evidence-based clinical nutrition. Practitioners should know how to determine risks and benefits of nutritional regimens and counsel pet owners accordingly. Currently, veterinary medical education and continuing education are not always based on rigorous assessment of evidence for or against particular management options. Still, studies have been published to establish the nutritional benefits of certain pet foods. Chapter 2 describes evidence-based clinical nutrition in detail and applies its concepts to various veterinary therapeutic foods.

Adjunctive Management: Drugs and Supplements

Most patients with cardiovascular disease in which nutritional management is used also receive drug therapy. In the past, drug-drug interactions received considerable attention but few investigators evaluated or discussed how nutrient levels might affect drug availability and pharmacokinetics and vice versa (Chapter 69). Because many cardiovascular patients are treated with a combination of veterinary therapeutic foods and drugs, potential food-drug or nutrient-drug interactions are important.

Table 36-5. Levels of key nutrients in selected commercial foods for dogs with cardiovascular disease compared to the recommended levels.*

Dry foods for Class Ia patients**	Energy density (kcal/cup)***	Na (%)	Taurine (%)†	Carnitine (%)†	P (%)	K (%)†	Mg (%)†
Recommended levels	**–**	**0.15-0.25**	**≥0.1**	**≥0.02**	**0.2-0.7**	**≥0.4**	**≥0.06**
Hill's Prescription Diet g/d Canine	358	0.21	0.1	na	0.41	0.61	0.068
Hill's Prescription Diet j/d Canine	356	0.17	0.13	0.04	0.54	0.83	0.139
Hill's Prescription Diet k/d Canine	396	0.23	0.12	na	0.24	0.67	0.107
Hill's Science Diet Mature Adult Active Longevity Original	363	0.18	0.13	na	0.58	0.83	0.109
Hill's Science Diet Mature Adult Large Breed	357	0.17	0.13	0.03	0.59	0.82	0.108
Hill's Science Diet Mature Adult Small Bites	363	0.18	0.13	na	0.58	0.83	0.109
Medi-Cal Early Cardiac	300	0.3	0.2	0.1	0.8	0.8	0.1
Purina Veterinary Diets NF KidNey Function	459	0.22	na	na	0.29	0.86	0.070
Royal Canin Veterinary Diet Early Cardiac EC 22	291	0.19	0.22	na	0.77	0.82	0.077
Moist foods for Class Ia patients**	**Energy density (kcal/can)*****	**Na (%)**	**Taurine (%)†**	**Carnitine (%)†**	**P (%)**	**K (%)†**	**Mg (%)†**
Recommended levels	**–**	**0.15-0.25**	**≥0.1**	**≥0.02**	**0.2-0.7**	**≥0.4**	**≥0.06**
Hill's Prescription Diet g/d Canine	377/13 oz.	0.22	0.11	na	0.41	0.78	0.067
Hill's Prescription Diet j/d Canine	498/13 oz.	0.19	0.12	0.03	0.56	0.81	0.112
Hill's Prescription Diet k/d Canine	458/13 oz.	0.19	0.11	na	0.22	0.37	0.141
Hill's Science Diet Mature Adult Active Longevity Gourmet Beef Entrée	164/5.8 oz. 368/13 oz.	0.16	0.12	0.02	0.52	0.76	0.104
Hill's Science Diet Mature Adult Active Longevity Savory Chicken Entrée	155/5.8 oz. 347/13 oz.	0.16	0.12	na	0.57	0.7	0.111
Hills Science Diet Mature Adult Active Longevity Gourmet Turkey Entrée	369/13 oz.	0.17	0.12	na	0.62	0.83	0.107
Iams Veterinary Formula Stress/Weight Gain Formula Maximum-Calorie	333/6 oz.	0.24	0.33	na	0.83	1.01	0.089
Medi-Cal Renal MP	532/380 g	0.2	na	na	0.4	1.5	na
Purina Veterinary Diet NF KidNey Function Formula	498/12.5 oz.	0.24	na	na	0.30	0.72	0.080
Dry foods for Class Ib, II and III patients	**Energy density (kcal/cup)*****	**Na (%)**	**Taurine (%)†**	**Carnitine (%)†**	**P (%)**	**K (%)†**	**Mg (%)†**
Recommended levels	**–**	**0.08-0.15**	**≥0.1**	**≥0.02**	**0.2-0.7**	**≥0.4**	**≥0.06**
Hill's Prescription Diet h/d Canine	407	0.08	0.14	0.03	0.54	0.8	0.122
Medi-Cal Renal LP	283	0.1	na	na	0.3	0.7	na
Medi-Cal Renal MP	336	0.1	na	na	0.4	0.7	na
Moist foods for Class Ib, II and III patients	**Energy density (kcal/can)*****	**Na (%)**	**Taurine (%)†**	**Carnitine (%)†**	**P (%)**	**K (%)†**	**Mg (%)†**
Recommended levels	**–**	**0.08-0.15**	**≥0.1**	**≥0.02**	**0.2-0.7**	**≥0.4**	**≥0.06**
Hill's Prescription Diet h/d Canine	480/13 oz.	0.11	0.21	0.03	0.57	0.81	0.131
Medi-Cal Renal LP	643/385 g	0.1	na	na	0.2	1.0	na
Purina Veterinary Diet CV Cardiovascular Formula	638/12.5 oz.	0.12	0.24	na	0.40	1.21	0.060

Key: Na = sodium, P = phosphorus, K = potassium, Mg = magnesium, na = information not available from the manufacturer, g = grams.
*Values are on a dry matter basis unless otherwise stated.
**Also recommended for Class Ib, II and III patients when ACE inhibitors are used, especially when used in combination with diuretics.
***As fed energy values (kcal/cup or can) are useful for determining the amount to feed; these values can be converted to an amount of food to feed by dividing the energy density of the food (as fed basis) by the patient's daily energy requirement (DER); cup = 8-oz. measuring cup; to convert kcal to kJ, multiply kcal by 4.184. Providing the right amount of food is vital for managing patients with cardiovascular disease. Overweight patients should be fed foods with reduced energy as part of a weight-reduction program (Chapter 27). Patients suffering from cardiac cachexia may need more energy than otherwise normal pets. Body condition scoring should be used frequently to determine the patient's response to the amount of food fed.
†See discussion under "Adjunctive Management: Drugs and Supplements" in the "Feeding Plan" section if additional supplementation is required beyond that present in foods in this table.

Table 36-6. Levels of key nutrients in selected commercial foods for cats with cardiovascular disease compared to the recommended levels.*

Dry foods	Energy density (kcal/cup)**	Na (%)	Taurine (%)***	P (%)	K (%)***	Mg (%)***
Recommended levels	**–**	**0.07-0.30**	**≥0.3**	**0.3-0.7**	**≥0.52**	**≥0.04**
Hill's Prescription Diet g/d Feline	297	0.32	0.14	0.54	0.77	0.049
Hill's Prescription Diet k/d Feline	477	0.24	0.16	0.46	0.75	0.058
Hill's Science Diet Mature Adult Active Longevity Original	475	0.32	0.2	0.69	0.88	0.069
Medi-Cal Mature Formula	355	0.4	0.4	0.8	1.0	na
Medi-Cal Reduced Protein	440	0.3	0.4	0.6	0.8	na
Medi-Cal Renal LP	409	0.2	0.2	0.5	1.0	na
Purina Veterinary Diets NF KidNey Function	398	0.2	0.18	0.41	0.88	0.10
Moist foods	**Energy density (kcal/can)****	**Na (%)**	**Taurine (%)*****	**P (%)**	**K (%)*****	**Mg (%)*****
Recommended levels	**–**	**0.07-0.30**	**≥0.3**	**0.3-0.7**	**≥0.52**	**≥0.04**
Hill's Prescription Diet g/d Feline	165/5.5 oz.	0.32	0.44	0.52	0.72	0.088
Hill's Prescription Diet k/d with Chicken Feline	183/5.5 oz.	0.3	0.42	0.38	1.18	0.049
Hill's Science Diet Mature Adult Active Longevity Gourmet Turkey Entrée Minced	87/3 oz. 160/5.5 oz.	0.28	0.48	0.64	0.84	0.072
Iams Veterinary Formula Stress/Weight Gain Formula Maximum-Calorie	333/6 oz.	0.24	0.33	0.83	1.01	0.089
Medi-Cal Mature Formula	205/170 g	0.3	0.3	0.6	0.7	na
Medi-Cal Reduced Protein	265/170 g	0.2	0.3	0.5	0.7	na
Medi-Cal Renal LP	125/85 g pouch	0.6	0.8	0.5	1.1	na
Purina Veterinary Diets CV Cardiovascular Formula	223/5.5 oz.	0.2	0.31	0.92	1.33	0.07
Purina Veterinary Diets NF KidNey Function	234/5.5 oz.	0.16	0.45	0.52	0.96	0.10

Key: Na = sodium, P = phosphorus, K = potassium, Mg = magnesium, na = information not available from the manufacturer.
*Values are on a dry matter basis unless otherwise stated.
**As fed energy values (kcal/cup or can) are useful for determining amount to feed; These values can be converted to an amount of food to feed by dividing the energy density of the food (as fed basis) by the patient's daily energy requirement (DER); cup = 8-oz. measuring cup; to convert kcal to kJ, multiply kcal by 4.184. Providing the right amount of food is vital for managing patients with cardiovascular disease. Overweight patients should be fed foods with reduced energy as part of a weight-reduction program (Chapter 27). Patients suffering from cardiac cachexia may need more energy than otherwise normal pets. Body condition scoring should be used frequently to determine the patient's response to the amount of food fed.
***See discussion under "Adjunctive Management: Drugs and Supplements" in the "Feeding Plan" section if additional supplementation is required beyond that present in foods in this table.

Diuretics

Diuretics continue to be a pharmacologic mainstay of acute therapy for heart failure. Sodium restriction, ACE inhibition, venodilating drugs and diuretics represent the major available methods for preload reduction.

Sodium chloride restriction is a key component of CHF treatment even with the use of diuretics. Well-controlled studies have demonstrated that loop diuretics such as furosemide given once daily fail to achieve a negative sodium balance in people with high sodium intake (Wilcox et al, 1983). Although there is an impressive natriuresis for several hours after furosemide administration, a compensatory increase in sodium reabsorption in the next 24 hours exactly matches the earlier losses (Wilcox et al, 1983). Thus, it is essential to limit sodium intake to ensure negative sodium balance. Balance studies with normal people have demonstrated that significant negative sodium balance can be predictably obtained with loop diuretics if sodium intake is limited to 20 mEq/day (roughly equivalent to 460 mg sodium or 1.2 g sodium chloride per day) (Kokko, 1994). This level of sodium restriction in people is equivalent to that achieved with use of foods formulated for patients with cardiovascular disease (**Tables 36-5** and **36-6**).

Blood volume contraction and circulatory impairment are potential complications of aggressive diuretic therapy. These complications can exacerbate pre-existing renal disease, alter excretion of drugs dependent on renal elimination and reduce cardiac output by reducing cardiac filling pressures (Fox, 1992). Reduced levels of sodium in the food have been implicated, but have not been proven to contribute to volume depletion from excessive diuresis (Fox, 1992). Fractional excretion of sodium in urine actually decreases in normal dogs fed a sodium-restricted food (Navar et al, 1982). The influence of diuretics on sodium and chloride balance in dogs with heart disease and failure fed sodium- and chloride-restricted foods has not been evaluated.

Furosemide contributes to hypokalemia and hypomagnesemia because of increased urinary loss of potassium and mag-

Table 36-7. Sodium content of selected human foods.*

Food	Amount	Sodium (mg)
Bread, cereals and potatoes		
Recommended		
Macaroni	1 cup	1-10
Potato	1 (medium)	<5
Puffed wheat	1 oz.	1-10
Rice (polished)	1/2 cup	1-10
Spaghetti	1 cup	1-10
Not recommended		
Bread	1 slice	200
Corn chips	1 oz.	230
Potato chips	1 oz.	300
Pretzel	1	275
Margarine and oil		
Recommended		
Unsalted margarine	1 tsp	0-1
Vegetable shortening	1 tbs	0-1
Not recommended		
Mayonnaise	1 tbs	60-90
Dairy products		
Not recommended		
American cheese	1 oz.	200-300
Butter	1 tsp	50
Cottage cheese	3 oz.	200-300
Cream cheese	1 1/2 oz.	100-120
Milk (regular and skim)	1 cup	122
Meats, poultry, fish		
Recommended		
Beef (fresh)	3 1/2 oz.	50
Chicken (no skin)		
Light meat	3 1/2 oz.	64
Dark meat	3 1/2 oz.	86
Lamb (fresh)	3 1/2 oz.	84
Pork (fresh)	3 1/2 oz.	62
Turkey (no skin)		
Light meat	3 1/2 oz.	82
Dark meat	3 1/2 oz.	98
Not recommended		
Bacon	2 slices	385
Egg	1	70
Frankfurter	1	560
Ham (processed)	3 oz.	940
Tuna (canned)	1 can	320
Vegetables (fresh or dietetic canned)		
Recommended		
Corn	1/2 cup	<5
Cucumber	1/2 cup	<5
Green beans	1/2 cup	<5
Green pepper	1/4 cup	<5
Lettuce	1/4 cup	<5
Peas	1/2 cup	<5
Tomato	1	<5
Not recommended		
Most canned vegetables	1/2 cup	190-450
Fruits		
Most fresh and canned fruits are low in sodium and are permitted		
Other food items		
Not recommended		
Macaroni with cheese	1 cup	1,000
Peanut butter	1 tbs	81
Pizza (cheese)	1 slice	650
Desserts		
Recommended		
Sherbet	1/2 cup	15-25
Not recommended		
Cookies	1	35-100
Gelatins	1/2 cup	60-85
Ice cream	1/2 cup	60-85
Puddings	1/2 cup	100-200

*Sodium amounts are on an as fed basis; adapted from Morris ML Jr, Ettinger SJ. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine, 4th ed. Philadelphia, PA: WB Saunders Co, 1995; 237.

nesium (Fox, 1992). The role of magnesium and potassium in the development of cardiac dysrhythmias has not received attention beyond the recognition that digitalis toxicosis appears to be much more dysrhythmogenic in hypomagnesemic and hypokalemic patients (Edwards, 1991). Hypomagnesemia may potentiate cardiac dysrhythmias caused by catecholamine release and is also associated with increased vascular reactivity (Bean and Varghese, 1994).

Conflicting reports have been published about the serum electrolyte and magnesium concentrations of dogs with CHF. A study of 113 dogs with CHF identified only four dogs with hypomagnesemia (Edwards, 1991). Three of the four hypomagnesemic dogs received combined therapy with a commercial sodium-restricted veterinary therapeutic food, furosemide and either hydralazine or enalapril. In another study, furosemide-treated dogs with heart failure had significantly lower serum magnesium and potassium values than did age-matched healthy controls (Cobb and Mitchell, 1991). A third study showed no significant differences in serum magnesium concentrations between clinically normal dogs, dogs with heart failure before any treatment, heart-failure dogs treated only with furosemide and heart-failure dogs treated with furosemide and digoxin (O'Keefe and Sisson, 1993). The feeding history was not included in the last two studies; therefore, specific food-diuretic interactions could not be interpreted. Normal dogs treated with a commercial sodium-restricted veterinary therapeutic food and furosemide for four weeks had no significant change in serum potassium concentrations (Roudebush et al, 1994).

Several studies have shown that the RAA system is not activated in human patients with moderate heart failure in the absence of diuretic therapy (Kubo, 1990; Bayliss et al, 1987). The major increase in plasma renin activity and plasma aldosterone concentration occurs with the introduction of diuretic drugs into the treatment regimen rather than as a result of the disease process itself. Furosemide apparently stimulates renin release by inhibiting chloride transport in the ascending limb of the loop of Henle, even if blood volume contraction is prevented (Kotchen et al, 1981). Treatment of normal geriatric dogs with moderate doses of furosemide profoundly stimulates the RAA system, irrespective of the sodium level in the food (Roudebush and Allen, 1996; Lovern et al, 2001). Use of furosemide with either hydralazine or enalapril also stimulates the RAA system in dogs with heart failure due to acquired mitral valve regurgitation (Haggstrom et al, 1996).

Although diuretics will remain important first-line drugs for management of acute cardiogenic pulmonary edema, findings in people suggest that diuretics continue to stimulate the RAA system and may play a pivotal role in the progressive self-perpetuating cycle of heart failure (Kubo, 1990). Veterinary cardiologists now recommend against the use of diuretic monotherapy early in the management of symptomatic heart failure (Keene and Rush, 1995; Keene and Bonagura, 2009). Diuretics should be reserved for managing more advanced heart failure in patients already receiving moderately sodium chloride-restricted foods, ACE inhibitors, pimobendan or combination thera-

py. Feeding patients foods without excess sodium chloride may allow lower dosages of diuretics to be used for control of the clinical signs of CHF.

Sodium, chloride, potassium and magnesium levels vary in commercial veterinary therapeutic foods for dogs and cats with cardiovascular disease (**Tables 36-5** and **36-6**). These nutrients in regular commercial foods vary markedly. Mineral levels should be considered when using concurrent diuretic therapy.

Long-term furosemide therapy may be associated with clinically significant thiamin deficiency, due to excessive urinary loss of thiamin, and may contribute to impaired cardiac performance in patients with CHF (Seligman et al, 1991). Patients receiving long-term diuretic therapy should be given supplements containing thiamin and other water-soluble vitamins or be fed a commercial food with increased concentrations of these vitamins. Veterinary therapeutic foods for patients with cardiac and renal disease are often formulated with higher levels of water-soluble vitamins to offset excessive urinary losses.

ACE Inhibitors

Enalapril, benazepril, ramipril and lisinopril, all ACE inhibitors, are commonly used to treat dogs and cats with CHF. Inhibition of the conversion of angiotensin I to angiotensin II results in vascular dilatation and decreased circulating plasma aldosterone concentrations. Angiotensin II and aldosterone play important roles in the maintenance of vascular volume and potassium balance. Both increase the reabsorption of sodium and chloride, and aldosterone promotes the excretion of potassium.

The use of ACE inhibitors in human patients with severe renal insufficiency or in patients given potassium supplements may increase the risk for hyperkalemia (Warren and O'Connor, 1980; Dzau et al, 1980; Rotmensch et al, 1988). In a study, more than half the dogs with CHF developed mild serum potassium elevations when treated with a commercial sodium-restricted veterinary therapeutic food, furosemide and captopril (Roudebush et al, 1994). Another study confirmed that heart-failure dogs treated with furosemide, digoxin and an ACE inhibitor had significantly higher mean serum potassium concentrations when compared with clinically normal dogs, dogs with heart failure before any treatment, heart-failure dogs treated only with furosemide and heart-failure dogs treated with furosemide and digoxin (O'Keefe and Sisson, 1993). Mild elevations in serum potassium concentrations have also been observed in dogs treated with enalapril (COVE, 1995). In another study, serum potassium concentration decreased in a subset of heart-failure dogs treated with ACE inhibitors and furosemide, although the specific feeding history was not reported (Cobb and Mitchell, 1991).

When mild hyperkalemia occurs in people with heart failure, reducing oral potassium intake and discontinuing potassium-sparing diuretics is recommended (Rotmensch et al, 1988). Although clinically significant hyperkalemia (serum potassium 6.5 mEq/l) is uncommon, the use of ACE inhibitors in dogs with CHF or renal insufficiency fed commercial or veterinary therapeutic foods with high potassium content may increase the risk for hyperkalemia (Roudebush et al, 1994).

Table 36-8. Low sodium commercial treats for dogs with cardiovascular disease.

Treats	Sodium (%DM)
Recommended sodium range for dogs with cardiac disease	**0.08 to 0.25**
Hill's Science Diet Adult Treats Medium/Large Bone with Real Chicken	0.23
Hill's Science Diet Adult Light Treats Medium/Large Bone with Real Chicken	0.24
Hill's Science Diet Jerky Plus with Real Beef and Vegetables	0.29
Medi-Cal Medi-Treats	0.1
Purina Veterinary Diets Lite Snackers Canine Formula	0.21
Royal Canin Veterinary Diet Treats for Dogs	0.21

Key: DM = dry matter.

Table 36-9. Daily sodium intake for a dog and a cat eating various foods.

Daily sodium consumption for a 15-kg dog eating 935 kcal/day

Food	Sodium intake (mg/day)
Grocery moist food[a]	2,338
Grocery dry food[b]	944
Specialty dry food[c]	552
Geriatric dry food[d]	430
Renal moist food[e]	468
Cardiac dry food[f]	159
Cardiac dry food and 1 slice bread	370
Renal moist food and 30 g cheese	700

[a]Pedigree with Chopped Beef
[b]Purina Dog Chow
[c]Hill's Science Diet Adult Original Dog Food
[d]Hill's Science Diet Mature Adult 7+ Original Dog Food
[e]Purina Veterinary Diets NF KidNey Function Canine Formula
[f]Hill's Prescription Diet h/d Canine

Daily sodium consumption for a 4-kg cat eating 270 kcal/day

Food	Sodium intake (mg/day)
Grocery moist food[g]	823
Grocery dry food[h]	405
Specialty dry food[i]	232
Geriatric moist food[j]	184
Renal moist food[k]	135
Renal dry food[l]	151
Renal dry food and 1/2 can tuna	295

[g]Fancy Feast Elegant Medleys White Meat Chicken Florentine
[h]Purina Cat Chow Complete Formula
[i]Hill's Science Diet Adult Original Cat Food
[j]Hill's Science Diet Turkey Entrée Mature Adult 7+ Cat Food
[k]Purina Veterinary Diets NF KidNey Function Feline Formula
[l]Hills Prescription Diet k/d Feline

Functional renal insufficiency occurs in up to one-third of human patients with severe CHF treated with sodium chloride restriction, ACE inhibitors and diuretics (Parker et al, 1987). This decline in renal function has been attributed to loss of angiotensin II-mediated systemic and intrarenal vasoconstrictor effects, which maintain renal perfusion pressure and glomerular filtration rate in low-output heart failure. Functional renal insufficiency appears to be alleviated in human patients when efforts are made to replenish total body stores of

Box 36-1. Palatability of Low-Salt Foods.

The question often arises whether sodium chloride enhances palatability of foods for dogs and cats. Sodium chloride and other inorganic salts stimulate specific taste chemosensory neural groups in these species. This finding suggests that dogs and cats can indeed taste sodium chloride and other inorganic salts. These "taste" groups are also stimulated by simple sugars in dogs and specific amino acids in dogs and cats. Standard palatability testing indicates that dogs prefer the taste of a moist food as the level of sodium chloride is increased, whereas increasing levels of salt in a dry food have no effect on palatability of the food. Palatability enhancers added topically to dry pet foods probably mask any taste effects of sodium chloride or other salts. Many foods with reduced sodium chloride levels for use in patients with cardiovascular disease have comparable or better palatability than grocery or specialty brand pet foods.

The Bibliography for **Box 36-1** can be found at www.markmorris.org.

Box 36-2. Use of Low-Salt Foods in Chronic Respiratory Diseases.

Avoiding excess sodium chloride may also be important in patients with some forms of chronic respiratory disease such as chronic bronchitis or asthma. Both epidemiologic and experimental evidence in people suggest that high sodium chloride intake may increase airway responsiveness and exacerbate clinical signs associated with asthma. When some people with asthma are subjected to salt loading, clinical signs worsen, lung function deteriorates and the need for antiasthmatic drugs increases. However, not all studies in people with asthma show benefits of avoiding excess dietary sodium. A serum-borne factor in human patients with airway hyperresponsiveness stimulates increased sodium influx into cells. Reduced sodium levels in food also result in increased levels of vasoactive intestinal peptide (VIP) in the plasma and lung; VIP acts as a bronchodilator. Although similar canine and feline studies have not been completed, foods that avoid excess salt may be helpful in conjunction with other forms of therapy in animals with chronic bronchitis or asthma-like clinical signs.

The Bibliography for **Box 36-2** can be found at www.markmorris.org.

sodium by reducing the diuretic dosage and liberalizing sodium intake (Parker et al, 1987). Renal insufficiency is a potential complication of ACE inhibitor therapy in dogs with CHF, but the role of sodium restriction is unknown (Roudebush et al, 1994; Longhofer et al, 1993; DeLillis and Kittleson, 1992). Four of 10 heart-failure dogs treated with captopril, furosemide and a sodium-restricted veterinary therapeutic food developed azotemia during the first five weeks of treatment; one of these dogs developed clinical signs of uremia (Roudebush et al, 1994). Two of the dogs that developed severe azotemia had isosthenuria on the initial urinalysis, which suggested some degree of pre-existing renal insufficiency. Azotemia is a more frequent complication when canine heart failure is treated with furosemide and enalapril rather than with furosemide alone (DeLillis and Kittleson, 1992).

Drug-induced azotemia in heart failure patients is treated by reducing the diuretic dose (usually at least by half–skip a dose if there is not active pulmonary edema); if that fails to resolve the problem, the ACE inhibitor dose can be reduced by half, the sodium intake can be increased to the next level (**Tables 36-5** and **36-6**) or a combination of these tactics may be used.

Management of Hyponatremia

The correction of hyponatremia associated with CHF has been evaluated in people but not in domestic animals. The combined administration of an ACE inhibitor and furosemide (but usually not of either agent alone) usually reverses CHF-associated hyponatremia in people, at least in part (Oster et al, 1994). The reversal of hyponatremia probably results from the combined effects of the ACE inhibitor (i.e., decreased thirst, decreased proximal tubular reabsorption of sodium chloride, interference with the hydro-osmotic effect of AVP) and the loop diuretic (i.e., increased distal delivery of glomerular filtrate, reduction in urine osmolality) acting to offset the pathophysiologic factors that impair excretion of water (Oster et al, 1994; Packer et al, 1984). Studies are needed to determine whether similar measures are effective in reversing CHF-associated hyponatremia in animals. Hyponatremia secondary to severely decreased cardiac output and inappropriate secretion of ADH would not be expected to resolve with either further diuretic therapy, or with ACE inhibition. In this case, increasing cardiac output (generally accomplished by inotropic stimulation, afterload reduction or a combination of the two) would be needed, and pimobendan would be the most easily available potentially effective therapy.

Pimobendan

Pimobendan is an inodilator drug (combination positive inotrope and vasodilator) approved by the FDA for the treatment of heart failure in dogs in 2007 in the United States.[d] This drug, used at an oral dose of 0.3 mg/kg twice daily in combination with an ACE inhibitor and furosemide, is now part of the standard medical therapy for dogs in heart failure from either chronic valvular heart disease or dilated cardiomyopathy. There are no known dietary considerations that influence the pharmacodynamic effects of pimobendan. The drug appears to be associated with a dramatic and helpful appetite stimulating effect in many patients. It is not approved by the FDA for use in cats.

Cardiac Glycosides

Pimobendan has largely supplanted the routine use of digoxin in dogs and cats in sinus rhythm, at least until their heart failure becomes refractory to standard treatment with pimobendan, furosemide, an ACE inhibitor and moderate dietary salt

restriction. Cardiac glycosides have been used for more than two centuries and are still widely prescribed to manage cardiac disorders in dogs and cats when atrial fibrillation is present. Appropriate use of cardiac glycosides is based on an appreciation of the nutritional factors that influence the pharmacokinetic properties of these drugs.

Absorption of cardiac glycosides is influenced by the formulation of the drug and its administration in relation to meals (Chapter 69). Because administering digoxin or digitoxin with food may result in up to a 50% reduction in serum concentrations, these drugs are best given between meals (Snyder and Atkins, 1992). The body condition of the patient can also influence the pharmacokinetics of these drugs. Digoxin is minimally distributed in adipose tissue; the dosage of the drug should be based on lean body weight even for obese patients. Digitoxin is more lipid soluble than digoxin; so its dosage need not be adjusted for overweight animals.

The dosage of digoxin for cats is influenced by concurrent drug and nutritional therapy. The digoxin dose should be reduced by one-third if the cat is receiving concomitant furosemide, aspirin and a sodium-restricted veterinary therapeutic food (Atkins et al, 1988).

Metabolic derangements associated with increased risk of digoxin toxicosis include hypokalemia, hypomagnesemia, hypercalcemia, renal insufficiency, hypothyroidism and obesity (Snyder and Atkins, 1992). Serum electrolyte and magnesium concentrations should be measured and corrections made before starting cardiac glycoside therapy.

Potassium and/or Magnesium Supplementation

Electrolyte abnormalities, including hypokalemia, hyperkalemia and hypomagnesemia, are potential complications of drug therapy in patients with cardiovascular disease. Patients receiving diuretic therapy should receive adequate amounts of potassium and magnesium. Patients treated with ACE inhibitors may be predisposed to mild hyperkalemia; so their food should not contain excess levels of potassium. If hyperkalemia develops, switch to a food with a lower potassium level and discontinue any potassium supplementation. Loop or thiazide diuretics should be considered instead of potassium-sparing ones. Chronic kidney disease is often a concomitant disease of patients with cardiovascular disorders. If hypokalemia develops, feed a food with a higher potassium level or supplement the existing food with 3 to 5 mEq or mmol of potassium/kg body weight per day. If hypomagnesemia develops, feed a food with a higher magnesium content or provide oral magnesium supplementation (magnesium oxide, 20 to 40 mg/kg body weight per day).

Taurine Supplementation

Cats and dogs with myocardial failure may benefit from taurine supplementation to their regular food or use of foods that already contain increased levels of taurine. Patients with documented taurine deficiency are more likely to respond favorably to taurine supplementation. In dogs, the association between taurine deficiency and dilated cardiomyopathy is strongest in American cocker spaniels and golden retrievers (Kramer et al, 1995; Kittleson et al, 1997, 1991; Pion et al, 1998). Cats should receive 250- to 500-mg taurine per os daily (Pion et al, 1989), whereas dogs should receive 500- to 1,000-mg taurine per os three times daily (Pion et al, 1998). Some foods formulated for nutritional management of cardiovascular disease usually already contain increased levels of taurine (**Tables 36-5** and **36-6**). Patients eating these foods usually do not need additional taurine supplementation. **Table 36-10** lists levels of taurine found in various types of natural foods.

Table 36-10. Taurine concentrations (mg/kg dry matter) in selected natural food sources.

Source	Concentration
Beef muscle, uncooked	1,200
Chicken muscle, uncooked	1,100
Cod fish, uncooked	1,000
Lamb muscle, uncooked	1,600
Mouse carcass	7,000
Pork muscle, uncooked	1,600
Tuna, canned	2,500

Taurine supplementation of feline foods can be discontinued within 12 to 16 weeks if: 1) clinical signs of heart failure have resolved, 2) echocardiographic values are near normal and 3) the cat will eat a food known to support normal whole blood taurine concentrations. The length of time needed for taurine supplementation of canine foods is currently unknown.

L-Carnitine Supplementation

The recommended oral dosage for dogs with myocardial L-carnitine deficiency is 50- to 100-mg L-carnitine/kg body weight three times daily (Keene, 1992). Dogs weighing 25 to 40 kg are most often affected and should receive 2 g of L-carnitine mixed with food three times daily. This high oral dosage will elevate plasma L-carnitine concentration 10 to 20 times above usual pretreatment values (Keene et al, 1991). These high plasma L-carnitine levels will usually, but not always, raise myocardial L-carnitine concentrations into the normal range. The cost of this level of L-carnitine supplementation is approximately $80 (U.S.) per month for a large-breed dog. L-carnitine is usually available in human health food stores.

Dogs that respond dramatically to L-carnitine therapy do so in a reasonably predictable manner. Owners often report generalized improvement in clinical signs within one to four weeks and echocardiographic improvement is noted after eight to 12 weeks of supplementation. Improvement may continue for about six to eight months, at which time patients often reach a plateau and though they appear clinically normal they have depressed ventricular function as determined by echocardiography (Keene, 1992).

Assess and Determine the Feeding Method

The method of feeding is often not altered in the nutritional management of cardiovascular disease. If a new food is fed, the amount to feed can be determined from the product label or other supporting materials. The food dosage may need to be

changed if the caloric density of the new food differs from that of the previous food. The food dosage is usually divided into two or more meals per day. The food dosage and feeding method should be altered if the patient's body weight and condition are not optimal. If the patient has a normal body condition score (2.5/5 to 3.5/5), the amount of food it was fed previously (energy basis) was probably appropriate. To determine the starting point for the amount of new food to feed, if the patient's body condition score is within the normal range (2.5/5 to 3.5/5), the amount of calories were appropriate. If the energy density of the previous food is available, the number of calories consumed per day (daily energy requirement [DER]) can be determined by multiplying the energy density of the food (kcal/cup and/or can) by the number of cups and/or cans fed. Then the amount of new food to feed can be obtained by dividing the DER value by the energy density of the new food. The energy densities of foods for heart disease are included in **Tables 36-5** and **36-6**. Manufacturers' feeding information can also be used to determine an initial amount of new food to feed. Body weight should be monitored for a few weeks after the food change is accomplished.

Food dosage should be modified for patients with obesity or cachexia. A diary maintained by the client is helpful for documenting what types and quantities of foods and supplements are being offered and eaten by the patient. This caloric intake can be compared with the number of calories that are usually needed to maintain ideal body weight and condition in that patient.

Obesity causes profound changes that can complicate cardiovascular disorders. Obese patients should undergo management with a calorie-restricted food and client education should focus on the importance of the pet achieving an ideal body weight and condition (Chapter 27). The veterinary health care team should emphasize the potentially damaging effects of obesity in patients with heart disease to clients to enlist their active participation in a successful weight-management program.

For clinical nutrition to be effective, there needs to be good compliance. Enabling compliance includes limiting access to other foods and knowing who feeds the patient. If the patient comes from a household with multiple pets, it should be determined whether the pet with cardiovascular disease has access to other pets' food. Access to other food (table food, other pets' food, etc.) may contribute to cardiovascular disease and thus should be denied (Chapter 1).

Occasionally, it is difficult to get a patient to accept a change to a lower salt commercial food. This can occur because of: 1) advanced illness associated with heart failure, 2) established feeding habits of older patients and their owners, 3) anorexia associated with concurrent renal failure and some cardiac drugs and 4) the "all or nothing" approach to feeding, rather than slowly changing to the new food. Changing the eating habits of most dogs is relatively easy, but changing the feeding habits and preconceptions (e.g., "low-salt food is always unpalatable") of some pet owners and veterinarians is often much more difficult. Results of feeding studies using hospitalized dogs have shown that most dogs will readily accept a food that is very low in sodium chloride by the third day (Ross, 1987). For individual dogs, these foods can be made more palatable by warming the food or adding flavor enhancers (low-sodium soup or tomato sauce; sweeteners such as honey or syrup). Use of foods that are very low in sodium chloride in advanced heart disease and failure will be much easier if the dog has already been fed a low-sodium food (Tables 13-4 and 14-3 for dogs and Tables 20-4 and 21-4 for cats).

REASSESSMENT

In general, the survival of patients with heart failure is related to the degree of myocardial failure, whereas their clinical signs are related more to CHF and its compensatory mechanisms. The overall objectives of treatment for chronic heart failure, as for almost any cardiovascular disease, are threefold: 1) prevention (prevent myocardial damage, prevent recurrence of heart failure), 2) relief of clinical signs (eliminate edema and fluid retention, increase exercise capacity, reduce fatigue and respiratory compromise) and 3) improvement of prognosis (reduce mortality).

Dogs and cats with suspected cardiovascular disease should undergo a routine serum biochemistry profile and urinalysis before any nutritional or drug therapy is initiated. Dogs and cats with heart failure and evidence of preexisting renal disease, including isosthenuria, may be at increased risk for developing azotemia during combined food-drug therapy. There are no universal recommendations for controlling: levels of sodium, chloride and potassium; fluid intake; ACE inhibition and diuretic administration for patients with cardiovascular disease. Rather, each patient should be monitored frequently (weekly for the first four to six weeks). Reassessment should include: 1) measurement of body weight, 2) assessment of body condition, 3) determination of serum electrolyte and magnesium concentrations and 4) evaluation of renal function.

FEEDING PLANS FOR PATIENTS WITH CHYLOTHORAX

Depending on the chronicity of the disease, amount of pleural effusion and prior treatment attempts, dogs and cats with chylothorax may be emaciated and dehydrated. The goal of medical management is to support the metabolic and nutritional needs of the patient until the effusion spontaneously resolves, specific therapy for an underlying disease is instituted (e.g., chemotherapy, radiation therapy or both for a mediastinal mass; surgical correction of diaphragmatic hernia) or the patient's thoracic duct is ligated.

Dehydration and electrolyte abnormalities should be corrected before initiating nutritional support. Serious hyponatremia and hyperkalemia occur in dogs with chylothorax and should be corrected, especially if anesthesia is planned for placement of a thoracic tube or exploratory thoracotomy (Willard et al, 1991). Parenteral nutrition is a proven way to reduce the quantity of

lymph flow through the thoracic duct in human patients with chylothorax and can be used in feline and canine patients (Chapter 26). No clinical trials to evaluate the efficacy of parenteral nutrition in patients with chylothorax have been reported.

In the past, feeding a low-fat homemade or commercial food supplemented with medium-chain triglycerides was recommended for patients with chylothorax because it was thought to minimize thoracic duct flow. However, newer information challenged this concept and showed that thoracic duct flow may not be altered significantly by nutritional changes in dogs (Sikkema et al, 1993). Until more information is available, the primary management goals for chylothorax should be to meet the overall nutritional needs of the patient rather than focusing on nutritional changes designed to reduce chyle production. In most patients, medical and nutritional management are usually temporary means to support the patient until surgery (Birchard et al, 1988; Fossum et al, 1991). Fewer than 20% of cats with idiopathic chylothorax respond to long-term medical and nutritional management alone (Fossum et al, 1991).

ENDNOTES

a. Pipers F. Merial U.S. Personal communication. 2002.
b. Metabolic Analysis Lab, Inc., 1202 Ann Street, Madison, WI, USA.
c. Shelton GD. Director, Comparative Neuromuscular Laboratory, School of Medicine, University of California-San Diego, LaJolla, CA, USA.
d. Pimobendan. (Vetmedin). Boehringer Ingelheim, USA.

REFERENCES

The references for **Chapter 36** can be found at www.markmorris.org.

CASE 36-1

Congestive Heart Failure in a Beagle Crossbred Dog

Bruce W. Keene, DVM, Dipl. ACVIM (Cardiology)
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina, USA

Patient Assessment

An 11-year-old, neutered female beagle crossbred dog weighing 10 kg was admitted to the hospital with a three-month history of weight loss and reduced appetite. The patient had been short of breath for the past 24 hours and would not lie down the previous night. The dog had been examined by a veterinarian two months earlier for coughing and exercise intolerance. At that time a tentative diagnosis of tracheobronchitis was made and the patient was treated with a trimethoprim-sulfadiazine combination for seven days and a sustained-release theophylline compound for three weeks. Clinical signs improved some during the first week of therapy.

The dog's vaccinations were current. Yearly heartworm antigen tests were negative for the past five years. The patient received ivermectin monthly for heartworm prevention, and except for intermittent flea problems and mild periodontal disease, had been exceptionally healthy its entire life.

On presentation, the dog's rectal temperature was 38.9°C (102.1°F), the pulse 160/min. and the respiratory rate 70/min. The patient appeared alert and anxious, with rapid, labored breathing. Mucous membranes were pale pink and the capillary refill time was slightly slow. A modest amount of periodontal disease and dental calculus was noted.

The bronchovesicular sounds were louder than normal and end-inspiratory crackles were heard diffusely over the lung fields bilaterally, accompanied by some expiratory wheezes. The precordial impulse was normally located and the arterial pulses were rapid but regular. A 3/6 holosystolic (regurgitant quality) murmur heard best at the left cardiac apex and radiating somewhat to the heart base was auscultated. A softer, regurgitant quality systolic murmur was audible at the right hemithorax. The jugular veins were modestly distended and a systolic jugular venous pulse was present. The abdomen was nonpainful. The liver was descended about 2 cm below the costal arch. Body condition score was 2/5. The rest of the physical examination was unremarkable.

Results of the initial laboratory tests included: complete blood count (normal); urinalysis (urine specific gravity = 1.022 [reference range = 1.001 to 1.070], dipstick and sediment examination were normal); and serum biochemistry profile (normal, except for a mild elevation in serum creatinine concentration). Generalized cardiomegaly with especially prominent left atrial and left ventricular enlargement was evident radiographically. Pulmonary venous distention and air bronchograms typical of cardiogenic pulmonary edema were also visualized (**Figures 1A** and **1B**).

The clinical diagnosis was congestive heart failure (CHF) secondary to chronic valvular heart disease (endocardiosis) and mitral/tricuspid regurgitation.

Assess the Food and Feeding Method

The dog was fed a mixture of commercial moist and dry dog food, with 10 to 20% of the intake from lean meat and vegetable table foods.

Questions

1. What are nutrients of concern and general nutritional recommendations for patients with cardiac disease and CHF?
2. What are the potential interactions between pharmacologic and nutritional prescriptions that might be made for this patient?
3. What is the patient's daily energy requirement (DER)?

Answers and Discussion

1. General nutritional recommendations for patients with cardiac disease and CHF include: avoid excess sodium and chloride; ensure adequate magnesium intake; ensure adequate potassium intake, if using diuretics; avoid excess potassium intake, if using angiotensin-converting enzyme (ACE) inhibitor drugs; ensure adequate energy and protein intake; avoid excess phosphorus and protein intake, especially when renal disease is present; and provide additional taurine and carnitine, if myocardial failure is present.
2. Most patients with advanced heart disease and failure are treated with a combination of nutritional management and drug therapy. The interaction between drugs and nutrient levels in foods used in cardiovascular patients is an important consideration.

   Furosemide may contribute to hypokalemia and hypomagnesemia (especially in patients with anorexia) by increasing urinary loss of potassium and magnesium. Hypokalemia and hypomagnesemia may potentiate cardiac dysrhythmias. Patients receiving diuretic therapy should be encouraged to eat a food that provides moderate, but not excessive, intake of these nutrients (0.10 to 0.15% magnesium on a dry matter basis; 0.6 to 0.9% potassium on a dry matter basis).

   Mild elevations in serum potassium concentrations have been noted in some dogs treated with ACE inhibitors such as captopril and enalapril. Although clinically significant hyperkalemia (serum potassium >6.5 mEq/l) is uncommon, the use of ACE inhibitors in dogs with CHF or renal insufficiency fed commercial or veterinary therapeutic foods with high potassium content may increase the risk for hyperkalemia.

   Hypotension and renal insufficiency are two common complications of ACE inhibitor therapy. When these complications occur, the dosage of the ACE inhibitor drug is often reduced. An alternative method is to replete total body sodium concentrations by reducing the dosage of diuretic and increasing the daily sodium intake of the animal. This may be successful in reversing hypotension or renal insufficiency without having to change the ACE inhibitor drug dosage.
3. This patient's calculated resting energy requirement (RER), based on a body weight of 10 kg, is approximately 370 kcal/day (1,548 kJ/day). However, the RER is probably higher because of the patient's increased heart and respiratory rates. Calculation of RER based on an estimated ideal body weight of 12 kg can be used and would result in an RER of 430 kcal/day (1,799 kJ/day). The dog's DER would be 520 to 600 kcal/day (2,176 to 2,510 kJ/day). Frequent monitoring of body condition is important so that appropriate adjustments to energy intake can be made.

Therapy Including Feeding Plan

The patient was treated initially with a diuretic (furosemide, 3 mg/kg body weight subcutaneously) and nitroglycerine (5 mg/24-hr transdermal patch), and was placed in an oxygen-enriched environment. Within four hours, breathing was less labored and oxygen supplementation was discontinued. A second dose of furosemide (2 mg/kg body weight orally) was administered and water was offered free choice. The dog spent a quiet night.

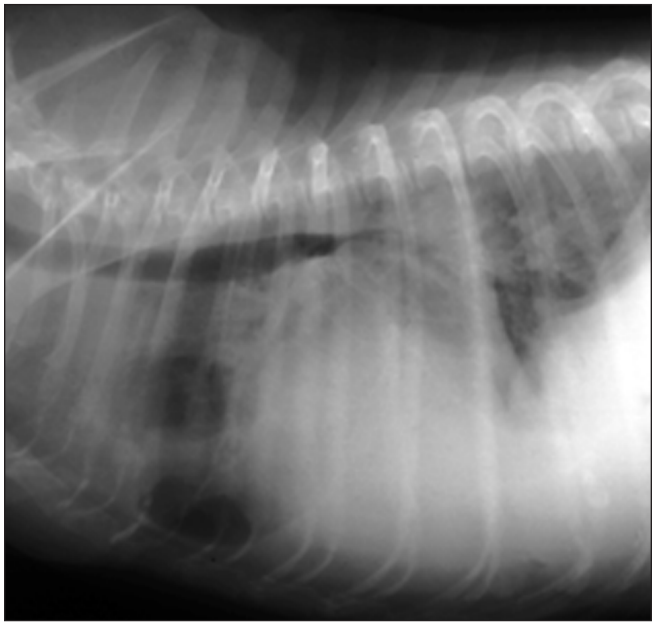
The next day, an electrocardiogram confirmed the presence of a sinus rhythm with evidence of left atrial and ventricular enlargement. An echocardiogram disclosed thickened mitral and tricuspid valve leaflets typical of endocardiosis (**Figure 2**). Also, severe mitral and tricuspid regurgitation was seen on color flow Doppler. Enalapril was initiated (0.5 mg/kg body weight per os, twice daily), furosemide was continued (1 mg/kg body weight per os, twice daily) and digoxin was begun (0.006 mg/kg body weight per os, twice daily).

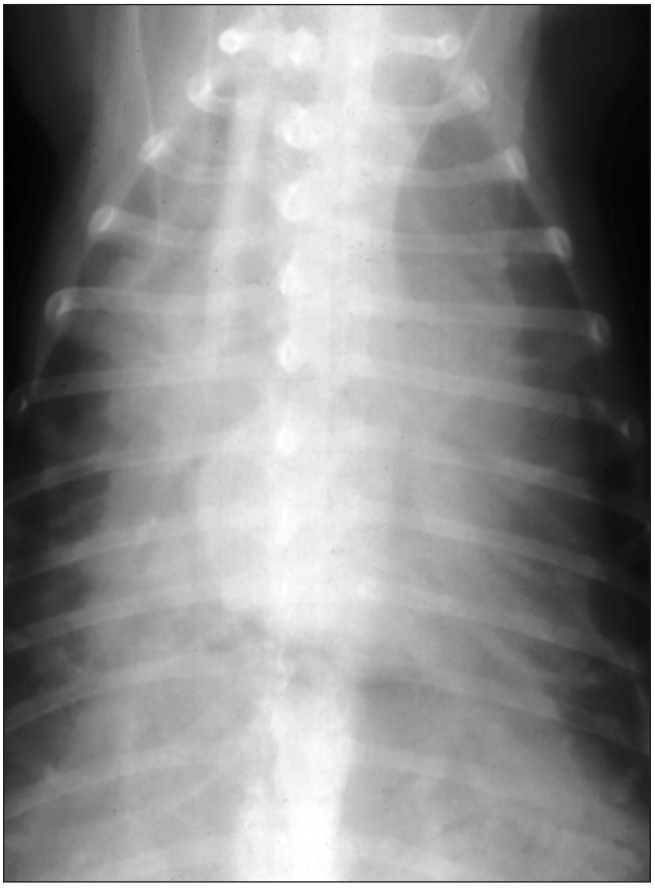
The dog was fed one can of Prescription Diet k/d Canine[a] (570 kcal/can; 2,384 kJ/can) per day and discharged from the hospital. The owners were instructed to return with the dog in five days for further evaluation.

Progress Notes

During the recheck examination, the owners reported that the dog was doing well. The body weight remained stable at 10 kg, the serum digoxin concentration was 1.4 ng/ml (therapeutic range = 1.0 to 2.0 ng/ml) and serum electrolyte, urea nitrogen and creatinine concentrations were within normal ranges. Rechecks were scheduled at three-month intervals, or sooner if clinical problems arose. The owners were instructed to adjust the furosemide dosage as needed to keep the dog comfortable, within a range of 0.5 to 2.0 mg/kg body weight once to twice daily.

The patient remained well for about eight months, when it was admitted to the hospital for evaluation of mild dyspnea. The owners reported that they had been gradually increasing the furosemide dosage, which was now consistently at 2 mg/kg body weight per os, twice daily. Houseguests had fed the dog pretzels and potato chips several hours before presentation. Auscultation revealed





Figures 1A (above) and 1B (right). Lateral and ventrodorsal thoracic radiographs taken on the day of admission to the hospital. Generalized cardiomegaly with prominent left atrial and ventricular enlargement is present. Pulmonary venous distention and air bronchograms typical of cardiogenic pulmonary edema are also visualized.

some end-inspiratory crackles over the lung fields. An additional dose of 2 mg/kg body weight of furosemide was administered subcutaneously. Serum urea nitrogen, creatinine and electrolyte concentrations were within normal limits. The serum digoxin concentration was 1.2 ng/ml.

The food was changed to moist Prescription Diet h/d Canine[a] (583 kcal/can; 2,439 kJ/can), which is lower in sodium than the food fed previously. Three days later, the owners reported that the dog was feeling well. Its serum biochemistry values continued to be normal.

Approximately 10 months later, another episode of severe pulmonary edema occurred that was unassociated with any known nutritional indiscretion. This condition was unresponsive to 12 hours of intensive preload and afterload reducing therapy (increasing doses of furosemide, the arterial dilator hydralazine and nitroglycerine). The dog was euthanatized at an emergency clinic at the owner's request. Postmortem examination revealed a ruptured primary chorda tendinea to be the cause of the dramatically worsened mitral regurgitation and unresponsive pulmonary edema.

Endnote

a. Hill's Pet Nutrition Inc., Topeka, KS, USA.

Bibliography

Keene BW, Bonagura JB. Management of heart failure in dogs. In: Bonagura JD, Twedt DC, eds. Current Veterinary Therapy XIV. Philadelphia, PA: Saunders Elsevier, 2009; 769-780.

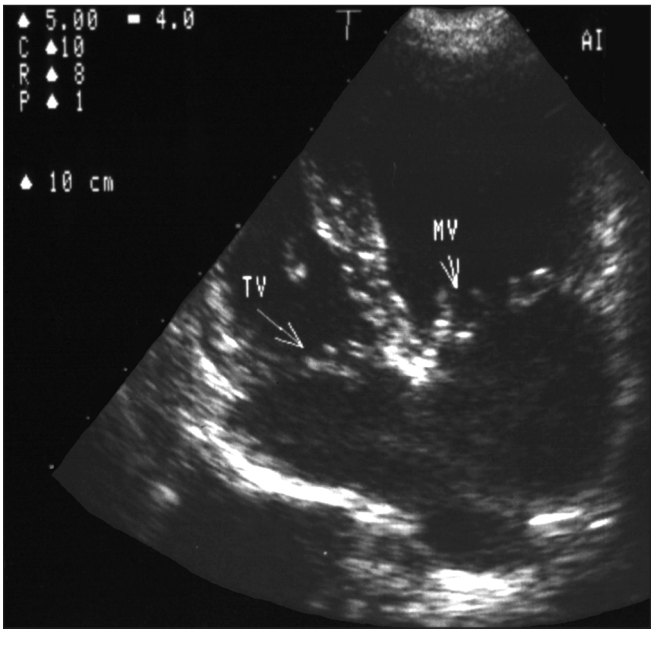


Figure 2. An echocardiogram obtained on the second day of hospitalization shows thickened mitral (MV) and tricuspid (TV) valve leaflets typical of endocardiosis.

CASE 36-2

Dilated Cardiomyopathy in an American Cocker Spaniel Dog

Bruce W. Keene, DVM, Dipl. ACVIM (Cardiology)
College of Veterinary Medicine
North Carolina State University
Raleigh, North Carolina, USA

Patient Assessment

A nine-year-old, male black American cocker spaniel dog was examined for dyspnea and lethargy that began two days after a routine elective surgical procedure (removal of a subcutaneous mass). The dog was thin (body condition score 2/5) and weighed 12 kg. Vaccinations were current and the dog received heartworm preventive medication. The dog had not had any major health problems in the past.

The heart rate was 180 beats/min. and regular, the respiratory rate 76 breaths/min. and the rectal temperature 39.9°C (103.8°F). The mucous membranes were dusky pink, with slow capillary refill. A soft (1/6 to 2/6) holosystolic murmur was heard best at the left cardiac apex, accompanied by a diastolic gallop sound (felt to be S3). The lung sounds were loud with some inspiratory crackles heard bilaterally. Otitis externa was noted bilaterally. An incision behind the right shoulder oozed slightly on palpation.

Thoracic radiographs revealed generalized, severe cardiomegaly with alveolar pulmonary edema (**Figures 1A** and **1B**). An echocardiogram revealed a left ventricular diameter of 5.68 cm in diastole (extremely dilated), with only an 8% shortening fraction (normal = 30 to 45%), but no major structural lesions were found on any valves (**Figure 2**). The echocardiographic findings were consistent with a diagnosis of dilated cardiomyopathy.

Results of an arterial blood gas analysis revealed hypoxemia and hyperventilation (PaO_2 = 71 mm Hg [reference range = 92.1 ± 5.6], pH = 7.4 [7.4], $PaCO_2$ = 30.8 mm Hg [36.8 ± 3.0]). Results of a complete blood count included normal red cell indices (packed cell volume = 39% [reference range = 38 to 57]), with an elevated leukocyte count (23,900/µl [reference range = 6.1 to 17.4]) consisting of a neutrophilia with a left shift (2,868 bands/µl [reference range = 0 to 300]). The platelet count was normal. Results of a serum biochemistry profile (including albumin, creatinine, urea nitrogen, electrolytes and liver enzymes) were within normal limits. Urinalysis disclosed an inactive sediment with a urine specific gravity of 1.024 (reference range = 1.001 to 1.070). The taurine concentration in a sample of whole blood was decreased (28.6 µmol/l; normal = 40.0 to 120.0), as was the plasma concentration of L-carnitine (plasma free carnitine 4.2 µmol/l; normal = 8.0 to 36.0).

Assess the Food and Feeding Method

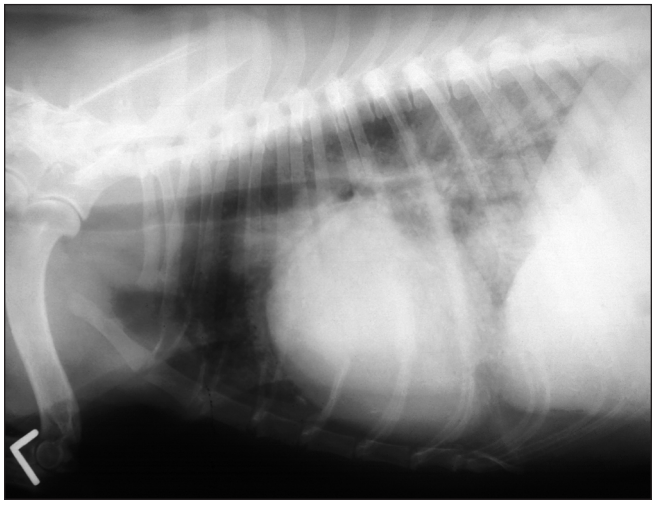
The dog was fed a variety of dry commercial dog foods, free choice.

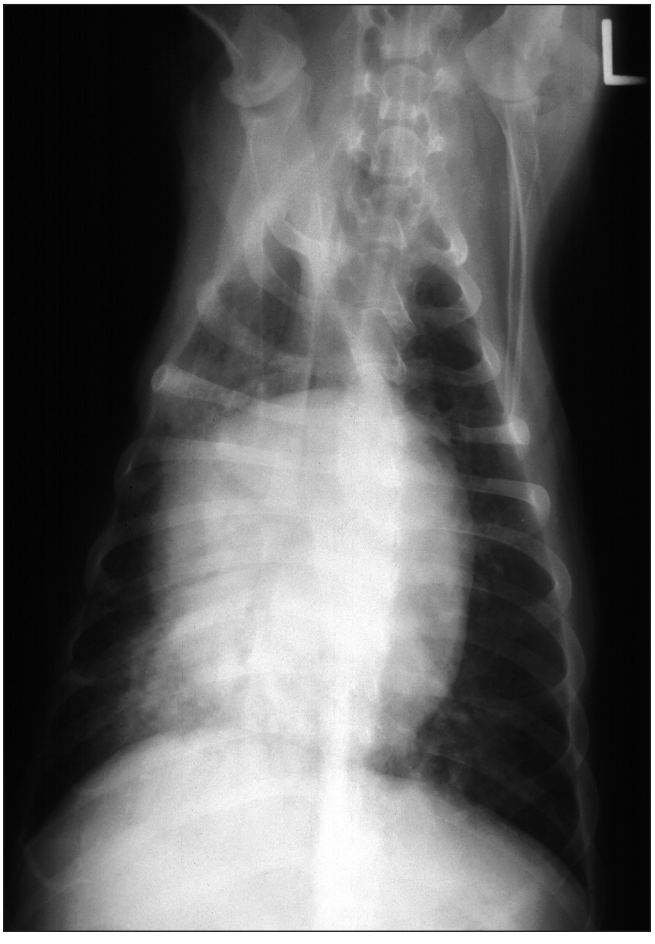
Questions

1. What is the feeding plan for this patient?
2. Should this dog be given nutritional supplementation?

Answers and Discussion

1. General nutritional recommendations for patients with cardiac disease and congestive heart failure (CHF) include the following: avoid excess sodium and chloride; ensure adequate magnesium intake; ensure adequate potassium intake, if using diuretics; avoid excess potassium intake, if using angiotensin-converting enzyme (ACE) inhibitor drugs; ensure adequate energy and protein intake; avoid excess phosphorus and protein intake, especially with evidence of concurrent renal disease; and provide additional taurine and carnitine, if myocardial failure is present. This patient's calculated resting energy requirement (RER), based on the current body weight of 12 kg, is approximately 430 kcal/day (1,806 kJ/day). However, the RER is probably higher because of the patient's increased heart and respiratory rates. The dog's daily energy requirement (DER) would be 600 to 700 kcal/day (2,510 to 2,928 kJ/ day). Frequent monitoring of body condition helps guide appropriate adjustments to this energy calculation.
2. Because of the suspected association of carnitine and taurine deficiency with dilated cardiomyopathy in American cocker spaniel dogs, supplementation with L-carnitine (1 g per os, three times daily) and taurine (500 mg per os, twice daily) was also begun. In this case, the whole blood taurine and plasma carnitine concentrations were depressed, justifying use of these supplements. In many cases of L-carnitine deficiency, the plasma carnitine concentration is "normal" (for dogs fed commercial dry foods), although endomyocardial biopsy may disclose myocardial carnitine deficiency. The relationship between blood and myocardial taurine concentrations is less well defined, but it seems prudent to supplement the food of American cocker spaniels with both taurine and L-carnitine.





Figures 1A (above) and 1B (right). Lateral and ventrodorsal radiographs taken at the time of admission. Generalized cardiomegaly and pulmonary edema consistent with CHF are present.

Therapy Including Feeding Plan

Therapy was initiated with furosemide (2 mg/kg body weight subcutaneously, twice daily), enalapril (0.5 mg/kg body weight per os, twice daily), digoxin (0.006 mg/kg body weight per os, twice daily) and nitroglycerine (0.2 mg/hr transdermal patch, applied for the initial 12 hours of hospitalization). After culture of the surgical wound, a first-generation cephalosporin was given orally. The dog was maintained in an oxygen-enriched environment (40% oxygen) and its respiratory rate was monitored hourly.

A commercial veterinary therapeutic food designed for patients with cardiovascular disease (Prescription Diet h/d Canine[a]) was initially offered free choice, but was refused by the dog. A different commercial veterinary therapeutic food (Prescription Diet k/d Canine) was offered two days later when the azotemia was beginning to resolve; this food was readily accepted. This food avoids excess sodium, chloride, phosphorus, potassium and protein found in regular commercial dog foods (**Table 36-5**).

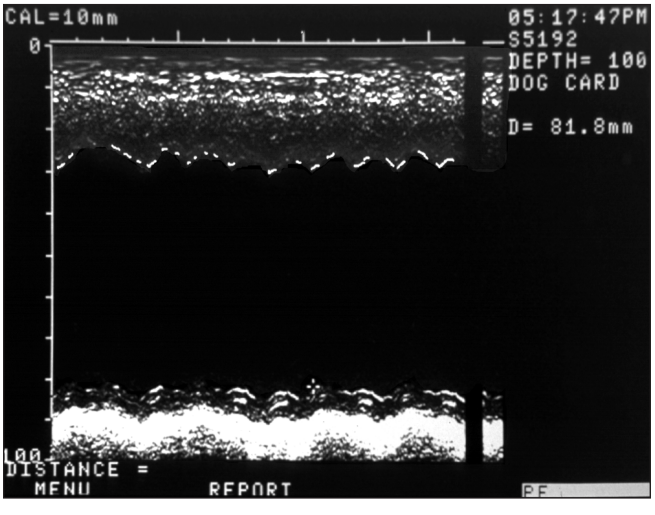


Figure 2. M-mode echocardiography reveals a marked increase in ventricular volume due to myocardial failure.

Progress Notes

The next day, the dog weighed 0.5 kg less, was afebrile, depressed and refused food, but was breathing much easier. Oxygen supplementation and nitroglycerine were discontinued. A serum biochemistry profile revealed that the serum urea nitrogen and creatinine concentrations had risen dramatically. An intravenous catheter was placed and maintenance fluid therapy was initiated with a relatively low-sodium physiologic electrolyte solution. Digoxin was withheld for 24 hours, and furosemide and enalapril were discontinued for 12 hours. Dobutamine (2.5 µg/kg body weight/min., increased to 5 µg/kg body weight/min. four hours later) was begun by continuous intravenous infusion to improve cardiac and renal function. An electrocardiogram was monitored continuously during dobutamine therapy for ventricular ectopic activity or other tachyarrhythmias.

The patient was much brighter and more active the following day. The serum urea nitrogen and creatinine concentrations had decreased. Fluid therapy and enalapril were continued, and the dobutamine drip was tapered over 12 hours. That evening, furosemide and enalapril were administered. The serum urea nitrogen and creatinine concentrations were normal the next day. The

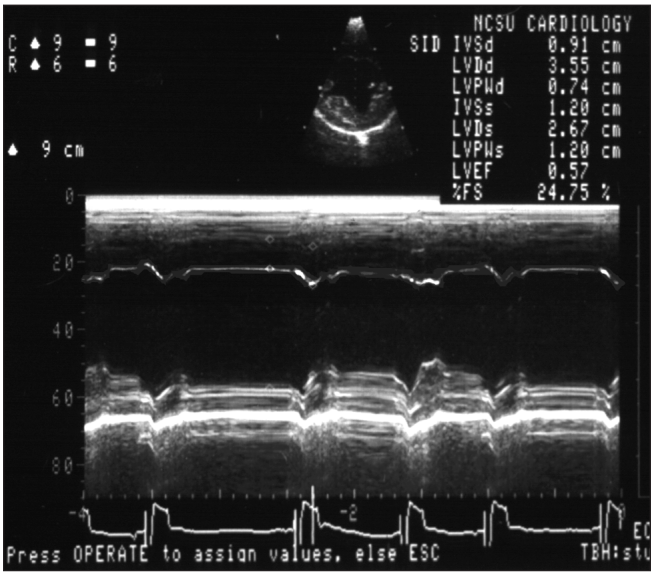
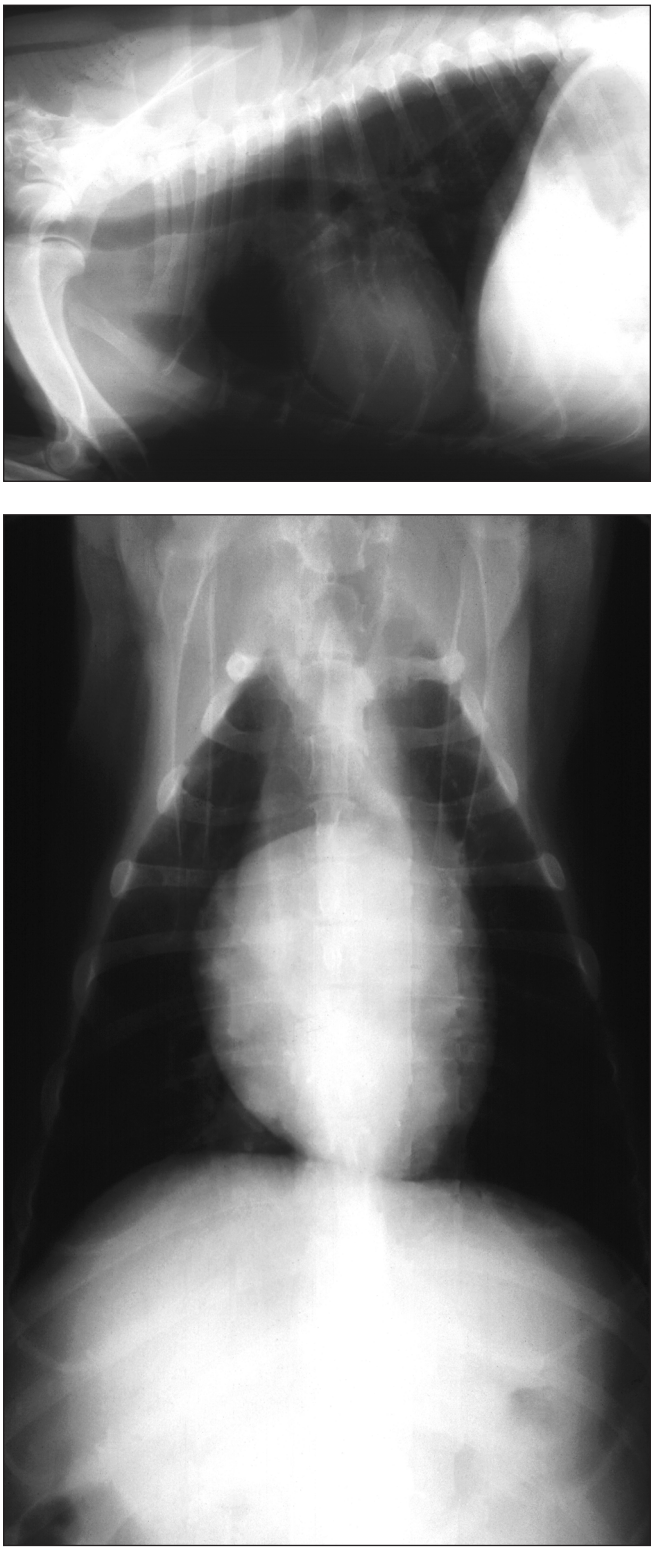


Figure 3. M-mode echocardiography one year after the initial admission for heart failure reveals normal left ventricular volume and function.

dog was now drinking and ate the veterinary therapeutic food that was offered (Prescription Diet k/d, one can). Fluid therapy was discontinued and digoxin (0.006 mg/kg body weight per os, twice daily), enalapril (0.5 mg/kg body weight per os, twice daily) and furosemide (1 mg/kg body weight per os, twice daily) were administered.

The dog improved and was able to go home four days after entering the hospital. Five days later, the owner reported that the patient was feeling better than it had in months. One and one-third cans of the veterinary therapeutic food were fed to meet the increased DER expected in the home environment. Three months postadmission, an echocardiogram and chest radiographs showed some improvement in fractional shortening, and complete resolution of pulmonary edema and pulmonary venous distention. Results of a serum biochemistry profile were normal. Furosemide was discontinued at that time. Body weight was now 13.2 kg. Digoxin, enalapril, k/d Canine and taurine and L-carnitine supplementation were continued. The food was fed in the same amount.

One year after the initial admission, an echocardiogram (**Figure 3**) disclosed remarkable reduction in left ventricular size and improved left ventricular systolic function (left ventricular diastolic diameter 3.55 cm; left ventricular shortening fraction 24.75%). Thoracic radiographs revealed no cardiomegaly or pulmonary edema (**Figures 4A** and **4B**). The owner had discontinued digoxin and enalapril approximately 10 months after the first admission (he had gone out of town and not started therapy again when he returned), although he continued to feed Prescription Diet k/d Canine and administer the taurine and L-carnitine supplements. The dog weighed 13.6 kg and had a body condition score of 3/5. The dog did well for three additional years, maintaining its improved ventricular function.



Figures 4A (top) and 4B (above). Lateral and ventrodorsal radiographs taken one year after the initial admission for heart failure reveal normal cardiac size and no evidence of pulmonary edema.

Four years after the initial diagnosis, the patient developed ascites. The heart and lungs were unchanged and the central venous pressure was normal. Ultrasonographic evaluation of the abdomen revealed a mass originating in the left adrenal gland, with intravascular invasion and extension into the right adrenal gland and obstruction of the caudal vena cava. Body weight was 10.5 kg with cachexia (body condition score of 1/5). A pheochromocytoma was diagnosed at postmortem examination.

Endnote

a. Hill's Pet Nutrition Inc., Topeka, KS, USA.

Bibliography

Freeman LM, Rush JE, Brown DJ, et al. Relationship between circulating and dietary taurine concentrations in dogs with dilated cardiomyopathy. Veterinary Therapeutics 2001; 2: 370-378.

Keene BW, Bonagura JB. Management of heart failure in dogs. In: Bonagura JD, Twedt DC, eds. Current Veterinary Therapy XIV. Philadelphia, PA: Saunders Elsevier, 2009; 769-780.

Kittleson MD, Keene BW, Pion PD, et al. Results of the Multicenter Spaniel Trial (MUST): Taurine- and carnitine-responsive dilated cardiomyopathy in American Cocker spaniels with decreased plasma taurine concentration. Journal of Veterinary Internal Medicine 1997; 11: 204-211.

Kramer GA, Kittleson MD, Fox PR, et al. Plasma taurine concentrations in normal dogs and dogs with heart disease. Journal of Veterinary Internal Medicine 1995; 9: 252-258.