Mythology of Protein Restriction for Dogs with Reduced Renal Function

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Dietary protein restriction has been widely accepted as a form of nutritional management for animals with reduced renal function for over four decades. While scientific evidence has not been presented to justify this practice, it is particularly used in dogs. Advertising claims suggest that dogs with a list of urinary problems could benefit from protein restriction including those with renal insufficiency, progressive renal failure, acute renal failure, normal aging, polydipsia/polyuria, glomerulonephritis, urinary tract infection, urolithiasis, and prostatitis. The most widely accepted of these is the notion that dogs with reduced renal function or advanced age will benefit from reduced dietary protein intake.

In recent years, 10 experimental studies using dogs have been published that clarify the controversy of protein restriction. A multicenter study conducted in human medicine is also noteworthy to review.

A number of false assumptions about the need for reduced protein intake in regard to renal disease have been perpetuated in the literature for many years, including:

- Increased urea load causes increased workload for the kidneys.
- High dietary protein intake injures kidneys.
- High dietary protein intake causes hyperkalemia.
- High dietary protein intake causes acidosis.
- Protein intake results in uremic toxins
- Reduced protein intake slows the progression of renal disease.

Recent evidence in dogs challenges the validity of the above assumptions and redirects the questions about factors that lead to the progression of renal failure. The beliefs about protein restriction will be discussed as a medical myth. The question of why the practice of reduced protein intake persists despite the lack of supportive scientific evidence is explored.

History of Protein Restriction

Two general reasons are most commonly given to support the reduction of dietary protein in animals with renal disease. First, reduced protein may result in reduced azotemia, which limits the nausea of renal failure and allows animals to continue eating. While this premise is widely accepted, its clinical importance has not been quantified. Second, reduced protein intake may influence the course of renal failure. The origin of these notions provides some insight into their appeal and durability.

The first suggestion in the literature that ingestion of protein aggravates the clinical condition of human patients with renal insufficiency dates back to 1920. Ambard reported that uremic patients were often wasted and did poorly when they ingested meat.[1] This clinical description led to efforts to alleviate the so-called "toxins of uremia" by reducing dietary protein. Newburgh and Curtis in 1928 reported the development of renal lesions in rats fed varying quantities of protein and suggested that rats fed high quantities of protein containing 75% dry liver developed renal lesions more quickly than those fed moderate protein or casein diets.[2] Rodents have been widely used to study possi-

ble causative factors of progression of renal failure. Some strains of rats have a high incidence of spontaneous glomerular and tubular lesions associated with age alone.[3–8] The progression and severity can be enhanced by increased dietary protein,[2,9,10] sodium,[4] and phosphate.[11] Surgical ablation of renal mass hastens glomerular lesions as does diabetes in these rats.[12–14] While these observations are limited to certain strains of rats, they have influenced many investigators by establishing the possibility of a dietary protein-induced nephropathy in other species.

The first published data in the dog linking dietary protein to renal function appeared in the 1930s. It was reported that in normal dogs glomerular filtration rate (GFR), renal blood flow (RBF), and urea clearance could be acutely increased by high protein feeding.[15–17] Subsequent studies by Pitts indicated that intravenous infusion of amino acids dramatically increased renal hemodynamics.[18]

Evidence that high protein diets enhance renal function in normal dogs has led to confusion among veterinarians who have been told for decades that low protein diets may be beneficial for kidney function.

It should be remembered that during the 1930s and 1940s the basic parameters of kidney function were first being studied. For example, blood urea concentration as an accurate measure of kidney function and the concept of extrarenal azotemia were first reported at that time.[19] It was then believed that the kidney expended considerable energy to excrete urea into the urine and that moderate restriction of protein was beneficial to human patients as contended by Addis.[20] This concept fell out of favor in human medicine when it was realized that renal work is tied closely to active sodium reabsorption and that urea is passively handled. Special dietary restrictions were not thought to be needed in human patients with chronic renal failure because of the lack of evidence that a normal protein intake had a deleterious effect on the kidney. Addis reported that urea production, urea excretion, and blood urea nitrogen (BUN) increased in normal subjects when dietary protein was increased. The uselessness of urea clearance and the limitations of creatinine clearance were not appreciated at that time.[21]

In 1941, Allison et al. reported on 10 dogs with kidney disease as measured by increased BUN and decreased urine specific gravity, which they felt correlated well and were of clinical significance in determining kidney damage. They were unaware of the extrarenal and renal factors separate from GFR that might influence BUN and reported that serum creatinine concentration was not a reliable indicator of kidney damage.[22] Morris subsequently developed, produced, and sold a reduced-protein diet, KD, for dogs with renal failure. He and others were influenced by the erroneous work hypertrophy concept for urea excretion advanced by Addis.[20] While experimental or clinical data were never published to support the value of this or other diets, the concept was broadly accepted without challenge in the veterinary literature.[23] Diets were promoted as lowering BUN and reducing urine volume.

The notion that high protein feeding to dogs may be harmful was even adopted by the National Research Council (NRC) of the National Academy of Sciences in 1972.[24] It was stated that high protein found in some commercial diets increases the workload of the liver and kidney and contributes to renal disease in dogs. There is no evidence to support this view, and the recommendation has been dropped. In contrast, there is evidence that high protein diets enhance renal function in normal dogs. This has led to confusion among veterinarians who have been told for decades that low protein diets may be beneficial for kidney function and therefore high protein diets may be deleterious to normal dogs.

While the Addis hypothesis of work hypertrophy to excrete urea is erroneous, a more modern concept associated with glomerular hyperfiltration was proposed in the 1980s by Brenner.[25] This hypothesis states that after any significant loss of renal function, surviving nephrons subsequently undergo functional and structural changes including increases in single nephron GFR and glomerular capillary pressure increases. These changes are referred to as glomerular hyperfiltration and glomerular hypertension. Micropuncture studies in rats indicate that a progressive decline in renal function is observed as a consequence of these adaptations. In addition, glomerular enlargement, hypertrophy, and glomerular mesangial deposits lead to a progressive glomerulosclerosis and eventual nephron loss. Surviving nephrons undergo further increases in filtration rate, capillary pressure, and size, setting up a vicious cycle of pathogenic renal injury. A reduction in dietary protein

and/or calories has been shown to limit this process in some strains of rats.[26] If this mechanism were operative in the dog, there would be good rationale to limit dietary protein.

Experimental Studies in Dogs

Because of the confusion in the veterinary literature and the lack of evidence to support the use of reduced protein diets, a number of experimental studies have been performed in recent years. These studies have utilized the standard experimental model of reduced renal function and have addressed many questions when dogs received varied forms and quantities of protein at different levels of renal function. These studies represent a major quantity of work that required the sacrifice of hundreds of dogs to deliver in the aggregate a clarification of the possible role of dietary protein in the initiation, maintenance, and progression of renal dysfunction.

The measurement of progression of renal failure requires specific definition. In these studies the use of clinical signs, reduced urinary concentration capacity, elevated BUN, and elevated plasma creatinine have limited ability to detect efficacy of protein restriction. Likewise, the presence of hyperphosphatemia, acidosis, and proteinuria may be misleading depending on the experimental model and diet and may not represent a precise measure of progression. The sole most reliable method is the measure of GFR using inulin or labeled iothalamate. This is considered the gold standard to indicate progression of disease, and all other measures are considered secondary.

Progression to failure may also be estimated on the basis of morphologic measures. The agreement of morphologic and functional measures is extremely complex and appears to vary with the form of renal disease or experimental model. A synthesis or comparison of functional and morphologic measures may be helpful in some cases. However, results may or may not agree. Although histologic or electron microscopic alterations may indicate something about the pathophysiology, their relationship to progression of failure may be difficult to quantify. It is commonly difficult to quantify histologic lesions because they are not uniformly distributed, there may be confusion due to compensatory hypertrophy and hyperplasia, and in some forms of disease fibrosis may obscure histologic architecture.

Results of the 10 experimental studies on dogs have failed to provide evidence of the benefit of reduced dietary protein to influence the course of renal failure.

Results of the 10 experimental studies on dogs have failed to provide evidence of the benefit of reduced dietary protein to influence the course of renal failure.[27–36] The results of these studies should allow veterinarians to disabuse themselves of the six assumptions related to protein intake set forth at the beginning of this article. It is clear that the concept of increased workload, protein intake causing injury to the kidneys, and reduced protein intake slowing the progression of renal disease are incorrect. The other three assumptions dealing with hyperkalemia, acidosis, and uremic toxin require comment. Hyperkalemia was not found in the above studies related to increased dietary protein. The ability to excrete potassium and maintain a normal serum potassium concentration until the very last stages of chronic renal failure has been studied in detail in dogs.[37,38] The secretory mechanism in the distal tubule represents the major site for enhanced potassium excretion during renal failure. Potassium balance is maintained in chronically uremic dogs even in the presence of changing rates of potassium intake, changing rates of excretion of sodium, phosphorus, and ammonium. Acidosis is also uncommon due to altered tubular mechanisms in dogs with reduced renal function.[39–41] The dog is unique in that the fractional reabsorption of bicarbonate increases after reduced kidney function. This enhanced ability to reabsorb bicarbonate prevents acidosis and is present in spite of tubular adjustment to regulate other electrolytes such as sodium, potassium, and phosphate. Finally, the concept of dietary protein being responsible for so-called "uremic toxin" has not been proven in any species despite extensive study.[42]

Dietary Protein and Progression of Renal Failure in Humans

The controversy of dietary protein restriction in humans had been perpetuated by anecdotal reports and uncontrolled clinical studies since the early 1960s. In view of the Brenner hypothesis, the National Institutes of Health funded an extended multicenter study, which recruited 585 patients with chronic renal failure. Patients were fed a standard protein diet and a low-protein diet for 18 to 45 months. Measurement of GFR and standard chemistry measurements were used. The mean decline in GFR at 3 years did not significantly differ between diet groups.[43] Among patients with

more severe renal insufficiency, a very low protein diet compared to a low protein diet did not significantly slow the progression of renal disease.

Advantages and Disadvantages of Dietary Protein Restriction in Dogs

Based on the previous data, the only advantages appear to be a lowering of BUN and the possibility of reduced nausea. Quantifying the value of these effects has not been reported in dogs. On the contrary, there appear to be disadvantages to reduced protein intake. These include reduced kidney function as measured by GFR and renal plasma flow, possibility of a negative nitrogen balance, and the promotion of a catabolic state in the presence of proteinuria. In practical application the use of a vague dietary recommendation appears to lead to complacency about long-term surveillance of the animal or the need for individualized specific treatment. Because some sort of management appears available, the search for a more specific etiologic diagnosis is usually not mounted. Finally, the use of arbitrary diets leads to a delusion of ourselves and clients about treatment and increases the cost to owners.

Disadvantages to reduced protein intake include reduced kidney function as measured by GFR and renal plasma flow, possibility of a negative nitrogen balance, and the promotion of a catabolic state in the presence of proteinuria.

Why Is Dietary Alteration Still Used if There Is No Proven Benefit?

The continued use of protein restriction in the absence of scientific evidence deserves thoughtful consideration. I would suggest that the dogma and mythology of a possible benefit are so embedded in the thought process of veterinarians and owners that these cannot be easily dislodged despite the scientific evidence. I would refer to this as the myth of dietary protein and characterize it as a negative myth.

What is a myth? A myth is a way of making sense of a difficult and senseless world. Myths give a society a degree of relief from neurotic guilt and excessive anxiety. Philosophers, psychiatrists, and theologians tell us that humans have always needed myths. Myths are a self-interpretation of our inner selves in relation to a larger world. All societies and individuals are built on a series of myths that are not readily apparent. If we are not given myths by society, we invent them to make sense of our personal experiences.[44]

There are both positive and negative myths. Positive myths support and validate our self-worth. They provide guidance and support. These positive myths are used as important patterns in human consciousness, which allow us to cope with a difficult world, as we are reminded by the psychiatrist Rollo May,[44] Carl Jung,[45] and philosophers Mortimer Adler[46] and Joseph Campbell.[47] There are many in our contemporary popular culture, though profoundly mistaken, who consider all myths as falsehood. I would consider a truly negative myth as one that misleads or has destructive effects. These could be termed pseudomyths or exaggeration and they appear to be almost magical. These are associated with beliefs without benefit or responsibility.

There are many types of myths: personal, societal, and professional. We use personal myths to develop our identity, image, and moral values. We use myths to define ourselves in a community. Societal myths include the New World, the Western frontier, the lone cowboy, national heroes, and the so-called American Dream. Professional myths in veterinary medicine include the images associated with the stories of James Herriott, the gentle doctor as projected by our organized profession, and the power of healing related to modern science.

Are there conflicts between science and myth? As it turns out, many of our scientific theories are a kind of mythology. Many scientific discoveries begin as myths or have their original questions in myths. In many ways, science is the critique of myth (W.B. Yeats).[44]

Why Relate Protein Restriction to Myth?

I suggest that we have used the myth of dietary protein restriction because it is psychologically reassuring in the face of life-threatening illness. Chronic renal failure presents multiple difficult problems in the absence of adequate medical treatment despite all efforts to date. In the absence of dialysis, which is not practical for the vast majority of animals, and renal transplantation, which is not successful

in the dog because of immunologic barriers, medical treatment has little to offer. Most cases are presented late in their natural course, are usually irreversible, and are usually attendant with a uniform pattern of failure and eventual death over months. Because of these factors, a sense of frustration, embarrassment, and even guilt arises in the veterinarian and owner. Veterinarians grasp for something to offer to maintain our professional position, status, and power in this dilemma with the owner. Dietary protein restriction is simple, relatively inexpensive, and usually not harmful and has the ring of authority. We can offer vague but firm assurance of its value since it has been on the scene for so long. Owners sense this dilemma and appreciate our efforts. This is an ideal circumstance to trap oneself and the client in a false myth.

Why Have We Chosen to Keep the Reduced Protein Myth?

The myth has been maintained even in the past decade despite negative scientific evidence because the dogma has persisted about its value for the past 40 years. If we as professionals are uncertain about the facts concerning a controversy, we are likely to put ourselves in someone else's hands who appears to have authority. Power to command this authority is in the hands of commercial advertisements that promote these special products with misleading messages. Marketing is aggressively aimed at veterinarians and owners alike. There is a profit motive for veterinarians to sell these diets. The public has a nutritional mania and preoccupation with diet in our society. Dietary change has assumed the status of medical treatment using such terms as intervention, maintenance, and correction. The profession and the public do not appreciate that advertising claims come without proof in the case of diets. Owners can easily be enrolled to accept such diet change because they feel they are involved in doing something constructive. Professional responsibility has been lost in this case. The situation can remind us that we are part of an uncritical profession with little review or standards. When scientific proof fails to justify a practice, a false myth may likely live on.

In conclusion, the continued existence of this false myth about dietary protein is an uncomfortable reminder of the lack of sophistication, lack of critical thought, and reliance on oversimplified and attractive dogma that persists in our profession. This is only one example of many false myths, misinformation, and partial truths that are repeated from decade to decade. Until a more critical approach with standards and oversight are brought to bear in our profession, we will likely continue to be ensnared in false myths despite the presence of sound science.

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