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# Nutritional therapies to improve health: lessons from companion animals

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Companion animals represent an under-utilised resource. The present paper is designed to encourage collaborative studies. Dogs and cats are out-bred animals that are willing to consume a consistent diet for long periods, so are ideal candidates for prospective studies of naturally-occurring disease. In some studies the effect of diet on survival has been substantial. Food restriction, for example, slows the development of osteoarthritis and increases the lifespan of Labrador retrievers by 2 years, protein and P restriction more than doubles the median survival time of dogs and cats with chronic kidney disease and adding *n*-3 fats and arginine to the diet of dogs with stage 3 lymphoma improves median survival time by one-quarter. Obesity is also very common in both dogs and cats and is also associated with disease as in human subjects. When interpreting these results, however, it is essential to take into account pathophysiological differences among species. Dogs and cats do not display all the characteristics of metabolic disease in human subjects, they metabolise fat well and atherosclerosis and cardiac infarction are uncommon. Such differences should not, however, preclude further study because differences among species often clarify knowledge. Monitoring of disease in companion animals may also provide a surveillance system for the safety of the food supply, as illustrated by recent outbreaks of acute renal failure and liver failure in cats and dogs in the USA caused respectively by melamine and mycotoxin contamination of pet foods.

**Health and disease: Nutritional therapy: Food safety: Cats and dogs**

To 'improve' health implies either the lack of health (i.e. disease) or the threat of lack of health in the future. 'Nutritional therapies to improve health', therefore, represents a substantial topic and it is difficult to do justice to all the work of the many scientists studying companion animal nutrition. The present paper cannot therefore be comprehensive, but is an eclectic overview with an emphasis on the effect of diet on clear clinical benefits such as prolonged survival. The intention is to illustrate how the study of nutrition of dogs and cats still has a role to play in developing the understanding of the role nutrition may play in health and disease and to encourage collaborative studies between veterinarians and biochemists, epidemiologists and other scientists studying nutrition in other species to the betterment of man as well as dogs and cats.

Unfortunately, the use of companion animals for nutrition research has been in decline. The National Research Council have recently published an updated summary of the current understanding of the nutrient requirements of dogs and cats[1]. This publication has increased considerably in size compared with the previous version but appearances can be deceiving. It does include new chapters that document the increased understanding of the importance of carbohydrates, for example, but the advances documented in other chapters are relatively small. There have been few new studies of the requirements for vitamins and minerals in companion animals and the chapter on physical activity and environment is largely based on studies published >20 years ago. Dogs and cats have become somewhat unfashionable because they are expensive to keep, regulations for their use have increased and

**Abbreviations:** BW, body weight; ME, metabolisable energy.

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because pet food companies who have provided the funds for many of the recent studies of nutrition in companion animals have become shy of 'invasive' research. It may be argued, however, that the study animals of a more intermediate size between rodents and human subjects will contribute to a better understanding of metabolic processes, especially when there are differences among species. Nutrient requirements seem to be similar relative to metabolic body weight among species[2–4], so comparisons among species are possible when the allometry of requirements and toxicity is understood. Differences in requirements among species when they occur, such as the requirement for taurine in cats[5,6], then often illuminate rather than cloud understanding.

Dogs and cats, like rodents, are also ideal candidates for long-term controlled prospective trials. Unlike human subjects, dogs and cats do not require variation in the food they consume and will consume standardised complete diets for long periods provided the diets are palatable and are introduced slowly when animals are not nauseous from their disease. The diseases of dogs and cats also evolve over a shorter lifespan than in human subjects, allowing early resolution. Some diseases, such as lymphoma, are more common in certain breeds, but dogs and cats are more out-bred than rodents. The value of using dogs to investigate the genetic basis of disease[7,8] has recently been highlighted, and there is a great opportunity to study the interaction between genetics and nutrition in companion animals[9–11].

## Treatment of disease

There is a dearth of well-described controlled randomised prospective clinical trials of the effect of diet on naturally-occurring diseases of dogs and cats. Within veterinary medicine there has been a proliferation of diets for the nutritional management of various disease states[12]. Such diets include those for the treatment of chronic kidney disease, diabetes mellitus, osteoarthritis, chronic heart failure, hepatic encephalopathy, cancer, intestinal disease and dietary allergies, as well as for the dissolution and prevention of uroliths, weight control, the moderation of cognitive dysfunction and the prevention of formation of dental calculus. Reports of studies that have been performed in support of these diets, however, have often left much to be desired. The composition of the diet is often described incompletely because pet food companies consider the composition of their diets to be proprietary and editors are often reluctant to include more than the analysis of the major nutrients. This situation makes any trial that uses a commercial diet difficult to interpret or to apply in a wider setting. Furthermore, many studies change more than one nutrient so that it is difficult to ascertain which nutrient or combination of nutrients is responsible for the effect observed. The amount of diet consumed and the conditions in which animals are maintained are also often not described, and many investigators measure changes in metabolism rather than more substantive measures of benefit such as a clinical response or survival. As a result, there is much controversy as to the usefulness of using diet to treat dogs and cats with disease. The authors of the National Research Council recommendations[1], it should be noted, have confined their recommendations to normal animals and the maintenance of health, rather than the treatment of disease.

The dietary treatment of chronic kidney disease in dogs and cats has received considerable attention because the prevalence in cats and dogs is high. Diets designed for the treatment of chronic renal failure typically contain less protein and P than most diets designed for maintenance of normal animals. They also often contain increased amounts of fish oil and moderate amounts of Na and are designed to moderate acidosis. P restriction has been shown to slow the progression of disease and adding fish oil has been shown to slow the development of pathological changes in the kidney in the nephrectomised dog model[13,14], but the value of protein restriction in slowing progression of disease remains uncertain[15]. Nevertheless, prospective controlled clinical trials have shown that survival is prolonged more than twofold in animals with chronic kidney disease when animals are fed commercial 'kidney' diets with less protein and P compared with when cats are fed normal maintenance diets. Thus, median survival time (d) is increased from 188 to 594 in thirty-eight dogs (randomised)[16] and from 264 to 633 in fifty cats (not randomised)[17]. Such numbers are compelling despite the failings in the description of experimental detail discussed earlier. As some cats with renal failure will not eat readily, simply providing a renal diet and water via a feeding tube may be sufficient to prolong the cat's life and reduce an owner's perception of the need for transplantation.

Malignant tumors are relatively common in some breeds of dogs and in cats but there has been only one prospective trial examining the effect of diet on survival. Adding fish oil to the diet in high concentrations and a modest increase in dietary arginine increases median survival from 270 d to 350 d in dogs with stage III lymphoma receiving regular chemotherapy (doxorubicin)[18]; there is a correlation between survival and DHA concentrations in the blood. This increase is only modest, but a retrospective study has reported that in dogs with mammary carcinomas fed lower-fat diets containing <39 % metabolisable energy (ME) as fat median survival is increased from 6 months to 3 years when dietary protein is increased from <23 % ME to >27 % ME[19].

Cardiac infarction is rare in dogs and cats but cardiac failure occurs secondary to cardiomyopathy or chronic valvular disease. A retrospective study of 180 dogs with heart failure has found that dogs that gain weight during the course of their disease and dogs that consume more *n*-3 fats survive longer than those that do not[20]. A prospective randomised controlled study of Boxer dogs with arrhythmogenic right ventricular cardiomyopathy has reported a decrease by more than half in the median frequency of abnormal heart beats (ventricular premature contractions) in dogs fed fish oil but not in dogs fed flax or sunflower oil[21].

The dietary management of cats with diabetes has received some attention. A prospective randomised controlled trial involving sixteen cats with diabetes maintained on insulin has found that including 120 g insoluble fibre/kg

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DM reduces postprandial blood glucose, although body weight is not changed by either high- or low-fibre diets[22]. Another trial has found that significantly more cats (68% *v.* 41%) revert to a non-insulin-dependent state when fed a canned diet containing almost no carbohydrate or fibre than when fed a moderate-carbohydrate higher-fibre canned food[23].

## Prevention of disease

Dogs and cats in developed societies are mostly fed complete and balanced foods made by commercial manufacturers to conform to the current understanding of the essential nutrient requirements of these species. Nutritional deficiencies are therefore uncommon in normal animals, except when human food in unbalanced proportions provides the preponderance of energy[24]. The debate among companion animal nutritionists, therefore, currently revolves around whether increased or decreased amounts of some nutrients may be beneficial.

Urolithiasis is common in dogs and cats and can result in life-threatening obstruction of the urinary tract. For many years cat foods have been mostly designed to produce acid urine to reduce the risk of struvite urolithiasis. This approach has been very successful but the number of oxalate uroliths submitted to analytical laboratories has increased as the number of struvite uroliths has decreased[25]. To compensate for this development some diets are being produced that contain higher concentrations of Na (>2 g/4184 kJ (1000 kcal)) to promote diuresis and thus lower the concentration of urine solutes. The long-term benefit of this approach has yet to be adequately evaluated in clinical patients.

Improvements in learning and retention of learned behaviour have been reported in old beagles supplemented with a cocktail of antioxidants (/kg; 1050 mg DL-α-tocopheryl acetate, 260 mg L-carnitine, 128 mg DL-α-lipoic acid, 80 mg Stay-C (Argent Laboratories, Redmond, WA, USA; mono-, di- and triphosphate esters of L-ascorbic acid providing 150 g ascorbic acid/kg dry weight) and 10 g each of spinach flakes, tomato pomace, grape pomace, carrot granules and citrus pulp)[26,27] or α-lipoic acid combined with L-carnatine[28]. This improvement has been shown to be enhanced in animals receiving behavioural enrichment[29]. The prevalence of cognitive dysfunction in pet dogs is, however, uncertain and increased concentrations of antioxidants are not always beneficial. In racing greyhounds, for example, high doses (1 g daily) of vitamin C appears to reduce performance[30].

Obesity is the commonest nutritional disease of companion animals. In various countries the prevalence has been reported as being from 19% to 52% in domestic cats[31–34] and from 22% to 44% in dogs[31,35–37]. Orthopedic, endocrine, cardiac, respiratory, neoplastic, urinary, reproductive and dermatological disease and reduced resistance to infection have been associated with obesity in dogs and cats[38]. A prospective randomised controlled trial has shown that food restriction prolongs survival in Labrador retrievers kept in kennels with runs[39]. Overweight dogs (median body condition score 6·9 on a nine-point scale) have been found to require medication for osteoarthritis 3 years earlier, and median survival is 2 years shorter than that for lean dogs (median body condition score 4·6) fed 75% of the amount of food fed to their paired littermates. It has also been reported that racing greyhounds run 0·7 km/h faster when they are fed 85% free-choice food and weigh 6% less[40]. Labrador retrievers are prone to osteoarthritis and racing greyhounds have a normal body condition that is lower than that of other breeds (3·5 on a nine-point scale), so it remains to be determined whether similar effects would be obtained with other breeds.

There are also important metabolic differences between dogs and cats and human subjects that must be taken into account before dogs and cats should be considered as potential models of metabolic syndrome in human subjects. Both obese dogs and obese cats can develop insulin resistance[41]. Overweight cats also commonly develop non-insulin-dependent diabetes mellitus but dogs usually develop insulin-dependent diabetes mellitus[42]. Only a very small increase in blood pressure has been documented as dogs gain weight, although the amount of change is affected by the type of fat in the diet[43,44]. Lipoprotein concentrations also change slightly in association with insulin resistance in dogs fed energy-dense diets[45,46], but such changes may not have the same consequences as in human subjects because most of the lipoprotein in fasted dogs and cats is HDL and the prevalence of atherosclerosis and cardiac infarction in dogs and cats is very low[47].

Dogs derive twice as much energy from fat oxidation at rest and during exercise and starvation as human subjects[48,49]. The distance beagle dogs could run before exhaustion has been reported to increase from 24 km to 48 km when the fat in their diet is increased from 30% ME to ≥ 50% ME[50]. Dogs undertaking endurance exercise use glycogen more slowly as fat intake increases[51]. In contrast, in human athletes carbohydrate loading increases stamina by increasing glycogen in muscle without affecting the rate of glycogen use[52]. However, fat oxidation does not increase with exercise in untrained dogs because increased lactic acid concentrations limit fat utilisation[53,54]. Untrained dogs may represent a better model for study than trained dogs.

When studying companion animals it is also essential to take account of differences in energy consumption. The National Research Council recommendations for adult maintenance are based on studies involving adult laboratory dogs consuming a mean of 544 kJ (130 kcal)/kg body weight (BW)$^{0.75}$ daily and average lean adult laboratory cats consuming a mean of 418 kJ (100 kcal)/kg BW$^{0.67}$ daily[1]. Nevertheless, many pet and laboratory animals are overweight, their activity and the conditions in which they are kept can be quite varied and there is great variation in the energy requirements among different breeds and among individual animals. As a result, many pet adult dogs require much less energy for maintenance than 544 kJ (130 kcal)/kg BW$^{0.75}$ daily and some working dogs require much more. Similarly, pet cats often require much more or less than the mean of 418 kJ (100 kcal)/kg BW$^{0.67}$ daily. Even in dogs that are undertaking no exercise and consuming no food in a thermoneutral environment ME requirements have been measured to vary from 201 to



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477 kJ (48 to 114 kcal)/kg $BW^{0·75}$ daily, whereas average ME requirements in fed dogs may vary from 352 kJ (84 kcal)/kg $BW^{0·75}$ daily in resting dogs to as much as 4393 kJ (1050 kcal)/kg $BW^{0·75}$ daily in dogs racing long distances while pulling a sled[1]. Thus, the amount of food consumed needs to be individualised for each pet or participant in a study if each dog or cat is to maintain body weight. Unfortunately, many reports do not describe the amount or energy density of food, which makes comparison among studies difficult. Only if food and ME intake, the ME and nutrient density of the food and any change in BW, body conditioning score and extent of muscle wasting are reported can a better understanding of the relationship between energy and nutrient requirements in sick and healthy animals be achieved.

## Conclusion

Companion animals represent a valuable comparatively-unexploited resource for the study of the effect of diet on the prevention and treatment of disease. Discoveries can be made with relatively small numbers of animals in carefully-controlled prospective randomised trials provided account is taken of differences in metabolism, metabolic body size and individual variation in energy requirements. Pet animals also have the potential to act as sentinels for contamination of the food supply. In the last 24 months melamine and cyanuric acid contamination has been identified as causing acute renal failure in cats[55,56]. The amount of protein in protein supplements added to pet food was being assessed using the Kjeldahl method to measure N rather than measuring protein directly. Melamine had been added to a protein supplement by a supplier because it is an inexpensive source of N and would falsely suggest a high protein content. Melamine was thought not to be toxic until many cats were noticed to be dying from acute renal failure when fed chunk and gravy pet foods. The melamine used contained cyanuric acid, which co-precipitated to form uroliths obstructing urine flow in the kidney. Mycotoxin contamination has also been identified as causing liver failure in dogs[57] and dog treats made from pig ears have been found to be contaminated with Salmonella[58]. As groups of animals are often fed a fairly standard diet, identification of the source of contamination can be easier when increases in the incidence of unusual diseases among animals fed the same food give reason to suspect contamination before human food becomes affected[59].

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