MANAGEMENT OF CHRONIC CONGESTIVE HEART FAILURE IN SMALL ANIMALS

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Introduction

A good understanding of the underlying pathophysiology is required to enable a sensible approach to the treatment and management of heart failure. Systolic dysfunction predominates in most heart failure patients, but others suffer from diseases that primarily impair diastolic performance. The general approach to treatment is greatly influenced by these distinctions, which must be clinically determined. Almost all heart failure treatments are palliative rather than curative. Therapy is usually directed at correcting the specific functional abnormalities responsible for the patient's clinical signs. The goals of therapy can be divided into three major groups. The first aim is to control salt and water retention and relieve oedema and effusions. The second goal is to improve pump function and therefore cardiac output. The last objective is to reduce afterload (Table 1).

TABLE 1: Goals of therapy in heart failure

I	**Control of salt and water retention/relieve oedema**
	Low sodium diets
	Loop, thiazide, potassium sparing diuretics
	Venous and mixed vasodilators
	ACE inhibitors
	Physical removal of fluid
II	**Improve pump function**
	Improve diastolic filling
	Control heart rate
	Abolish arrhythmia
	Improve ventricular relaxation
	Improve contractility
	Digitalis glycosides
	Calcium sensitizers
	Sympathomimetic drugs
	Reverse or modify myocardial and vascular remodelling
	ACE-inhibitors
	β-blocking agents
II	**Reduce workload**
	Reduce afterload
	ACE inhibitors
	Arterial or mixed vasodilators
	Reduce physical activity
	Avoid environmental stressors
	Weight reduction in the obese

It should be emphasised that the efficacies of drugs that are used to treat heart failure depend very much on drug type, underlying disease and individual patient response. There are no set rules and it is important to regularly monitor a patient with heart failure. The treatment should be adapted depending on the clinical evaluation of the patient.

Congestive heart failure

Several classifications have been used to characterise heart failure. From a practical and therapeutic point of view it is preferable to subdivide congestive heart failure into acute, life-threatening failure and more chronic, congestive heart failure. This paper will concentrate on the treatment of chronic heart failure.

Chronic congestive heart failure

Treatment of International Small Animal Cardiac Health Council System of Heart failure Classification (ISACHA) (Table 2) Class IA and IB patients with dilated cardiomyopathy (DCM) or mitral regurgitation remains controversial. Currently, no drugs have been shown to alter the natural course of heart diseases or prolong survival in these patients.

In Class II patients the major therapeutic goal is to relieve the clinical signs (cough, exercise intolerance, ascites) and to improve quality of life.

For Class III patients long-term treatment should be implemented after the acutely ill patient is stabilised (see treatment of acute heart failure).

Control of oedema and effusions

Diuretics

Diuretics are essential in the control of congestive heart failure (Fig. 1). Single-agent therapy with diuretics is usually not advocated since these drugs activate neuro-endocrine responses that might hasten the progression of heart failure. Frusemide is the most commonly used diuretic in small animal medicine. It is potent and has few side effects. Once the clinical signs of congestive heart failure are controlled, attempts should be made to reduce the diuretic dose. If very high dosages of frusemide (more than cumulative dose of 6-8 mg/kg/day) are required to control the heart failure,

another diuretic should be added to the existing treatment. The author prefers to use the potassium sparing diuretic spironolactone. It is not advisable to wait until the maximum dose of frusemide is reached before adding in spironolactone: it has anti-aldosterone and other potentially beneficial effects which will speed the patient's recovery (see later).

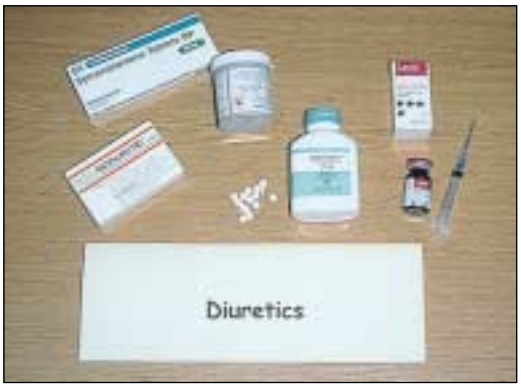

Fig. 1
The different diuretics: frusemide (tablets and injectable), spironolactone, hydrochlorothiazide and Moduretic®.

Loop diuretics

Frusemide (1-3 mg/kg q 8-12 hrs in dogs; 1-2 mg/kg q 12 hrs in cats) is a sulphonamide type of loop diuretic. It inhibits the reabsorption of electrolytes in the thick ascending loop of Henle. Frusemide also decreases reabsorption of sodium and chloride in the distal renal tubule. Frusemide diuresis results in enhanced excretion of sodium, chloride, potassium, hydrogen, calcium, magnesium and possibly phosphate.

Potassium sparing diuretics

Spironolactone (Aldactone® 2-4 mg/kg PO q 24 hrs in dogs and cats) is well absorbed by the gastrointestinal tract and is rapidly and extensively metabolised to the active product, canrenone. Canrenone is structurally similar to aldosterone, and its effect results from competitive binding to aldosterone's binding sites in the distal tubule. The use of spironolactone for congestive heart failure has been advocated for several other reasons. It is theorised that spironolactone can reduce myocardial fibrosis in patients with heart disease, and it may help restore normal baroreceptor function in heart failure. However spironolactone interferes with the synthesis of testosterone and may cause associated endocrine abnormalities. Hyperkalaemia may result if ACE inhibitors, NSAIDs or potassium supplements are concurrently administered and therefore serum potassium levels should be repetitively monitored.

Triamterene (dogs: 2-4 mg/kg/day) competitively displaces aldosterone from its binding sites and directly inhibits the distal tubular transport of potassium.

Amiloride (as combination preparation with thiazide diuretic in Moduretic®, 1-3 mg/kg q 12-24 hrs in the dog)

TABLE 2: International small animal cardiac health council system of heart failure classification

Class	Criteria
IA	Heart disease present No clinical signs No signs of compensation (no left ventricle volume overload)
IB	Heart disease present No clinical signs Signs of compensation on echocardiography or radiography (e.g. left ventricle volume overload or left atrial enlargement)
II	Heart disease present, with mild or moderate signs of heart failure Clinical signs of backward failure on exertion or excitement At rest, no clinical evidence of poor systolic function Treatment is indicated
IIIA	Heart disease present, with clinical signs of advanced heart failure Clinical signs even at rest Cardiomegaly apparent on echocardiography or radiography Death or severe debilitation likely without treatment Home treatment is possible
IIIB	Heart disease present, with clinical signs of advanced heart failure Clinical signs even at rest Cardiomegaly apparent on echocardiography or radiography Death or severe debilitation likely without treatment Hospitalisation and intensive care treatment is required

is another potassium-sparing diuretic that has some structural similarities to triamterene. Amiloride has actions in addition to producing diuresis in experimental dogs. It prolongs action potential duration and refractory period and it also causes vasodilation.

Thiazide diuretics

The thiazides act primarily by reducing membrane permeability in the distal convoluted tubule to sodium and chloride. They promote potassium loss at this site and promote large increases of sodium loss in the urine with only mildly increasing the volume of urine. The thiazides are ineffective when renal blood flow is low, which may explain their lack of efficacy in patients with severe congestive heart failure. Thiazides also decrease glomerular filtration rate and should be used carefully in animals with a prerenal azotaemia. **Chlorothiazide** (Saluric® 20-40 mg/kg PO q 12 hrs in dogs and cats) and **hydroclorothiazide** (Vetidrex® 1-5 mg/kg PO q 12 hrs in dogs and 2-4 mg/kg PO q 12 hrs in cats) are the two most commonly used thiazide diuretics in veterinary medicine. Adverse effects of the thiazide diuretics include a reduced glucose tolerance, hypokalaemia, hyponatraemia and volume contraction. Their use in animals with renal impairment is contra-indicated because it tends to reduce renal blood flow.

Thoracocentesis

Pleural effusion is difficult to clear with diuretics and thoracocentesis is only required if the pleural effusion causes respiratory distress.

Abdominocentesis

It is not advisable to drain ascites unless the effusion is compromising respiration or creates discomfort. Ascitic fluid is relatively protein rich and repetitive drainage may induce hypoproteinaemia.

Counteracting the detrimental neuro-endocrine activation

Angiotensin Converting Enzyme inhibitors (Table 3)

ACE-inhibitors should be given to all patients unless specific contraindications exist. Activation of the renin-angiotension-aldosterone system is responsible for many features of congestive heart failure (see pathophysiology). ACE inhibitors have a number of beneficial effects:

- ***Vasodilator***: arteriolar and venous dilation occurs as a direct result of the decreased concentration of angiotensin II. ACE inhibitors decrease systemic vascular resistance by approximately 25-30 %.
- ***Anti-aldosterone effect***: sodium and water excretion is enhanced when the stimulus for aldosterone secretion is lessened. The ability of ACE-inhibitors to decrease plasma aldosterone secretion may become attenuated or lost with time (‘aldosterone escape’).
- ***Attenuation of sympathetic drive***: ACE-inhibitors prevent via angiotensin II inhibition the central and peripheral effects of the sympathetic nervous system.
- ***Renoprotection***: levels of bradykinin and renoprotective prostaglandins are allowed to accumulate.
- ***Prevention of remodelling and fibrosis*** of the myocardium and vascular smooth muscle.

Currently available ACE inhibitors in veterinary medicine are **enalapril, benazepril** and **ramipril** (Fig. 2). It is difficult to determine the optimal dose for any ACE inhibitor or to compare relative efficacy of the drugs available. It is suggested that once daily dosing is sufficient, however giving an ACE inhibitor every 12 hours may be beneficial and preferable to increasing the diuretic dose.

Fig. 2
The different ACE inhibitors: enalapril, benazepril, ramipril.

TABLE 3: Angiotensin converting enzyme inhibitors

Drug	Preparation	Dose
Benazepril	5, 20 mg tablets Fortekor® (Novartis)	0.25-0.5 mg/kg PO once daily
Enalapril	1, 2.5, 5, 10, 20 mg tablets Enacard® (Merial)	0.5 mg/kg per os q 12-24 hrs
Ramipril	1.25, 2.5, 5 mg tablets Vasotop® (Intervet)	0.125 mg/ kg per os q 24 hrs

Aldosterone antagonists

Despite adequate inhibition of ACE, aldosterone levels may build up. In right-sided heart failure, this may, in part be due to impaired liver function resulting from chronic hepatic venous congestion; however, increased aldosterone is also mediated via other mechanisms. **Spironolactone** is the drug of choice if this occurs, as it acts as an aldosterone antagonist.

β-blockers (Table 4)

One of the most profound changes in attitude towards β-blockade has been in the field of dilated cardiomyopathy. β-blockers have traditionally been considered to be contraindicated in myocardial failure, because of their adverse acute haemodynamic effects (negative inotropy). It now appears that long-term use of β-adrenergic antagonists (> 3 months) is associated with improvement in systolic function in human patients with idiopathic dilated cardiomyopathy and ischaemic heart disease. It was initially believed that the mechanism was related to reversal of the down regulation of β-receptors that occurs with chronically elevated catecholamine levels, but it now appears that the improvement is related to an increase in contractile function in cardiac myocytes themselves, which may be a result of an increase in contractile elements. Certain strict guidelines are recommended for commencing therapy with β-adrenergic antagonists in animals with myocardial failure. Patients must be stable and compensated (i.e. no congestive signs) and the doses must be extremely low initially and titrated upwards very slowly at 1-2 week intervals. The author recommends their use in experienced hands only. Currently used β-blockers are **propanolol** and **atenolol**. Propanolol is a non-selective β-blocker, where atenolol and metoprolol are selective β_1-blockers. **Carvedilol**, a non-selective β-blocker which has additional vasodilatory effects via α_1 blockade, is still under investigation in veterinary medicine, but has shown to be very promising in human patients with DCM.

Digoxin

As well as being a positive inotrope (see later), **digoxin** has modulatory effects on the sympathetic nervous system which may underlie many of its favourable effects in heart failure. Digoxin restores baroreceptor sensitivity and therefore decreases sympathetic tone. These favourable vagomimetic effects of digoxin are seen even at low doses and so levels at the lower end of the therapeutic range are usually sufficient (< 1.5 ng/ml).

Improving cardiac output

Improving contractility

Digoxin

The positive inotropic action of **digoxin** is achieved through an increase in intracellular calcium concentration via inhibition of the sodium/potassium ATP-ase pump. Consequently an increase in the myocardial tension is generated during contraction. Digoxin is a comparatively weak positive inotrope with a narrow margin of safety. In most cases digitalis glycosides can be administered orally, starting at maintenance dosage (Lanoxin® tablets, GlaxoWellcome; dogs 0.22 mg/m2). The bioavailability of digoxin varies between different dosage routes (tablets = 60% and elixir 75%) and generic brands (Lanoxin® recommended). Rapid intravenous digitalisation is rarely necessary in dogs with heart failure except to control certain supraventricular arrhythmias. Because of its narrow therapeutic safety margin, and the individual variation in absorption, metabolism and response, the patient should be observed closely. The most common adverse reactions seen with digoxin are either gastrointestinal or cardiac in nature. The gastrointestinal signs (anorexia, vomiting, diarrhoea) seem to precede the cardiac side-effects (rhythm disturbances). If these side effects occur the drug should be withdrawn and after disappearance of the toxicity effects (48 hours) digoxin can be reintroduced at half the initial dosage. Monitoring therapeutic levels can be helpful in deciding whether the non-specific gastrointestinal signs are secondary to digoxin toxicity or not (range 0.8-2.0 ng/ml). A patient on long-term therapy should be monitored intermittently for changes which may predispose the animal to the development of toxicosis (renal failure, hypokalaemia, reduction in muscle mass). Since there is no predictable relationship between serum level and effect, levels should be measured in patients where the effect appears inadequate or excessive. Serum should be collected 8-hours post tablet and samples should only be taken after a steady state has been achieved (7-10 days). Because digoxin's beneficial vagomimetic effects are obtained at low serum levels,

TABLE 4: β - Blocking agents

Drug	Mechanism	Preparation	Dose
Propanolol	β1, β2	10, 40, 80, 160 mg tablets Inderal® (Zeneca)	Dogs: 0.2-1.0 mg/kg PO q 8 hrs Cats: 2.5-5.0 mg/cat PO q 8 hrs
Atenolol	β1	25,50, 100 mg tablets Tenormin® (Stuart)	Dogs: 0.5-2 mg/kg PO q 12 hrs Cats: 6.25-12.5 mg/kg/cat PO q 24 hrs

and considering the narrow safety margin in some animals, the author aims for serum levels less than 1.5 ng/ml.

Pimobendan

Pimobendan (Vetmedin® 0.2-0.6 mg/kg/day in dogs divided over 2 doses) is a novel agent (inodilator) for the treatment of canine congestive heart failure. It has a dual mode of action, acting directly on the heart as a calcium sensitiser to increase myocardial contractility and on the peripheral circulation through selective phosphodiesterase III inhibition to produce both peripheral and coronary vasodilation. It has shown promise in the treatment of DCM in association with other drugs including frusemide, ACE inhibitors and digoxin. Its benefits in congestive heart failure secondary to mitral valve endocardiosis are currently under investigation. At the time of writing, there is no evidence to suggest that pimobendan replaces an ACE-inhibitor, and the author only uses the drug as an addition to the traditional treatment with diuretics, ACE-inhibitors and digoxin.

Improving diastolic filling

Control heart rate and improve ventricular relaxation

β-blocking agents (**propanolol**, **atenolol**, see Table 4) and calcium channel blockers (diltiazem, Hypercard® 10 mg/ cat PO q 8 hrs) have been, because of their negative chronotrope effect, advocated to improve left ventricular filling and cardiac performance in cats with hypertrophic cardiomoypathy (Fig. 3). β-blockers are

Fig. 3
β-blockers: propanolol (tablets and injectable) and atenolol (tablets).

generally more effective than calcium-channel blockers in reducing heart rate. There is at present much debate but no comparative clinical trials to determine which drug is most beneficial in feline cardiomyopathies. Calcium-channel blockers have also arteriodilatory (including coronary arteries) action (Fig. 4). They reduce afterload and increase the pressure gradient in the left ventricular outflow tract when hypertrophic obstructive cardiomyopathy is present and are therefore theoretically contraindicated. Because calcium-channel blockers have positve lusitrope properties they might be beneficial in non- obstructive hypertrophic cardiomyopathy and in early restrictive cardiomyopathy. β-blockers are contraindicated when concurrent asthma is present because they cause bronchoconstriction.

Fig. 4
Calcium channel blockers.

In dogs with left ventricular hypertrophy secondary to severe aortic stenosis or right ventricular hypertrophy secondary to severe pulmonic stenosis, β-blockers remain the drug of choice. They improve filling by slowing the heart rate and they protect against malignant ventricular arrhythmias, a common cause of sudden death in animals with severe aortic stenosis.

Reducing workload

ACE-inhibitors

ACE-inhibitors reduce afterload by vasodilation. For more details see above.

Hydralazine

Hydralazine (Apresoline® 0.5-3 mg/kg q 8-12 hrs in dogs) is a very potent arteriodilator. It is more efficient in treating pulmonary oedema secondary mitral regurgitation than in treating oedema due to dilated cardiomyopathy. When used in dogs that are already receiving an ACE-inhibitor, addition of hydralazine should be done with extreme care. The author only uses hydralazine in the intensive care and emergency setting (fulminant refractory pulmonary oedema), where haemodynamic parameters can be measured.

Physical activity

An animal in chronic congestive heart failure should be encouraged to exercise to within its capabilities (a golden cage is not a lifestyle). Fit muscles are better able to withstand the reduced delivery of nutrients than unfit muscles. However, sudden increases in exercise should be avoided.

Weight

Weight reduction is strongly recommended in obese animals.

Controlling arrhythmias

The most commonly encountered arrhythmias in congestive heart failure are atrial fibrillation, supraventricular tachycardia and ventricular tachycardia. Substantial haemodynamic and clinical improvement can often be realised by successful treatment. More details are discussed in a separate article.

Nutrition

Salt and water intake

Marked restriction of sodium is no longer advocated for dogs with congestive heart failure. Such diets are usually unpalatable and it is important that an animal in congestive heart failure has a proper calorie and protein intake. Additionally, reduction in sodium intake will activitate the RAAS system. It is important that sodium intake is kept constant. Water should never be restricted in dogs on diuretics.

L-Carnitine

L-carnitine is critical for the metabolism of fatty acids, which are the major energy substrate within the myocardium. **L-carnitine** is expensive and should only be supplemented (50-100 mg/kg q 8 hrs) in animals with a L-carnitine deficiency-induced cardiomyopathy. Significant improvement in echocardiographic parameters should be recognised within three months of treatment to confirm a response.

Taurine

The role of taurine deficiency in canine DCM is less clear than in feline DCM. Animals with proven taurine deficiency-induced myocardial failure (plasma level < 50 ng/ml) should be supplemented with **taurine** (dogs 500 mg/20 kg q 12hrs; cat 250 mg q 12 hrs).

Fish oil

Fish oil administration has been shown to decrease cardiac cachexia in dogs with heart failure. It contains **omega-3 fatty acids**, **eicosapentaenoic acid** and **doxosahexanaenoic acid** which decrease the production of cytokines and inflammatory mediators and therefore improves appetite. The author commonly prescribes **cod liver oil** in animals with advanced dilated cardiomyopathy and signs of cardiac cachexia.

Patient monitoring

It is important to regularly monitor a patient with congestive heart failure. Every patient will react differently to different treatments. Where necessary, the treatment should be adapted appropriately depending on the clinical findings. There is no doubt that repetitive monitoring by experienced individuals improves quality and duration of life.

Further reading

Kittleson, M. D. and Kienle, R. D. (1998) **Small Animal Cardiovascular Medicine**. Mosby.

Fox, P. R., Sisson, D. and Moise, N. S. (1999) **Textbook of Canine and Feline Cardiology**. Second Edition. W. B. Saunders company.

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These multiple choice questions are based on the above text. Readers are invited to answer the questions as part of the RCVS CPD remote learning program. ***Answers appear on the inside back cover****. In the editorial panel's view, the percentage scored, should reflect the appropriate proportion of the total time spent reading the article, which can then be recorded on the RCVS CPD recording form.*

1. What is spironolactone's other beneficial effect in CHF beside its diuretic effect?

a. It interferes with testosterone production.
b. It produces a hyperkalaemia.
c. It is a vasodilator.
d. It reduces myocardial fibrosis.

2. Abdominocentesis should be performed in:

a. Every animal with ascites.
b. The animal where the ascites compromises respiratory function.
c. Hypoproteinaemic animals.
d. Animals where diuretics do not reduce the ascites.

3. Pimobendan is:

a. An ACE-inhibitor.
b. An anti-arrhytmic drug.
c. An inodilator.
d. A calcium-channel blocker.

4. β-blockers might await a great future in myocardial failure because:

a. They are positive inotropic drugs.
b. They counteract β- down regulation which occurs in chronic congestive heart failure.
c. They improve contractile function of the myocytes themselves, probably by increasing the amount of contractile elements.
d. They improve diastolic filling.

5. Amiloride might have other beneficial properties in the dog beside its diuretic efffect:

a. Anti-hypertensive properties.
b. Anti-arrhythmic properties.
c. Positive inotropic feaures.
d. Positive lusitrope effects.