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The Use of Reduced Protein Diets in the Management of Canine Renal Failure

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Renal failure can be defined as the clinical state in which the functionally damaged kidney can no longer compensate for its decreased capacity. 1 Metabolic waste products are not removed completely, and the body can no longer maintain homeostasis. Renal function can be evaluated in terms of glomerular filtration rate (as measured by inulin or creatinine clearance), renal blood flow, tubular secretion, serum creatinine concentration, and the ability to concentrate urine. 1-4 Conservative medical management has often involved the use of low protein diets to slow or prevent the progression of renal failure and associated uremic complications. Recent literature has argued against low protein diets, advocating normal to high protein diets instead. This paper will address the efficacy of low protein diets in the management of renal failure.

When a kidney suffers the loss of functioning nephrons, regardless of the cause, the normal physiologic response is for the surviving nephrons to hypertrophy and increase their rate of filtration. 5-7 In renal failure there is a reduction in the number of filtering nephrons, but those remaining have an increased glomerular filtration rate (GFR). 4,6 The total GFR will be reduced below normal despite the increase in single nephron GFR (SNGFR). The term “hyperfiltration” is used to describe the condition when the SNGFR exceeds normal levels. The actual increase in SNGFR correlates closely with the amount of renal mass lost. A more severe loss of functional nephrons will cause a greater increase in SNGFR. 4,6,7.

Glomerular filtration rate and renal blood flow (RBF) also increase with the level of protein in an animal’s diet. 3,8,9 The GFR in dogs fed a single meal of meat has been shown to increase from 40 - 100%. 3 While the exact mechanism of increased GFR with increased protein intake is not known, it is thought to be unrelated to levels of protein metabolites such as urea, sulfate, or hydrogen ions. 5,7 One of the proposed theories is that a circulating hormone or mediator is responsible for the elevated GFR and RBF. Glucagon has been suggested as a possible mediator, since its release from the pancreas is triggered by protein ingestion. Furthermore, glucagon has been shown to increase GFR and RBF, possibly by vasodilation of the preglomerular vessels. 2,3,7,8 Additional theories relating protein intake to changes in renal hemodynamics have been suggested, and include alterations in plasma amino acid levels, or the release of hormones (other than glucagon) which cause vasodilation. 2,7

Conversely, when a low protein diet is fed the GFR is decreased in both normal and renal failure dogs. 2,4,6 In one study 4, rats underwent severe (five-sixths) renal ablation and contralateral nephrectomy, and were then maintained on high or low protein diets. Those fed a 24% dry weight protein diet had a higher GFR than rats fed a 6% dry weight protein diet.

It is established that GFR can increase as a normal physiologic response to the loss of functioning nephrons, and in response to protein levels in the diet. Some researchers feel that an increased GFR is a favorable condition in an animal that has compromised renal function. 10 Others feel that the immediate benefit of improved renal function may be diminished by degenerative structural changes that have been shown to occur with prolonged hyperfiltration in rats. 1,4,6

Hyperfiltration has been incriminated in the development of proteinuria and glomerular lesions in rats with reduced renal mass. 4,6 In the previously cited study 4 in which rats with experimentally induced renal failure were placed on diets containing 24% and 6% protein, the group consuming

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24% protein had a wide range of histologic glomerular abnormalities within one week. Proteinuria was also observed in the same group after one week. Those rats fed a low protein diet had notably fewer glomerular lesions after one week.

One proposed mechanism for glomerular pathology in rats is that hyperfiltration, which causes an increase in capillary hydrostatic pressure, damages the microvasculature of the glomerulus, resulting in increased glomerular permeability. It is thought that the size and charge selectivity of the glomerular membrane is lost, resulting in proteinuria. Damage to the glomerular vasculature may also cause an influx of protein and other molecules into the mesangium, causing cellular proliferation and matrix formation, which is the forerunner of sclerotic changes. It has been suggested in the rat that chronic hyperfiltration in a single nephron results in glomerular sclerosis. As that individual nephron function is lost, another nephron will be recruited for hyperfiltration, causing the cycle to continue.

The fact that hyperfiltration exists in renal failure is well accepted. Many researchers believe that low protein diets help to alleviate the hemodynamic changes that occur with hyperfiltration and hence protect against the progression of renal failure through glomerular sclerosis. Others feel that the reduced renal function (as measured by RBF, GFR, and tubular secretion) associated with low protein diets is a more significant and detrimental result.

Several studies have shown a much higher incidence of uremic complications in renal failure dogs fed high protein diets. It should be noted that in addition to different protein levels, the experimental diets varied in carbohydrate, fat, mineral and electrolyte content. In one study, done by Polzin et al., in which renal failure was experimentally induced, 6 out of 11 dogs on a high protein diet (44.4% dry weight protein) died of uremic complications, characterized by hypothermia, dehydration, oral ulcers, anorexia, vomiting and depression. These signs were not seen in any dogs

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**FIGURE 1.** Hypothetical scheme relating compensatory glomerular hemodynamic changes in surviving glomeruli to pathologic changes in those nephron units.6
fed diets containing moderate (17.2% dry weight) or restricted (8.2% dry weight) protein diets. The two lower protein groups also appeared to be more active, had better hair quality, and less severe proteinuria. Dogs fed restricted and moderate protein diets had significantly lower serum urea nitrogen levels than dogs fed the high protein diet, however there was not a significant difference in serum creatinine levels between the groups. All three groups showed a significant decline in inulin clearance (a measure of GFR) following the surgical induction of renal failure. Dogs on the moderate protein diet had a steady increase in inulin clearance throughout the study, and by week 32 had greater inulin clearance than dogs on the high protein diet. Dogs on the restricted protein diet consistently had the lowest inulin clearance.

The study was conducted over a forty week period, during which time the renal function of the high protein group remained stable. Therefore, it cannot be concluded from this study that high protein intake is a causative factor in the progression of renal failure. However, one cannot rule out the possibility that renal function remained stable due to hyperfiltration and hypertrophy, and that declining GFR may not be detected until the residual nephrons have reached their compensatory limit. The study does seem to incriminate high protein diets as a factor in the increased mortality and clinical signs of uremia in that diet group.

It is thought that uremia may contribute to infections due to an impaired immune response. An interesting finding in the study mentioned above is that 7 of 11 dogs on the high protein diet had pneumonia, which did not afflict the dogs on reduced protein diets. Necropsy revealed atrophy of lymphatic tissues in the high protein group non-survivors, supporting the theory of immunodeficiency. A reduced protein diet may result in depletion of total protein and albumin levels, but it does not affect the dogs on restricted protein diets. Necropsy revealed atrophy of lymphatic tissues in the high protein group non-survivors, supporting the theory of immunodeficiency.

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It was the conclusion of Polzin et al. that "reduced protein diets were of benefit in reducing mortality, preventing clinical signs of uremia and lowering SUN concentrations in dogs with chronic renal failure when compared with that in dogs fed a 44.4% protein diet".

Finco and Barsanti did a prospective study with client-owned renal failure dogs. The dogs were placed in three diet groups with protein levels of 11%, 4.3%, and 1.2% on an as-fed basis. (These values can be converted to dry weight protein based on the typical 70% moisture content of canned dog foods. Henceforth, the respective values of 36.6%, 14.3% and 4.0% will be used.) Owner compliance in feeding only the specified diet must be considered as a variable in this study.

Dogs fed the high (36.6% dry weight) protein diet maintained their elevated baseline SUN levels, and appeared thin and unthrifty throughout the study. The owners reported good appetite, attitude, and activity level despite considerable weight loss. The restricted (4.0% dry weight) protein group had the most complications and the shortest mean survival time, which may be attributed to more severe renal failure as evidenced by a significantly lower initial hematocrit. The restricted protein diet was the least palatable, which contributed to anorexia and weight loss, and several dogs became hypoalbuminemic. The SUN levels decreased markedly from the baseline levels, apparently due to reduced protein intake, since renal function (as measured by serum creatinine concentration) remained stable.

Several dogs in both the moderate (14.3% dry weight) and restricted protein groups developed metabolic acidemia, with clinical signs such as tachypnea, shivering and lethargy. The signs were resolved following the addition of sodium bicarbonate to their regime. Two dogs on the moderate protein diet had a marked increase in serum creatinine concentration which apparently coincided with the acidemia, as the level returned to near baseline when sodium bicarbonate was administered. The dogs on the moderate protein diet had the longest mean survival time (they were also the youngest, and least anemic at the start of the study), gained weight, and were judged to have the best quality of life. This group looked and behaved like normal dogs, in contrast to the high and low protein groups.

In a second study, Polzin found that induced renal failure dogs fed diets of 17.2% and 8.2% dry weight protein had variable degrees of hyperchloremic metabolic acidosis, as opposed to dogs on a 44.4% dry weight protein diet. Several dogs on the lowest protein diet also had hypoalbuminemia and hypercholesterolemia.

Polzin, Finco and Barsanti tend to favor the moderate protein diet, with protein levels in the range of 14-18% dry weight for the management of dogs in renal failure. This protein level appears to provide an adequate level of nutrition without aggravating, and often improving, the uremic status of the dog. Renal function appears to remain stable, as evidenced by consistent serum creatinine concentrations in both studies. Polzin found that
protein diet. Survival time, appearance, and quality of life were favorable in the moderate protein groups.

Bovee et al. found in a thirteen month study with induced renal failure dogs, that dogs fed a 19% dry weight protein diet had lower GFR and RBF, as well as lower SUN and plasma protein than dogs fed 56% and 27% dry weight protein diets. The slight increase in SUN (though still within the normal range) in dogs on the highest protein diet was due to increased protein intake rather than reduced renal function, as serum creatinine was not significantly elevated, and creatinine clearance was higher than in the two lower protein groups.

In the same study, it was found that dogs on high protein diets were more resistant to experimentally induced Escherichia coli pyelonephritis. Experimental induction of renal failure included combinations of ligation of renal artery branches, contralateral nephrectomy, and surgical induction of E. coli pyelonephritis. Dogs fed the high protein diet had negative urine cultures after 45 days, and a more rapid return to normal peripheral leukocyte count than dogs on a moderate protein diet, which had significant urine bacterial cultures for four months. This concurs with previous findings in which there is increased antibacterial activity in urine of human and canine patients fed high protein diets or urea supplements. The antibacterial effect is most likely due to decreased urine pH and increased urea excretion.

Throughout the study the serum creatinine, SUN, hemograms, total protein and urinalysis values of dogs on all three diets were within normal limits, which makes the original premise that the dogs were in renal failure somewhat doubtful. The urinary antibacterial effect of high protein diets is of questionable significance in the management of renal failure dogs. The study does not report any variation in subjective criteria, such as appearance or attitude, between the groups.

There is a lack of consensus regarding the appropriate level of dietary protein for dogs in moderate renal failure, and further research is needed. A paradox exists between the apparent desirable and deleterious effects of low protein intake. Low protein diets tend to reduce hyperfiltration which is the normal compensatory response to nephron damage and decreased renal function. It has not been shown conclusively that hyperfiltration due to high protein levels causes glomerular sclerosis, and consequently decreased renal function in the dog, though it has been suggested in the rat. However, the majority of clinical evidence is in favor of the use of reduced protein diets in managing moderate renal failure.

The major complication in reducing protein intake is determining the appropriate timing and degree of protein restriction. Patients with reduced renal function that are given protein in excess of maintenance requirements will have increased retention of nitrogenous metabolites and hence uremic symptoms. Conversely, if the protein intake is below maintenance requirements, the dog will eventually become protein depleted, with a reduction in body mass and plasma proteins. Extremely low protein diets also tend to have poor palatability.

Prior to restricting protein intake, the practitioner should thoroughly evaluate the dog's renal function and nutritional status. Parameters that should be measured include body weight, hydration, general body and coat condition, serum creatinine, urea nitrogen, albumin, calcium, and phosphate levels, complete blood count, and urinalysis.

A large number of metabolites have been incriminated as uremic toxins, and many are intermediate or end products of protein metabolism. Excesses of certain hormones such as gastrin, growth hormone, glucagon, renin and parathyroid hormone have also been linked to the uremic syndrome. Fluctuations in serum urea nitrogen have been used extensively to monitor renal function, and although urea is considered to be a minor uremic toxin, its concentration reflects that of the more toxic uremic compounds. Clinical signs of uremia are usually not evident until SUN levels reach 60-80 mg/dl. SUN levels can be significantly altered by nonrenal factors such as dietary protein levels, hydration status, and tissue catabolism, all of which can vary in a renal failure patient. The previous studies used declining SUN levels as an indication of reduced uremia, which was supported by subjective and objective data. It is generally accepted in the veterinary literature that reduced protein diets will reduce SUN as well as other uremic toxin levels, thereby minimizing the severity of clinical signs associated with the uremic syndrome.

Serum creatinine can be used as a very reliable indicator of renal function, and is minimally influenced by diet or nonrenal causes. The SUN/creatinine ratio has been used as a means of normalizing the SUN according to renal function.

Cowgill and Spangler have proposed a direct relationship between the SUN/creatinine ratio and protein intake. Polzin also confirmed this relation-
ship in his study with induced renal failure dogs. Given the patient's serum creatinine level, a maximum dietary protein intake can be estimated which would maintain the SUN within a desired range. (Figure 2).

A progressive decline in renal function, as evidenced by an increased serum creatinine concentration, will require an adjustment in protein intake in order to maintain an acceptable SUN level. When serum creatinine levels reach 4.0 - 5.0 mg/dl, the commercial diets will not provide sufficient protein restriction. (Figure 3). Prescription diets provide adequate restriction and homemade diets with high quality protein sources are acceptable. Prescription diets often have low levels of sodium which is helpful in minimizing hypertension in renal failure dogs.

A minimal protein level in a dog's diet is 1.25-1.60 gm/kg/day of high-biologic value protein. An additional gram of protein should be added to the diet to compensate for each gram of protein lost in the urine. A 24-hour urine collection or a single urine sample can be used for quantitative estimation of proteinuria by determining the urine protein to creatinine ratio.

The patient should be monitored by the owner and the practitioner for signs of protein malnutrition. A significant reduction in muscle mass, progressive weight loss, or reduction in packed cell volume and serum albumin levels would indicate an insufficient supply of dietary protein. The diet should be adjusted accordingly, until the dog can maintain an acceptable physical condition and the uremic state can be controlled.

**SUMMARY**

The use of reduced protein diets in the management of canine renal failure is a controversial issue. It is well-accepted that there is a direct correlation between protein intake and renal blood flow and...
glomerular filtration rate. Studies show that reduced protein diets have lower RBF and GFR as compared to diets with normal or high protein content. On the surface the improvement in GFR and RBF would appear to be advantageous; however, some researchers feel that hyperfiltration can contribute to the progression of renal failure. Experimentally induced renal failure rats have developed glomerular sclerosis when fed a high protein diet. It has not been proven in the dog that hyperfiltration leads to glomerular degeneration, and further research is needed.

Renal failure is a very complex disease, and can be manifested by many systemic changes. Though dietary protein plays a significant role, other factors such as phosphorus should not be overlooked. One of the drawbacks of the research cited in this paper is that the studies evaluated commercially available products, so protein was not the only variable. However, based on experimental and clinical findings cited it is our recommendation that a moderately restricted protein diet (14-18% dry weight) be fed to dogs in renal failure, especially those with signs of uremia. The link between serum urea nitrogen levels and protein intake is well-established in the dog, and it is generally accepted that the levels of other uremic toxins can also fluctuate in relation to dietary protein. Since serum creatinine concentration is a more accurate gauge of renal function, it should be considered when prescribing the appropriate protein intake. The overall status of the dog should be evaluated on a regular basis, with the prevailing goal of providing the best quality of life for the renal failure patient.

REFERENCES