

# Recent advances in the dietary management of chronic renal failure in cats

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## Summary

Dietary modification is recognised as a corner-stone in the management of chronic renal failure (CRF), which is a common, generally progressive, condition in the geriatric cat. Key recommendations have included restriction of dietary phosphate and protein; however, there have been few reports of dietary intervention studies in cats with naturally occurring CRF. The study reported here showed that a diet restricted in phosphate and protein, together with oral phosphate binders in some cats, was able to bring about significant reductions in plasma phosphate and parathyroid hormone (PTH) concentrations in a group of cats with naturally occurring CRF, compared with a group not receiving this regimen. Median survival time in the group receiving dietary management was also significantly greater, and the results suggested that the management regimen might have slowed the progression of CRF.

## Introduction

Chronic renal failure (CRF) is commonly diagnosed in the geriatric cat, and is the most frequently observed manifestation of renal disease in this species. It represents the end stage of a number of renal diseases, and may thus result from neoplastic, immune-mediated, infectious, iatrogenic, metabolic, congenital, toxic, traumatic, or obstructive processes. It is usually insidious in onset, and is generally considered to be a progressive condition in which existing renal damage is irreversible.

The kidneys have a considerable functional reserve capacity, and as renal tissue is progressively destroyed the surviving nephrons undergo hypertrophy and hyperplasia to compensate for loss of functional mass. It is not until at least 65–75% of renal tissue is destroyed that these compensatory mechanisms are overcome, resulting in decreased glomerular filtration rate, decreased tubular transport and the development of azotaemia. Overt clinical signs may not be apparent until this stage is reached and for this reason, early cases of CRF may go undetected.

The kidney performs many vital functions, all of which may be affected in CRF. Nevertheless, it is generally agreed that some of the key metabolic abnormalities and clinical signs associated with CRF are consequences of the accumulation of nitrogenous waste products and of the failure to excrete phosphorus. Dietary manipulation has long been considered a corner-stone in the conservative medical management of CRF, although it only represents one aspect of a therapeutic regimen. The goals of dietary management may be summarised as follows:

- to meet the patient's nutrient and energy requirements
- to ameliorate clinical signs of uraemia (where present)
- to minimise electrolyte, vitamin and mineral disturbances
- to try to slow progression of CRF

Several independent studies have evaluated nutritional intervention in renal ablation models of CRF in cats (Ross *et al.* 1982; Adams *et al.* 1994; Finco *et al.* 1998). The 'remnant kidney' model of renal failure used in these studies is produced by infarcting a large portion of one kidney and removing the other kidney. The remaining surviving nephrons are normal in function and morphology, but subsequently undergo changes to accommodate functional demands (Finco *et al.* 1998).

Our studies have focused on dietary intervention in naturally occurring CRF in cats. An earlier Waltham study (Harte *et al.* 1993; 1994) showed that a commercial canned diet restricted in phosphorus (0.23 g/MJ metabolisable energy [ME]) and protein (15.4 g/MJ ME) resulted in improvements in physical condition, haematological parameters and decreased azotaemia in cats with naturally occurring CRF, compared with a control diet providing 0.48 g phosphorus and 23.6 g protein/MJ ME. This study provided the basis for our subsequent work, described below, the objectives of

which were to evaluate the effects of protein and phosphorus restriction on azotaemia, plasma phosphate and parathyroid hormone (PTH) concentrations, and survival of cats with naturally occurring CRF (Barber *et al.* 1996; 1999; Elliott *et al.* 1998).

## Materials and methods

Cats in stable CRF which were presented to three veterinary hospitals were considered for inclusion in the study. CRF was diagnosed on the basis of persistent azotaemia (plasma creatinine concentration above the laboratory reference range of 180 mmol/l). Cats with signs of extrarenal disease or with prerenal azotaemia were excluded, as were cats in which CRF was a result of glomerular disease leading to severe protein-losing nephropathy. The owners of all cats entering the study were offered treatment of their pets, using dietary management with a commercially available diet<sup>1</sup> designed for the management of feline CRF. This diet was moderately restricted in protein, phosphorus and sodium, and had increased concentrations of B group vitamins compared with typical feline diets. In addition, the canned formulation, which was fed to most of the cats, had a higher fat content (Table 1). This diet was used from December 1993 until December 1996. A new version of the canned diet<sup>3</sup> with a lower phosphorus content (0.16 g/MJ) and a slightly reduced calcium content (0.33 g/MJ) was introduced in December 1996, following recognition of the benefits of phosphorus restriction.

Dietary management was offered to all the cat owners, but some were not able or not willing to introduce the veterinary diet effectively over a period of four weeks. These cats were assigned to the 'normal' phosphate and protein group (NPD) and continued to be fed other commercially available maintenance cat foods with varying amounts of fresh meat and fish.

Cases were initially evaluated on approximately a monthly basis, and then at two monthly intervals if considered stable. On each evaluation the cat was weighed, a full clinical examination was completed, and blood and urine samples were collected. Owners were questioned about their cats' general well being, adherence to dietary management and any prescribed treatments. Plasma phosphate and PTH concentrations were monitored in both groups. In the group receiving the phosphate and protein restricted diet (RPD) therapy was adjusted if plasma phosphate concentrations increased markedly, if a slight increase was maintained over a number of visits, or if PTH concentrations failed to decrease or started increasing. Phosphate restriction was initially achieved with diet alone, but where this was considered insufficient, aluminium hydroxide gel, either as a liquid<sup>4</sup> or dried formulation<sup>5</sup> was introduced. The dose was titrated on an individual case basis. Phosphate binders were not used in the NPD group. Other complications of CRF (hypokalaemia, hypertension, and urinary tract infections) were managed as and when they were recognised.

The age and body weights of the cats at the start of the study, and the pre-treatment plasma creatinine, phosphate and PTH concentrations in the RPD and NPD groups were compared using an unpaired *t* test. The plasma creatinine, phosphate and PTH concentrations at the mid-survival time point (in those cats that died or were euthanased) were compared between the two groups using an unpaired *t* test. Survival times of cats in the two groups were compared using a Mann Whitney U test. In all tests  $P < 0.05$  was taken to indicate significance.

## Results

Twenty-two cats were fed the phosphate and protein restricted diet and were considered to be adequately phosphate restricted, whereas fifteen owners were not

**Table 1** Typical analysis of a commercially available veterinary diet<sup>1</sup> fed to 22 cats with naturally occurring chronic renal failure.

Nutrient	Content (g / MJ) in		
	Canned diet	Dry diet	Maintenance diet <sup>2</sup>
Protein	14.4	13.2	28.9
Fat	21.2	11.2	17.3
Nitrogen free extract	3.1	22.8	6.5
Ash	2.5	2.3	4.9
Calcium	0.41	0.33	1.26
Phosphorus	0.25	0.17	1.14
Sodium	0.14	0.11	0.64

<sup>1</sup>Whiskas® Low Protein Diet (Waltham): Masterfoods, Bruck, Austria (canned) and Whiskas® Low Phosphorus Low Protein Diet Effem, Minden, Germany (dry)

<sup>2</sup>Typical analysis of a canned cat food (Whiskas® Supermeat, Pedigree Masterfoods, UK) is provided for comparison

<sup>3</sup>Whiskas® Low Phosphorus Low Protein Diet (Waltham): Masterfoods, Bruck, Austria (canned)

<sup>4</sup>Aludrox®, Wyeth Laboratories, Maidenhead, UK

<sup>5</sup>Alu-Cap®, Riker Laboratories, Loughborough, UK

able or willing to introduce the diet. There were no significant differences between the groups in initial plasma creatinine concentrations, body weight, or age.

Plasma creatinine concentration remained stable in the RPD group, whereas it tended to increase in the NPD group ( $P = 0.077$ ); the difference between the groups was not significant at the mid-survival time point. Thirteen (59%) of the protein and phosphate restricted cats died ( $n = 5$ ), or were euthanased ( $n = 8$ ), with a median survival time of 581 days. Eleven (73%) of the cats which did not receive the phosphate and protein restricted diet were euthanased, with a median survival time of 252 days. The median survival time was significantly shorter ( $P = 0.017$ ) in the NPD group than in the RPD group (Elliott *et al.* 1998).

Progressive renal failure, as judged by increases in plasma creatinine concentration, was the reason for death or euthanasia in four (31%) of the cats in the RPD group and eight (73%) of the cats in the NPD group (Elliott *et al.* 1998).

Detailed results of plasma phosphate and PTH concentrations are presented from the 13 cats in the RPD group and 11 cats in the NPD group died (Table 2) (Elliott *et al.* 1998). Plasma phosphate and PTH concentrations did not differ significantly between the two groups at the initial diagnosis of renal failure. Eight of the 13 cats in the RPD group and six of the 11 cats in the NPD group had plasma phosphate concentrations above the laboratory reference range (0.68–1.86 mmol/l) at the start of the study. Plasma PTH concentrations were above the laboratory reference range (2.9–25.0 pg/ml) in all of the cats of both groups at the start of the study. Control of plasma PTH was initially achieved using diet alone in 11 cats (85%) of the RPD group; phosphate binders were started in the remaining two cats in this group at days 63 and 66. Phosphate binders were used at a later stage (126 to 714 days) in a further four cats to maintain the control of PTH secretion that had originally been achieved by diet alone.

The effect of dietary phosphate restriction was evaluated by comparing the plasma phosphate and PTH concentrations of the cats at their mid-survival time point. Plasma phosphate and PTH concentrations were both significantly lower ( $P < 0.01$ ) in the RPD group at this time when compared with the values in the NPD group (Table 2). These data indicate that the treatment

regimen adopted for the RPD group was effective in maintaining control of plasma phosphate and PTH concentrations over a prolonged period of the study, whereas those animals which did not receive a phosphate-restricted diet tended to show progressive increases in plasma PTH and phosphate over time.

## Discussion

The data from this study show that dietary management of cats with naturally occurring CRF using a commercially available phosphate and protein restricted diet as part of a management regimen, can bring about significant decreases in plasma phosphate and PTH concentrations, and significantly increase survival time compared with cats not receiving dietary management. To the authors' knowledge this is the first time that these clinical benefits have been shown in naturally occurring CRF. It is also possible, based on the observations about causes of death or euthanasia, that the regimen slowed the progression of CRF.

The precise mechanism(s) for these effects were not determined by this study, but may have related to the changes in plasma phosphate or PTH concentrations. Hyperphosphataemia is a commonly recognised biochemical disturbance of cats with renal failure (DiBartola *et al.* 1987), the primary mechanism for which is phosphate retention due to decreased glomerular filtration rate. Phosphate retention may promote soft tissue calcification and plays an important role in the pathogenesis of renal secondary hyperparathyroidism (Barber and Elliott 1998). Correction of hyperphosphataemia by dietary phosphorus restriction is an accepted method of managing cats with CRF, and its efficacy in controlling renal secondary hyperparathyroidism in cats has been demonstrated (Barber *et al.* 1999). The diet used in this study was considered restricted in phosphorus compared with typical maintenance foods (Table 1), the concentration being similar to the minimum phosphorus recommendation of 0.30 g/MJ for adult maintenance (NRC 1986; WCPN 1993). The lower plasma phosphate and PTH concentrations in the RPD group at the mid-survival time point is thus attributed to the use of this diet, together with oral phosphate binders in some cats.

**Table 2** Plasma phosphate and parathyroid hormone (PTH) concentrations (mean  $\pm$  SE) in cats with chronic renal failure managed with a phosphate and protein restricted diet (RPD;  $n = 13$ ) or without dietary phosphate and protein restriction (NPD;  $n = 11$ ).

Treatment group	Plasma phosphate concentration (mmol/l)		Plasma PTH concentration (pg/ml)	
	Initial	Mid-survival	Initial	Mid-survival
RPD	2.07 $\pm$ 0.26	1.32 $\pm$ 0.12 <sup>1</sup>	140.0 $\pm$ 30.8	75.9 $\pm$ 23.9 <sup>1</sup>
NPD	1.97 $\pm$ 0.22	2.64 $\pm$ 0.35 <sup>1</sup>	153.6 $\pm$ 58.4	345.6 $\pm$ 76.2 <sup>1</sup>

<sup>1</sup>Values within a column sharing a superscript are significantly ( $P < 0.01$ ) different.

The diet also varied from typical maintenance foods in a number of other nutrients (Table 1). The protein content was approximately half that of the canned cat food quoted for comparison, and was between the minimum recommendations for growth of 11.5 g protein / MJ (NRC 1986) and 15 g/MJ (WCPN 1993: the latter value incorporates a 25% increment over the NRC minimum requirement to allow for variation in protein source and digestibility). In addition, the diet was restricted in sodium compared with typical foods, and was supplemented with water-soluble vitamins. The canned formulation was also higher in fat and energy (on an as fed basis) than typical cat foods. Which of these factors, either alone or in combination with the use of phosphate binders in some cats, led to the effects on survival remains speculative.

Three studies conducted at North American universities have studied dietary intervention in induced renal failure in cats. Dietary protein intake has been evaluated previously in two studies of induced renal failure (Adams *et al.* 1994; Finco *et al.* 1998). Adams *et al.* (1994) showed that restriction of dietary protein (to approximately 2.7 g/kg/d) and energy (approximately 235 kJ/d) intake resulted in fewer renal lesions in cats with induced renal failure, than consumption of approximately 6.8 g protein/kg/d and 315 kJ/d. The higher protein and energy intake resulted in weight gain over the course of the study and the development of significant glomerular and tubulointerstitial lesions. No decrement in renal function was observed in either group of cats over the one-year study. Finco *et al.* (1998) did not find an effect of different protein intakes (approximately 5.3 or 9.0 g/kg/d) and showed only minor effects of energy intake on the development of renal lesions. None of the groups studied showed a decrement in renal function over the study period, although one individual developed severe uraemia, and those renal lesions that developed were considered mild. These data suggested that factors other than protein or energy intake may have been involved in the effects seen by Adams *et al.* (1994); one possibility is phosphorus intake, which was approximately 17% less in the cats on the lower protein and energy intake. Serum phosphorus concentrations were significantly higher in the high protein / high energy group (1.76 mmol/l) than in the low protein / low energy group (1.44 mmol/l) although the concentrations did not exceed the laboratory reference range in either group (Adams *et al.* 1994).

Ross *et al.* (1982) studied the effect of phosphorus intake on the development of renal lesions in cats with induced renal failure. A phosphate-restricted diet (phosphorus content 0.42% dry matter) resulted in significantly lower serum phosphate (range approximately 1.13 to 1.17 mmol/l) and PTH concentrations than a diet with a 'normal' phosphate content (1.56% dry matter) (serum phosphate concentrations approximately 1.93 – 2.58 mmol/l). In addition, renal mineralisation, fibrosis, and cell infiltration occurred in the kidneys of the cats fed the

higher phosphorus level, whereas the kidneys of the cats fed the restricted phosphate diet showed little or no change. Taken together, the data from these studies of induced renal failure suggest that protein intake is not an important factor in progression of renal damage in the remnant kidney model in the cat, whereas phosphorus intake, and perhaps other factors, may be of importance.

It is not clear whether results from studies using the remnant kidney model can be applied to clinical disease. The acute reduction in renal mass and residual normal tissue might not properly be equated with naturally occurring CRF, which may be more gradual in onset and result from a series of insults or an ongoing disease process. Progression to end-stage renal failure did not occur in one year in any of the groups in the studies of induced renal failure considered above, which is in contrast with the observations from the NPD group described here.

Energy intake was not recorded in the clinical study described here, although the data on body weight show that it met the maintenance requirements of the cats, suggesting that it approximated 250 – 290 kJ/kg/d. In contrast with the study of Adams *et al.* (1994) weight gain did not occur in either group. Based on the assumed energy intake for maintenance, protein intake in the RPD group was estimated to be approximately 4 g/kg/d; in the NPD group it was probably approximately twice this amount. Protein intake in the NPD group was thus probably similar to that in the high protein groups in the study of Finco *et al.* (1998) which did not develop significant renal lesions. If comparisons can be drawn between naturally occurring disease and the remnant kidney model, these observations suggest that restriction of protein intake may not have been a major factor in the clinical benefits seen in the study reported here.

Ross *et al.* (1981) provided limited analytical data; however, it is estimated that the phosphorus contents of their diets were approximately 0.20 and 0.74 g/MJ. The high phosphorus diet resulted in hyperparathyroidism, significantly increased serum phosphorus concentrations and the development of renal lesions. The serum phosphorus concentrations of the cats fed this diet were broadly similar to those reported at the mid-survival time point in the NPD group of the study reported here. The low phosphorus diet used by Ross *et al.* (1981) was not associated with the development of renal lesions; its phosphorus content was within the range of the diets used in the study reported here. If comparisons between these studies can be drawn, the data suggest that phosphate restriction may have been more important than protein restriction in the increased life span and slowing of progression that were observed. Nevertheless, further research should be conducted in cats with naturally occurring chronic renal failure to define the mechanism for the beneficial effects observed in the study reported here.

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