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Veterinary clinical nutrition: success stories: an overview

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In this overview of success stories in veterinary clinical nutrition topics in cats and dogs reviewed include the dietary management of chronic kidney disease, dissolution of urinary tract uroliths by dietary modification, the recognition that taurine and L-carnitine deficiencies can cause dilated cardiomyopathy; that clinical signs associated with feline hyperthyroidism (caused by a benign adenoma) can be controlled by a low-iodine diet alone; that dietary management of canine osteoarthritis can also reduce non-steroidal anti-inflammatory drug doses; and that disease-free intervals and survival times can be statistically longer in dogs with Stage III lymphoma managed with diet. As we discover more about nutrigenetics and nutrigenomics, and as we expand our basic understanding of idiopathic diseases we are bound to identify more nutritionally related causes, and be able to develop novel dietary strategies to manage disease processes, including the formulation of diets designed to alter gene expression to obtain beneficial clinical outcomes.

Clinical nutrition: Dilated cardiomyopathy: Hyperthyroidism: Chronic kidney disease

There are differences between human and pet nutrition which suggest potentially better compliance with veterinary clinical nutrition recommendations. We have free choice to access any foodstuffs we can afford from a vast array of global products in our shops. Over time we develop personal food preferences, but we are influenced by peer pressure from family, friends, cultural background and sometimes religious beliefs. Scientific evidence presented by the medical profession to encourage healthy eating is often ignored and lack of compliance is resulting in an epidemic of diet-related health issues, notably obesity, associated mobility problems and type 2 diabetes mellitus.

Pets, on the other hand, rely on food provided to them by their owner and have a relatively narrow range available except in households that feed leftovers. There is little opportunity to self-select foods except for hunters (cats) and scavengers (dogs) and whilst pressure to eat as much food as possible as quickly as possible can occur in multi-dog households, there is no peer pressure to eat

unusual products or to eat excessively. Nevertheless, obesity is a major problem with 45 % of pets in the UK considered overweight and, although we know owners could easily adhere to veterinary advice about nutrition in clinical disease, non-compliance is a significant problem with only 21 % compliance reported for feeding therapeutic diets on veterinary recommendation⁽¹⁾.

The present paper is about success stories in veterinary clinical nutrition, but I should mention that we still see many health issues associated with errors in feeding pets, including obesity in both cats and dogs; there is a growing trend to feed raw diets with little or no control over ensuring nutritional adequacy or prevention of transmission of infectious diseases (both to pets and owners). Other common diet-related health issues include foreign body obstructions in the gastrointestinal tract and metabolic bone disease (nutritional secondary hyperparathyroidism) due to feeding an all meat diet which is deficient in minerals, including calcium. This condition results in demineralisation of the skeleton causing

Abbreviation: DCM, dilated cardiomyopathy.

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thinning of the bone cortices and spontaneous fractures. In other situations, excessive mineral intake, especially calcium, can result in serious developmental disease, including angular deformities and osteochondrosis in young growing large and giant breed puppies.

In disease situations veterinary objectives are:

- (1) Ensure nutritional intake, using special feeding techniques such as tube feeding, or parenteral nutrition if necessary;
- (2) Meet the energy requirements of the animal, which may be higher or lower than usual depending on the disease, and select the most appropriate nutrients to supply the energy;
- (3) Meet all other essential nutrient requirements, which may be altered by the disease situation. In some situations otherwise non-essential nutrients may become 'conditionally essential', for example glutamine in severe gastrointestinal disease;
- (4) Avoid or minimise the intake of nutrients that may be detrimental in the disease;
- (5) Increase the intake of nutrients that may be beneficial in the disease.

Nutritional interventions in pets may simply be an adjunct to conventional treatment, but in many situations dietary manipulation is an essential part of successful disease management, and increasingly nutritional management alone can offer an alternative to conventional therapy.

It would be wrong to attribute the development of clinical nutrition in pets to one man, but when tracing its history it is impossible not to mention Dr Mark Morris Senior, who was a notable character in the veterinary profession in the USA. At a time when veterinary practices were predominantly providing farm animal or mixed animal services in 1928 he opened only the second exclusively small animal hospital on the Continent. He was the first President of the American Animal Hospital Association and in 1939 he created a renal diet to help prolong the life of Buddy a dog owned by one of his blind clients. News of the success of this diet spread throughout the profession; he initially made the diet in his own kitchen, but eventually he was forced to seek an outside pet food manufacturer to deal with the volume of orders. Over the years he founded both the veterinary research Institute Mark Morris Associates and the now global Hill's Pet Nutrition Company in Topeka Kansas.

Dietary management of chronic kidney disease

As in 1939, chronic kidney disease is still common in cats and dogs and is responsible for thousands of deaths every year. The kidneys normally filter blood, retain beneficial substances such as protein, and excrete waste products such as urea and creatinine into the urine. Typical clinical signs of chronic kidney disease are increased thirst and urination, weight loss and in later stages halitosis due to uraemia. End stage renal failure results in vomiting

Table 1. Dietary management in chronic kidney disease (CKD)

Nutrient control	Reason
Controlled (relatively low) protein intake	To reduce nitrogenous waste product production e.g. urea (toxic) To reduce workload stress (glomerular filtration rate) on surviving nephrons To reduce protein-derived phosphate intake
Controlled (relatively low) phosphate intake	To reduce phosphate retention and hyperparathyroidism
Controlled (relatively low) sodium intake	Hypertension is very common in association with CKD

inappetence and a moribund state with no urine being produced followed by neurological signs, coma and death. By the time animals are struggling to concentrate their urine they only have 33% of their functioning nephrons left; by the time they have high urea and creatinine in their blood the animals only have 25% nephrons left. They are also retaining phosphate which stimulates parathyroid hormone secretion (a condition called hyperparathyroidism) which in turn activates osteoclasts in the bone to break down and release calcium and phosphate into the blood. Bones demineralise and at the same time soft tissues can become calcified, including glomeruli in the kidneys, so this hastens the loss of functioning nephrons. Dietary management aims to delay the rate of loss of surviving nephrons.

The formulation of canine and feline renal diets has changed only slightly over the years; they mainly involve the modifications listed in Table 1 and other features may include supplementation with *n*-3 fatty acids, B-complex vitamins and antioxidants.

A systematic review published in 2010⁽²⁾ reaffirmed that scientific evidence still supports dietary management as the most important intervention that can prolong survival time in canine chronic kidney disease (Table 2).

In a prospective study in cats (*n* 50)⁽³⁾ feeding a veterinary renal diet was associated with a reduction in plasma phosphate and urea concentrations and prevented the increase in plasma PTH concentrations seen in cats not receiving the diet; cats fed the veterinary diet survived for longer compared with those that were not (median survival times 633 v. 264 d).

Dissolution of uroliths (calculi)

According to Medscape⁽⁴⁾ 'Medical therapy alone cannot rid the patient of struvite calculi and is typically adjunctive in nature'. However, in the cat and dog struvite uroliths can reliably be dissolved *in situ* in the urinary bladder averting the need for surgical removal. In dogs clinical signs of increased frequency of urination, straining and passing small amounts of blood typically appear suddenly and the dog is presented to a veterinary practice within 48 h. On radiographs there are usually large and small stones present (Fig. 1) and these can be dissolved within a 3-week period unless there is a urinary tract

Table 2. The scientific evidence to support strategies for managing chronic kidney disease (CKD)⁽²⁾

Grade 1 evidence (highest)	Grade 2 evidence
Therapeutic renal foods (stages 3 and 4 CKD)	Angiotensin-converting enzyme inhibitors (proteinuric CKD)
Calcitriol therapy – vitamin D (hyperparathyroidism in dogs with CKD)	Therapeutic renal foods (proteinuric CKD)



Fig. 1. (Colour online) Struvite uroliths surgically removed from the urinary bladder of a dog.

infection present that does not respond to antibiotic therapy (Figs 2–4). In cats a recent study has shown that dissolution can be achieved in 10–16 d⁽⁵⁾. Clinical signs can resolve within a few days of starting dissolution and because of the risk of residual small stones dissolution still has to be done following surgical removal to reduce the possibility of a stone nidus encouraging further mineral precipitation and formation of a new stone. Consequently, experts at the University of Minnesota now consider surgical intervention in dogs with struvite uroliths to be professional negligence⁽⁶⁾.

Successful medical dissolution can also be achieved for urate and cystine uroliths in dogs.

Recognition that nutrient deficiencies can cause dilated cardiomyopathy

Idiopathic dilated cardiomyopathy (DCM) was common in both cats and dogs (Fig. 5) and it was not until the 1980s that an underlying nutritional deficiency was discovered as a cause. It had been known since 1975 that deficiency of the β -amino acid taurine could cause central retinal degeneration and blindness in cats⁽⁷⁾ and whilst investigating the underlying mechanisms involved in this condition researchers at the University of Davis, California noted that several cats in their small research colony developed DCM. Staff cardiologist Paul Pion determined that the condition responded to taurine in these taurine-depleted cats and he went on to diagnose

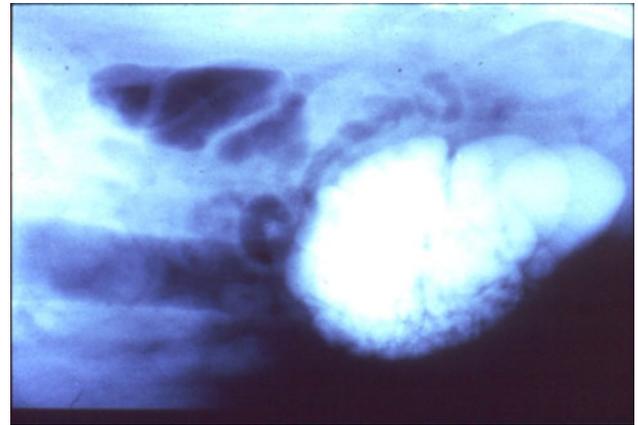


Fig. 2. (Colour online) Radiograph of the urinary bladder containing struvite uroliths in a dog.

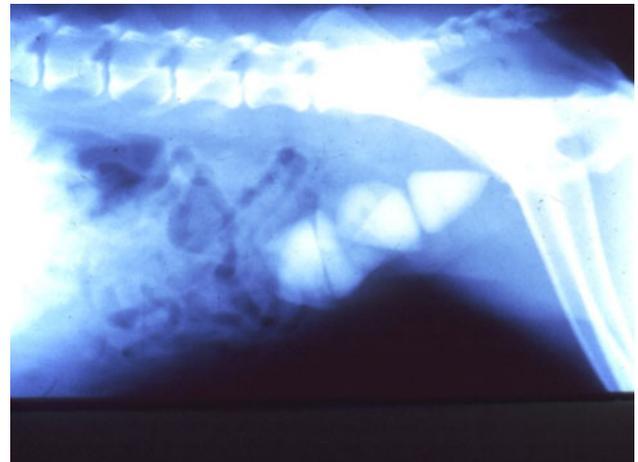


Fig. 3. (Colour online) Radiograph of the same dog as in Fig 1 1 week after starting dissolution using diet. The small stones have all gone and the large stones are smaller and less radiodense.

taurine deficiency and response to supplementation in feline outpatients diagnosed with idiopathic DCM⁽⁸⁾.

In Pion's study⁽⁸⁾ low plasma taurine concentrations associated with echocardiographic evidence of myocardial failure were observed in twenty-one cats fed commercial cat foods and in two of eleven cats fed a purified diet containing marginally low concentrations of taurine for 4 years. Oral supplementation of taurine resulted in increased plasma taurine concentrations and was associated with normalisation of left ventricular function in both groups of cats. In a follow-up study⁽⁹⁾, 1-year survival rate was 58% (twenty-one of thirty-six cats with a known outcome) in the taurine-treated group compared with a 1-year survival rate of 13% (four of thirty-one cats with a known outcome) in a retrospectively evaluated population of thirty-three cats with DCM.

It emerged that although adequate taurine to meet known nutritional requirements was being added to canned cat foods, processing reduced bioavailability

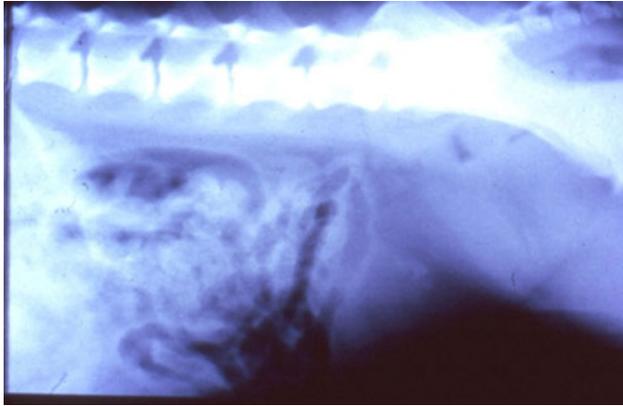


Fig. 4. (Colour online) Radiograph of the same dog as in Figs 2 and 3 3 weeks after starting dissolution using diet.



Fig. 6. (Colour online) Hyperthyroidism in cats is a common debilitating disease which can be controlled using a diet low in iodine content.



Fig. 5. Dilated cardiomyopathy in cats (and some breeds of dog) can be caused by taurine deficiency.

and so some (but not all) cats could not meet their daily requirement and became depleted. As a result more taurine is now added to complete cat foods and dietary deficiency as a cause of DCM is rarely seen. Discovery that taurine deficiency could cause DCM in cats prompted investigations into taurine status in dogs with DCM, and in some breeds a direct association has also been found, notably in Cocker Spaniels, Newfoundlands, Golden Retrievers and Beagles⁽¹⁰⁾.

Certain breeds of dog (including the Doberman, Boxer, American Cocker Spaniel and Great Dane) have also been shown to develop DCM caused by L-carnitine deficiency and some dogs with this condition respond to dietary supplementation with L-carnitine (50 mg/kg body weight three times daily)^(11,12).

Remission of signs of hyperthyroidism in cats with thyroid adenoma by dietary manipulation alone

Feline hyperthyroidism caused by a benign thyroid adenoma is the commonest endocrine disorder in cats with an estimated prevalence of 1/300 cats (Fig. 6). Clinical signs

can be severe and distressing and include weight loss, increased appetite, tachycardia, hyperactivity, polydipsia, polyuria, vomiting and eventually heart failure.

Until recently treatment options included surgical excision, radioactive iodine therapy, or lifetime medical treatment with carbimazole or methimazole. All of these interventions have potential complications; they do not work in all cases and may be inappropriate options for some cats.

The introduction of an iodine-restricted complete diet for cats with hyperthyroidism was seen as a major development for veterinarians. The diet does not directly affect the adenoma, but due to the inability of the tumour to produce thyroid hormone clinical signs resolve within 2–3 weeks. The diet has been shown to be effective in all cases, provided the cat does not eat other foods containing iodine. The recommended iodine content in food is 0.5–2 mg/kg. In hyperthyroid cats fed a diet containing 0.14 or 0.19 mg/kg (canned and dry respectively) total thyroxine can return to the reference interval, with 90 % of cats becoming euthyroid after 12 weeks of exclusive feeding⁽¹³⁾.

There is a problem when the afflicted cat lives in a multi-cat household, because this diet is inappropriate for a cat that does not have hyperthyroidism and so under such situations controlled access is needed, which means preventing access, either by feeding in separate rooms or by using newer technology such as a microchip-controlled pet feeder.

Dietary management in osteoarthritis reducing non-steroidal anti-inflammatory drug dose

The strongest scientific evidence based on several randomised controlled trials supports the clinical benefits to patients of weight reduction or the use of special diets formulated for dogs and cats with osteoarthritis. These incorporate ingredients such as glucosamine, chondroitin, *n*-3 fatty acids or green-lipped mussel extract. In addition to improving mobility dietary manipulation

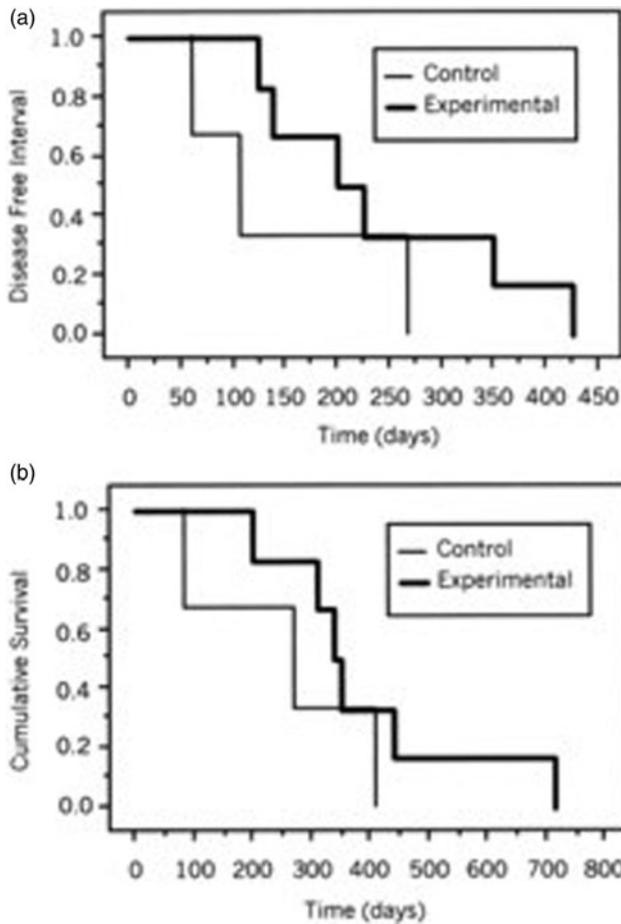


Fig. 7. Figure showing (a) the disease free interval and (b) survival times of dogs with lymphoma managed with (experimental) or without (control) dietary management.

can reduce the required dose for non-steroidal anti-inflammatory drugs. In one study 46% of dogs with osteoarthritis fed a therapeutic diet ($n = 52$) had dose reductions and a more rapid decrease in daily carprofen dosage than dogs in a control group fed a regular maintenance diet ($n = 57$)⁽¹⁴⁾.

Dietary management in canine lymphoma

There are many proposed mechanism by which dietary manipulation could alter the progression of neoplasia, but there are few clinical studies demonstrating efficacy. In a canine study⁽¹⁵⁾ thirty-two dogs with lymphoma were randomised to receive either a diet supplemented with menhaden fish oil and arginine or an identical control diet supplemented with soyabean oil. Dogs fed the special diet had significantly ($P < 0.05$) higher mean serum levels of the $n-3$ fatty acids DHA (C22:6) and EPA (C20:5) compared with controls. Higher serum levels of C22:6 and C20:5 were associated with lesser ($P < 0.05$) plasma lactic acid responses to intravenous glucose and diet tolerance testing. Increasing C22:6 levels were also significantly ($P < 0.05$) associated with

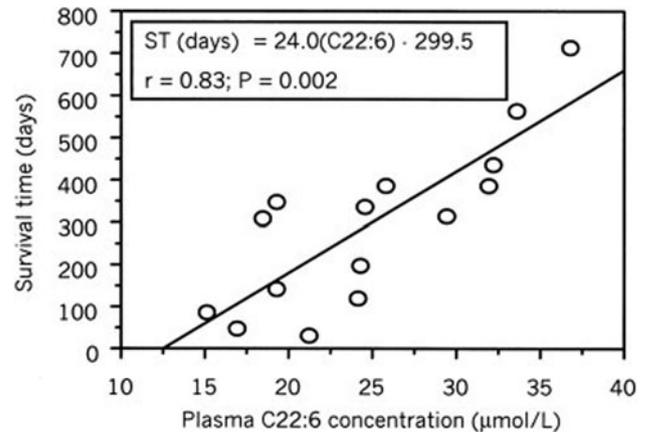


Fig. 8. Relationship between survival time and plasma docosahexaenoic acid (C22:6 fatty acid) concentration in dogs with lymphoma.

longer disease-free intervals and survival times for dogs with Stage III lymphoma fed the experimental diet (Figs 7–8). This study resulted in a diet formulated for use as an aid in the management of dogs with lymphoma.

Summary

There have been some outstanding, important developments in the field of veterinary clinical nutrition in the past 30 years, and I have highlighted just a few in this overview. As we discover more about nutrigenetics and nutrigenomics, and as we expand our basic understanding of idiopathic diseases we are bound to identify more nutritionally related causes, and be able to develop novel dietary strategies to manage disease processes. Indeed, special diets are already being formulated using selected ingredients with the intention of altering gene expression to achieve clinical outcomes.

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Conflicts of Interest

None.

Authorship

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References

1. American Animal Hospital Association (2009) *Compliance: Taking Quality Care to the Next Level. A Report of the 2009 AAHA Compliance Follow-Up Study* Published by the American Animal Hospital Association, 12575 West Bayaud Avenue, Lakewood, Colorado 80228. Available at: aaha.net.org.
2. Roudebush P, Polzin DJ, Adams LG *et al.* (2010) An evidence-based review of therapies for canine chronic kidney disease. *J Small Anim Pract* **51**, 244–252.
3. Elliott JM, Rawlings PJ, Markwell ND *et al.* (2000) Survival of cats with naturally occurring chronic renal failure: effect of dietary management. *J Small Anim Pract* **41**, 235–242.
4. Medscape. (2010) Available at: <http://emedicine.medscape.com/article/439127-treatment> (accessed August 2015).
5. Lulich JP, Kruger JM, Macleay JM *et al.* (2013) Efficacy of two commercially available, low-magnesium, urine-acidifying dry foods for the dissolution of struvite uroliths in cats. *J Am Vet Med Assoc* **243**, 1147–1153.
6. Lulich JP (2015) (University of Minnesota) *Proc Lower Urinary Tract Disease Symp Prague 2015 Published by Hill's Pet Nutrition*, Topeka Kansas.
7. Hayes KC, Carey RE & Schmidt SY (1975) Retinal degeneration associated with taurine deficiency in the cat. *Science* **188**, 949–951.
8. Pion PD, Kittleson MD, Rogers QR *et al.* (1987) Myocardial failure in cats associated with low plasma taurine: a reversible cardiomyopathy. *Science* **237**, 764–768.
9. Pion PD, Kittleson MD, Thomas WP *et al.* (1992) Response of cats with dilated cardiomyopathy to taurine supplementation. *J Am Vet Med Assoc* **201**, 275–284.
10. Kittleson MD, Keene B, Pion PD *et al.* (1997) Results of the multicenter spaniel trial (MUST): taurine- and carnitine-responsive dilated cardiomyopathy in American cocker spaniels with decreased plasma taurine concentration. *J Vet Intern Med* **11**, 204–211.
11. Keene BW, Kittleson MD, Rush JE *et al.* (1989) Myocardial carnitine deficiency associated dilated cardiomyopathy in Doberman pinschers. *J Vet Intern Med* **3**, 126.
12. Keene BW, Panciera DP, Atkins CE *et al.* (1991) Myocardial L-carnitine deficiency in a family of dogs with dilated cardiomyopathy. *J Am Vet Med Assoc* **198**, 647–650.
13. Melendez L (2012) The rise and fall of thyroxin: dietary support of feline thyroid health. In *The Rise and Fall of Thyroxin, Hill's Global Symp of Feline Hyperthyroidism*, Barcelona, pp. 22–26.
14. Fritsch DA, Allen TA, Dodd CE *et al.* (2010) A multicenter study of the effect of dietary supplementation with fish oil omega-3 fatty acids on carprofen dosage in dogs with osteoarthritis. *J Am Vet Med Assoc* **236**, 535–539.
15. Ogilvie GK, Fettman MJ, Mallinckrodt CH *et al.* (2000) Effect of fish oil, arginine, and doxorubicin chemotherapy on remission and survival time for dogs with lymphoma: a double-blind, randomized placebo-controlled study. *Cancer* **88**, 1916–1928.