The Effect of Diet on Lower Urinary Tract Diseases in Cats[1]

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ABSTRACT Because dietary ingredients and feeding patterns influence the volume, pH and solute concentration of urine, diet can contribute to the etiology, management or prevention of recurrence of some causes of lower urinary tract disease. Most research assessing the effect of diet has focused on the latter two aspects, primarily because of interest in struvite urolithiasis. Manipulation of urine pH through dietary means has proven an effective tool for the management and prevention of struvite urolithiasis; acidification of urine, however, may be a risk factor for calcium oxalate urolithiasis, which now appears to occur with approximately equal frequency in cats. Prediction of urine pH from dietary analysis would thus be a valuable tool, but considerable further research is required before this can be achieved with commercial canned foods. With the growing importance of urolith types other than struvite, alternatives to the measurement of urine pH are required to assess critically the likely beneficial (or detrimental) effects of manipulation of nutrient profile. Measurement of urinary saturation may permit the development and fine tuning of nutrient profiles aimed at controlling lower urinary tract diseases in cats that are associated with a range of different mineral types. The majority of cats with signs of lower urinary tract disease do not, however, have urolithiasis; indeed, no specific cause can be established in most of these cats. Recent observations suggest that recurrence rates of signs in cats classified as having idiopathic lower urinary tract disease may be more than halved if affected animals are maintained on high, rather than low moisture content diets. J. Nutr. 128: 2753S–2757S, 1998.

KEY WORDS: • *cats* • *lower urinary tract diseases* • *urine volume* • *urine pH* • *urinary saturation*

Clinical disorders of the lower urinary tract of cats are not new phenomena. Kirk (1925), for example, described "retention of urine" as a very common condition in cats. He also noted that the most common cause of the problem was obstruction of the urethra by a sabulous material; less frequent causes were cystic or urethral calculi. Blount (1931) noted that seven different types of urinary calculi could occur in cats, and that "triple phosphates" (presumably magnesium ammonium phosphate) were present in the majority of calculi deposited in alkaline urine. Milks (1935) recorded only one urethral calculus from a cat in his own studies, but suggested that there was evidence indicating that they were fairly common in cats. This is in contrast to the observations of Krabbe (1949) who noted no examples of "real stone formers" in a series of over 1000 cats seen at the Royal Veterinary and Agricultural College in Copenhagen throughout the 1930s and 1940s. "Sedimentation" of the urine was reported, however, in ~1% of cases. These observations demonstrate that uroliths and urethral plugs have afflicted cats for many years. Although they are difficult to relate to more recent data, the observation by Krabbe of an ~1% incidence is strikingly similar to the estimates of 0.64 and 0.85% reported more recently in Europe and the U.S. (Lawler et al. 1985, Walker et al. 1977).

The term feline urological syndrome (FUS)[3] was coined in 1970 to describe "the feline disease syndrome characterized by dysuria, urethral obstruction, urolithiasis and hematuria . . ." (Osbaldiston and Taussig 1970). Interestingly, despite use of the term urolithiasis in the definition of FUS, no occurrences of urolithiasis appeared among the cases reported (Osbaldiston and Taussig 1970). A study of 46 cats with "FUS" led to the conclusion that "FUS . . . may not be a single disease entity, but rather a group of separate urological problems." Thus the term FUS describes the presence of signs of lower urinary tract disease without implying any specific cause. Subsequent epidemiologic studies identified many risk factors associated with FUS (Willeberg 1984). Proposed dietary influences, the results of many diet-related studies and the fact that struvite (the stone most commonly associated with FUS) is composed of magnesium, ammonium and phosphorus led toward the conclusion that most cases of FUS were diet induced and away from investigation of other potential causes. Noting the confusion that subsequently arose surrounding the term FUS, it has been proposed that it be used either as a synonym for lower urinary tract disorders in cats (Osborne et al. 1984) (Osbaldiston and Taussig's original meaning) or abandoned altogether

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[3] Abbreviations used: RUS, feline urological syndrome; PRSL, potential renal solute load; UTI, urinary tract infection.

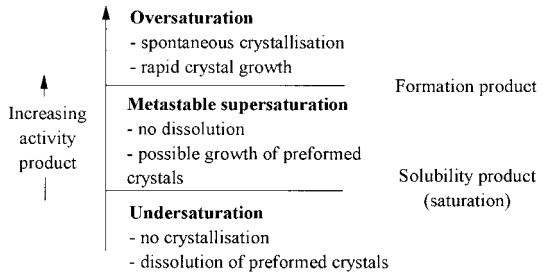

FIGURE 1 Effect of changing activity product on saturation and its effect on crystallization and crystal growth. Modified from Markwell and Buffington (1994) with permission.

(Markwell and Buffington 1994). It has been proposed that signs of lower urinary tract disease in the absence of a specific diagnosis be simply called idiopathic lower urinary tract disease; in cases in which a specific cause is identified, the appropriate descriptive term should be used (Markwell and Buffington 1994).

WHAT ARE THE MAIN CAUSES OF SIGNS OF LOWER URINARY TRACT DISEASE IN CATS IN THE 1990S?

Two detailed investigations of specific causes of signs of lower urinary tract disease in cats have been reported. The first study described 143 cases of hematuria and dysuria, collected between 1982 and 1985 (Osborne et al. 1989, Kruger et al. 1991). Urethral plugs were present in 32 cases, urolithiasis without urinary tract infection (UTI) in 30 cases, UTI alone in two cases and UTI with uroliths in two cases. Seventy-seven cases were classified as idiopathic. Idiopathic disease was present in ~69% of the nonobstructed cats.

In a more recent study, 132 cats with signs of lower urinary tract disease were evaluated by the Ohio State University urology service (Buffington et al. 1997). Twelve of these cats had urethral obstruction and a further 11 had concurrent systemic disease. Etiologies were not reported in the obstructed cats. Specific causes for the signs of lower urinary tract disease were identified in 29 of the remaining cats. Urolithiasis (eight struvite, seven calcium oxalate, one unknown) was present in 16 cats (14.7% of nonobstructed cats without concurrent systemic disease), anatomic defects in 12 (this included one of the cats with urolithiasis), neoplasia in 2 (this included one cat with urolithiasis), and urinary tract infection in 1. Ten cats were considered to have behavioral abnormalities and 70 had idiopathic cystitis (64.2% of nonobstructed cats without concurrent systemic disease). These data stress the importance of idiopathic disease; it is interesting to note that the proportion of nonobstructed cases with idiopathic disease was similar in both studies, despite the 10-y gap between them. The more recent study does show, however, that urolithiasis remains an important cause of lower urinary tract disease in cats. It also suggests that two types of urolith predominate (struvite and calcium oxalate), an observation supported by extensive data on quantitative analysis of uroliths (Kirk et al. 1995, Osborne et al. 1995a and 1995b).

DOES DIETARY MODIFICATION HAVE A ROLE IN THE MANAGEMENT OR PREVENTION OF ANY OF THE LOWER URINARY TRACT DISEASES SEEN IN CATS IN THE 1990S?

Diet can contribute to the etiology, management or prevention of recurrence of some of these causes of lower urinary tract disease because dietary ingredients and feeding patterns influence the volume, pH and solute concentration of urine. Knowledge of these effects of diet and of the specific cause of signs in individual cases of lower urinary tract disease enables identification of those cases in which modification of the diet may truly be of value. Augmenting urine volume may be a reasonable prophylactic measure for a number of types of lower urinary tract disease. If the influence of diet on this parameter is set aside, dietary modifications may be appropriate only in the cases of lower urinary tract disease in which precipitation of minerals plays a significant part [based on the data cited above, urethral plugs were present in~22% and uroliths in ~13–22% of cases of lower urinary tract disease (Buffington et al. 1997, Kruger et al. 1991, Osborne et al. 1989)]. Furthermore, although dietary recommendations appropriate to the management of some mineral types are well developed, those for other types (particularly calcium oxalate) require extensive further research.

DOES AUGMENTING URINE VOLUME HAVE A ROLE IN MANAGING OR PREVENTING ANY OF THE LOWER URINARY TRACT DISEASES SEEN IN CATS IN THE 1990S?

Most research relating diet to lower urinary tract disease in cats has focused on mineral content, or more recently, on the effect of diet on urinary pH; much less research has been devoted to the effect of diet on urine volume or specific gravity. It can be predicted from theoretical considerations that increasing urine volume for a given solute load has a greater influence on the likelihood of struvite crystal formation than a reduction in urinary magnesium concentration (Markwell and Buffington 1994, Marshall and Robertson 1976). This concept has also been demonstrated experimentally in studies of struvite activity product in feline urine (Buffington et al. 1990).

In addition, enhancing urine volume may increase the frequency of urination, which should hasten crystalloid and crystal transit time through the urinary tract, thus reducing the potential for crystal growth. Holme demonstrated that hematuria, induced in cats by feeding a high magnesium, low moisture–containing diet, could be abolished by feeding the same diet as a slurry containing 80% water (Holme 1977). Of particular importance, perhaps, are recent observations in cats classified as having idiopathic lower urinary tract disease. The proportion of cats showing recurrence of lower urinary tract disease was significantly less in a group fed a canned, commercial acidifying diet (11%) than in another group fed the dry formulation of the same product (39%) (Markwell et al. 1998). The mechanism for this effect was not determined in the study, but was considered likely to be the result of changes in the concentration or type of solutes in urine and/or changes in urine volume.

Epidemiologic studies of signs of lower urinary tract disease conducted in the 1970s implicated dry cat foods as a risk factor (Reif et al. 1977, Walker et al. 1977, Willeberg 1984); more recently, consumption of dry foods has been implicated as a risk factor specifically for idiopathic lower urinary tract disease (Buffington et al. 1997). Multiple diet-related factors may be involved with this increased risk, but included within these is the tendency for cats to produce smaller volumes of more concentrated urine when fed dry foods (Burger et al. 1980, Gaskell 1985). Explanations originally offered for these observations were that cats might not repair a water deficit as well as dogs, and that cats fed dry foods take in less water. These interpretations clearly require further discussion.

TABLE 1

Results from regression of mean urine pH values on dietary base excess (BE) in cats fed canned foods[1]

Base excess calculation	*P*-value	R^2(%)	Regression equation
A 2[Ca] + 2[Mg] + [K] + [Na] − 2[P] − 2[Met] − [Cl]	<0.001	24.0	pH = 6.53 + 0.00321 BE(A)
B 2[Ca] + 2[Mg] + [K] + [Na] − 1.8[P] − 2[Met] − [Cl]	<0.001	27.7	pH = 6.45 + 0.00328 BE(B)
C 2[Ca] + 2[Mg] + [K] + [Na] − 2[P] −2[Met] − [Cl] − 2[Cys]	<0.001	21.6	pH = 6.57 + 0.00297 BE(C)
D 2[Ca] + 2[Mg] + [K] + [Na] − 1.8[P] − 2[Met] − [Cl] − 2[Cys]	<0.001	22.9	pH = 6.51 + 0.00295 BE(D)

[1] Units are mmol/kg dry matter; data from Smith et al. (1995).

In studies of five cats and three dogs, Adolph (1947) found that both species incurred similar water deficits in 48°C environments when water was available. After heat exposure without available water, dogs replaced moderate, but not severe deficits more rapidly than did cats. Both species, however, drank proportionately more than humans when dehydration exceeded 5%. These results suggest that differences in response to dehydration between dogs and cats, if they exist at all, are relatively small and probably not clinically relevant as a risk factor for lower urinary tract disease.

It is also doubtful that cats reduce water intake in some unusual way when fed dry foods. It has been shown that cats fed diets containing differing amounts of moisture drink quite different amounts of water (Burger et al. 1980). A large number of these differences may be accounted for by changes in the potential renal solute load (PRSL) of the diets fed. The PRSL of a diet is the amount of solute, i.e., minerals and nitrogen, that must be excreted in the urine (Kohn and DiBartola 1992, Ziegler and Fomon 1989). The PRSL has been estimated as the urea (mg nitrogen/28) plus the sum of the sodium, chloride, phosphorus and potassium content of the diet (mg N/28 + Na + Cl + K + P) (O'Connor and Potts 1969). Calculations of PRSL reveal that the majority of diet-induced changes in water intake (Burger et al. 1980, Jackson and Tovey 1977, Kane et al. 1981), or urine formation (Sauer et al. 1985) reported in several studies can be explained by the solute load of the diet.

Similar data were reported in another study involving cats fed a single diet to which increasing amounts of water were added (Gaskell 1985). When the water content of the food was 10 or 45%, total water intake, urine volume and specific gravity were not different among groups. When the water content of the food was increased to 75%, however, total water intake and urine volume increased, and urine specific gravity decreased. Because the diet was the same in all cases, water intake (from food) probably increased as a consequence of increased food intake to meet energy needs from the water-diluted diet. Thus the differences in urine volumes and specific gravities observed in some of the studies discussed may be more a reflection of differences in the PRSL and/or the energy content of dry and wet diets, rather than moisture content per se. In consequence, if a cat is changed from a dry to a wet diet as part of a management program for lower urinary tract disease, it is important to ensure that the intended increases in urine volume and decreases in specific gravity actually occur.

DOES MANIPULATING URINE PH HAVE A ROLE IN MANAGING OR PREVENTING ANY OF THE LOWER URINARY TRACT DISEASES SEEN IN CATS IN THE 1990S?

Dietary manipulation has been a mainstay of the management and prevention of struvite urolithiasis in cats for some years, primarily because of the influence of dietary ingredients on urine pH. Urine pH is a much more important determinant of struvite formation than is the magnesium content of the diet (Buffington et al. 1985, Buffington 1988, Marshall and Robertson 1976, Taton et al. 1984). Changing pH has a proportionately much greater effect on changing struvite activity product (solute activity is the concentration of crystalloid that is free to react with other solutes in a solution, and is the ultimate determinant of crystal formation) than changing the concentration of one or more of the crystalloid components of struvite. Reduction of urinary pH through dietary manipulation is thus the most reliable means of creating urine that is undersaturated with struvite; under these circumstances, crystallization and crystal growth will not occur, and preformed material will dissolve (**Fig. 1**) (Buffington 1988, Markwell and Buffington 1994). Acidification of the urine may not be appropriate, however, in the management of other types of urolith. It has been suggested, for example, from epidemiologic data that acidifying diets, and in particular those that result in a urine pH <6.29, may increase the risk of calcium oxalate formation (Kirk et al. 1995, Osborne et al. 1995b). Given this background, the ability to predict the likely urinary pH resulting from consumption of a particular diet from its analysis would be of considerable value.

Major dietary contributors of acid include the oxidation of sulfur amino acids and the balance of metabolizable anions and cations (Brosnan and Brosnan 1982, Patience and Wolynetz 1990). Oxidation of organic cations yields hydrogen ions, whereas oxidation of organic anions consumes them (Lennon et al. 1966). The net concentration of these organic ions can be measured indirectly by analyzing inorganic cations and anions in the diet (Austic and Patience 1988). This approach to predicting the influence of diet on urine pH and acid base balance has been evaluated in a number of species, including humans (Lennon et al. 1966), pigs (Patience and Wolynetz 1990) and cats (Kienzle et al. 1991, Kienzle and Schuknecht 1993, Kienzle and Wilms-Eilers 1994).

The initial studies reported in cats evaluated whether the dietary "base excess" [calculated from the sum of "alkalogenic" components (calcium, magnesium, sodium and potassium) minus the sum of "acidifying" components (phosphorus, chloride, methionine and cysteine)] could be used to predict urinary pH (Kienzle et al. 1991, Kienzle and Schuknecht 1993). These studies suggested that there was a highly significant correlation between dietary base excess and mean urine pH. They involved, however, only six wet and four dry commercial diets. We have conducted studies to determine if the same principle could be applied across a much wider range of canned commercial foods. In the course of these studies, 32 canned diets from a range of manufacturers were evaluated (Smith et al. 1995). These were fed to groups of four to eight healthy, adult cats for between 10 and 23 d. The cats were housed individ-

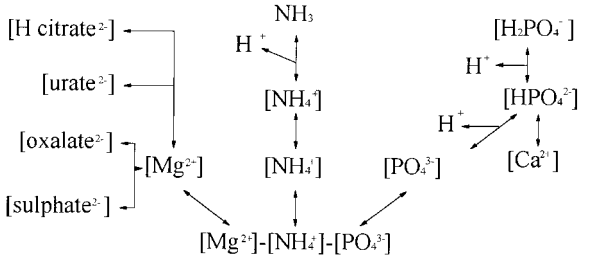

FIGURE 2 Some solutes affecting crystallization in urine. Other factors affecting crystal formation include time, temperature, and the presence, absence and effectiveness of endogenous protein crystallization inhibitors.

ually in purpose-built lodges, and urine pH was measured continuously using an automated system that has been described previously (Markwell and Smith 1993). Dietary analyses were used to calculate the base excess for each food using four different equations (**Table 1**). Individual mean urine pH values were then regressed on individual base excess intakes (calculated for each cat during each trial using its mean food intake) to investigate the suitability of a linear relationship. Although all four methods of calculating dietary base excess provided significant linear relationships, none of the resultant regression equations explained >28% of the variability seen in urine pH values (Table 1).

A second approach to evaluating the data was to establish whether various combinations of the individual components used to calculate dietary base excess could be used to predict urinary pH. When the individual intakes of each component were regressed against individual urine pH results, the best linear regression procedure suggested a more effective relationship to be the following:

$$pH = 6.42 + 0.572[Ca] + 0.727[Na] + 0.674[K] - 0.731[P] - 0.546[\text{methionine}] - 0.183[Cl]$$

(units are g/100 g diet as fed). This relationship accounted for 35.5% of the variation seen in pH values. The signs of the coefficients were in agreement with expectations, i.e., increases in pH were positively correlated with the calcium, sodium and potassium content, and negatively correlated with the methionine and phosphorus content of the diet. These data indicate that dietary content may explain a significant proportion of the variation seen in the urine pH of meal-fed cats. More research is required, however, before dietary analysis can be used to yield an accurate prediction of the urine pH of cats fed commercial canned foods.

DIET AND URINARY SATURATION

The primary goal of dietary manipulation to alter urinary pH and solute concentration is to achieve urine that is undersaturated with calculogenic crystalloids, although as described above, enhancement of urine volume may have the added benefit of increasing the frequency of urination, and hence reducing retention time. Undersaturation of urine is a prerequisite for urolith dissolution, and supersaturation with calculogenic crystalloids is an essential requirement for formation of a crystal nucleus, the initial step in development of a urine crystal (Fig. 1) (Buffington 1988, Markwell and Buffington 1994, Osborne et al. 1995a).

The study of the effects of diet on urinary saturation requires determination of solute activity. Although the concentration of ions in a solution, e.g., a urine sample, can be measured relatively easily, this is not a measure of activity because an individual ion may form a complex with many other ions; magnesium, for example, may form complexes with phosphate, citrate, oxalate and sulfate (**Fig. 2**). The extent to which these complexes form can be predicted from known dissociation constants, allowing free ion concentrations to be predicted. Noncomplexed ions are further restricted in their movement by the nonspecific effect of other ions in solution, an effect that varies with the electrical field strength of the solution. This effect is represented by the term "activity coefficient" (Senior and Finlayson 1986). Computer programs are available to calculate urinary saturations (Werness et al. 1985), although a series of complex analyses are required after collection. One further limitation is that the calculations do not account for some additional factors such as urine proteins which may influence crystal formation. Despite these difficulties, measurement of activity products provides a more critical appraisal of the likely beneficial, or detrimental effects of manipulation of nutrient profile than, for example, assessment of urine pH. These techniques may permit the development and fine tuning of nutrient profiles in cats with the aim of controlling lower urinary tract diseases associated with a range of different mineral types.

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