Chapter 46

Feline Lower Urinary Tract Diseases

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"There is a great difference between knowing and understanding: you can know a lot about something and not really understand it."
Charles F. Kettering

CLINICAL IMPORTANCE

Diseases of the feline lower urinary tract involve the urinary bladder or urethra and may be associated with varying combinations of signs including dysuria, hematuria, pollakiuria, stranguria and periuria (i.e., urinating in inappropriate locations). Feline lower urinary tract diseases (FLUTD) encompass many diverse causes; however, this chapter will focus primarily on the three most common: 1) idiopathic lower urinary tract disease, often called feline idiopathic cystitis (FIC), 2) urolithiasis and 3) urethral plugs. Nutritional management is an important component in the treatment of cats with these lower urinary tract disorders. Nutritional management is recommended for cats with FIC together with environmental enrichment and behavioral management. Nutritional management also is indicated for dissolving struvite uroliths and decreasing risk for recurrence of struvite uroliths and urethral plugs and calcium oxalate uroliths.

The true incidence of the various forms of FLUTD is unknown; however, previous estimates in the United States and the United Kingdom have been approximately 0.85 and 1.5% per year, respectively (Lawler et al, 1985; Willeberg, 1984). These estimates were based on presence of clinical signs and did not consider subsets of cats with specific diagnoses, such as struvite urolithiasis or FIC. In a 1995 survey of primary care veterinary hospitals in the U.S., prevalence of lower urinary tract disorders among 15,226 cats was 3% (Lund et al, 1999). The proportional morbidity ratio (i.e., frequency with which cases are seen at a veterinary hospital) of cats with lower urinary tract diseases has been reported to be 4.6% of those evaluated in primary care hospitals and 7 to 8% of those at North American veterinary teaching hospitals (Bartges, 1997; Kirk et al, 2001; Lekcharoensuk et al, 2001). Proportional morbidity ratios, however, are not reliable estimates of disease incidence because they are affected by other parameters including type of veterinary hospital, interest and expertise of veterinarians at the hospital and economic status of clients served by the hospital.

Another measure of the importance of a clinical problem is the degree of owner concern and recognition. In an animal health survey prepared for the Morris Animal Foundation, 1,211 owners indicated that their top feline health concerns were urinary diseases (n = 576; 48%), dental problems (29%), cancer (27%) and feline leukemia virus infection (27%) (MAF, 1998). In a survey of current and previous donors, kidney and urinary disease (43%) were the most common feline health concerns identified by respondents (MAF, 2005). According to

Table 46-1. Prevalence of feline lower urinary tract diseases in four clinical studies.

Diagnosis*	Occurrence among cats with lower urinary tract signs (%)			
Idiopathic (FIC)	63	55	64	57
Urethral obstruction	19	21**	na	58***
Urethral plugs	nr	21	na	10
Uroliths	19	23	15	22
Behavioral disorder	nr	nr	9	0
Incontinence	4	0	0	0
Bacterial UTI	3†	3	1	8
Anatomic anomaly	0.3	nr	11	0
Neoplasia	0.3	0	2	0
Unknown	0	0	0	3
	Study characteristics			
Study type	Retrospective††	Prospective†††	Prospective‡	Prospective‡‡
Population	All clinical presentations	All clinical presentations	Non-obstructed clinical presentations	All clinical presentations
Collection period	1980-1997	1982-1985	1993-1995	2000-2002
Cases (n)	22,908	141	109	77

Key: FIC = feline idiopathic cystitis, na = not applicable, nr = not reported, UTI = urinary tract infection.
*Some cats had multiple disorders.
**All cats had urethral obstruction associated with urethral plugs.
***Included 24 cats with FIC, 13 cats with uroliths and eight cats with urethral plugs.
†Another 9% were reported to have undefined infection
††Adapted from Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. Journal of the American Veterinary Medical Association 2001; 218: 1429-1435.
†††Adapted from Kruger JM, Osborne CA, Goyal SM, et al. Clinical evaluation of cats with lower urinary tract disease. Journal of the American Veterinary Medical Association 1991; 199: 211-216.
‡Adapted from Buffington CAT, Chew DJ, Kendall MS, et al. Clinical evaluation of cats with non-obstructive lower urinary tract disease: 109 cases (1993-1995). Journal of the American Veterinary Medical Association 1997; 210: 45-50.
‡‡Adapted from Gerber B, Boretti FS, Kley S, et al. Evaluation of clinical signs and causes of lower urinary tract disease in European cats. Journal of Small Animal Practice 2005; 46: 571-577.

Table 46-2. Prevalence of lower urinary tract diseases in 81 cats over 10 years of age evaluated at the University of Georgia Veterinary Teaching Hospital between 1980 and 1995.*

Disorders	Cats (%)
UTI	46
UTI and uroliths	17
Uroliths	10
Urethral plugs	7
Trauma	7
FIC	5
Incontinence	5
Neoplasia	3

Key: UTI = urinary tract infection, FIC = feline idiopathic cystitis.
*Adapted from Bartges JW. Lower urinary tract disease in geriatric cats. In: Proceedings. 15th Annual Veterinary Medical Forum, American College of Veterinary Internal Medicine, Lake Buena Vista, FL, 1997: 322-324.

data from VPI Pet Insurance, lower urinary tract disease was the most common reason pet owners filed a claim for reimbursement of veterinary expenses for their cats in 2006; gastric upsets and kidney disease were the second and third most common reasons (2007). Finally, inappropriate elimination often accompanies FLUTD and is the most common behavioral problem for which pet owners seek professional counsel. It also is the primary behavioral reason why pet owners relinquish their cats to shelters (Beaver, 1989; Neilson, 2003; Salman et al, 2000). Therefore, correct diagnosis and management of underlying causes of periuria are important for maintaining the pet-family bond.

CAUSES OF FLUTD

Many different lower urinary tract diseases occur in cats; however, only a few are common and these may differ depending on the cat's age, presence of concomitant diseases and geographic location. If clinical signs are present and a specific cause is not identified after appropriate evaluation, FIC is the most likely diagnosis. Based on findings from four clinical studies, the three most common lower urinary tract diseases in cats are FIC, urolithiasis and urethral plugs (Lekcharoensuk et al, 2001; Kruger et al, 1991; Buffington et al, 1997; Gerber et al, 2005) (**Table 46-1**). In cats older than 10 years, urinary tract infection (UTI) and uroliths were the most common causes of lower urinary tract signs (**Table 46-2**) (Bartges, 1997). In a study from Norway, 33% of 134 cats with stranguria, dysuria, hematuria and pollakiuria were diagnosed with UTI based on culture of urine obtained by cystocentesis, catheterization or voiding (Eggertsdóttir et al, 2007). No significant difference existed in occurrence of UTI based on methods of sampling in this study. In contrast to previous studies, in which most cats were evaluated at teaching hospitals, 97% of cats in the Norwegian study were first-opinion cases and only 3% were referred. Before the approach to management of cats with signs of FLUTD is modified, further evaluation is needed to determine if UTI is a common occurrence in first-opinion cases, and whether there are geographic differences.

Uroliths and urethral plugs are named based on their mineral composition, which is determined by quantitative analysis.

Usually one mineral type predominates; however, the composition may be mixed in some uroliths and plugs. Different mineral types may be dispersed throughout the urolith (i.e., mixed urolith) or organized into separate, discrete bands or layers (i.e., compound urolith). The most common mineral types identified in feline uroliths are struvite (magnesium ammonium phosphate) (**Figures 46-1** and **46-2**) and calcium oxalate (**Figure 46-3**) (Houston et al, 2003; Cannon et al, 2007).[a] Rarely, uroliths are composed of non-mineral substances (e.g., dried solidified blood) (Westropp et al, 2006). Although there have been changes in trends over the past 25 years, struvite and calcium oxalate have remained the most common uroliths in cats (**Table 46-3**). The most recently collected data reveal that struvite is the most common feline urolith followed by calcium oxalate and purine (e.g., urate) (**Table 46-4**). Since 1981, struvite has consistently been the most common mineral type identified in urethral plugs, representing 81 to 87% of plugs analyzed in the U.S. and Canada (**Table 46-5**) (Houston et al, 2003).[a]

Over the past 25 years, several changing trends have been noted in occurrence of feline uroliths (Cannon et al, 2007; Picavet et al, 2007).[a] In 1981, 78% of feline uroliths evaluated at the Minnesota Urolith Center (University of Minnesota) were struvite and only 2% were calcium oxalate.[a] From 1994 to 2001, however, occurrence of calcium oxalate uroliths increased to 55% and struvite decreased to 33%. In 1994, 77% of uroliths from cats in Benelux (Belgium, The Netherlands and Luxemburg) were struvite and 12% were calcium oxalate; however, by 2003, struvite uroliths had decreased to 32% and calcium oxalate had increased to 61% (Picavet et al, 2007). At the Canadian Urolith Centre (University of Guelph, Ontario), approximately 50% of feline urinary bladder uroliths analyzed from 1998 to 2003 were calcium oxalate and 44% were struvite (Houston et al, 2003). Since 2001, the number of struvite uroliths analyzed at the Minnesota Urolith Center has consistently increased whereas the number of calcium oxalate uroliths has decreased (**Figure 46-4**). At the Gerald V. Ling Urinary Stone Analysis Laboratory (University of California, Davis), struvite-containing uroliths were the predominant mineral type analyzed from 1985 to 1993. Thereafter, calcium oxalate became more common (Cannon et al, 2007). From 2002 to 2004; however, 44% of feline uroliths submitted were struvite and 40% were calcium oxalate. The cause(s) for these changing trends is unknown and needs further study.

Urethral obstruction is a complication of both uroliths and urethral plugs, particularly in male cats (Bovee et al, 1979; Kruger et al, 1991; Gerber et al, 2007). During the past 20 years, the number of perineal urethrostomies performed at veterinary teaching hospitals in the U.S. and Canada has declined, which has paralleled a similar decline in the frequency of urethral obstructions, urethral plugs or urethroliths (**Figure 46-5**) (Lekcharoensuk et al, 2002). These trends coincide with widespread use of specially formulated foods to minimize struvite crystalluria in cats. This is important considering that struvite has consistently been the predominant mineral type in feline urethral plugs during the same time period.

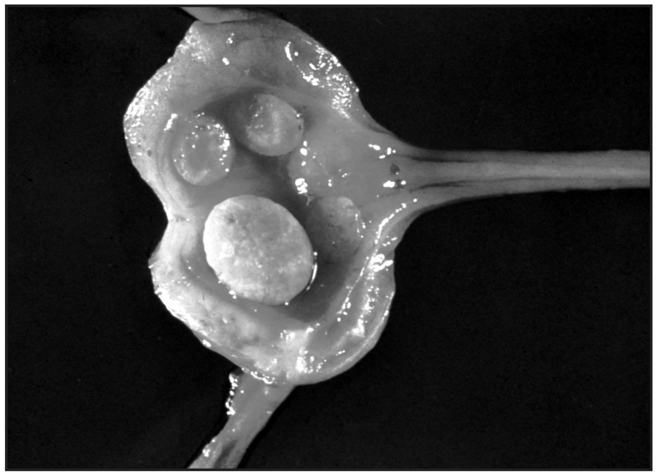

Figure 46-1. Urinary bladder from a cat with struvite urolithiasis. Note the thickened urinary bladder wall and several struvite uroliths within the urinary bladder lumen.

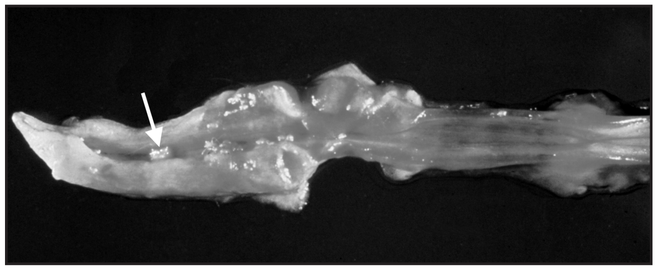

Figure 46-2. Penis and urethra from a cat with urethral obstruction. Note the small struvite urolith (white arrow) in the penile urethra. Uroliths consist of small amounts of matrix and macroscopic crystalline mineral concretions. They are less common causes of urethral obstruction in male cats than urethral plugs (**Figure 46-12**).

Figure 46-3. Calcium oxalate dihydrate urolith removed from the urinary bladder of a cat with hematuria and dysuria.

Although data from urolith centers are helpful, this information cannot be used to determine incidence (i.e., rate of occurrence of new cases in the population) or prevalence (i.e., total number of urolith cases during a given time) of urolith types. Not all cats with uroliths are diagnosed or treated (e.g., they may not receive veterinary care). In addition, not all uroliths are submitted for quantitative analysis and not all laboratories routine-

Table 46-3. Mineral composition of feline uroliths submitted for quantitative analysis to three centers.

Predominant mineral type	Uroliths submitted during collection period (%)		
Struvite	43.5	43	44
Calcium oxalate	45.4	53	50
Purine	5.0*	10**	3
Compound	3.4	–	–
Mixed	1.0	13***	–
Matrix	0.9	–	–
Calcium phosphate, apatite and brushite	0.3	6	0.1
Cystine	0.1	0.1	–
Silica	0.04	0.4	–
Dry solidified blood	Included with matrix	1	–
Summary information for data sources			
Urolith center	Minnesota Urolith Center†	Gerald V. Ling Urinary Stone Laboratory††	Canadian Urolith Centre†††
Collection period	1981-2008	1985-2004	1998-2003
Uroliths (n)	102,191	5,230	4,866

*Includes uroliths that contained 70 to 100% urate, uric acid or xanthine.
**Includes uroliths that contained any amount of urate.
***Includes mixed and compound uroliths.
†Adapted from Osborne CA, Lulich JP. Unpublished data. Minnesota Urolith Center. University of Minnesota, St Paul, 2009.
††Adapted from Cannon AB, Westropp JL, Ruby AL, et al. Evaluation of trends in urolith composition in cats: 5,230 cases (1985-2004). Journal of the American Veterinary Medical Association 2007; 237: 570-576.
†††Adapted from Houston DM, Moore AE, Favrin MG, et al. Feline urethral plugs and bladder uroliths: A review of 5,484 submissions 1998-2003. Canadian Veterinary Journal 2003; 44(12): 974-977.

Table 46-4. Mineral composition of 11,416 feline uroliths analyzed quantitatively at the Minnesota Urolith Center in 2008.*

Mineral type	Percent
Struvite	49
Calcium oxalate	39
Urate/uric acid	4.9
Compound/matrix/mixed	4.29/0.7/1.0
Calcium phosphate	0.2
Cystine	0.04
Xanthine	<0.01

*Adapted from Osborne CA, Lulich JP. Unpublished data. Minnesota Urolith Center. University of Minnesota, St Paul, 2009.

Table 46-5. Mineral composition of feline urethral plugs submitted for quantitative analysis to two centers.

Predominant mineral type	Urethral plugs submitted during collection period (%)	
Struvite	83.8	81
Calcium oxalate	0.94	6.6
Calcium phosphate	0.55	2.4
Urate	0.13*	1.1
Cystine	0	0.16
Silica	0	0.5
Mixed	2.46	3.6
Matrix (no crystals)	11.11	4.5
Summary information for data sources		
Center location	Minnesota Urolith Center**	Canadian Urolith Centre***
Plugs (n)	6,704	618
Collection period	1981-2008	1998-2003

*Includes eight ammonium acid urate plugs and one xanthine plug.
**Adapted from Osborne CA, Lulich JP. Unpublished data. Minnesota Urolith Center. University of Minnesota, St Paul, 2009.
***Adapted from Houston DM, Moore AE, Favrin MG, et al. Feline urethral plugs and bladder uroliths: A review of 5,484 submissions 1998-2003. Canadian Veterinary Journal 2003; 44(12): 974-977.

ly report urolith data annually. In addition, some urolith types are more likely to be submitted for evaluation than others. For example, struvite uroliths can be dissolved with nutritional management; however, calcium oxalate uroliths are more likely to be removed and submitted for quantitative analysis. This could result in an underestimation of the occurrence of struvite uroliths and overestimation for calcium oxalate uroliths.

Regarding trends in occurrence of feline uroliths, several relevant questions remain unanswered: 1) What is the incidence (i.e., rate of occurrence among all cats, not only those presented for veterinary evaluation) of uroliths and has it changed over the past decades? 2) How has the apparent aging feline population affected the relative frequency of different urolith types (e.g., has this contributed to increased diagnosis of calcium oxalate uroliths)? 3) Does the occurrence of calcium oxalate uroliths appear greater because fewer struvite uroliths are submitted for analysis due to the availability of struvite dissolution protocols? 4) What role has nutritional management played in managing or causing uroliths? 5) Are there common factors that explain increased occurrence of calcium oxalate uroliths in cats, dogs and people? 6) During the time that calcium oxalate uroliths were more common in cats from North America, why were struvite uroliths more common elsewhere (e.g., Australia, Japan)? and 7) Why have most urethral plugs been composed of struvite for more than 25 years whereas other mineral types of uroliths have changed?

PATIENT ASSESSMENT

Each cat presenting with lower urinary tract signs should be thoroughly evaluated to identify the underlying cause(s). To guide initial assessment and need for emergency treatment (e.g., urethral obstruction), it is helpful to categorize patients into one of four clinical presentations, realizing that some cats may have features of several presentations (**Table 46-6**) (Lulich, 2007). A thorough history, physical examination and diagnostic evaluation including urinalysis and some form of diagnostic imaging (i.e., abdominal radiography and/or ultrasound) are indicated for every patient. Individualized treatment recommendations can be made based on these findings.

History

The nutritional history should include information about specific brand(s) of food fed, form (dry, moist, semi-moist or a combination), method of feeding (meal fed, free choice) and whether table food, supplements or treats are offered. Access to other food should also be determined (e.g., other pets in the household that eat different foods, access to food at other households or in the outdoor environment). Trends in water consumption (i.e., increased, decreased, unchanged) should also be noted.

Pet owners should be questioned carefully about: 1) duration and progression of clinical signs (same, better, worse), 2) whether the episode was the patient's first or a recurrence, 3) interval between episodes, 4) previous treatments (medical, surgical, nutritional) and response to therapy, 5) presence of other illnesses, injuries or trauma (current or previous) and 6) presence of systemic signs (e.g., inappetence, vomiting, diarrhea, weight loss). Questions should be asked to determine presence or absence of dysuria, pollakiuria, urinary incontinence, periuria, discolored urine and uroliths or urethral plugs voided during urination. Approximate urine volume and any changes in volume should be determined to distinguish between pollakiuria and polyuria. Owners should be asked about pharmaceutical agents that may be risk factors for urolithiasis (e.g., allopurinol may predispose to xanthine uroliths, excessive use of urinary acidifiers may predispose cats to calcium-containing uroliths).

Physical Examination

The urinary bladder should be palpated carefully to evaluate its size, shape, surface contours and thickness of the bladder wall. The presence of pain or masses within the urinary bladder lumen should also be assessed. Most feline urocystoliths cannot be detected by abdominal palpation; however, hearing a "grating" sound during palpation of the urinary bladder strongly suggests their presence. In male cats, the penis and prepuce should be examined for urethral abnormalities. The kidneys should be evaluated for size, shape, surface contour and symmetry. If possible, the patient should be observed during urination to evaluate the size of its urine stream and detect abnormalities such as discolored urine, pollakiuria, dysuria and stranguria.

Diagnostic Evaluation

Initial diagnostic evaluation of all cats with lower urinary tract signs should include urinalysis and some form of diagnostic imaging (i.e., plain abdominal radiographs, abdominal ultrasound). Additional tests may be indicated in some patients. Because urine sediment examination is an unreliable means of detecting UTI, quantitative urine culture should be performed in all cats with lower urinary tract signs. (See Urine Culture below.) Contrast urethrocystography should be performed to exclude small or radiolucent uroliths, urethral plugs and anatomic defects. If available, cystoscopy can also be used to detect and evaluate disorders of the lower urinary tract (e.g., uroliths, neoplasia). In cats with systemic signs of illness (e.g., inappetence, vomiting, weight loss), a complete blood count and serum biochemistry analysis are indicated; however, these tests are unlikely to be helpful in cats with signs limited to the lower urinary tract.

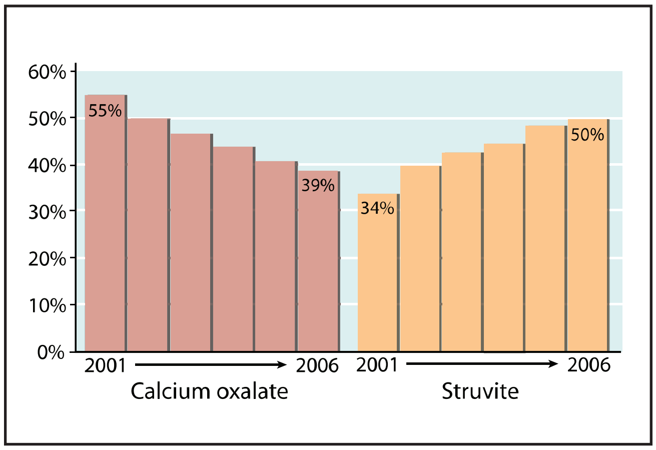

Figure 46-4. Occurrence of calcium oxalate and struvite uroliths analyzed at the Minnesota Urolith Center from 2001-2006. During this six-year period, the number of calcium oxalate uroliths gradually declined with a concomitant increase in struvite uroliths. (Adapted from Osborne CA, Lulich JP. Unpublished data. Minnesota Urolith Center, University of Minnesota, St Paul, 2007.)

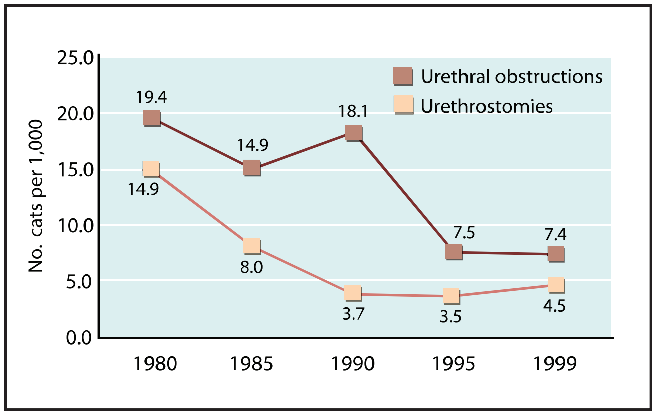

Figure 46-5. The frequency of feline perineal urethrostomies performed at veterinary teaching hospitals in Canada and the United States declined during a 20-year period and paralleled a similar decline in frequency of urethral obstructions and urethral plugs or urethroliths. (Adapted from Lekcharoensuk C, Osborne CA, Lulich JP. Evaluation of trends in frequency of urethrostomy for treatment of urethral obstruction in cats. Journal of the American Veterinary Medical Association 2002; 221: 502-505.)

Urinalysis

Complete urinalysis including determination of specific gravity, dipstick analysis and sediment examination is indicated in all cats with lower urinary tract signs. Because many cats with lower urinary tract diseases have pollakiuria, obtaining an adequate sample for urinalysis may be challenging. Whenever possible, urine should be collected before treatment and evaluated as soon as possible. This is especially important for patients with crystalluria because crystals may begin to form immediately in urine as its temperature decreases. Microscopic examination of urine sediment is essential to confirm the presence of hematuria, pyuria and crystalluria. Examination of unstained urine sediment, however, is an unreliable method of detecting bacteriuria. When compared

Table 46-6. Clinical presentations of cats with various lower urinary tract diseases.*

Presentation	Nonobstructive periuria	Obstructive dysuria	Behavioral periuria**	Urinary incontinence
Probable diagnoses	FIC Uroliths Infection Neoplasia	Urethral plugs Urethroliths Urethral strictures Functional obstruction Blood clots Foreign material	Toileting preferences/ aversions and/or marking with or without medical causes of lower urinary tract disease (e.g., FIC, uroliths, UTI, others)	Neurologic incontinence Anatomic abnormalities Partial obstruction
Initial tests	Urinalysis Diagnostic imaging	Abdominal radiographs Urinalysis	Urinalysis Diagnostic imaging	Neurologic examination Urinalysis Diagnostic imaging
Ancillary tests	Urine culture Abdominal ultrasound Contrast urethrocystography	Serum biochemistry profile Urine culture Contrast urethrocystography Complete blood count	Urine culture Abdominal ultrasound Contrast urethrocystography Coagulation profile Complete blood count	Urine culture Abdominal ultrasound Contrast urethrocystography Intravenous urography Cystoscopy

Key: FIC = feline idiopathic cystitis, UTI = urinary tract infection.
*Adapted from Lulich JP. FLUTD: Are you missing the correct diagnosis? In: Proceedings. Hill's Symposium on Feline Lower Urinary Tract Disease, 2007: 12-19 (www.hillsvet.com/conferenceproceedings).
**May occur with or without hematuria and signs of urinary tract inflammation.

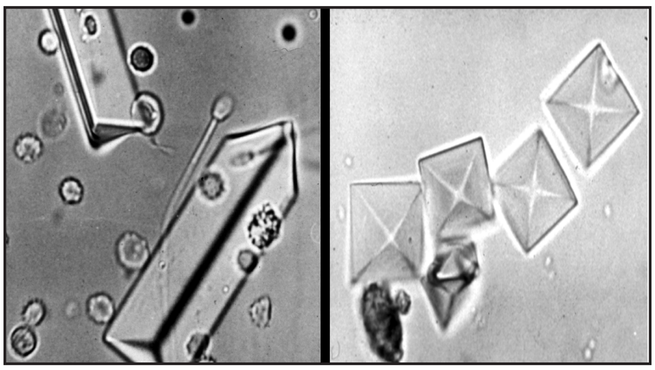

Figure 46-6. Magnesium ammonium phosphate (struvite) crystals (left) typically are colorless, orthorhombic, coffin-like prisms. Struvite crystals may have square or rectangular dimensions, vary in size, may have three to six sides and often have oblique ends. Calcium oxalate dihydrate crystals (right) typically are colorless and have a characteristic octahedral or envelope shape; they resemble small squares with corners connected by intersecting diagonal lines.

with quantitative urine culture, microscopic examination of unstained urine sediment was associated with only an 11% positive predictive value (i.e., the proportion of cats with a positive test that were correctly diagnosed) (Swenson et al, 2004). Bacteria may also be difficult to visualize by routine microscopic examination of urine sediment. Approximately 10,000 rod-shaped bacteria per ml of urine are required for visualization by light microscopy in unstained preparations of urine sediment. Cocci may not be consistently detected if fewer than 100,000 per ml are present. Inability to detect bacteria in urine sediment, therefore, does not exclude their presence. Staining of urine sediment with Wright's, Gram's or new methylene blue stain may significantly improve detection of bacteriuria (Swenson et al, 2004a).

Results of urinalysis are used to: 1) help determine underlying cause(s) of lower urinary tract signs, 2) detect conditions that may predispose to formation of uroliths or urethral plugs, 3) infer mineral composition of uroliths or urethral plugs (**Figure 46-6**) and 4) evaluate response to treatment or preventive measures. Hematuria is a common finding in cats with most lower urinary tract disorders; however, it is uncommon in cats with behavioral periuria (unless it results from a previous medical disorder). Pyuria is uncommon in cats with nonobstructive FIC and behavioral periuria and more often occurs with urolithiasis, urethral obstruction and UTI (Kruger et al, 1991; Osborne et al, 1990).

Several factors influence the number of crystals present in the urine sediment. Because storage at room temperature or refrigeration of urine samples may cause in vitro crystal formation, fresh urine samples should be evaluated ideally within 30 minutes of collection (Sturgess et al, 2001; Albasan et al, 2003). Other factors that affect the presence of crystalluria include volume of urine centrifuged, centrifugation speed and volume of sediment re-suspended and transferred to the microscope slide for evaluation. Consequently, it is difficult to attach clinical significance to the number of crystals observed. In addition to evaluating crystal type, sediment should be evaluated for tendencies of crystals to aggregate. Detection of large aggregates of struvite or calcium oxalate crystals is an important finding when monitoring effectiveness of preventive measures. Crystals only form when urine is supersaturated with crystallogenic materials. Therefore, crystalluria is a risk factor for formation of uroliths and urethral plugs. However, crystalluria alone is not diagnostic for uroliths or urethral plugs (**Box 46-1**). Conversely, urolithiasis is possible without associated crystalluria (Kruger et al, 1991). Crystalluria should be interpreted in the context of the patient's medical history, laboratory methods used and complete diagnostic findings.

Box 46-1. Managing Cats with Crystalluria.

Detection of crystalluria on microscopic examination of urine sediment does not mean a cat subsequently will develop urolithiasis; however, it does indicate increased risk for urolith development. Crystalluria in cats with normal anatomy and physiology of the urinary tract is usually of no clinical significance; these crystals are voided before they grow to sufficient size to interfere with urinary tract function and health.

Crystals that form in vitro after a urine specimen is collected are often of no clinical importance. Temperature, evaporation and pH are in vitro variables that may cause a urine specimen to become oversaturated, leading to crystal formation. Importantly, in vitro conditions may cause crystals to dissolve or grow. It is possible that urine kept at room temperature after collection may lose carbon dioxide into the atmosphere, which could affect pH, and subsequently, presence of crystalluria. However, a recent study found that urinary pH was not affected by storage time or temperature. Analysis of stored urine from cats consuming a mixture of moist and dry food was associated with significant increases in struvite crystalluria compared with evaluation of a fresh urine sample. In another study that included 31 dogs and eight cats, calcium oxalate and struvite crystals formed in vitro in urine that was stored at either room or refrigeration temperature. However, this phenomenon occurred more commonly at refrigeration temperature. In addition, length of crystals that formed in vitro was significantly increased in urine stored at refrigeration temperature compared with samples stored at room temperature.

Bacterial contamination of urine specimens also may affect crystalluria. Urease-producing bacteria (e.g., *Staphylococcus* spp., *Proteus* spp.) alkalinize urine, possibly altering crystal composition and disrupting cellular components in urine (e.g., red and white blood cells). Other bacteria produce acid metabolites with similar consequences. To prevent bacterial overgrowth, urine samples should be refrigerated if they cannot be evaluated promptly. However, this is not ideal for evaluation of crystalluria.

The nutritional history, including water intake, must be considered when evaluating significance of crystalluria. Cats consuming moist food are less likely to have crystalluria than those eating dry food exclusively. In addition, results of urine sediment examination may not accurately reflect what occurs in the home environment if cats are fed different foods in the hospital before urine collection.

Crystalluria should not be used as the sole criterion to predict mineral type of confirmed uroliths; only quantitative analysis of a retrieved urolith can provide that information. However, crystalluria can be used along with other factors (e.g., history, age, breed, urinary pH, radiographic appearance, other urinalysis findings and biochemistry profile results) to predict mineral type. Uroliths may be present in cats without crystalluria. In this case, factors that influenced formation and growth of crystals may be absent transiently. Factors typically responsible for this phenomenon include food changes, anorexia, increased water intake, different urinary pH values and in vitro changes in urine specimens that are not fresh. The crystal type may be different from the urolith type in some cases. This dichotomy exists when cats are assumed to have one urolith type, which is not confirmed by quantitative analysis (e.g., assumed to have struvite uroliths and fed according to struvite dissolution or preventive protocols, when in reality the cat has calcium oxalate uroliths and calcium oxalate crystalluria). Finally, cats may have more than one crystal type concurrently (e.g., struvite and calcium oxalate crystals may be identified in the same urine sample).

Struvite crystals may occur in: 1) normal cats, 2) cats with infection-induced struvite uroliths, 3) cats with sterile struvite uroliths, 4) cats with non-struvite uroliths, 5) cats with uroliths of mixed mineral type and 6) cats with urinary tract disease other than uroliths (e.g., feline idiopathic cystitis). Calcium oxalate dihydrate crystals occur uncommonly in normal cats. Large quantities of these crystals alone or in combination with calcium oxalate monohydrate crystals in fresh urine specimens probably indicate a hypercalciuric or hyperoxaluric disorder (e.g., ethylene glycol toxicity, calcium oxalate urolithiasis).

Should all cats with crystalluria be treated? In the absence of urolithiasis or a history of urolithiasis, cats with struvite or calcium oxalate crystalluria should be monitored serially. Cystine, ammonium urate or xanthine crystalluria should be investigated and the cause treated. Frequent detection of large crystals and aggregates of crystals in a fresh urine sample may be clinically important, especially if the cat has a history of urolith formation. In this case, preventive nutritional management should be implemented, and the cat should be encouraged to increase water intake. Finally, urine sediment examination should be performed periodically to monitor effectiveness of preventive therapy in patients with a history of uroliths.

The Bibliography for **Box 46-1** can be found at www.markmorris.org.

Urinary pH

Urinary pH influences formation of several crystal types. Although exceptions occur, crystal types tend to form and persist at certain urinary pH ranges (**Table 46-7**) (Osborne et al, 1995). In general, struvite uroliths are associated with more alkaline urinary pH values (>6.4) and calcium oxalate uroliths are associated with lower urinary pH values. Overlapping values can be detected; however, in cats with either urolith type. The method of measuring urinary pH should be considered because the urine dipstick method is not as accurate as a pH meter. In addition, urinary pH varies throughout the day due to the influence of food, time of eating, method of feeding and amount of food consumed. Consequently, it is difficult to interpret a single urinary pH value, especially if the type of food and time of eating are unknown. Furthermore, it has been reported that simply putting a cat in a carrier and traveling to a veterinary hospital can increase urinary pH (Buffington and Chew, 1996).

In laboratories, pH meters with glass and reference electrodes are used to make pH measurements. The electrode must be calibrated periodically against buffers of known pH. For clinical purposes, urinary pH can be measured with pH meters or indicator paper. Most multi-test reagent strips and test tapes use indicator paper impregnated with two indicator dyes: methyl red and bromthymol blue. The typical pH range is

Table 46-7. Clinical and diagnostic findings associated with the most common feline uroliths.*

Parameters	Struvite	Calcium oxalate	Purine (urate)
Breed predisposition	Chartreux Domestic longhair Domestic shorthair Foreign shorthair Himalayan Manx Oriental shorthair Ragdoll Siamese	Burmese British shorthair Exotic shorthair Foreign shorthair Havana brown Himalayan Persian Ragdoll Scottish fold Domestic shorthair	Siamese
Gender predisposition	Female >male Neutered >intact	Male >female	Neutered >intact
Common age (years)	Younger (<7 years)	Middle-aged to older (>7 years)	Young (if associated with portosystemic shunt)
Serum biochemistries	Normal	Hypercalcemia Acidemia (decreased TCO_2)	Normal (idiopathic) Evidence of hepatic disease (low urea nitrogen, increased ammonia)
Urinary pH**	Slightly acidic (>6.5) or alkaline	Acidic to neutral	Acidic to neutral
Bacteria	Usually sterile Occasionally associated with urease-producing bacteria	Usually sterile May be present in cats with infection secondary to uroliths	Usually sterile May be present in cats with infection secondary to uroliths
Typical crystals	Colorless, coffin-lid prisms, sometimes shaped like squares	Monohydrate–oval, dumbbell shaped Dihydrate-squares with diagonal lines	Spherical, tan in color May be green/brown Thorn apple appearance
Radiopacity	1+ to 4+	3+ to 4+	0 to 2+
Radiographic appearance	Rough or smooth, round or faceted, sometimes disk-shaped	Rough or smooth, usually small, occasionally jackstone shaped	Smooth, occasionally irregular

*Adapted from Osborne CA, Kruger JM, Lulich JP, et al. Disorders of the feline lower urinary tract. In: Osborne CA, Finco DR, eds. Canine and Feline Nephrology and Urology. Baltimore, MD: Williams & Wilkins 1995; 651.
**Concomitant infection with urease-producing bacteria may cause alkaline urine in cats with uroliths.

Table 46-8. Possible risk factors for urinary tract infection in cats.

- Age (≥10 years)
- Female gender
- Urinary tract procedures
  - Urethral catheterization
  - Perineal urethrostomy
- Urolithiasis
- Systemic diseases
  - Chronic kidney disease
  - Hyperthyroidism
  - Diabetes mellitus

roughly from 5.0 (orange) to 9.0 (blue). According to most manufacturers, pH values measured with indicator paper are only accurate to within 0.5 pH units. For best results, indicator squares on reagent strips should be compared with the manufacturer's color standards in well-illuminated areas, as directed by product instructions. Urine reagent strips may be used to estimate pH for routine urinalysis; however, they should not be relied on when accurate pH measurements are needed for diagnosis, prevention and management of disease (Johnson et al, 2007).

Relatively inexpensive microprocessor-based, pocket-sized pH meters[b] have become available and are more accurate for measuring urinary pH than reagent strips (Heuter et al, 1998; Raskin et al, 2002; Johnson et al, 2007). These instruments can be used in veterinary hospitals or by pet owners at home. A study in cats revealed that portable pH meters were more accurate than pH paper or reagent test strips for measuring urinary pH in healthy cats (Raskin et al, 2002). Another study of hospitalized dogs compared hand-held pH meters, pH paper and reagent strips with a bench top pH meter, considered the gold standard for measuring pH. Results revealed that pH paper and reagent strips had poor to moderate agreement with the reference method, whereas, hand-held pH meters had nearly perfect agreement (Johnson et al, 2007). Based on these studies, a portable or bench top pH meter should be used when accurate urinary pH measurements are crucial for diagnosis or treatment.

Urine Culture

Urine culture should be done in all cats with lower urinary tract signs or in asymptomatic cats when there is increased risk of UTI (**Table 46-8**). Quantitative bacterial culture of urine collected by cystocentesis is the gold standard for diagnosis of UTI. For most accurate results, urine should be cultured within 30 minutes of collection or refrigerated because multiplication or destruction of bacteria may occur within one hour. If urine samples cannot be processed immediately, other alternatives such as inoculating culture plates in the hospital or using special storage media should be considered (Bartges, 2004). Growth of any bacteria from a sample of urine collected by cystocentesis is abnormal; contamination during collection should be suspected if multiple organisms are cultured. If a UTI is diagnosed, antimicrobial susceptibility testing is indicated to select appropriate treatment, especially in cats with pyelonephritis, recurrent infections or those that have been receiving antimicrobials.

Radiography

Radiography of the urinary tract (including the entire urethra in male cats) is a valuable diagnostic procedure that allows for detection of most feline uroliths and crystalline-matrix urethral plugs (Johnston et al, 1996). Radiography can determine the size, shape, location and number of uroliths. Relative radiodensity of uroliths can be used to make a rough guess of mineral composition (**Table 46-7**). Struvite and calcium oxalate uroliths are usually radiodense, whereas urate uroliths often are radiolucent. Radiographic shape, contour and size can be used as an inexact predictor of mineral composition. Struvite uroliths can be smooth or rough, round or faceted. Calcium oxalate dihydrate uroliths are usually small, rough and round to oval. Calcium oxalate monohydrate uroliths are usually small, smooth and round. Occasionally, calcium oxalate monohydrate uroliths have a "jackstone" appearance. The size and number of urocystoliths does not predict whether medical dissolution (if applicable) will be successful. Survey radiography or ultrasonography may fail to detect small uroliths (i.e., less than three mm in diameter); however, uroliths greater than one mm in diameter usually can be detected with double-contrast cystography if excessive contrast medium is not infused (Osborne et al, 1996).

Radiographic abnormalities also may be detected in the kidneys and ureters, especially in feline patients with calcium oxalate urolithiasis. The overwhelming majority of feline nephroliths are composed of calcium salts; only a small percentage of nephroliths are struvite (Kyles et al, 2005; Cannon et al, 2007).[a] Nephroliths must be differentiated from dystrophic or metastatic calcification of renal parenchyma, calcified mesenteric lymph nodes and ingesta or medications in the intestinal tract.

Contrast radiography is indicated in cats with recurrent or persistent clinical signs that do not respond to appropriate treatment. Contrast studies can be used to identify radiolucent uroliths, small uroliths or space-occupying lesions of the urinary tract such as neoplasia. Double-contrast radiography is helpful in evaluating urinary bladder wall thickness. Retrograde urethrography may be necessary in cases of urethral disease or obstruction. Patients with FIC may have normal findings or abnormalities including focal or diffuse thickening of the urinary bladder wall, irregularities of the urinary bladder mucosa or filling defects (Scrivani et al, 1998).

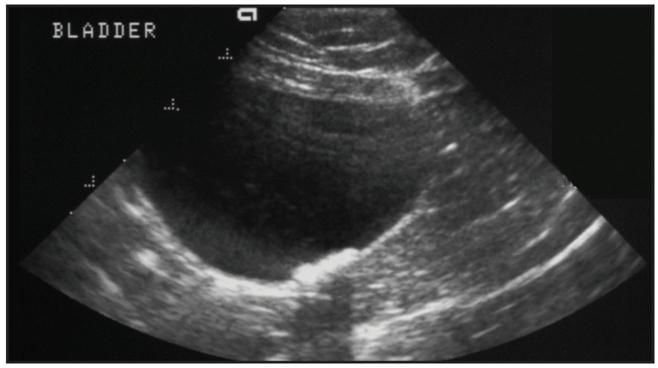

Figure 46-7. Sagittal plane urinary bladder sonogram of a cat with a history of lower urinary tract signs and several previous episodes of urethral obstruction. Note the presence of several hyperechoic densities in the urinary bladder, with acoustic shadowing below. These findings are typical of urinary bladder uroliths. After surgical removal, the uroliths were confirmed to be composed of calcium oxalate.

Ultrasonography

Ultrasonography is a rapid, safe, noninvasive imaging technique for evaluating the urinary bladder. Results often are unique, or at least complementary, compared with other diagnostic procedures; however, ultrasonography should not be viewed as a replacement for other tests including survey radiography (Widmer et al, 2004; Lulich, 2007). Factors affecting accuracy of ultrasonographic evaluation of the lower urinary tract include size and superficial location of the urinary bladder, inaccessible location of much of the urethra within the bony pelvis, degree of urinary bladder distention and presence of urinary bladder disease. Caudal abdominal structures are most readily visualized when the urinary bladder is full. In addition, when there is minimal distention, the urinary bladder mucosa develops folds that misrepresent wall thickness and mucosal contour (Widmer et al, 2004). Minimal transducer pressure should be used when scanning the urinary bladder to avoid displacement away from the transducer; this is especially important in cats with minimal urinary bladder distention.

Urinary bladder ultrasonography may be used to identify uroliths, masses or signs of chronic inflammation. Radiopaque and radiolucent uroliths in the urinary bladder have high echogenicity with characteristic acoustic shadowing (**Figure 46-7**). They tend to gravitate to the most dependent part of the urinary bladder with movement of the patient. Small uroliths may be difficult to distinguish from mineralization of the urinary bladder wall and should be displaced by shaking the urinary bladder during ultrasonography (Widmer et al, 2004). Blood clots also shift location with patient movement; however, they do not cause acoustic shadowing. Diffuse thickening of the urinary bladder mucosa is typical of chronic inflammation from any cause; however, it also may occur with neoplasia, especially lymphoma in cats. Thickening of the mucosa must be interpreted carefully in patients that have a partially filled urinary bladder because mucosal folds may appear in this situation in the absence of disease. Discrete

Table 46-9. Contact information for urolith analysis laboratories.

Antech Diagnostics – East
111 Marcus Ave.
Lake Success, NY 11042
800.872.1001

Antech Diagnostics – West
17672 Cowan Ave.
Irvine, CA 92614
800.745.4725

Canadian Veterinary Urolith Centre
Laboratory Services Division
University of Guelph
95 Stone Road West
P.O. Box 3650
Guelph, ON N1H8J7

Gerald V. Ling Urinary Stone Analysis Laboratory
Department of Medicine
Room 3106 MSI-A
School of Veterinary Medicine
Davis, CA 95616
Phone: 530.752.3228
Fax: 530.752.0414
www.vetmed.ucdavis.edu/vme/labs.htm

Laboratory for Stone Research
81 Wyman Street
P.O. Box 129
Newton, MA 02168

Louis C. Herring and Company
1111 South Orange Ave.
Orlando, FL 32806-1236
P.O. Box 2191
Orlando, FL 32802
Phone: 407.841.770
Fax: 407.422.8896
www.herringlab.com

Minnesota Urolith Center
University of Minnesota
1352 Boyd Ave.
St. Paul, MN 55108
Phone: 612.625.4221
Fax: 612.624.0751
www.cvm.umn.edu/depts/minnesotaurolithcenter

Urolithiasis Laboratory
P.O. Box 25375
Houston, TX 77265-5375
800.235.4846
www.urolithiasis-lab.com

masses, often located in the apex of the body of the urinary bladder, suggest urinary bladder neoplasia, which is rare in cats (Forrester, 2006; Wilson et al, 2007).

Urethrocystoscopy
Transurethral cystoscopy (or urethrocystoscopy) is becoming an increasingly important diagnostic method for evaluating the urethra and urinary bladder of cats. However, its availability may be limited to certain specialty hospitals. Patients with recurrent or persistent lower urinary tract signs despite normal findings on routinely available diagnostic tests (i.e., urinalysis, urine culture and diagnostic imaging) are candidates. The lower urinary tract of nearly all female cats weighing more that 3.0 kg can be evaluated with one of several small rigid cystoscopes. Urethrocystoscopy may be the method of choice for evaluating female cats with signs of periuria, pollakiuria, dysuria or stranguria. Observation of submucosal petechial hemorrhages (glomerulations), in the absence of other lesions, supports a diagnosis of FIC.

Serum Biochemistry Profiles
Serum biochemistry profiles are not generally helpful in most cats with FLUTD unless there are systemic signs of illness, urolithiasis or frequent recurrences of FLUTD with no obvious cause (**Table 46-7**). Hypercalcemia has been reported to occur in 14 to 35% of cats with calcium oxalate uroliths (Osborne et al, 1996a; Kyles et al, 2005). These patients should be evaluated for underlying causes of hypercalcemia (e.g., hyperparathyroidism, neoplasia and hypervitaminosis D); in most cases, however, a cause is not evident and idiopathic hypercalcemia is diagnosed (McClain et al, 1999; Midkiff et al, 2000; Savary et al, 2000). Presumably, persistent hypercalcemia increases the risk of forming calcium-containing uroliths by increasing excretion of calcium in urine. However, it is possible that processes involved with formation of calcium-containing uroliths and hypercalcemia are unrelated. Acidemia and serum total CO_2 less than 18 mEq/l, were reported in 64% of non-azotemic cats with calcium oxalate uroliths and 92% of cats with concurrent azotemia and uroliths (Osborne et al, 1996a). Metabolic acidosis may contribute to calcium-containing urolith formation because it promotes mobilization of calcium from bone and inhibits renal tubular reabsorption of calcium. Most urate uroliths in cats do not have an identifiable cause; however, serum biochemistry abnormalities (e.g., low urea nitrogen, increased ammonia) may occur in those with concurrent hepatic disease or portosystemic shunts.

Urolith Analysis
Recommendations for urolith dissolution and prevention are based on mineral composition of uroliths; therefore, it is important to analyze uroliths whenever possible. In addition to surgical removal, several less invasive techniques for obtaining uroliths should be considered. These methods include retrieval with a urinary catheter, voiding urohydropropulsion and voiding into an empty or plastic bead-filled litter box (Lulich et al, 1993). Ideally, all uroliths retrieved from a cat should be analyzed by a urolith diagnostic laboratory to determine specific mineral type(s) (**Table 46-9**).

Uroliths can be analyzed qualitatively or quantitatively. Qualitative analysis uses spot tests to identify radicals and ions; however, these tests do not reveal the proportion of mineral types and do not detect certain mineral crystals (e.g., silica) and drug crystals (e.g., sulfadiazine). Qualitative tests lack sensitivity and specificity for analyzing feline and canine uroliths (Osborne et al, 1996; Bovee and McGuire, 1984; Ruby and Ling, 1986). Investigators at the Minnesota Urolith Center examined 223 uroliths by qualitative and quantitative methods

Table 46-10. Reported risk factors for selected feline lower urinary tract diseases.*

Parameters	Feline idiopathic cystitis	Struvite uroliths	Calcium oxalate uroliths
Patient characteristics	Four to 10 years old Breeds (purebred, longhaired, Persian) Neutered Overweight Lazy/little exercise	Younger cats (<7 years) Breeds (**Table 46-7**) Female Neutered Urinary tract infection (urease positive)	Older cats (>7 years) Breeds (**Table 46-7**) Male Neutered
Environmental conditions	Multi-cat household Less freedom to leave house Provided with litter box Living in conflict with another cat Moving within last three months High number of rainfall days in month before signs		Indoor environment
Nutritional factors	Fed dry cat food Decreased water intake	Alkalinizing foods (urinary pH >6.5) Magnesium content 0.14 to 0.56% (0.36 to 1.4 mg/kcal) Phosphorus content 1.27 to 1.88% (3.17 to 4.70 mg/kcal) Sodium content 0.57 to 1.48% (1.43 to 3.7 mg of Na/kcal) Fiber content ≥2.7 (≥0.71 g/100 kcal)	Dry foods 7 to 7.9% moisture Excessively acidifying foods (urinary pH = 5.8 to 6.29) Feeding single brand Sodium content 0.2 to 0.3% (0.48 to 0.77 mg/kcal) Potassium content 0.04 to 0.06% (0.95 to 1.6 mg/kcal) Protein content 21 to 32% (5.15 to 7.98 g/100 kcal) Magnesium content 0.04 to 0.07% (0.09 to 0.18 mg/kcal) or 0.14 to 0.56% (0.36 to 1.4 mg/kcal) Phosphorus content 0.34 to 0.70% (0.85 to 1.76 mg/kcal) or 1.27 to 1.88% (3.17 to 4.70 mg/kcal) Calcium content 0.39 to 0.82% (0.97 to 2.05 mg/kcal) or 1.5 to 2.0% (3.76 to 5.06 mg/kcal)

*Nutrient values expressed on a percent dry matter basis and assume a food energy density of 4 kcal metabolizable energy/g (17.6 kJ/g); however, dry matter nutrient content of foods with energy densities substatially higher or lower than 4 kcal/g will be under- or overreresented, respectively. Thus, the energy basis nutrient values in this table (parenthetical values) are more accurate.

and found that qualitative methods yielded false-negative results in 38.1% of the uroliths and false-positive results in 6.7% (Ulrich et al, 1996). These two methods agreed in only 43.1% of the analyses. Uroliths, therefore, should be analyzed quantitatively to obtain the most accurate information about mineral content.

Quantitative analytical methods include optical crystallography, x-ray diffraction, infrared spectroscopy and electron scanning microscopy (Ulrich et al, 1996). In optical crystallography, crystalline material is removed from representative areas of the urolith using a dissecting microscope. The optical characteristics (e.g., refractive index and birefringence) of the crystalline material then are determined by polarizing microscopy and compared with known standards to determine mineral composition. Methods such as infrared spectroscopy are used if results of optical crystallography are inconclusive.

Different minerals may be deposited in layers (i.e., compound) or mixed throughout the urolith. Although one mineral type predominates, the composition of uroliths frequently is mixed. Thus, sampling and reporting results from different parts of the urolith become important when considering urolith dissolution and prevention. The following terms are sometimes used: the "nidus" is where growth of the urolith apparently started; it is not necessarily the geometric center. "Shells" are one or more complete outer layers of the urolith. "Surface crystals" refer to an incomplete outermost layer. Grossly visible layers do not always mean different mineral composition. The layers represent different phases of deposition and may be composed of the same or different minerals.

Risk Factors

Many studies have evaluated risk factors for FLUTD including patient characteristics, environmental conditions and various nutritional factors (**Table 46-10**) (Buffington et al, 1997, 2006; Houston et al, 2003; Kirk et al, 1995; Cameron et al, 2004; Lekcharoensuk et al, 2000, 2001, 2001a; Walker et al, 1977; Jones et al, 1997; Thumchai et al, 1996). For some risk factors, findings are consistent between studies, whereas others are different (e.g., living in a multi-cat household has been associated with increased risk of FIC in some studies but not in others). It is important to keep in mind that risk factors identified in epidemiologic studies show associations between certain factors and the disease of interest; additional study is necessary to show a cause-and-effect relationship. For exam-

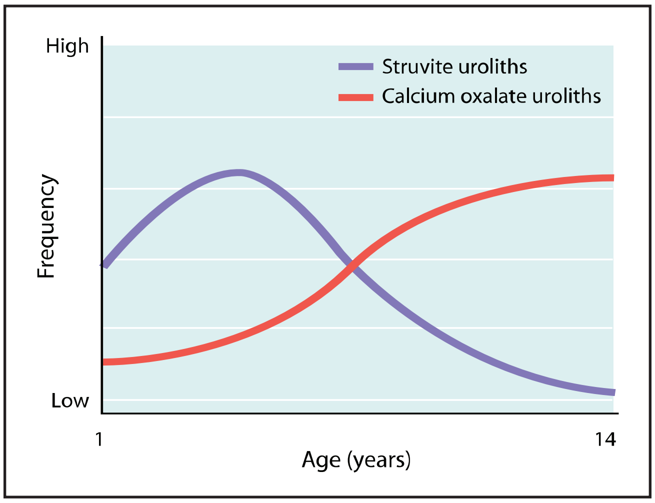

Figure 46-8. Relationship between urolith mineral type and age in cats. Note that struvite urolithiasis occurs more frequently in younger cats, whereas calcium oxalate urolithiasis occurs more frequently in older cats.

ple, it is likely that feeding a therapeutic renal food is associated with (i.e., is a risk factor for) chronic kidney disease; however, this does not mean it causes kidney disease. Finally, individual cats in a population are rarely exposed to a single risk factor; it is likely that FIC is a multifactorial disease and effects of interaction between multiple risk factors are challenging to evaluate (Willeburg, 1984).

Patient Characteristics

Patient factors that may affect risk for various types of FLUTD include age, breed, gender, neuter status, body condition and miscellaneous factors.

AGE

Review of data from the Veterinary Medical Database (1980-1990) revealed that lower urinary tract disease is most prevalent in cats between one and 10 years of age (Bartges, 1997). Another study using information from the same database (1980-1997) revealed that cats between four and seven years of age had the highest risk of lower urinary disease in general (Lekcharoensuk et al, 2001). Cats between four and 10 years of age had increased risk for urocystolithiasis, urethral obstructions and FIC, whereas, cats older than 10 years were at increased risk for UTI and neoplasia (Lekcharoensuk et al, 2001). Compared with younger to middle-aged cats, UTI is more commonly diagnosed in older cats (Lees, 1984; Bartges, 1997; Lekcharoensuk et al, 2001). In one study of cats with lower urinary tract disease that were 10 years of age and older, 63% had UTI (46% had UTI only and 17% had UTI combined with uroliths) (Bartges, 1997).

In general, cats with struvite uroliths tend to be younger and those with calcium oxalate uroliths older (**Figure 46-8**) (Thumchai et al, 1996; Cannon et al, 2007). In one study, cats with struvite uroliths (5.75 ± 3.12 years [mean age ± standard deviation]) were significantly younger than cats with calcium oxalate uroliths (7.5 ± 3.42 years) (Lekcharoensuk et al, 2000). Cats four years of age and older but younger than seven years had the highest risk of developing struvite uroliths. Cats older than seven years, but younger than 10 years, had the highest risk of developing calcium oxalate uroliths.

BREED

Several breeds of cats have increased risk for lower urinary tract disorders; however, there is so much overlap that it is difficult to draw meaningful conclusions (**Tables 46-7** and **46-10**) (Thumchai et al, 1996; Lekcharoensuk et al, 2000; Cannon et al, 2007). In one study, Persian, Himalayan and manx cats had increased risk for lower urinary tract diseases in general, whereas Siamese cats had decreased risk (Lekcharoensuk et al, 2001). Breeds with increased risk of developing urocystoliths were Persian, Himalayan and Russian blue (Lekcharoensuk et al, 2001). No breed predilection was observed for urethral obstruction (Lekcharoensuk et al, 2001). Breeds reported to have decreased risk for struvite uroliths include Burmese, Persian, Himalayan, Rex, Abyssinian, Russian blue, Birman, Siamese and mixed-breed cats (Thumchai et al, 1996; Lekcharoensuk et al, 2000). However, Siamese cats were reported to have significantly more struvite uroliths than other breeds in another study (Cannon et al, 2007). Birman, Abyssinian, Siamese and mixed-breed cats had significantly lower risk of developing calcium oxalate uroliths in one study (Lekcharoensuk et al, 2000). Persian cats had significantly fewer urate uroliths than other breeds in another study (Cannon et al, 2007).

GENDER

Neutered males and females had increased risk of lower urinary tract diseases overall and intact females had decreased risk in one epidemiologic study (Lekcharoensuk et al, 2001). Male cats are at increased risk for calcium oxalate uroliths, whereas females are at greater risk for struvite uroliths (Thumchai et al, 1996; Lekcharoensuk et al, 2000; Houston et al, 2003; Cannon et al, 2007). In one study, however, there was no gender predilection for cats with calcium oxalate uroliths (Kirk et al, 1995). Neutered cats are reported to have increased risk for both struvite and calcium oxalate uroliths compared with sexually intact cats (Lekcharoensuk et al, 2000). Neutered males are at increased risk for urethral obstruction (Lekcharoensuk et al, 2001). UTI is more common in female than male cats (Bailiff et al, 2006; Lekcharoensuk et al, 2001).

BODY CONDITION

Being overweight or obese has been a risk factor for lower urinary tract diseases in older and more recent studies (Walker et al, 1977; Cameron et al, 2004; Willeburg, 1984). Overweight cats (defined as ≥6.8 kg) had increased risk for lower urinary tract diseases when compared with cats weighing less than 6.8 kg (Lekcharoensuk et al, 2001). In a study of more than 8,000 cats in the U.S., nearly 29% were overweight, which was associated with urinary tract disease (Lund et al, 2005).

MISCELLANEOUS FACTORS

Cats described as lazy, or that exercise little, appear at increased risk for lower urinary tract disorders (Walker et al, 1977; Jones et al, 1997). It may be that these cats are overweight, which also is a risk factor for lower urinary tract diseases. In a study of indoor-housed cats, significantly more owners of those with lower urinary tract signs observed gastrointestinal signs, scratching and fearful, nervous or aggressive behaviors than owners of healthy cats (Buffington et al, 2006).

Environment

Living in a multi-cat household has been identified as a risk factor for lower urinary tract disorders in some studies (Walker et al, 1977; Jones et al, 1997). Cats that live indoors (or have restricted access to the outdoors) and/or are provided a litter box are also at increased risk for lower urinary tract diseases (Walker et al, 1977; Jones et al, 1997; Kirk et al, 1995). Conditions that may cause increased stress (e.g., living in conflict with another cat or moving to another home) have been associated with FIC (Jones et al, 1997; Cameron et al, 2004).

Nutritional Factors

Decreased moisture content of foods (feeding dry food) and/or decreased water intake have been associated with increased risk of FIC and calcium oxalate uroliths but not struvite uroliths (Walker et al, 1977; Kirk et al, 1995; Lekcharoensuk et al, 2001a). In one study, cats fed foods with a high moisture content (74.4 to 81.2%) were about a third as likely to develop calcium oxalate uroliths as were cats fed foods low in moisture (7 to 7.9%) (Lekcharoensuk et al, 2001a). In another study, cats with FIC were significantly more likely to eat dry pet food exclusively (59%) compared with cats in the general population (19%); however, this study did not include a control group (Buffington et al, 1997). Instead, results of a survey conducted by another organization regarding feeding practices of pet owners were used. These survey results differ from other studies, which show 95 to 99% of cat owners feed either dry food exclusively or a mixture of dry and moist (Habits and Practices, 2002; Gunn-Moore and Shenoy, 2004). Eating dry cat food has been associated with increased occurrence of FIC, whereas eating food with higher moisture content (e.g., canned food) has been associated with decreased occurrence (Walker et al, 1977; Jones et al, 1997; Willeberg, 1984). In addition, feeding moist food to cats with FIC has been associated with reduced recurrence of clinical signs compared with feeding dry food (Markwell et al, 1999). Additional study, however, is needed to determine if dry food causes FIC. As noted previously, more than 95% of owners feed their cats dry food exclusively or a combination of dry and moist food, yet the reported incidence of lower urinary tract diseases overall is less than 2% (Habits and Practices, 2002; Gunn-Moore and Shenoy, 2004; Lawler et al, 1985; Willeberg, 1984).

The source of water (e.g., tap vs. well) is not believed to be a contributing factor in cats with lower urinary tract disorders; however, it has not been carefully evaluated. In an epidemiologic study, water sources for cats with calcium oxalate uroliths (i.e., municipal, well or bottled) were similar to those for hospital control cats; more than 80% of cats in both groups received water from municipal supplies (Kirk et al, 1995). Mineral content of water is expressed as parts per million whereas mineral content of food is expressed as parts per hundred. Therefore, even water with high mineral content (i.e., "hard water") would contribute little to the total daily mineral intake compared with the amount supplied in food (Kirk et al, 1995).

A case-control study was performed to identify nutritional factors associated with struvite and calcium oxalate uroliths in cats (Lekcharoensuk et al, 2001a). Data were collected from cats whose uroliths were submitted to the Minnesota Urolith Center between 1990 and 1992. A content-validated questionnaire was mailed to owners to obtain information about their cat's food (e.g., types and quantities fed), feeding methods, mineral and vitamin supplements and source of drinking water. Nutrient information and expected urinary pH ranges for each food were obtained from pet food manufacturers. Data from 290 cats with magnesium ammonium phosphate uroliths and 216 cats with calcium oxalate uroliths were compared with data from 827 control cats without urinary tract disease. Distributions for breed, age, gender, body condition and living environment were significantly different between case and control cats; therefore, multivariate analyses were performed to adjust for potential confounding variables. The authors identified several associations between food components and occurrence of uroliths. Cats fed foods with high amounts of magnesium, phosphorus, fiber, calcium, sodium, chloride or potassium, or moderate protein content had increased risk of struvite uroliths (Lekcharoensuk et al, 2001a). In addition, cats fed foods formulated to produce urinary pH values between 6.5 and 6.9 were two times as likely to develop struvite uroliths as cats fed foods formulated to produce a urinary pH between 5.99 and 6.15. Cats fed foods with low amounts of sodium, potassium or protein, low or high amounts of magnesium, phosphorus or calcium, or those formulated to produce an overly acidified urinary pH had increased risk for calcium oxalate uroliths (Lekcharoensuk et al, 2001a) (**Table 46-10**). Increased dietary magnesium was previously associated with struvite urolith formation; however, presence of a concomitant alkaline urinary pH was likely a more important factor (Taton et al, 1984; Buffington et al, 1985, 1990).

To date, the strongest association with occurrence of calcium oxalate urolithiasis has been use of acidifying foods (Kirk et al, 1995; Lekcharoensuk et al, 2001a). It has been hypothesized that uniform use of these foods for managing struvite disease may be the cause for increased occurrence of calcium oxalate uroliths in cats (Buffington et al, 1994; Kirk et al, 1995; Thumchai et al, 1996; Lekcharoensuk et al, 2001a). In one epidemiologic study, cats with calcium oxalate urolithiasis were more than three times as likely as hospital control cats to have been fed foods that typically promote urinary pH equal to or lower than 6.29 (Kirk et al, 1995). In another study, cats fed foods formulated to produce urinary pH values between 5.99 and 6.15 were three times as likely to develop calcium oxalate uroliths as cats fed foods formulated to produce urinary pH values ranging from 6.5 to 6.9 (Lekcharoensuk et al, 2001a). Although two studies have identified that feeding acidifying foods is associated with calcium oxalate uroliths in cats, additional evaluation is necessary to show a cause-and-effect relationship and to determine what specific nutritional factors (e.g., magnesium content, degree of acidifying potential) are involved. It is of interest to note that normal urinary pH values in feral cats are reported to be 5.97 ± 0.10 (range, 5.54 to 6.57) in females and 6.37 ± 0.07 (range, 5.73 to 7.39) in males (Cottam et al, 2002). Both studies described above evaluated data collected from 1990 to 1992, when occurrence of calcium oxalate uroliths was increasing. Since 2001, occurrence of struvite uroliths has been increasing and calcium oxalate has been decreasing. Therefore, additional study is needed to identify more current risk factors and causes for recent trends of feline urolithiasis. It seems likely that multiple factors (e.g., nutritional, presence and function of urolith inhibitors, genetic predisposition) play a role in formation of calcium oxalate uroliths in susceptible cats.

Pathogenesis

Feline Idiopathic Cystitis

The clinical course of FIC is characterized by episodes of lower urinary tract signs that usually resolve spontaneously within three to five days, with or without treatment (Barsanti et al, 1982; Gunn-Moore and Shenoy, 2004). Although not evaluated in a large number of cases, it appears that 39 to 65% of cats with FIC will have recurrence of signs within a six- to 12-month period (Barsanti et al, 1982; Markwell et al, 1999; Kruger et al, 2003; Gunn-Moore and Shenoy, 2004). Many cats have multiple recurrences within a year. In a study involving 70 cats with FIC, 63 (90%) had multiple episodes of lower urinary tract signs; 30 (43%) cats had at least three episodes in the year before diagnosis (Buffington et al, 1997). In a study of 15 untreated cats with acute FIC, eight (53%) had one or more episodes of recurrent signs of lower urinary tract disease with 22 events reported over a period of 7,942 days at risk (Kruger et al, 2003). The overall incidence rate was 2.6 events per 1,000 days at risk. Survival analysis revealed that increasing number of prior episodes of lower urinary tract signs was associated with a significantly higher risk, whereas increasing age was associated with a significantly lower risk of recurrence of clinical signs. In another study, cats with FIC experienced a mean of five recurrences in six months (Gunn-Moore and Shenoy, 2004).

FIC shares many features in common with human interstitial cystitis and has been called feline interstitial cystitis when cystoscopic examination reveals characteristic findings (Buffington et al, 1997, 1996a, 1996b). Comparisons are based on clinical signs and diagnostic features. All of the National Institutes of Health (NIH) criteria (i.e., history, laboratory evaluation, cystoscopy and cystometrics) for interstitial cystitis in human patients have been applied to cats (Gao et al, 1994). Affected people and cats present as adults with symptoms/signs of variable severity that are influenced by stress. Spontaneous remissions occur in people and cats. According to NIH criteria, the diagnosis in people also requires cystoscopic lesions, either glomerulations or Hunner's ulcer. Glomerulations are submucosal petechial hemorrhages, whereas Hunner's ulcer is a small area of brownish-red mucosa, surrounded by a network of radiating vessels. Veterinary investigators report that lesions indistinguishable from glomerulations are observed commonly during cystoscopic examination of cats with FIC (Osborn et al, 1994; Buffington et al, 1997). A single case report describes a cat with FIC and findings of Hunner's ulcer (Clasper, 1990).

The pathogenesis of FIC appears to involve a variety of abnormalities affecting the urinary bladder, nervous system and hypothalamic-pituitary-adrenal axis (Westropp et al, 2004, 2005). One study of patients with FIC revealed abnormally low amounts of urinary glycosaminoglycans (GAG) compared with normal controls (Buffington et al, 1996b). In contrast, studies of urinary GAG in human patients with interstitial cystitis have yielded variable results (Akcay et al, 1999; Erickson et al, 1997; Hurst et al, 1993). The surface layer covering the urinary bladder mucosa includes GAG. A defective GAG layer or damaged urothelium may allow irritating substances in the urine to contact sensory nerve endings, which transmit action potentials through the spinal cord to the brain, resulting in perception of pain. In addition, there may be local release of neurotransmitters (e.g., substance P) and other inflammatory mediators (e.g., histamine) within the urinary bladder mucosa, which interact with receptors on vessel walls causing vascular permeability and leakage (i.e., neurogenic inflammation) (Westropp et al, 2005). Studies have shown that patients with FIC have increased urinary bladder permeability and leakage of ions across the urothelium compared with normal cats (Lavalle et al, 2000; Gao et al, 1994; Westropp et al, 2006a). Histologic changes associated with FIC generally are nonspecific and may include an intact or damaged urothelium with submucosal edema, dilatation of submucosal blood vessels, submucosal hemorrhage and sometimes increased mast cell density (Westropp et al, 2005). There is no correlation between histologic lesions, cystoscopic findings and clinical signs in patients with FIC. Cats may have remission of clinical signs but persistently abnormal cystoscopic findings (Westropp et al, 2005).

Several neurohormonal abnormalities have been described in patients with FIC and may play a role in its pathogenesis. A significant increase in tyrosine hydroxylase immunoreactivity was identified in the locus coeruleus (a nucleus in the brainstem) of patients with FIC compared with findings in healthy control cats (Reche Júnior and Buffington, 1998; Welk et al, 2003). Urinary bladder distention stimulates neuronal activity in the locus coeruleus, the origin of the descending excitatory pathway to the urinary bladder. Tyrosine hydroxylase is the rate-limiting enzyme involved in synthesis of catecholamines (e.g., norepinephrine). Chronic stress can increase tyrosine hydroxylase activity in the locus coeruleus with subsequent increases in autonomic outflow. It is possible this may play a role in the waxing and waning of clinical signs observed in patients with FIC, particularly in response to environmental stressors (Westropp et al, 2005). Patients with FIC also have increased plasma norepinephrine concentrations (Buffington and Pecak, 2001; Westropp et al, 2006a). In a study evaluating effects of stress, patients with FIC had significantly increased plasma concentrations of catecholamines, including norepinephrine, compared with healthy cats (Westropp et al, 2006a).

Abnormalities also have been identified in the hypothalamic-pituitary-adrenal axis of cats with FIC. Those with FIC had significantly decreased cortisol response to administration of synthetic adrenocorticotropic hormone compared with that of healthy cats (Westropp et al, 2003). In the same study, adrenal gland volume was significantly lower in cats with FIC compared with healthy cats; however, there were no correlations between adrenal size and cortisol production (Westropp et al, 2003, 2005). In another study of the effects of stress, there was no significant difference in urinary cortisol:creatinine ratios between patients with FIC and healthy cats (Westropp et al, 2006a). Based on studies conducted to date, it appears there is dissociation between the response of the sympathetic nervous system and the hypothalamic-pituitary-adrenal axis to stress in patients with FIC.

Although many risk factors have been identified in patients with FIC, additional evaluation is likely needed to identify its definitive cause(s). Based on current understanding of pathogenesis, it appears that abnormalities are not limited to the urinary bladder and interactions between other systems (e.g., nervous and endocrine) are likely involved. This possibility must be considered when formulating a treatment plan, which should include a multimodal approach (i.e., decreasing environmental stress, nutritional management, behavioral modification, pain management) for all patients with FIC.

Urolithiasis

Uroliths, or urinary calculi, are composed primarily of crystalline mineral concretions with a small amount of organic matrix. Urolithiasis is a multifaceted process that begins with microcrystals in urine and ends with mature uroliths somewhere in the urinary tract (Osborne and Kruger, 1984). Urolith formation occurs in two separate phases-initiation of the crystal nidus and continued growth to form a urolith. In general, there are four factors involved in formation of uroliths: 1) oversaturation of urine with calculogenic crystalloids, which may result from increased urinary excretion of these substances or increased urine concentration (e.g., due to decreased water intake), 2) decreased solubility of crystalloids in urine (e.g., struvite is less soluble in alkaline urine), 3) presence or absence of crystallization inhibiters or promoters in urine and 4) retention of crystals/uroliths within the urinary tract.

In its simplest form, initiation and growth of uroliths involves chemical precipitation of dissolved ions or molecules from a solution that has become oversaturated with respect to those components (**Figure 46-9**). From a physiochemical perspective, the degree of saturation or undersaturation of urine influences the probability that precipitates will form, or if already present, will dissolve. Relatively simple diagrams depict states of saturation of any solution (**Figures 46-10** and **46-11**). These diagrams provide the framework for understanding the concept of how nutritional management influences probability of urolith formation or dissolution. Units and numerical values

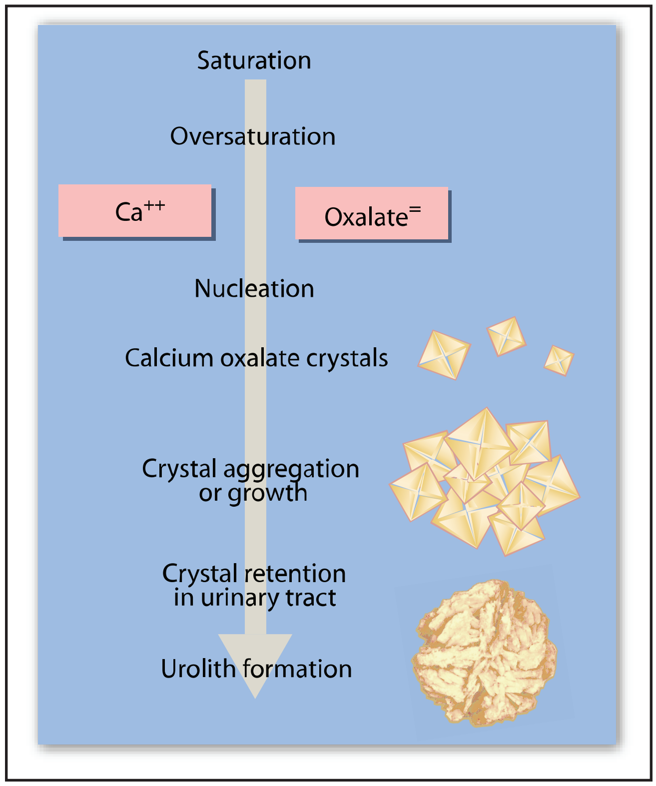

Figure 46-9. Increasing saturation of urine with urolith-forming constituents (e.g., calcium, oxalate) results in crystal growth, aggregation and ultimately urolith formation, if the components are retained in the urinary tract. (Adapted from Bartges JW, Osborne CA, Lulich JP, et al. Methods for evaluating treatment of uroliths. Veterinary Clinics of North America: Small Animal Practice 1999; 29: 46.)

are not included in these diagrams because they differ for each of the urolith components and measurement technique; however, the general features apply to all crystalline materials. At concentrations below the solubility product (i.e., in the undersaturation zone), it is impossible for crystals to form and crystals added to such a solution would dissolve. However, crystals may grow if added to a solution with a concentration greater than the solubility product. The formation product is the concentration at which crystals will begin to spontaneously precipitate in the absence of preformed crystalline material. Although the solubility product is constant for a pure crystalline material, the formation product is much more difficult to demonstrate; therefore, this area is illustrated by a shaded band rather than a line (**Figure 46-11**). Strictly speaking, the ionic activities (not concentrations) of the species govern the described solubility principles. Ionic activities are influenced by the presence of other ions in solution (i.e., ionic strength) and by the presence of other species that form complex ions, thereby reducing their "free" concentrations in solution.

The metastable zone is of most interest clinically; in this concentration range crystal growth and aggregation may occur or other factors (e.g., crystallization inhibitors) may impede or prevent crystallization (**Figure 46-11**). Risk factor reduction

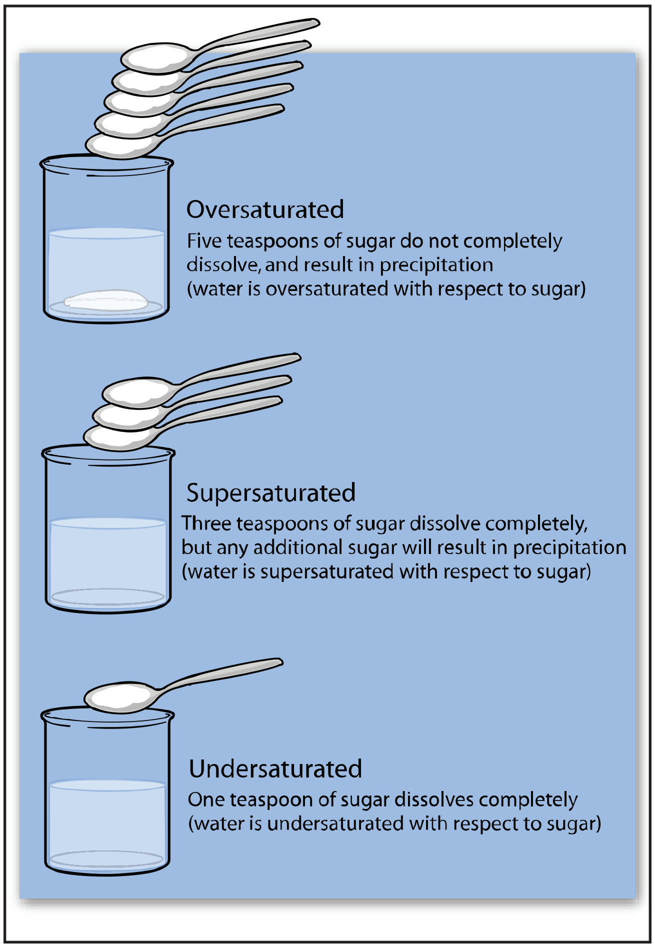

Figure 46-10. This diagram depicts a simplified explanation of effects of different levels of urine saturation (oversaturation, supersaturation [metastable] or undersaturation) on formation of uroliths. In this example, the liquid is tea and the mineral or crystalloid is sugar. As the amount of added sugar increases, the solution (tea) goes from being undersaturated (all the sugar completely dissolves) to being oversaturated (some of the sugar precipitates). Similar phenomena occur with mineral salts in urine. However, just as there are different outcomes when dissolving sugar in iced vs. hot tea, other factors (e.g., temperature, pH, crystalloid inhibitors) also affect saturation of urine with crystalloids. (Adapted and modified from Bartges JW, Osborne CA, Lulich JP, et al. Methods for evaluating treatment of uroliths. Veterinary Clinics of North America: Small Animal Practice 1999; 29: 47.)

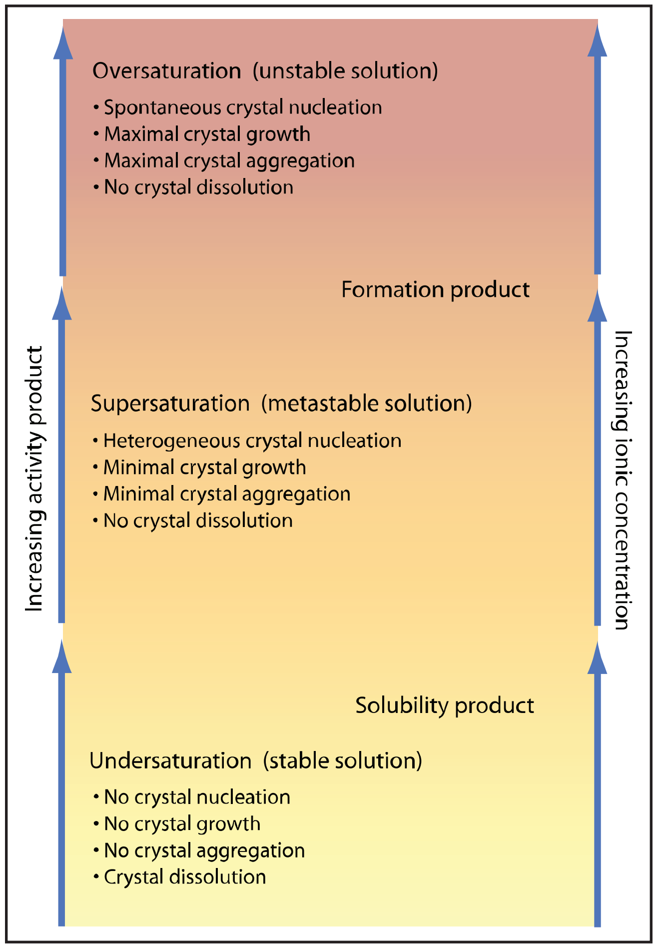

Figure 46-11. This diagram illustrates effects of differing degrees of urine saturation on risk of urolith formation. Increasing concentrations of urolith-forming substances result in metastable (supersaturated) and eventually, oversaturated urine. Crystal growth and aggregation may occur in the metastable zone. Presence of a nidus promotes nucleation (i.e., heterogeneous nucleation) and subsequent crystal formation. Inhibitors in urine may impede or prevent crystallization in the metastable zone. Spontaneous or homogenous nucleation occurs, however, when concentrations of urolith-forming substances increase to the point of oversaturation. After oversaturation occurs, inhibitors of crystal formation generally are ineffective. (Adapted from Bartges JW, Osborne CA, Lulich JP, et al. Methods for evaluating treatment of uroliths. Veterinary Clinics of North America: Small Animal Practice 1999; 29: 48.)

and nutritional intervention may be most beneficial with urine in this region. A precarious balance exists between crystal formation and inhibition in the metastable zone. Anatomic defects within the urinary tract that allow for stasis of metastable urine will lead to formation and growth of crystals. Urine containing microscopic impurities will facilitate crystal formation and growth. This process is called “heterogeneous nucleation.” Crystal formation is much less likely in urine without impurities (i.e., homogeneous solution) (Bartges et al, 1999). **Box 46-2** discusses laboratory techniques used to measure these changes in urine. A more detailed description of this entire process is found in Chapter 38.

STRUVITE UROLITHS

Struvite uroliths form as a result of oversaturation of urine with magnesium ammonium phosphate. This oversaturation can occur in the presence of infection with a urease-producing organism. However, in contrast to the situation in dogs, most struvite uroliths in cats form in sterile urine (Osborne et al, 1996a). Urinary magnesium levels are related to dietary intake; as the amount of dietary magnesium increases, urinary magnesium excretion increases linearly (Sauer et al, 1985; Pastoor, 1993). **Box 46-3** provides more information about the effects of urinary pH on struvite urolith formation.

Box 46-2. Determining Risk for Urolith Formation or Recurrence.

Analytical data indicate that urine often is supersaturated with respect to most common urolith components. Thus, the question is not why a specific patient formed a urolith, but rather why doesn't every patient form uroliths? Inhibitors in urine probably explain the less than predicted prevalence of urolith formation. The current therapeutic strategy is to reduce risk factors by decreasing the degree of supersaturation because we know less about changing urinary inhibitors. One way to express urinary saturation is to determine the relative supersaturation (RSS) of a calculogenic substance (e.g., struvite or calcium oxalate). RSS is determined by measuring the concentration of a number of urinary analytes, including sodium, calcium, oxalate, magnesium and potassium. The concentrations of these analytes are entered into a computer program that calculates the saturation of the urolith elements compared with a standard human urine sample. RSS has limitations because it is highly dependent on urine volume and involves comparison with standard values for human urine.

Another technique for predicting likelihood of crystal formation is the activity product ratio (APR) (**Figure 1**). The APR for calcium oxalate is the mathematical product of the activity of calcium and the activity of oxalate. Activity is different than simple concentration of the substance of interest in an aqueous solution. Activity refers to the ionic activity, which is influenced by the concentration of the substance of interest, other substances in urine and factors such as pH and temperature. Like RSS, APR involves measurement of a number of analytes (e.g., sodium, potassium, calcium, oxalate, magnesium) in urine that are entered into a computer program. Unlike RSS, however, the APR technique requires incubation of seed crystals (e.g., calcium oxalate) in an aliquot of urine. After incubation, urinary analytes are measured again and the post-incubation activity product is determined. Dividing the pre-incubation activity product by the post-incubation activity product yields the APR. An APR less than one indicates that crystals dissolved during incubation. The APR provides a better indication of risk of crystal formation than RSS because APR considers the influence of unmeasured inhibitors and promoters and is not unduly influenced by urine volume. APRs can be used to evaluate quantitatively the influence of nutrients, complete foods and drugs on the risk of crystal formation.

Several studies have reported effects of various foods on urinary saturation values for calcium oxalate and struvite (APR and/or RSS) in healthy cats; however, only one has reported these values in cats with a history of forming uroliths. Although decreasing values for urine saturation indicate decreased risk for urolith formation, these values serve as surrogate markers. There are no reported studies correlating urine saturation values (APR or RSS) in urolith-forming cats with rate of urolith recurrence.

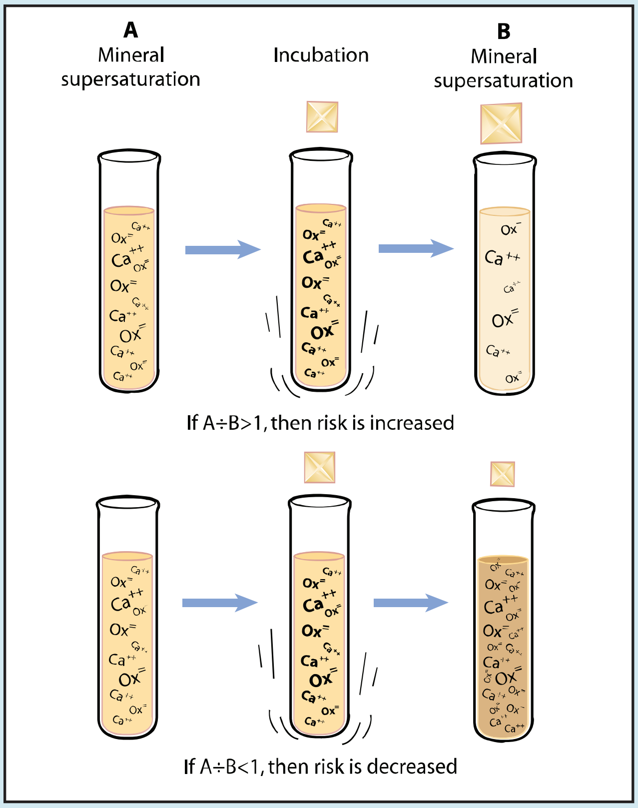

Figure 1. Schematic depicting how APRs are calculated. Urine from a cat is analyzed for pertinent minerals (Tube A) and then is incubated with a seed crystal. After incubation, the urine is analyzed for the same mineral constituents (Tube B). Dividing the pre-incubation activity product by the post-incubation activity product yields the APR. The risk of urolith formation increases with an APR greater than 1. This means the seed crystal has grown and the urine is supersaturated and/or contains inadequate concentrations of crystal inhibitors. The risk of urolith formation decreases with an APR less than 1. This means the seed crystal became smaller during the incubation process and the urine is undersaturated or contains adequate concentrations of crystal inhibitors.

The Bibliography for **Box 46-2** can be found at www.markmorris.org.

CALCIUM OXALATE UROLITHS

Based on a small study of cats with calcium oxalate uroliths and information extrapolated from canine and human patients, it seems reasonable that factors promoting hypercalciuria and/or hyperoxaluria are involved in the pathogenesis of calcium oxalate urolithiasis in cats (Lulich et al, 1991, 2004; Stevenson et al, 2004; Seiner et al, 2003, 2005). Hypercalciuria was identified in 10 cats with calcium oxalate uroliths; feeding a therapeutic food[c] formulated to prevent urolith recurrence was associated with a significant decrease in urine calcium excretion and urine calcium oxalate saturation compared with feeding their regular food. Hypercalcemia promotes urinary excretion of calcium and therefore may increase the risk of calcium oxalate urolithiasis. Mild hypercalcemia (11.1 to 13.5 mg/dl) has been identified in approximately 35% of cats with calcium oxalate uroliths (Osborne et al, 1996a). Radiopaque uroliths were diagnosed in seven of 20 cats (35%) with idiopathic hypercalcemia in one study; uroliths were removed from two

Box 46-3. Urinary pH, Ammonium and Anionic Phosphate.

Normal urinary concentration of total phosphate ions is high and not subject to great variation by dietary manipulation. Although complexes are formed between phosphate ions and calcium and magnesium ions, these complexes do not markedly decrease free phosphate ion concentration. The urinary variable that has the greatest impact on trivalent phosphate ion concentration is urinary pH. Urinary pH influences formation of struvite precipitates because it influences the amount of total urinary phosphorus present as the free trivalent phosphate ion. Concentration of the free trivalent ion depends on the position of the acid-base equilibria of the two principal phosphate species that exist in the normal urinary pH range: HPO_4^{2-} and $H_2PO_4^-$. As urinary pH increases, concentration of free trivalent ions increases, as monobasic and dibasic phosphates are deprotonated.

$$H_2PO_4^- = HPO_4^{2-} + H^+$$

$$HPO_4^{2-} = PO_4^{3-} + H^+$$

According to the above equations, an increase in hydrogen ion concentration will shift both equilibria to the left, resulting in lower concentrations of free trivalent phosphate (PO_4^{3-}). Decreasing urinary pH from 8.5 to 5.5, the approximate physiologic range for cats, results in a 14,000-fold decrease in free trivalent ion concentration, with no change in total urinary phosphate.

Urinary pH also influences concentration of ammonium ions. Ammonia generated by urease enzymes provides necessary ions that react with available hydrogen ions to increase urinary pH:

$$NH_3 + H^+ = NH_4^+$$

Reduction in urinary pH from the upper to the lower end of the physiologic range changes the ratio of NH_4^+ to NH_3 from 3.4:1 to 3,400:1. Thus, foods that produce moderately acidic urine increase urinary ammonium concentration. However, because the effect on free trivalent phosphate ion concentration is greater, the net effect of moderate urinary acidification is a reduced likelihood of struvite precipitation.

The Bibliography for **Box 46-3** can be found at www.markmorris.org.

cats and were confirmed to be calcium oxalate (Midkiff et al, 2000). In another study of 71 cats with hypercalcemia, eight of 11 had calcium oxalate uroliths; nine of the 11 cats with uroliths also had chronic kidney disease (Savary et al, 2000). The role of hypercalcemia in the pathogenesis of calcium oxalate uroliths requires further study; it is appropriate to screen patients for hypercalcemia and, when possible, manage the underlying cause.

Hyperoxaluria may result from increased dietary intake or endogenous production of oxalate from metabolism of ascorbic acid (vitamin C), glycine, glyoxylate or other substances. A study in healthy cats fed differing amounts of vitamin C ranging from 40 to 193 mg vitamin C/kg of food for approximately one month found no significant change in urinary oxalate excretion (Yu and Gross, 2005). However, the effects of vitamin C supplementation have not been studied in cats at risk for calcium oxalate urolithiasis. A large part of the metabolic pool of glyoxylate is transaminated to glycine by the enzyme alanine glyoxylate aminotransferase, which requires pyridoxine (vitamin B_6) as a cofactor (Menon and Koul, 1992). Pyridoxine deficiency has been associated with increased oxalate production and urinary excretion in cats but has not been associated with calcium oxalate uroliths in cats (Bai et al, 1989, 1991). Primary hyperoxaluria, due to reduced activity of hepatic D-glycerate dehydrogenase, has been recognized in a family of cats; however, the role of primary hyperoxaluria in cats with calcium oxalate uroliths is unknown (McKerrell et al, 1989).

Urinary oxalate is an important determinant of urinary calcium oxalate saturation because small increases in oxalate excretion profoundly influence the activity product ratio. Oxalate forms a number of complexes and salts in solution; the calcium salt is relatively insoluble and pH does not influence its solubility over the physiologic range. The calcium salt of oxalate is just as insoluble in the luminal content of the intestinal tract as in other complex solutions. Consequently, dietary calcium is an important determinant of oxalate availability and intestinal absorption. Sufficiently available dietary calcium in the intestinal lumen combines with oxalate to form insoluble complexes of calcium oxalate. This phenomenon reduces intestinal absorption and subsequently less renal excretion of calcium oxalate. In contrast, if dietary calcium is reduced without a concomitant reduction in dietary oxalate, intestinal absorption and urinary excretion of oxalate may increase.

Urine normally contains substances that modify and inhibit nucleation, growth and aggregation of crystals. This likely explains, in part, why urine of most human beings is continuously saturated with calcium oxalate, yet only a small percentage of the human population will form calcium oxalate uroliths during their lifetime. Inhibitors such as citrate, magnesium and pyrophosphate can form soluble complexes with calcium or oxalic acid, making them unavailable to form insoluble salts such as calcium oxalate (Khan et al, 1993). Low concentrations of urinary citrate are common in human patients with calcium oxalate uroliths and some recurrent urolith formers may have defective inhibitory substances (Hess et al, 1991; Parks and Coe, 1986). Magnesium is a potent inhibitor of calcium oxalate crystallization in vitro. Low excretion of magnesium in urine has been suggested as a possible risk factor for development of calcium-containing uroliths. In an experimental study in rats, administration of magnesium oxide prevented renal deposition of calcium oxalate crystals in hyperoxaluric rats (Khan et al, 1993). Magnesium presumably increased urinary pH and excretion of citrate and decreased urinary oxalate excretion. This effect of magnesium depends on which specific salt is used (e.g., magnesium oxide has an alkalinizing effect, whereas magnesium sulfate has an acidifying effect). Other substances such as mucoproteins (e.g., Tamm-Horsfall mucoprotein), nephrocalcin and osteopontin (uropontin) also may inhibit crystal nucleation, growth and/or aggregation; however, their role in preventing calcium oxalate uroliths in cats has not been evalu-

Table 46-11. Potential factors associated with formation of uncommon feline uroliths.

Factors	Causes	Pathogenesis
Urate		
Hyperuricosuria	Portosystemic shunt or severe hepatic disease	Decreased hepatic conversion of uric acid to allantoin, which is more soluble in urine
	Excessive purine intake	Promotes hyperuricemia with subsequent hyperuricosuria
Hyperammonuria	Excessive protein intake	Additional urea and glutamine available for conversion to ammonium (NH_4)
	Metabolic acidosis	Promotes metabolism of glutamine to NH_4
	Acidic urine	Ammonia (NH_3) is converted to NH_4, which is excreted in urine
	Hypokalemia	Results in intracellular acidosis (potassium exchanged for hydrogen) and subsequent excretion of NH_4
	Urinary tract infection with urease-producing organism	Converts urea in urine to NH_3 and NH_4
Aciduria	Acidic urine	Decreased solubility of uric acid in urine
Decreased urine volume	Decreased water intake	Increased urine concentration and saturation with uric acid Decreased urination causes retention of crystals and uroliths
Calcium phosphate		
Hypercalciuria	Hypercalcemia	Increased urinary calcium excretion
	Excessive vitamin D	Increased intestinal calcium absorption and suppressed parathyroid hormone secretion, which promotes calcium excretion
	Hypophosphatemia	Stimulates vitamin D production, which augments intestinal absorption of calcium
	Acidosis	Promotes skeletal release of calcium and inhibits renal tubular reabsorption of calcium
	Excessive calcium intake	Increases urinary calcium excretion
	Excessive sodium intake	Increases urinary calcium excretion
Hyperphosphaturia	Excessive phosphorus intake	Increased urinary phosphorus excretion
	Alkaline urine	Increases urine concentration and saturation of phosphate
Alkaline urine	Alkaline urine	Reduces solubility of calcium phosphates, especially brushite
Decreased urine volume	Decreased water intake	Increased urine concentration and saturation with calcium phosphate Decreased urination causes retention of crystals and uroliths

ated (Nakagawa et al, 1987; Hess, 1991; Asplin et al, 1991).

Although a cause-and-effect relationship remains to be established, feeding foods formulated to maintain an acidic urinary pH (≤6.29 in one study and between 5.99 and 6.15 in another study) has been associated with calcium oxalate uroliths in two epidemiologic studies of cats (Kirk et al, 1995; Lekcharoensuk et al, 2001a). Acidosis may cause mobilization of calcium from bone (along with buffers), resulting in increased urinary calcium excretion. In addition, metabolic acidosis is associated with decreased urinary citrate excretion and increased citrate metabolism by renal tubular cells.

OTHER UROLITHS

Pathogenesis of less commonly diagnosed urolith types is not well understood, although several factors may be involved in formation of uroliths composed of purine (e.g., ammonium acid urate, uric acid) or calcium phosphate (**Table 46-11**). An underlying metabolic disorder is likely in these patients; however, often one is not identified. Detection of certain crystals (i.e., ammonium urate, cystine and xanthine), even in patients without clinical signs, suggests an important underlying metabolic defect, but not all cats with these crystals will develop uroliths. UTI may be associated with uncommon urolith types, but there is little evidence to support that UTI is the cause of these uroliths. Xanthine uroliths have been reported to occur in seven cats that had not received allopurinol; an underlying cause was not obvious (Osborne et al, 1996a). Cystinuria, presumably due to a defect in renal tubular transport of certain amino acids including cystine, has been identified in a small number of cats with cystine uroliths (DiBartola et al, 1991; Osborne et al, 1996a).

Urethral Plugs

It is likely that urethral plugs result from different pathogenic mechanisms than uroliths. In contrast to uroliths, urethral plugs typically contain large amounts of matrix and tend to be soft, compressible and friable (**Figure 46-12**). Although most plugs contain crystalline minerals, some do not. On occasion, plugs can be composed almost completely of matrix, blood cells, inflammatory cells and sloughed tissue (**Table 46-5**). Matrix is the nondialysable portion of urethral plugs that remains after mild solvents have dissolved crystalline components. Matrix may provide the "glue" for urolith and plug formation (Osborne et al, 1996b). The exact composition of feline urethral plug matrix is unknown. It is possible that a major component of matrix is Tamm-Horsfall mucoprotein based on the observation that the urinary concentration of Tamm-Horsfall mucoprotein is increased in cats with a history of forming uroliths (Rhodes et al, 1992). Tamm-Horsfall mucoprotein may be a local host defense against bacterial and viral UTIs. Excess mucus may be secreted by cells within the urinary bladder and urethra in response to an irritant or inflammatory stimulus.

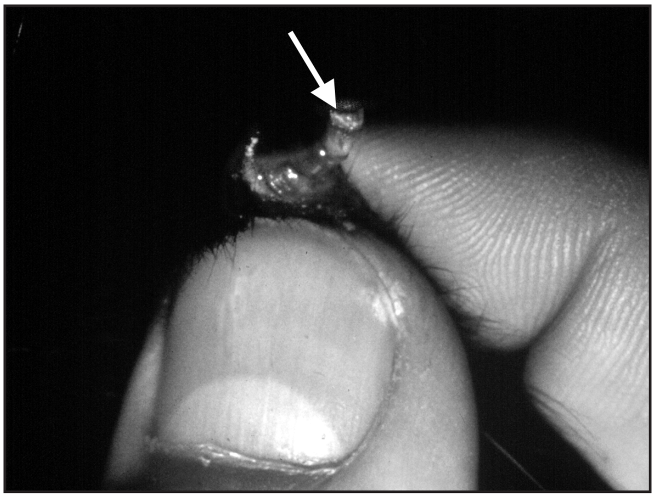

Figure 46-12. Note urethral plug (white arrow) extruding from the tip of the penis in a cat with urethral obstruction. Most urethral plugs are soft, compressible, friable and composed of large amounts of matrix mixed with smaller amounts of crystalline minerals. Although urethral plugs are diagnosed more often in male cats, due to occurrence of urethral obstruction, they also may occur in female cats.

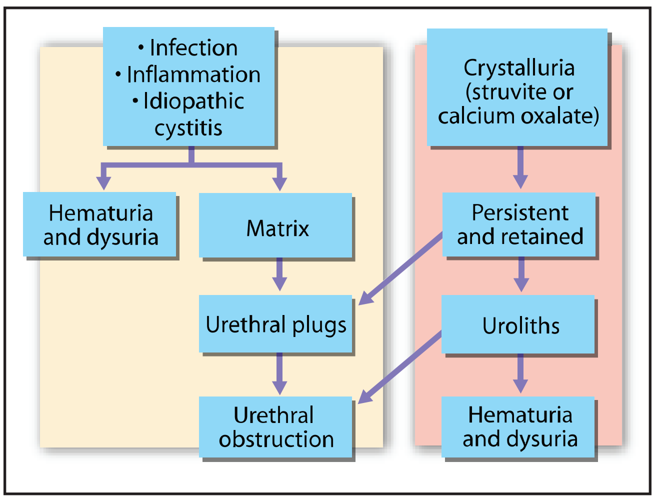

Figure 46-13. Unifying concept for pathogenesis of feline lower urinary tract disease. Infection or inflammation (e.g., idiopathic cystitis) results in clinical signs of lower urinary tract disease and production of excess matrix. Persistent crystalluria can combine with matrix to form urethral plugs or contribute to urolith formation and typical clinical signs. (Adapted from Osborne CA, Kruger JM, Lulich JP. Feline lower urinary tract disorders: Definition of terms and concepts. Veterinary Clinics of North America: Small Animal Practice 1996; 76: 169-179.)

Formation of matrix-crystalline urethral plugs hypothetically requires two simultaneous but unrelated events (**Figure 46-13**) (Osborne et al, 1992, 1996b, 1996c). One event is the formation of matrix that may result from some inflammatory process (e.g., idiopathic, bacterial or viral UTI). The other event is the formation of crystalline precipitates, most often struvite. If matrix forms without concomitant crystals, the noncrystalline gel is voided; however, nonobstructive dysuria and hematuria result. A more rigid plug forms in the presence of crystals that may cause urethral obstruction. The mineral composition of crystals can serve as the basis for preventive efforts. This process of plug formation has been compared with the formation of casts in renal tubular lumina. Urinary mucoprotein provides a gel that traps intact cells (producing cellular casts) or disintegrating cellular elements (producing granular casts). A more trivial analogy is the creation of fruit gelatin (**Figure 46-14**). The "gelatin" (i.e., matrix) traps pieces of "fruit" (i.e., crystals) as it forms.

Urinary Tract Infection

BACTERIAL INFECTION

Infection with urease-producing bacteria (e.g., *Staphylococcus* spp. and *Proteus* spp.) causes persistently alkaline urine, which may be associated with formation of struvite uroliths. It appears that most cats with struvite uroliths do not have UTI; however, urolith-induced changes in host-defense mechanisms may lead to bacterial colonization of the urinary tract (Osborne et al, 1996a). Thirty percent of feline patients with urocystoliths in one study had positive urine cultures (Osborne et al, 1990). In a study of uroliths from 150 cats, investigators cultured bacteria from a urolith or urine in 30 (41%) of 74 cats. Coagulase-positive staphylococci were cultured from uroliths or urine in 17 cats, representing 45% of bacteria isolated (Ling et al, 1990). In some cases, culture of urine may be negative or yield the same or different organisms than cultures from uroliths.

Although a cause-and-effect relationship has not been established, there is an increased occurrence of UTI in cats with systemic diseases. Of cats with chronic kidney disease, 10 to 50% are reported to have UTI; it isn't known if kidney disease causes UTI or if other factors (e.g., older age) are responsible (Lulich et al, 1992; McMahon et al, 2006; Mayer-Roenne et al, 2007). UTI also has been reported to occur in 12 to 13% of cats with diabetes mellitus and 12% of cats with hyperthyroidism (Bailiff et al, 2006; Mayer-Roenne et al, 2007).

Perineal urethrostomies are associated with significant postoperative sequelae, including urethral strictures, bacterial UTI and struvite urolithiasis (Osborne et al, 1991; Griffin et al, 1992; Bass et al, 2005). These postoperative sequelae can produce lower urinary tract signs. In a prospective clinical study of 30 male cats with intraluminal urethral obstruction and negative urine cultures, investigators randomly assigned cats to receive one of three treatments following relief of the obstruction: 1) nutritional management with a struvite dissolution food, 2) perineal urethrostomy or 3) nutritional management and perineal urethrostomy. During the one-year followup period, none of the cats receiving nutritional management alone had episodes of UTI, whereas episodes of bacterial UTI were documented in 50% of the group managed by surgery alone, and 40% of the group receiving nutritional management and surgery. Three of the infected cats from the urethrostomy-only group subsequently developed urocystoliths (Osborne et al, 1991). In a more recent study, one-year followup of 39 cats that had perineal urethrostomy revealed that 51.3% had complications (UTI in nine, stricture in two) or recurrent signs due to urolithiasis (five cats) or FIC (four cats) (Bass et al, 2005).

Several factors associated with perineal urethrostomies have been incriminated as risk factors for bacterial UTI. These include decreased length of the urethra after surgery, loss of normal penile urethral mucosal defense mechanisms, transurethral catheterization, wider external urethral orifices, impaired function of the striated urethralis muscle and decreased intraluminal pressure. Some cats have decreased postprostatic urethral pressure and decreased activity of the striated muscle sphincter after perineal urethrostomy, as determined by urethral pressure profiles and electromyographic changes (Gregory and Vasseur, 1983). These changes were linked to extensive tissue dissection and damage to the pudendal nerve during surgery.

A modified surgical procedure, designed to preserve function of the striated urethral sphincter, was evaluated in a group of healthy neutered male cats and a group of cats with persistent or recurrent urethral obstruction. All cats had normal urethral pressure profiles and electromyographic results postoperatively. Twenty-two percent of the cats with persistent or recurrent urethral obstruction had bacterial UTIs vs. none of the normal cats. These findings suggest that decreased urethral pressure does not predispose cats to ascending UTI (Griffin et al, 1989).

Vesicourachal diverticula were reported to occur in one of every four cats with dysuria, hematuria and/or urethral obstruction (Osborne et al, 1987). Vesicourachal diverticula can be congenital or acquired. Diverticula alter the normal flow of urine; thus in theory, they may predispose patients to UTI, infection-related urolithiasis and formation of urinary precipitates. It has been suggested that acquired diverticula occur as a result of increased intraluminal pressure due to urethral obstruction or hyperactivity of the detrusor muscle associated with inflammation. Spontaneous resolution of diverticula has been observed in cats (Osborne et al, 1987, 1989).

VIRAL INFECTION

Although not a consistent finding in cats with lower urinary tract signs, viral infections have been implicated as causative agents based on isolation of feline cell-associated herpesvirus, feline calicivirus (FCV) and syncytia-forming virus from cats with hematuria and dysuria alone or in combination with urethral obstruction (Kruger and Osborne, 1990). Calicivirus-like viral particles have been identified in crystalline/matrix urethral plugs from cats with obstructive lower urinary tract disease. Although standard cell culture inoculation methods with urine were negative for virus, investigators were able to induce bovine herpesvirus type 4 (BHV-4) infections experimentally in feline urinary bladders using tissue explantation techniques. However, the pathogenic role of BHV-4 in FLUTD remains unclear because the prevalence of BHV-4 antibodies in affected cats was not significantly different from that of clinically normal control cats (Kruger et al, 1991). In a study of 40 cats, researchers identified FCV in one female cat with FIC and one male cat with obstructive FIC; the FCV (FCV-U1 and FCV-U2) were genetically different from known field and vaccine strains (Rice et al, 2002). In a more recent epidemiologic study of 47 cats with nonobstructive FIC, 22 cats with obstructive FIC, 56 cats with signs of upper respiratory tract disease and 46 asymptomatic cats, FCV was detected by reverse transcription-polymerase chain reaction (RT-PCR) in urine from approximately 6% of cats with FIC or upper respiratory tract disease. FCV was not detected in urine from any asymptomatic cat. Mean FCV virus neutralizing antibody titers for cats with nonobstructive FIC, obstructive FIC and upper respiratory tract disease were significantly higher than the mean titers of asymptomatic control cats (Larson et al, 2007). Despite increasing evidence that FCV invades the urinary system and that cats with FIC have increased exposure to FCV, establishing a cause-and-effect relationship between FCV and FIC requires further investigation.

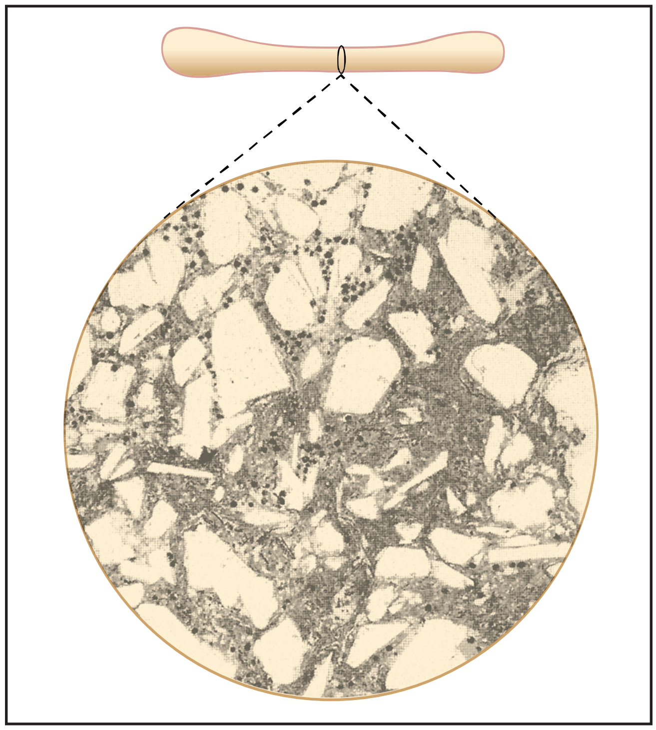

Figure 46-14. Diagram showing a cross-section of a matrix-crystalline urethral plug. Note the spaces previously occupied by struvite crystals are surrounded by matrix containing amorphous material, cellular debris and a small number of inflammatory cells. This phenomenon is analogous to a gelatin salad that contains various fruits or vegetables (depicting crystals, cells, cellular material) embedded in a gelatin matrix.

FUNGAL INFECTION

Fungal UTI is rarely diagnosed in cats; *Candida* spp. are the organisms most often isolated (Pressler et al, 2003; Jin and Lin, 2005). *Candida* spp. are considered a normal part of the genital mucosal flora and most patients with fungal UTI have underlying disorders that alter host defenses against opportunistic infection. Some treatments and concomitant disorders diagnosed in cats with fungal UTI have included administration of antimicrobials or corticosteroids, diabetes mellitus, kidney disease, indwelling urinary catheters, perineal urethrostomy and

Table 46-12. Key nutritional factors and recommended levels for managing cats with common lower urinary tract diseases.*

Factors	Dietary recommendations				
	FIC	Struvite dissolution	Struvite prevention	Calcium oxalate uroliths	Combined FIC, struvite and calcium oxalate prevention
Water	Moist foods are best	Moist foods are best	Moist foods are best	Moist foods are best	Moist foods are best
Magnesium (%)	–	0.04 to 0.09	0.04 to 0.14	0.07 to 0.14	0.07 to 0.14
Phosphorus (%)	–	0.45 to 1.1	0.5 to 0.9	0.5 to 1.0	0.5 to 0.9
Calcium (%)	–	–	–	0.6 to 1.0	0.6 to 1.0
Protein (%)	–	30 to 45	30 to 45	≥32	32 to 45
Sodium (%)	–	0.3 to 0.6	0.3 to 0.6	0.3 to 0.6	0.3 to 0.6
Urinary pH	–	5.8 to 6.2	6.0 to 6.4	≥6.2	6.2 to 6.4
Total omega 3 (%)	0.35 to 1.0	–	–	–	0.35 to 1.0

Key: FIC = feline idiopathic cystitis, Total omega 3 = total omega-3 fatty acids.
*Nutrients expressed on a dry matter basis unless otherwise stated.

Table 46-13. Key nutritional factors for preventing uncommon feline uroliths.

Factors	Dietary recommendations
Purine uroliths (urate, uric acid)	
Water	Promote water intake by using a moist food or other measures
Protein	Avoid excess dietary protein Recommend foods with 28 to 30% DM protein Recommend foods with low purine content Avoid proteins with high purine content such as liver, sardines and anchovies
Urinary pH	Use foods that maintain less acidic urine (6.6 to 6.8)
Calcium phosphate uroliths	
Water	Promote water intake by using a moist food or other measures
Calcium	Avoid excess dietary calcium Recommend foods with 0.6 to 0.8% DM calcium
Phosphorus	Avoid excess dietary phosphorus Recommend foods with <0.8% DM phosphorus
Sodium	Avoid excess dietary sodium Recommend foods with <0.30% DM sodium
Vitamin D	Avoid excess dietary vitamin D Recommend foods with <2,000 IU of vitamin D/kg DM

Key: DM = dry matter.

Table 46-14. Water intake and urine volume in cats fed dry or moist food.*

Volume (ml/day)	Moist food	Dry food
Water (in food)	246	6
Water (in addition to food)	32	221
Total water intake	278	227
Fecal water	27	44
Urine	166	79

*Adapted from Burger IH, Smith PM. Effects of diet on the urine characteristics of the cat. In: Proceedings. International Symposium on Nutrition, Malnutrition and Dietetics in the Dog and Cat, 1987: 71-73.

other lower urinary tract disorders (e.g., uroliths).

Key Nutritional Factors

Nutritional management plays a key role in successful treatment and/or prevention of the most common FLUTDs. Nutrition may be helpful for decreasing urine concentration of crystallogenic minerals and inflammatory mediators, increasing solubility of crystalloids in urine, promoting increased concentrations of crystallization inhibiters in urine and decreasing retention of crystals and/or uroliths within the urinary tract. When designing a therapeutic regimen for patients with FIC, struvite uroliths or urethral plugs, or calcium oxalate uroliths, consider the key nutritional factors discussed below. **Table 46-12** summarizes these key nutritional factors and recommended nutrient ranges for managing patients with common lower urinary tract disorders. **Table 46-13** summarizes key nutritional factors for cats with less common urolith types. Recommended ranges of nutrient levels of the key nutritional factors were determined by: 1) considering nutrient levels in foods evaluated in cats with various lower urinary tract diseases, 2) using information about risk factors from epidemiologic studies of cats with lower urinary tract signs and 3) extrapolation from studies in other species. Available evidence supporting effectiveness of different foods should be considered when planning treatment as well as each patient's response to treatment.

Water

The volume of water cats consume daily depends on the composition and quantity of food ingested and possibly feeding frequency. Although somewhat variable, most dry cat foods contain less than 10% water and moist foods (most often packaged in cans or pouches) contain more than 72% water. Healthy cats drink more water when eating dry food compared with moist food. The total volume of water ingested (i.e., drinking water plus water in food); however, is significantly greater and more water is excreted in urine than in feces when cats are fed moist food (**Table 46-14**) (Gaskell, 1989; Burger and Smith, 1987). The solute load of food also influences water consumption; urea is a major contributor to the renal solute load. Increasing the protein content of food increases the solute load (e.g., urea). Therefore, foods with higher protein content are associated with higher water intake. Metabolism of energy substrates yields endogenous water but the daily volume of endogenously produced water is small (approximately 10 to 15%) compared with the total daily water intake. Metabolism of fats provides the most water per gram whereas carbohydrate metabolism results in the most water per calorie. The amount of water generated differs slightly depending on the source of fat, chain length and degree of saturation. Feeding frequency also appears to affect water intake in cats. In a study of healthy adult cats, water intake (in addition to that consumed in the food) increased significantly when cats were fed two or three meals compared with a single meal each day. However, the study did not note whether the food was dry or moist (Kirschvink et al, 2005).

Of all treatments evaluated in controlled studies, the only one that has been associated with a statistically significant difference in recurrence of clinical signs in cats with FIC is feeding moist food (Barsanti et al, 1982; Gunn-Moore and Shenoy, 2004; Gunn-Moore and Cameron, 2004; Kruger et al, 2003; Kraijer et al, 2003; Osborne et al, 1996d; Markwell et al, 1999). During a one-year nonrandomized clinical study of cats with FIC, clinical signs recurred less often in cats fed moist food compared with cats fed the dry formulation of the same food[c] (**Figure 46-15**) (Markwell et al, 1999). In a six-month FIC study evaluating glucosamine hydrochloride[d] vs. placebo, cats receiving either treatment improved significantly compared with evaluations at the beginning of the study (**Figure 46-16**) (Gunn-Moore and Shenoy, 2004). Before the study, 95% of cats were fed either dry food exclusively or at least half of their daily intake was dry food. After starting the study, however, 36 (90%) owners increased the amount of moist food given to their cats, so that at least 50% of their daily intake was moist food. Owners began feeding moist food exclusively to 33 (82.5%) cats. In both studies described above, it is likely that increased consumption of moist food caused urine dilution, which was associated with clinical improvement in cats with FIC. However, other beneficial effects of feeding moist food (e.g., increased owner/cat interactions associated with delivery of canned meals) cannot be excluded.

Moist foods also are recommended in the management of urolithiasis and urethral plugs because they lead to production of less concentrated urine that is less saturated with crystalloids. Increased water consumption has been used as an effective strategy for controlling calcium oxalate uroliths in people, dogs and cattle. A case-controlled study of nutritional factors associated with urolithiasis in cats unexpectedly found no association between high-moisture foods and decreased risk for struvite uroliths (Lekcharoensuk et al, 2001a). However, cats fed high-moisture (74.4 to 81.2%) foods were about a third as likely to develop calcium oxalate uroliths as were cats fed low-moisture (7.0 to 7.9%) foods. The authors concluded that it is possible that increases in urine volume produced by moisture content of food may have less influence on struvite urolith formation than on calcium oxalate urolith formation.

Based on available information, patients with FIC and calcium oxalate uroliths should be fed foods that contain more than 74% moisture, as fed (e.g., foods in cans or pouches). Current evidence is less clear regarding beneficial effects of moist food for cats with struvite disease. However, it seems reasonable to also recommend moist foods for these cats as well, especially if

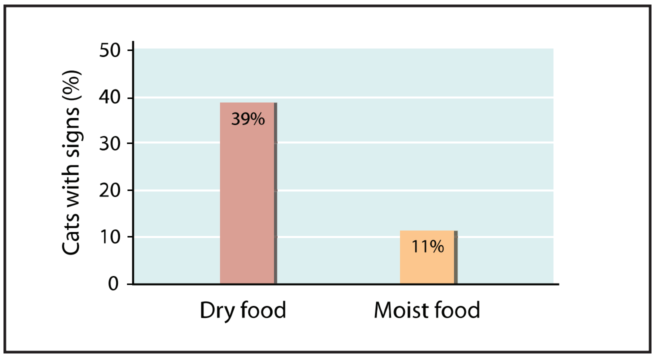

Figure 46-15. Results of a one-year study of 46 cats with feline idiopathic cystitis showed that recurrence of clinical signs was significantly greater in cats fed a dry food[c] (n = 28) compared with cats fed the moist version of the food (n = 18) (p = 0.04). After feeding the dry food, mean urine specific gravity values (measured at 2 weeks, 16 weeks, 6 months and 12 months) ranged from 1.050 to 1.051 whereas mean urine specific gravity values in cats eating moist food ranged from 1.032 to 1.041. (Adapted from Markwell PJ, Buffington CA, Chew DJ, et al. Clinical evaluation of commercially available urinary acidification diets in the management of idiopathic cystitis in cats. Journal of the American Veterinary Medical Association 1999; 214: 361-365.)

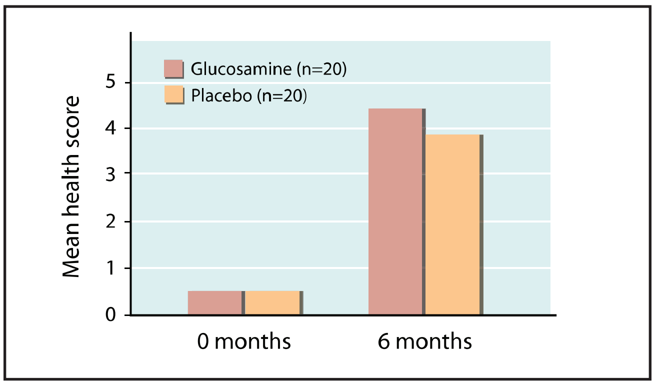

Figure 46-16. Mean health scores (0 = very severe cystitis, 5 = normal) from owner ratings at the beginning (0 months) and end (6 months) of a clinical study evaluating effects of glucosamine[d] compared with placebo in cats (n = 40) with feline idiopathic cystitis (FIC). There was no significant difference between groups (glucosamine or placebo) at baseline or after six months of treatment; however, mean health scores were significantly higher in both groups of cats at six months compared with baseline ($p < 0.001$). Mean urine specific gravity at the beginning of the study was 1.050 and it was significantly lower (1.036) when reassessed one month later. Most owners switched from feeding dry food to moist food after receiving educational material at the beginning of the study that included benefits of feeding moist food to cats with FIC. (Adapted from Gunn-Moore DA, Shenoy CM. Oral glucosamine and the management of feline idiopathic cystitis. Journal of Feline Medicine and Surgery 2004; 6: 219-225.)

there is recurrent disease in the face of feeding a dry struvite preventive food.

Magnesium

Avoiding excess dietary magnesium intake can reduce urinary concentration of magnesium, which decreases risk for struvite disease. In an epidemiologic study, risk of struvite uroliths was increased in cats fed foods higher in magnesium (Lekcharoensuk et al, 2001a). Excess magnesium is present in some commercial cat foods because they contain ingredients high in magnesium (e.g., high-ash meat and bone, fish and poultry meals). The recommended range of dietary magnesium for dissolving struvite uroliths in cats is 0.04 to 0.09% (dry matter [DM]). For preventing recurrence of struvite uroliths or urethral plugs, the recommended range of magnesium is 0.04 to 0.14% DM (**Table 46-12**).

Magnesium is considered to be an inhibitor of calcium oxalate crystal formation. Potential mechanisms for this inhibitory effect include increased urinary pH, increased urinary excretion of citrate and formation of magnesium oxalate complexes in urine, which are more soluble than calcium oxalate. Formation of magnesium oxalate, in theory, reduces the concentration of oxalate available for precipitation as calcium oxalate. Low urinary magnesium concentration has been suggested as a potential risk factor for formation of calcium-containing uroliths in cats (Lekcharoensuk et al, 2000, 2001). Clinical studies evaluating effectiveness of magnesium supplementation on recurrence of calcium oxalate uroliths in people have yielded conflicting results (Johansson et al, 1980; Ettinger et al, 1988; Schwartz et al, 2001). Addition of magnesium was associated with reduced calcium oxalate saturation in urine as demonstrated with in vitro studies using synthetic human urine (Kohri et al, 1988). In vitro studies demonstrated that physiologic concentrations of magnesium decreased rate of nucleation and growth of calcium oxalate crystals (Kohri et al, 1988; Li et al, 1985). However, excessive dietary magnesium may result in hypercalciuria, a risk factor for calcium oxalate urolithiasis (Fetner et al, 1978).

An epidemiologic study of nutritional factors associated with urolithiasis in cats demonstrated that foods with the lowest magnesium content (0.04 to 0.07% DM; 0.09 to 0.18 mg/kcal) were associated with increased risk of forming calcium oxalate uroliths when compared with foods that had moderate magnesium content (0.08 to 0.14% DM; 0.19 to 0.35 mg/kcal) (Lekcharoensuk et al, 2001a). Foods with the highest magnesium content (0.14 to 0.56% DM; 0.36 to 1.40 mg/kcal) also were associated with increased risk of developing calcium oxalate uroliths when compared with foods containing moderate amounts of magnesium. In another study of cats with calcium oxalate uroliths, the mean magnesium content (0.19 mg/kcal) of the food being fed at the time of urolith diagnosis was similar to that of the magnesium content of a urolith-prevention food[e] (0.2 mg/kcal), which significantly decreased urine calcium oxalate saturation compared with the regular food (Lulich et al, 2004). To minimize risk of calcium oxalate uroliths, foods should contain a moderate amount of magnesium (0.07 to 0.14% DM). Individual foods intended to reduce the recurrence of both struvite and calcium oxalate urolithiasis should also be within this range.

Phosphorus

Varying dietary phosphorus levels can alter urinary phosphate concentrations in cats, thereby influencing likelihood of urinary struvite precipitates. High-phosphorus foods have been associated with increased risk of struvite uroliths in cats (Lekcharoensuk et al, 2001a). The recommended range of dietary phosphorus for dissolving struvite uroliths is 0.45 to 1.1% DM phosphorus; for struvite prevention the recommended range is 0.5 to 0.9% DM (**Table 46-12**).

Urinary phosphate can exist in several states; anionic phosphate (PO_4^{-3}) is the important form in precipitation and dissolution of struvite. Urinary concentration of anionic phosphate is reversibly influenced by pH. (See Urinary pH below and **Box 46-3.**) Thus, as urine becomes more acidic, anionic phosphate is converted to monobasic and dibasic phosphate, thereby reducing the concentration of anionic phosphate available for forming struvite precipitates. As urine becomes more alkaline, the reaction proceeds in the opposite direction and concentration of anionic phosphate increases.

Compared with foods containing moderate amounts of phosphorus, both low- and high-phosphorus foods are associated with increased risk of calcium oxalate uroliths in cats. Reduction in dietary phosphorus may cause activation of vitamin D, which promotes intestinal absorption of calcium and subsequent urinary calcium excretion. Rats fed a very low-phosphorus food (0.07% DM) had marked hypercalciuria (Werness et al, 1981). Feeding this level of phosphorus for one week resulted in urine that was oversaturated with calcium oxalate and contained large amounts of calcium oxalate crystals. A possible explanation for increased risk of calcium oxalate uroliths associated with increased phosphorus intake is that excessive dietary phosphorus could form insoluble salts with dietary calcium, which in turn could increase availability of noncomplexed oxalic acid for intestinal absorption and renal excretion (Lekcharoensuk et al, 2001a).

The recommended range of dietary phosphorus for decreasing risk of calcium oxalate urolithiasis is 0.50 to 1.0% DM phosphorus (**Table 46-12**). The recommended range for the phosphorus content of foods intended for prevention of both struvite and calcium oxalate should be between 0.5 and 0.9% DM.

Calcium

Calcium availability from the gastrointestinal tract may be influenced by non-dietary and dietary factors. Intestinal absorption of calcium occurs primarily in the duodenum; transport of calcium across the gut is a saturable process that is vitamin D-dependent. In general, calcium absorption from the intestinal tract is inversely proportional to dietary intake. In other words, absorption is high from low-calcium foods and low from high-calcium foods. Other dietary factors (e.g., vitamin D, sucrose, fructose, glucose, xylose, dietary fiber, oxalic acid, phytic acid, protein and phosphorus) reportedly affect calcium availability.

Excessive dietary calcium should be avoided to prevent recurrence of calcium oxalate uroliths. The most important sources of excess calcium are commercial foods and mineral supplements containing high calcium levels. High intake of dietary calcium may lead to hypercalciuria and urolith formation in patients with intestinal hyperabsorption of calcium. Calcium-rich human foods (**Table 46-15**) should be avoided in patients at risk for calcium oxalate uroliths. In addition to foods naturally high in calcium, a number of different human foods (e.g., breads and breakfast cereals) and beverages are fortified with calcium. The amount of calcium added to these foods can be found on the product label.

Another potential unrecognized source of excess dietary calcium is vitamin-mineral supplements, especially calcium supplements. A wide variety of calcium supplements are available over the counter. These supplements differ in the amount of elemental calcium provided. Calcium carbonate, for example, contains 40% calcium (by weight), whereas calcium lactate and calcium gluconate contain 13 and 9% calcium, respectively. Little is known about the relative availability of calcium from different supplements. Calcium supplements differ not only in their calcium content, but also in their solubility. Increasing dietary calcium intake prevents dietary hyperoxaluria in human patients eating oxalate-rich foods (Pak, 1990). This finding presumably is due to decreased intestinal absorption of oxalate. However, women taking calcium supplements had a 79% increased risk of calcium oxalate uroliths (Curhan et al, 1995). The increased risk associated with calcium supplements may be due to timing of ingestion. If not taken with meals, calcium supplements may lead to increased urinary calcium excretion, without decreasing oxalate absorption in the gastrointestinal tract.

Excessive restriction of calcium should also be avoided; it may cause negative calcium balance and contribute to hyperoxaluria, which increases risk for calcium oxalate uroliths. Cats fed foods containing moderate amounts of calcium had decreased risk of developing calcium oxalate uroliths compared with cats fed either low or high amounts of calcium (Lekcharoensuk et al, 2001a). The recommended range of dietary calcium for decreasing risk of calcium oxalate uroliths is 0.6 to 1.0% DM. This is also the recommended range for the calcium content of foods intended for prevention of both struvite and calcium oxalate urolithiasis.

Protein

Excessive dietary protein intake should be avoided in patients at risk for struvite uroliths. Protein provides additional urea and glutamine, which are metabolized to ammonia and ammonium, respectively. Urinary excretion of ammonia and ammonium increases their availability to combine with magnesium and phosphate to form struvite crystals and uroliths. In addition, foods that have increased amounts of protein also tend to have increased phosphorus, which is a component of struvite uroliths. The recommended amount of dietary protein for struvite dissolution and prevention ranges from 30 to 45% DM protein.

The risk of calcium oxalate urolithiasis in people and dogs generally is considered to increase with ingestion of foods that are high in protein. During the last century, the predominant urolith type in people in the U.S. has shifted from struvite to calcium oxalate (Goldfarb, 1994). Cross-cultural studies have shown a shift from struvite to calcium oxalate uroliths with increasing industrialization (Samuel and Kasidas, 1995). The reason for the increased incidence of calcium oxalate in these human populations is unknown. However, dietary habits are thought to play a major role. Nutritional epidemiologic studies have emphasized the role of increased dietary intake of animal protein. This link seems plausible because the amount of animal protein in the diet correlates with industrialization. Dietary protein increases calcium, uric acid and possibly oxalate excretion and decreases urinary pH. Animal proteins are rich in sulfur-containing amino acids, which are metabolized to sulfate and thus may reduce urinary pH and increase urinary calcium and uric acid concentrations. High dietary protein intake reportedly increases urinary calcium excretion in dogs. The 24-hour urinary calcium excretion almost doubled when dogs were fed a food containing 31% DM protein compared with calcium excretion for dogs fed a food containing 10% DM protein (Bartges et al, 1995). The type of protein, duration of protein intake and phosphorus intake influence the effect of protein on calcium.

At present, available evidence does not support that excessive dietary protein is associated with calcium oxalate uroliths in cats. Healthy cats eating a high-protein food (13.7 g/100 kcal; 55% DM protein for a food with 4 kcal metabolizable energy [ME]/g DM) had increased water intake, urine volume and urinary pH; however, they did not have increased urinary calcium excretion (Funaba et al, 1996). In a case-controlled study of nutritional factors associated with urolithiasis, cats fed foods containing more than 7.98 g of protein/100 kcal (32% DM protein for a food with 4 kcal ME/g DM) were less likely to form calcium oxalate uroliths than cats fed low-protein foods (5.15 to 7.98 g/100 kcal; 21 to 32% DM protein for a food with 4 kcal ME/g DM) (Lekcharoensuk et al, 2001a). It is possible that increased urine volume associated with increased protein intake plays a role in decreasing risk of urolith formation. On the basis of current information, cats at risk for calcium oxalate uroliths should be fed foods with at least 32% DM protein. The protein content of foods intended for prevention of both struvite and calcium oxalate should be between 32 and 45% DM.

Table 46-15. Calcium-rich foods that should be avoided in cats at risk for calcium oxalate urolithiasis.*

Food item	Serving size	Calcium (mg)
Yogurt	1 cup (8 oz.)	415
Whole milk	1 cup (8 oz.)	291
Cheese	1 oz.	200-270
Ice cream or ice milk	1 cup (8 oz.)	176
Cottage cheese, creamed	1 cup (8 oz.)	136
Broccoli, cooked	1 large stalk	88

*Mineral supplements and some commercial cat foods contain much more calcium than these foods; therefore, a thorough and complete nutritional history is important for managing these patients.

Sodium

Increasing the salt (i.e., sodium chloride) content of food is an effective method for increasing water intake and causing subsequent urine dilution in healthy cats (Hawthorne and Markwell, 2004; Luckshander et al, 2004). However, most factors that promote natriuresis tend to increase urinary calcium excretion, which could increase risk for calcium oxalate uroliths. Calcium and sodium are reabsorbed at common sites in the renal tubules. Hypercalciuric people who form calcium-containing uroliths appear to have a proportionally greater increase in urinary calcium excretion than non-urolith formers. Increasing dietary sodium intake from 140 to 310 mmol/day increased urinary calcium excretion by 34% and decreased urinary citrate by 10% (Kok et al, 1990). However, urinary calcium and sodium excretion was not correlated in healthy people with low dietary calcium intake (Dawson-Hughes et al, 1996).

Effects of increased sodium intake on urinary excretion of calcium or urinary calcium oxalate saturation in cats with calcium oxalate uroliths have not been reported. Increased urinary excretion of calcium was identified in cats with mild, naturally occurring chronic kidney disease consuming a food with 1.2% DM sodium compared with consumption of a food containing 0.4% DM sodium (Kirk et al, 2006). Additional study of effects of increased sodium intake on urinary calcium excretion in cats with kidney disease is indicated because nephroliths and ureteroliths, which are most often calcium oxalate, are being diagnosed more often in cats with chronic kidney disease (Ross et al, 2005, 2007).

In healthy cats fed a high-salt food, urine calcium concentration and calcium oxalate saturation were not increased, although there was a significant increase in 24-hour urine calcium excretion (Biourge et al, 2001). This was likely due to dilution of calcium and other substances in urine associated with increased urine volume. In another study of healthy cats, increased dietary sodium was associated with increased water intake and urine volume and significantly decreased values for calcium oxalate urine saturation (Hawthorne and Markwell, 2004).

In an epidemiologic study, feeding foods containing less sodium (0.48 to 0.77 mg sodium/kcal; 0.19 to 0.31% DM, for a food with 4 kcal ME/g DM) was associated with calcium oxalate uroliths in cats (Lekcharoensuk et al, 2001a). Despite this finding, feeding a veterinary therapeutic food containing 0.67 mg sodium/kcal (0.27% DM for a food with 4 kcal ME/g DM) to calcium oxalate urolith-forming cats was associated with a significant decrease in urine calcium excretion and calcium oxalate saturation compared with eating their regular food (Lulich et al, 2004). The recommended range for dietary sodium intake in cats at risk for calcium oxalate uroliths is 0.3 to 0.6% DM sodium.

Varying levels of sodium have been used in foods[f,g] that have been shown to be effective for struvite dissolution in feline patients (Osborne et al, 1990; Houston et al, 2004). In lieu of other data, based on the sodium levels in these foods, a recommended range for sodium content for foods for struvite dissolution could be developed by simply bracketing the levels in these foods (e.g., 0.37 to 1.27% DM sodium). However, research indicates that urinary calcium excretion increases when healthy cats are fed a high-salt food (Biourge et al, 2001). Also, as mentioned above, cats prone to the development of calcium oxalate urolithiasis benefit from avoiding increased sodium intake (Lulich et al, 2004). Thus, to avoid excess calcium excretion and the possibility of formation of calcium oxalate crystals while feeding these types of foods, a sodium range of 0.3 to 0.6% DM is recommended in foods intended for struvite dissolution.

Cats fed foods containing 1.43 to 3.7 mg of sodium/kcal (0.57 to 1.48% DM, for a food with 4 kcal ME/g DM) were 4.1 times as likely to develop struvite uroliths as cats consuming foods with less sodium (0.48 to 0.77 mg/kcal; 0.19 to 0.31% DM, for a food with 4 kcal ME/g DM) (Lekcharoensuk et al, 2001a). In this epidemiologic study there was a significant correlation between high sodium and high phosphorus content in foods. It is possible that increased risk for struvite uroliths in cats eating high-sodium foods is related to the type of sodium salt (e.g., monosodium phosphate, sodium tripolyphosphate) used in foods. However, additional study is needed to confirm this. There are no reported studies evaluating effects of increased sodium intake in cats with naturally occurring struvite uroliths. The recommended range of dietary sodium intake for prevention of struvite disease in cats is 0.3 to 0.6% DM.

In order to cause production of dilute urine, food must contain more than 1% DM sodium. Many foods formulated for cats with lower urinary tract diseases contain between 0.3 and 0.6% DM sodium, whereas, some contain 1 to 1.4% DM sodium. The minimum recommended allowance of sodium for adult cats is 0.068% DM (NRC, 2006). According to the most recent information published by the National Research Council (NRC), it is difficult to suggest a safe upper limit of sodium for healthy adult cats (NRC, 2006). The NRC has concluded that as long as unlimited amounts of water are available, cats probably can tolerate reasonably high concentrations of dietary sodium; the safe upper limit for adult cats has been defined as greater than 1.5% DM. However, the safe upper limit of sodium for cats with chronic kidney disease, lower urinary tract disorders and other conditions (e.g., hypertension) is unknown. One study revealed that six cats with early kidney disease had significant increases of serum creatinine, urea nitrogen and phosphorus when consuming a food with 1.2% DM sodium for three months vs. when fed a food with 0.4% DM sodium (Kirk et al, 2006). Additional evaluation of effects of increased sodium intake is needed because most studies have either been of short duration (<6 months) or were performed in healthy cats. Pending availability of additional data (e.g., effects of high sodium intake in cats with calcium oxalate uroliths), orally administered sodium chloride should be used cautiously and with careful monitoring because of the potential for increased risk of calcium oxalate urolith formation in some patients (Bartges and Kirk, 2006).

Urinary pH

The kidneys eliminate acid that is produced as a result of normal metabolism, including digestion of food. Therefore, to

Box 46-4. Determining the Effect of Food on Urinary pH.

Several important effects of food on acid-base balance can be described by the anion-cation balance (ACB). Calculation of a food's ACB has been evaluated as a practical method for predicting the effect of a food on urinary pH. In this method, the ACB is calculated from the concentrations of alkaline and acid compounds in the food, expressed as mmol/kg dry matter, using the formula:
ACB = 49.9 (Calcium) + 82.3 (Magnesium) + 43.5 (Sodium) + 25.6 (Potassium) – 64.6 (Phosphorus) – 13.4 (Methionine) – 16.6 (Cysteine) – 28.2 (Chloride). Factors take into account atomic/molecular weight and valence (2 for phosphorus).

This method was evaluated in a study involving 10 commercial foods (moist and dry) and several additives. Feeding trials involved four to six cats per trial. Cats were fed the foods for two days and urine was collected for at least five days. During the eight hours after feeding, urinary pH was measured immediately after urination and urine excreted during the remainder of the day was tested the following morning. A highly significant correlation was seen between ACB of the food and the mean urinary pH. In the amounts used in this study, the addition of calcium carbonate and calcium lactate significantly increased urinary pH; dibasic calcium phosphate and ascorbic acid had no effect; and calcium chloride, ammonium chloride and phosphoric acid decreased urinary pH.

Another study was conducted recently to determine if urinary pH could be predicted using the nutrient components of feline foods. One-hundred-fifty foods (90 dry, 60 wet) were fed to groups of 10 adult cats to determine urinary pH of cats fed each food. Each food was fed for seven days and pH was determined on freshly voided urine on Days 5 to 7 of the study. Using stepwise regression, it was determined which cations, anions and sulfur-containing amino acids were of importance for predicting urinary pH. Separate formulas had to be used for dry and wet foods to maintain accuracy.

Although calculation of ACB may roughly estimate urinary pH and formulas can be used to predict urinary pH based on nutrient content of food, the most accepted method of comparing foods is to feed the food to a group of cats and compare urinary pH values. However, although most reputable cat food manufacturers provide urinary pH data for their products, no standard urinary pH testing protocol has been developed. Consequently, it is important to know the protocol used to measure urinary pH before comparing results from different companies or laboratories.

The Bibliography for **Box 46-4** can be found at www.markmorris.org.

define "normal" urinary pH, it is necessary to consider the "normal" or habitual diet. On a volume basis, the gastric content of feral cats is approximately 90% small mammals (e.g., mice, rats) (Coman and Brunner, 1972). In one study, the average urinary pH was approximately 6.3 when cats were fed a diet of rat carcasses (Vondruska, 1987). In another study, mean urinary pH was reported to be 5.97 for feral female cats and 6.37 for feral male cats eating a natural diet (Cottam et al, 2002).

The kidneys provide long-term defense against acid and alkali deviations; this process occurs continuously as endogenous acids are generated. The kidneys must conserve bicarbonate in the glomerular filtrate and regenerate bicarbonate degraded by the reaction with metabolic acids to maintain normal plasma bicarbonate levels. The kidneys can increase the amount of net acid excretion in urine and generate bicarbonate in response to exogenous acid loads. Normally, the kidneys synthesize urinary ammonia (NH_3) and thus ammonium (NH_4^+) almost exclusively. With chronic metabolic acidosis, more NH_3 is produced and urinary NH_4^+ ion concentration is increased. The kidneys excrete hydrogen ions (H^+) in the form of titratable acid (e.g., phosphoric acid) and NH_4^+ ions. Reduction of urinary pH greatly increases the ratio of NH_4^+ to NH_3. Acidifying foods, therefore, increase urinary concentration of NH_4^+ ions, one component of struvite. Although decreasing urinary pH theoretically increases urinary NH_4^+ concentration, the same change in urinary pH decreases anionic phosphate levels in urine. Thus, as urine becomes more acidic, precipitation of struvite becomes less likely.

The effect of a food on urinary pH is the net effect of its constituent nutrients (**Box 46-4**). Dietary acid is derived from several nutrients (**Table 46-16**) (Halperin and Jungas, 1983).

Table 46-16. Urine acidifying and alkalinizing pet food ingredients.

Protein sources that are acidifying ingredients
Poultry meal
Corn gluten meal
Other acidifying ingredients
Ammonium chloride*
Calcium chloride
Calcium sulfate
dl-methionine
Phosphoric acid
Alkalinizing ingredients
Calcium carbonate
Potassium citrate
Magnesium oxide

*Not approved in the United States as a food additive.

Sulfuric acid is formed when sulfur-containing amino acid (e.g., methionine and cysteine) residues of proteins are oxidized to sulfate. In general, animal-source protein ingredients contain more sulfur-containing amino acid residues than do plant-source proteins. Phosphorus has strong effects on acid-base balance, depending on its chemical form. Inorganic phosphorus can be ingested as phosphoric acid, monobasic and dibasic or anionic phosphate. Phosphoric acid is used in cat foods to enhance palatability, either separately or as a component of topically applied animal digests. Phosphoric acid has a strong acidifying effect. Monobasic phosphate also is acidifying, whereas dibasic phosphate has little effect on urinary pH (Kienzle et al, 1991). Anionic phosphate is alkalizing.

Mineral salts vary in their effect on urinary pH and thus are potential acid or base sources. Oxides and carbonates are alka-

Table 46-17. Effect of urinary pH on urine saturation values in healthy cats (n = 6).*

Food	Urinary pH	CaOx RSS	Struvite RSS
$NaHCO_3$	6.81 ± 0.33[b]	0.78 ± 0.53[a]	7.98 ± 4.62[b]
Control	6.18 ± 0.26[a]	0.71 ± 0.28[a]	1.61 ± 1.11[a]
NH_4Cl	5.81 ± 0.14[a]	1.66 ± 0.58[b]	1.16 ± 0.25[a]

Key: $NaHCO_3$ = sodium bicarbonate, NH_4Cl = ammonium chloride, CaOx = calcium oxalate, RSS = relative supersaturation.
*Significant differences within columns indicated by different superscripts. Adapted from Stevenson AE, Wrigglesworth DJ, Markwell PJ. Urine pH and urinary relative supersaturation in healthy adult cats In: Rodgers AL, Hibbert BE, Hess B, et al, eds. IXth International Symposium on Urolithiasis. Cape Town, South Africa, 2000: 818-820.

Table 46-18. Oxalate content of selected human foods.*

Product categories	Moderate to high oxalate	Low oxalate
Milk and dairy products	–	Milk** Cheese**
Meats	Liver Sardines	Beef Bacon Ham Lamb Shellfish Poultry
Fruits	Apples (green) Apricots Bananas Cherries Berries (most) Oranges/tangerines Pears Peel (lemon/lime/orange) Pineapple	Apples (red) Coconut (fresh) Cranberries Melons Peaches
Vegetables	Beans Carrots Celery Green beans Green peppers Greens (collards, mustard, turnips) Peas Soybean products Spinach Sweet potatoes Tofu Tomatoes	Asparagus Avocado Broccoli** Cabbage Corn (sweet) Cucumber
Breads/ grains/nuts	Bagels Bread (whole wheat) Cornbread Fig newtons Fruitcake Grits Oatmeal Most nuts Rice (brown)	Bread (white) Tortilla (corn) Pasta (boiled) Popped popcorn Rice (white)

*For information about oxalate content of additional foods see www.ohf.org
**High in calcium, therefore, may not be ideal for cats with calcium oxalate uroliths.

lizing. Differences in absorption of the cation and anion portion of a salt are important. Intestinal absorption of calcium and magnesium is relatively low. However, absorption of accompanying anions can be high and influences urinary pH. Nonmetabolizable anions (e.g., chloride, phosphate and sulfate) absorbed in excess of their accompanying cations are acidifying. For example, ammonium chloride, calcium chloride and calcium sulfate decrease urinary pH, and magnesium oxide and calcium carbonate increase urinary pH.

Urinary pH plays a critical role in managing cats with struvite disease but appears less important in cats with calcium oxalate uroliths. Struvite is highly soluble and is, therefore, less likely to precipitate in acidic urine (pH <6.5). Alterations in urinary pH have a proportionally greater effect on changing struvite activity product than changes in crystalloid (e.g., magnesium) concentrations. Decreasing urinary pH, therefore, is the most reliable means of producing urine undersaturated for struvite. Although acidifying foods have been associated with occurrence of calcium oxalate uroliths in cats, changes in urinary pH values over the physiologic range appear to have little effect on solubility of calcium oxalate (**Figure 46-17**) (Verplaetse et al, 1985; Yu and Gross, 2007; Stevenson et al, 2000). One study showed that pH changes between 4 and 11 had minimal effect on calcium oxalate solubility (Verplaetse et al, 1985). In a study of healthy cats fed three foods to produce different urinary pH values, reducing urinary pH from 6.81 to 6.18 had no significant effect on urine saturation for calcium oxalate (0.78 vs. 0.71) but significantly decreased struvite saturation (**Table 46-17**) (Stevenson et al, 2000).

The recommended urinary pH range for dissolving struvite uroliths is 5.8 to 6.2. To decrease risk for recurrence of struvite uroliths or urethral plugs, urinary pH should be 6.0 to 6.4; however, to decrease risk for recurrence of calcium oxalate uroliths, urinary pH should be at least 6.2. Thus, foods for prevention of both struvite and calcium oxalate urolithiasis should produce a urinary pH between 6.2 to 6.4.

Fatty Acids

Urinary bladder inflammation is characteristic of most lower urinary tract disorders including FIC and urolithiasis. Long-chain omega-3 (n-3) fatty acids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have potent antiinflammatory properties. These dietary fatty acids are absorbed and incorporated into cell membranes, including those of the urinary bladder, where they may alter production of inflammatory mediators. Antiinflammatory effects of omega-3 fatty acids such as EPA have been demonstrated in dogs with osteoarthritis and patients with dermatitis. Effects of omega-3 fatty acids have not been evaluated in cats with various lower urinary tract disorders; however, they appear to have beneficial urinary effects in studies of other species. Administration of EPA to rats prevented experimentally induced nephrocalcinosis and significantly decreased urinary calcium excretion compared with a placebo (Buck et al, 1991). In a second part of the study, 12 human patients with recurrent calcium oxalate uroliths and hypercalciuria had significantly decreased urinary calcium and oxalate excretion when treated with EPA for eight weeks. In another study, administration of EPA for three months to 88 people with recurrent urinary stones, primarily calcium oxalate, was associated with significantly decreased urinary calcium in those with hypercalciuria (Yasui et al, 2001).

The recommended range of dietary total omega-3 fatty acids (i.e., DHA and/or EPA) for managing inflammation associated with lower urinary tract diseases is 0.35 to 1.0% DM. This range was extrapolated from levels associated with antiinflammatory effects in other species. Additional study is needed to better define the therapeutic range of omega-3 fatty acids for managing patients with FIC and calcium oxalate uroliths.

Other Nutritional Factors

Antioxidants

Vitamin E has antioxidant properties that have been shown to decrease oxidative stress and damage caused by free radicals. Because oxidative stress is often associated with inflammation, antioxidants may help create an unfavorable environment for the development of uroliths. However, this has not been evaluated in cats with naturally occurring urolithiasis.

Vitamin C is also an antioxidant. However, a portion of urinary oxalate is derived from endogenous metabolism of vitamin C. In a controlled study of healthy cats fed differing amounts of vitamin C ranging from 40 to 193 mg vitamin C/kg of food for four weeks, there was no significant change in urinary oxalate excretion (Yu and Gross, 2005). Effects of vitamin C supplementation have not been studied in cats with calcium oxalate uroliths. Because cats do not have a dietary requirement for vitamin C, supplementation should be avoided in cats at risk for calcium oxalate uroliths (Bartges and Kirk, 2006). One source of vitamin C that should be avoided is cranberry concentrate tablets.

Oxalate

Excessive intake of oxalate is unlikely in dogs and cats eating most commercial foods but it could occur in pets receiving excessive amounts of certain human foods as treats. Foods that contain relatively high amounts of oxalate (e.g., spinach, carrots, liver, sardines) should be avoided in patients with a history of calcium oxalate uroliths. **Table 46-18** provides more information about the oxalate content in selected human foods.

Potassium

Transient negative potassium balance has been reported to occur in adult cats receiving long-term dietary acidification (i.e., for struvite urolith prevention) with phosphoric acid and NH_4Cl; potassium balance returned to normal by the end of both studies (Fettman et al, 1992; Ching et al, 1990). In an epidemiologic study, cats fed foods with higher amounts of potassium (2.17 to 3.20 mg/kcal; 0.87 to 1.28% DM for a food with 4 kcal ME/g DM) had decreased risk of calcium oxalate uroliths compared with cats that were eating foods with less potassium (0.95 to 1.60 mg/kcal; 0.35 to 0.64% DM for a food with 4 kcal ME/g DM) (Lekcharoensuk et al, 2001a). Additional study is needed to determine if potassium supplementation benefits cats with calcium oxalate uroliths. Based on current information, dietary potassium intake should exceed 0.65% DM in cats at risk for struvite disease and calcium oxalate uroliths. Most commercial foods are replete with potassium.

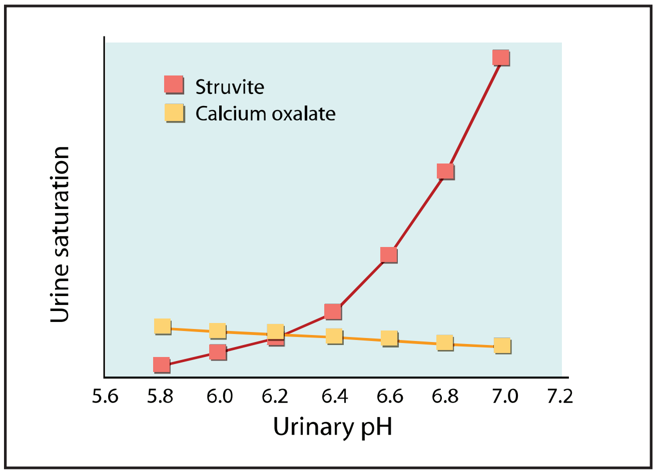

Figure 46-17. This graph demonstrates the relationship between urinary pH and urine saturation values for struvite and calcium oxalate. Data were collected from 21 adult cats (10 healthy and 11 urolith-forming cats) during consumption of a food (Hill's Prescription Diet c/d Multicare Feline) formulated to manage both struvite and calcium oxalate uroliths. Mineral type was not available for uroliths in most cats; however, calcium oxalate was presumed most likely due to location (eight cats had nephroliths), radiographic appearance and results of quantitative analysis for uroliths that were removed. Urine constituents (e.g., calcium oxalate, magnesium, phosphate) and pH were measured for each cat and used to calculate values for relative supersaturation (RSS). This was followed by a computer-modeling procedure to predict effect that changing only urinary pH would have on RSS values. Results were similar for both healthy and urolith-forming cats; therefore, all data are shown in one graph. Note that as urinary pH increases, urine saturation for struvite increases; however, as urinary pH decreases over the physiologic range, there is only a slight change in calcium oxalate saturation. In this model, reducing urinary pH from 7.4 to 6.4 decreased struvite saturation by 122 units but only increased calcium oxalate saturation by 0.9 units. (Adapted from Yu S, Gross KL. Dietary management of the three most common lower urinary tract diseases in cats. In: Proceedings. Hill's Symposium on Lower Urinary Tract Disease. Educational Concepts, 2007: 53-57.)

Vitamin B_6 (Pyridoxine)

Increases in urinary oxalic acid excretion have been observed in kittens fed pyridoxine-deficient foods. However, no studies have evaluated effects of vitamin B_6 in cats with calcium oxalate uroliths (Bai et al, 1989, 1991). No evidence suggests that supplementing vitamin B_6 beyond nutritional requirements benefits cats with calcium oxalate urolithiasis. Because most commercially available pet foods are well supplemented with vitamin B_6, it seems unlikely that additional supplementation would be helpful unless the primary food is homemade.

Vitamin D

Increased vitamin D intake should be avoided because it can lead to increased intestinal absorption of calcium with subse-

Table 46-19. Comparison of key nutritional factors in selected commercial veterinary therapeutic foods for reducing the recurrence of feline idiopathic cystitis, struvite disease (uroliths or urethral plugs) and/or calcium oxalate uroliths in cats.*

Moist foods**	Mg (%)	P (%)	Ca (%)	Protein (%)	Na (%)	Urinary pH	Total omega 3 (%)
Recommended levels	**0.07-0.14**	**0.5-0.9**	**0.6-1.0**	**32-45**	**0.3-0.6**	**6.2-6.4**	**0.35-1.0**
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.052	0.68	0.72	43.8	0.32	6.35	0.96
Hill's Prescription Diet c/d Multicare with Seafood Feline	0.054	0.71	0.62	44.8	0.33	6.4	0.62
Medi-Cal Urinary SO	na	1.20	1.20	43.5	1.1	6.4	na
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	0.97	0.96	50.6	0.62	6.0-6.4	na
Royal Canin Veterinary Diet Urinary SO in gel	0.10	1.36	1.02	41.3	1.02	6.0-6.3	na
Dry foods	**Mg (%)**	**P (%)**	**Ca (%)**	**Protein (%)**	**Na (%)**	**Urinary pH**	**Total omega 3 (%)**
Recommended levels	**0.07-0.14**	**0.5-0.9**	**0.6-1.0**	**32-45**	**0.3-0.6**	**6.2-6.4**	**0.35-1.0**
Hill's Prescription Diet c/d Multicare Feline	0.06	0.65	0.74	36.1	0.35	6.3	0.65
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.06	0.65	0.76	34.6	0.33	6.3	0.64
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	1.08	1.1	44.9	1.17	6.0-6.4	na

Key: Mg = magnesium, P = phosphorus, Ca = calcium, Na = sodium, total omega 3 = total omega-3 fatty acids, na = not available from manufacturer.
*Nutrients expressed on a dry matter basis unless otherwise stated.
**In general, it is recommended that moist foods be fed to cats with lower urinary tract disorders, especially those with feline idiopathic cystitis or calcium oxalate uroliths.

Table 46-20. Descriptions of grades used to classify evidence supporting treatments for cats with lower urinary tract diseases.*

Grade	Description of evidence
I	At least one properly designed, randomized, controlled clinical study performed in patients of the target species
II	Evidence from properly designed, randomized, controlled studies in animals of the target species with spontaneous disease in a laboratory or research animal colony setting
III	Appropriately controlled studies without randomization Appropriately designed case-control epidemiologic studies Studies using models of disease or simulations in the target species Dramatic results from uncontrolled studies Case series
IV	Studies conducted in other species Reports of expert committees Descriptive studies Case reports Pathophysiologic justification/rationale Opinions of respected experts

*Adapted from Roudebush P, Allen TA, Dodd CE, et al. Application of evidence-based medicine to veterinary clinical nutrition. Journal of the American Veterinary Medical Association 2004; 224: 1765-1771.

quent hypercalciuria and increased risk for oxalate uroliths. The minimum recommended allowance for vitamin D for adult cats is 280 IU/kg food (DM; for a food with 4 kcal ME/g DM) (NRC, 2006). However, cats at risk for calcium oxalate urolithiasis and those with hypercalcemia associated with calcium oxalate urolithiasis should be fed foods that do not exceed 2,000 IU/kg of food. Dietary supplements containing vitamin D should not be fed to at-risk cats.

Fiber

The role of dietary fiber has not been carefully evaluated in cats with lower urinary tract disorders. In an epidemiologic study of cats with uroliths, those fed high-fiber foods (0.71 to 11.57 g/100 kcal) were 2.12 times more likely to develop struvite uroliths than cats fed low-fiber foods (0.06 to 0.30 g/100 kcal) (Lekcharoensuk et al, 2001a). In the same study there was no association between dietary fiber and development of calcium oxalate uroliths. Dietary fiber may bind calcium in the small intestine, preventing its absorption. There are anecdotal reports that feeding foods with increased fiber helps control hypercalcemia in cats with concomitant calcium oxalate uroliths (McClain et al, 1999).

FEEDING PLANS

Successful management of cats with various lower urinary tract diseases requires a multifaceted approach and effective communication between health care team members and owners. Nutritional management plays a key role in the treatment of patients with FIC, struvite disease (uroliths and urethral plugs) and calcium oxalate uroliths. Environmental enrichment (e.g., stress reduction, litter box management) also should be implemented in patients with FIC and may be helpful for cats with other lower urinary tract disorders. For cats with persistent clinical signs, especially periuria, behavioral modification may also be needed to correcting the underlying medical disorder. Finally, other treatments such as pain management may be needed for some cats, especially during acute episodes.

Feeding plans for cats with various lower urinary tract diseases continue the iterative process and include the following steps: 1) assess and select the food, 2) assess and determine the feeding method and 3) reassess and modify the feeding plan, as

Table 46-21. Summary of evidence for treatments used to manage cats with idiopathic cystitis, struvite uroliths or urethral plugs and calcium oxalate uroliths.*

Feline idiopathic cystitis
Grade III
- Environmental enrichment/stress reduction
- Feeding moist food
- Long-term treatment with amitriptyline (6 to 9 months) for severe cases

Grade IV
- Increased salt intake to stimulate urine dilution
- Additional methods to stimulate water intake
- Analgesics and nonsteroidal antiinflammatory drugs during acute episodes
- Feline facial pheromone
- Glycosaminoglycans (pentosan polysulfate, glucosamine/chondroitin sulfate)
- Propantheline during acute episodes

Dissolution of struvite uroliths
Grade III
- Hill's Prescription Diet s/d Feline
- Medi-Cal Dissolution Formula

Grade IV
- Other therapeutic foods formulated to dissolve uroliths

Prevention of struvite urolith or urethral plug recurrence
Grade III
- Hill's Prescription Diet s/d (for urethral plug prevention)

Grade IV
- Other therapeutic foods formulated to prevent struvite disease

Decreasing risk of calcium oxalate recurrence**
Grade III
- Feeding moist food
- Hill's Prescription Diet x/d Feline (currently available as c/d Multicare Feline)

Grade IV
Other therapeutic foods formulated to prevent calcium oxalate
- Potassium citrate
- Thiazide diuretics
- Vitamin B_6
- Using other methods (in addition to moist food) to increase water intake

*Adapted from Forrester SD, Roudebush P. Evidence-based management of feline lower urinary tract disease. Veterinary Clinics of North America: Small Animal Practice 2007; 37: 533-558.
**Based on decreased urine calcium oxalate saturation or decreased risk in epidemiologic studies.

Table 46-22. Comparison of key nutritional factors in selected commercial veterinary therapeutic foods for reducing the recurrence of feline idiopathic cystitis.*

Moist foods**	Omega 3 (%)
Recommended levels	**0.35-1.00**
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.96
Hill's Prescription Diet c/d Multicare with Seafood Feline	0.62
Iams Veterinary Formula Urinary S Low pH/S Feline	na
Medi-Cal Veterinary Diet Urinary SO	na
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	na
Royal Canin Veterinary Diet Feline Urinary SO in Gel	na
Dry foods	**Omega 3 (%)**
Recommended levels	**0.35-1.00**
Hill's Prescription Diet c/d Multicare Feline	0.65
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.64
Medi-Cal Veterinary Diet Urinary SO	na
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	na

Key: Omega 3 = total omega-3 fatty acids, na = not available from manufacturer.
*Nutrients expressed on a dry matter basis.
**Moist foods are best because increased water intake is considered important in the management of feline idiopathic cystitis.

necessary. Four feeding plans are reviewed below, including treatment and prevention of FIC, dissolution of struvite uroliths, prevention of struvite urolithiasis and urethral plugs and managing cats with calcium oxalate urolithiasis.

Regarding the food assessment/selection step: more recently, several foods have been developed that are intended to simultaneously manage the combination of risk factors associated with FIC-, struvite- and calcium oxalate-based FLUTD. These foods are listed in **Table 46-19** and are compared to the composite key nutritional factors for these three forms of lower urinary tract disease. The use of this type of food is intended to simplify and improve the effectiveness of FLUTD prevention strategies. The following sections provide guidelines for successful implementation of feeding plan recommendations and other treatments that may improve outcome and enhance quality of life for cats and their owners. In addition to considering key nutritional factors, the quality of evidence supporting different treatments and foods should be evaluated (Roudebush et al, 2004; Forrester and Roudebush, 2007). **Tables 46-20** and **46-21** provide more information about evidence for treatments of cats with FLUTD.

Feline Idiopathic Cystitis

FIC is characterized by recurrent episodes of lower urinary tract signs that usually resolve within three to five days. Because of the nature of this disorder, complete elimination of episodes is unlikely. Therefore, goals of treatment are to improve quality of life by decreasing frequency of episodes and their severity. Environmental enrichment (e.g., stress reduction, litter box management) should also be implemented in patients with FIC. In cats with persistent clinical signs, especially periuria, behavioral modification may be needed in addition to correcting the underlying medical disorder. Other treatments such as pain management may be needed for some cats, especially during acute episodes. **Boxes 46-5**, **46-6**, and **46-7** include information about environmental enrichment, behavioral modification and pain management.

Assess and Select the Food

Moist foods are recommended for patients with FIC. Feeding moist food has been associated with increased daily water intake and urine volume in cats compared with feeding dry food (**Table 46-14**) (Burger and Smith, 1987; Gaskell, 1989). Beneficial effects have been observed in patients with FIC when urine specific gravity decreased from values around 1.050

Box 46-5. Ancillary Management for Patients with Feline Idiopathic Cystitis: Environmental Enrichment.

In addition to nutritional management, currently recommended treatment for patients with feline idiopathic cystitis (FIC) includes environmental enrichment, stress reduction and appropriate litter box maintenance. Recently, a prospective, uncontrolled study evaluated the effects of multimodal environmental modification in 46 client-owned cats with FIC. Significant reductions in lower urinary tract signs, fearfulness and nervousness were seen after treatment for 10 months, compared with the signs noted before using environmental enrichment.

Environmental enrichment includes providing opportunities for play/resting (e.g., horizontal and vertical surfaces for scratching, hiding places and climbing platforms). Food and water bowls should be clean and kept in safe places (e.g., not next to noisy appliances). Litter boxes should be clean and kept in locations that do not increase stress. An adequate number of litter boxes (generally defined as one more than the number of cats in the home) should be available. Most cats prefer clumping, unscented litter but individual preferences may differ for some cats and different strategies can be used to determine a cat's particular preference. More detailed and helpful information about environmental enrichment and litter box management is available elsewhere.

BEHAVIORAL MANAGEMENT

Even after successful implementation of strategies described above, some patients with FIC (or other lower urinary tract disorders) may continue to urinate in inappropriate locations. This undesirable behavioral pattern may be maintained for several reasons. Classic conditioning may play a role in persistent periuria. The litter box is associated with pain and discomfort that occurred when the cat urinated in the box previously; therefore, the cat might associate this experience with the litter box and avoid using it in the future. In this situation, it may help to change the location or physical characteristics of the litter box. It also is possible for cats to develop a litter box aversion secondary to lack of cleanliness, because the litter box may be used more frequently during episodes of FIC. If this happens, it may help to provide additional litter boxes and/or increase frequency of cleaning the litter box or changing litter. If a cat develops a litter box aversion secondary to FIC or experiences an urgency that causes elimination elsewhere, the possibility exists for development of a secondary location or substrate preference. In this situation, the litter box is not necessarily the problem; however, the cat may discover a better toileting option (e.g., a substrate that is softer, more absorbent, more accessible or cleaned more readily). To resolve this problem, the preferred inappropriate site should be made less attractive or unavailable while the litter box is improved to meet the preferences of the cat. Finally, the pain associated with an episode of FIC may result in increased irritability and subsequent social strife between previously friendly cats in the household. When signs of FIC resolve, cats may not return to their previously friendly relationship. In serious cases, full segregation and gradual reintroduction using desensitization and counter-conditioning may be necessary. Cats with persistent periuria can be very frustrating to manage and may be relinquished to a shelter if not handled appropriately. Therefore, consulting with a veterinary behaviorist (sooner rather than later) should be considered to increase chances of improving quality of life for the cat and the owner. **Boxes 46-6** and **46-7** provide more information about behavioral management of cats with inappropriate urination.

PAIN MANAGEMENT

Analgesics are indicated to manage patient discomfort during acute episodes of FIC. Drugs that have been used include buprenorphine[a] (0.03 mg/kg body weight administered topically via buccal mucosa every six to eight hours), butorphanol[b] (0.5 to 1 mg/kg body weight orally every six to eight hours) and meloxicam[c] (0.1 mg/kg body weight orally once daily for three to four days). Although other analgesics and nonsteroidal antiinflammatory agents may be appropriate, selection is often based on clinician preference or experience and whether the patient has concomitant conditions (e.g., kidney disease) that might preclude their use. No clinical studies have evaluated opioid analgesics (e.g., butorphanol, buprenorphine) or nonsteroidal antiinflammatory agents in patients with FIC.

FELINE FACIAL PHEROMONE

Synthetic feline facial pheromone therapy has been recommended to decrease signs of stress in patients with FIC. In a double-blind, placebo-controlled clinical study of 20 hospitalized cats (13 with lower urinary tract disease and seven apparently healthy), exposure to feline facial pheromone[d] was associated with significant increases in grooming, interest in food and food intake; these results suggested an anxiolytic effect in some cats. Another study evaluated effects of feline facial pheromone in 12 patients with FIC. Although no significant difference was seen between treatment of the environment with placebo and feline facial pheromone for two months, a trend was identified for cats exposed to facial pheromone. Exposed cats had fewer days with clinical signs of cystitis, a reduced number of episodes and reduced negative behavioral traits (e.g., less aggression and fear). Further study is needed; however, it seems reasonable to consider treatment with facial pheromones in cats with signs of stress or when clinical signs persist after implementing environmental enrichment and methods to increase water intake.

GLYCOSAMINOGLYCANS

Glycosaminoglycan (GAG) replacers such as pentosan polysulfate have been used in people with interstitial cystitis and have been recommended for patients with FIC. Anecdotally, these agents have

to values ranging from 1.032 to 1.041 (Markwell et al, 1999; Gunn-Moore and Shenoy, 2004). It is not known if FIC predisposes to urolith formation, but the presence of inflammatory cells and other products of inflammation could conceivably pose such a risk. Foods that are most similar to the key nutritional factor target ranges and/or have the best evidence for managing these uroliths should be considered for cats with FIC. **Tables 46-19** and **46-22** provide key nutritional factor information about selected veterinary therapeutic foods for managing patients with FIC compared with recommended levels of key nutritional factors. When possible, moist foods should be selected over dry foods.

been mentioned as useful. However, only one GAG has been critically evaluated. In a randomized, double-blinded, controlled clinical study, administration of glucosamine hydrochloride[e] (125 mg orally once daily) was not associated with any difference in clinical signs compared with cats that received placebo. If signs of FIC persist despite other treatments, GAGs (such as pentosan polysulfate[f] [8 mg/kg body weight orally q12h] or a combination of glucosamine and chondroitin sulfate[g] [250 mg/200 mg orally q24h]) may be attempted.

AMITRIPTYLINE

Amitriptyline[h] is a tricyclic antidepressant with anticholinergic, antihistaminic, sympatholytic, analgesic and antiinflammatory properties that has been used in treating people with interstitial cystitis and cats with FIC. In an uncontrolled study of cats with severe, recurrent FIC that failed to respond to other treatments, administration of amitriptyline for 12 months was associated with decreased clinical signs in nine (60%) of 15 cats during the last six months of treatment. A randomized, controlled clinical trial of amitriptyline treatment for seven days revealed no significant difference in rate of recovery from pollakiuria or hematuria; overall, clinical signs recurred significantly faster and more frequently in cats that had been treated with amitriptyline compared with control cats. In a similar study, amitriptyline combined with amoxicillin was no more effective than placebo and amoxicillin when given to cats with FIC for seven days. Based on current information, amitriptyline does not appear to be beneficial for short-term management of cats with FIC. It is possible that longer use (i.e., several months) may be helpful; however, this has not yet been demonstrated in a controlled, long-term clinical study.

ENDNOTES

a. Buprenex. Reckitt Benckiser Pharmaceuticals, Inc., Richmond, VA, USA.
b. Torbutrol and Torbugesic. Fort Dodge Animal Health, Fort Dodge, IA, USA.
c. Metacam. Boehringer Ingelheim Vetmedica, Inc., Saint Joseph, MO, USA.
d. Feliway. Veterinary Product Laboratories, Phoenix, AZ, USA.
e. Cystease. Ceva Animal Health, Chesam, United Kingdom.
f. Elmiron. Ortho McNeil Pharmaceutical, Inc., Raritan, NJ, USA.
g. Cosequin for Cats. Nutramax Laboratories, Inc., Edgewood, MO, USA.
h. Elavil. Astra-Zenaca, Wilmington, DE, USA.

The Bibliography for **Box 46-5** can be found at www.markmorris.org.

Assess and Determine the Feeding Method

Gradual transition to moist food and recommending other strategies to increase water intake should be part of initial management of patients with FIC. Cat owners may be hesitant to switch from dry to moist food and some believe their cat will not eat moist food. However, switching to moist food is possible in most situations if the change is made gradually; for some cats this many require a period of several weeks. Failure to make a gradual transition may result in refusal to eat the moist food or increased stress, which may cause recurrence of clinical signs. Therefore, moist food should be offered initially as a food option in a second dish next to the usual food (two-pan approach) (Westropp and Buffington, 2004; Buffington, 2007). If the cat consumes the moist food, the amount of moist food can be increased gradually while decreasing the amount of dry food correspondingly. **Table 46-23** lists tips for increasing water consumption.

Increasing frequency of feeding (i.e., dividing the daily amount of food into several meals) may increase daily water intake in cats. In a study of healthy cats with free access to water, feeding two or three meals per day was associated with a significant increase in total water intake compared with feeding a single meal (Kirschvink et al, 2005).

Reassessment

Clinicians should use their best judgment regarding the most appropriate times for reevaluating patients with FIC. Because of stress associated with hospital visits, it may be preferable to conduct evaluations by talking with owners more often than examining the patient. This allows for discussing effectiveness of current treatments and recommendations for changes if needed. If there are changes in the cat's clinical findings (e.g., increased severity or frequency of episodes) despite appropriate treatment, additional patient evaluation including urinalysis, urine culture and diagnostic imaging is indicated to detect other disorders (e.g., uroliths, UTI).

Feeding Plan for Struvite Urolith Dissolution

Treatment options for cats with struvite uroliths include dissolution by nutritional management and physical removal of uroliths (e.g., cystotomy, voiding urohydropropulsion, catheter retrieval, laser lithotripsy). Treatment selection depends on clinician experience, expertise and preference, availability of necessary equipment, patient factors and client preferences. Considering all factors, it is generally preferred to select the least invasive treatment that has the most evidence for effectiveness.

Two studies reported effects of feeding a dissolution food to cats with struvite uroliths (Osborne et al, 1990; Houston et al, 2004). In one study, 25 cats (13 males, 12 females) with 28 occurrences of struvite uroliths were fed a struvite dissolution food[f] (Osborne et al, 1990). Among cats in the study, there were 20 occurrences of sterile uroliths and eight with UTI (five urease-positive infections, three urease-negative infections). Mean time for sterile struvite urolith dissolution was 36 days (range, 14 to 141 days), while the average time for dissolution of uroliths associated with UTI was 44 days (range, 14 to 92 days). Clinical signs (gross hematuria and dysuria/pollakiuria) were present in 90% or more of urolith occurrences before nutritional management and were absent by the time of first reevaluation in two weeks. None of the cats developed urethral obstruction but perineal urethrostomy had been performed

Box 46-6. Behavioral Screen for Cats with Inappropriate Urination.*

All cats that urinate outside the litter box or in inappropriate places should receive a medical evaluation to identify and address underlying medical disease(s). In some cases, a primary medical reason for inappropriate urination will be identified, treatment implemented and the problem resolved. However, in other cases there will be no primary medical problem identified or even after resolution/control of an identified medical issue, inappropriate urination continues. In the latter case, the medical problem may have been the initiating cause but behavioral issues maintain inappropriate urination, despite successful control/resolution of primary medical problems. For cats with continued inappropriate urination despite diagnosis and management of all primary medical issues, the following questions should be considered:

Question**	Answer
1. Does your cat urinate on vertical surfaces outside the litter box?	☐YES ☐NO
2. Does your cat urinate on horizontal surfaces outside the litter box?	☐YES ☐NO
3. Does your cat seek out certain targets for urination?	☐YES ☐NO
4. Do these targets have a common quality (e.g. all soft, absorbent materials, certain room, always slick surfaces)?	☐YES ☐NO
5. Is the quantity of urine deposited very small?	☐YES ☐NO
6. Does your cat defecate outside the litter box?	☐YES ☐NO
7. Does your cat ever use the litter box?	☐YES ☐NO
8. Does your cat dig in its litter when it uses the litter box?	☐YES ☐NO
9. Is there more than one cat in the household?	☐YES ☐NO
10. Does your cat ever fight or appear frightened of other pets or people in the household?	☐YES ☐NO
11. Are the litter boxes all in the same site/room/area/floor of the home?	☐YES ☐NO

Total number of litter boxes in the house . . . . ________

Indicate number of boxes with each characteristic:

Box style:
- Covered . . . . ____
- Uncovered . . . . ____
- Large . . . . ____
- Medium . . . . ____
- Small . . . . ____
- With plastic liner . . . . ____

Litter type:
- Unscented . . . . ____
- Scented . . . . ____
- Clumping (sand-like) . . . . ____
- Recycled paper (pellets) . . . . ____
- Crystal (silica) . . . . ____
- Non-clumping clay . . . . ____
- Wheat clumping . . . . ____
- Corn clumping . . . . ____
- Pine . . . . ____
- Other . . . . ____

Cleaning schedule for litter boxes	Check rate
Scooping:	
Multiple times per day	☐
Once per day	☐
Once every other day	☐
Twice a week	☐
Once a week or less often	☐
Complete box change (wash, new litter):	
Daily	☐
Weekly	☐
Every two weeks	☐
Monthly	☐
Every 2-3 months	☐
Every 3-6 months	☐
Every year or more	☐
Never	☐

*Adapted from Neilson JC. FLUTD: When should you call the behaviorist? In: Proceedings. Hill's Symposium on Feline Lower Urinary Tract Disease, 2007: 20-28 (www.hillsvet.com/conferenceproceedings).
**"YES" answers for Questions 1 and 5 may indicate urine marking.

previously in 10 of the male cats. In another study, 32 cats (10 males, 22 females) with struvite uroliths were fed either a dry or moist version of a dissolution food[g] (Houston et al, 2004). Mean time for dissolution in cats eating moist food (3.73 weeks) was not significantly different from those eating dry food (4.82 weeks) ($p = 0.066$). Clinical signs resolved in an average of 19 days after beginning nutritional management. No occurrences of urethral obstruction were reported. Approximately 30% of cats had radiographic evidence of urolith disappearance after two weeks of feeding the dissolution food. Time to resolution of clinical signs or urolith dissolution did not differ significantly with the number of uroliths.

Box 46-7. Behavioral Management for Cats with Inappropriate Urination.*

Cats that urinate and/or defecate outside the litter box can do so for a variety of reasons including disease, communication (e.g., marking) and toileting preferences/aversions. Sometimes the medical problem can be an initiating factor for toileting problems. For example, medically triggered urgency to urinate causes the cat to select a convenient location like the bed; but even with resolution of the medical problem, the new behavior persists. These cats develop a new preference for toileting. (e.g., the bed is convenient, nicely absorbent and is cleaned readily) or have such negative associations with the litter box (e.g., painful urination when they were ill) that they persist in using a new, alternative, inappropriate site. Issues that should be addressed in cases of inappropriate elimination are listed below.

Resources	Recommendations	Explanations/consequences
Number of litter boxes	Number of litter boxes = number of cats +1	Too few litter boxes may result in problems that cause a cat to seek alternative toileting sites. These problems may include: volume of excrement in the litter box; box occupied by another cat; box being guarded by another cat.
Location of litter boxes	Should be spread throughout environment in easily accessible locations	Clustering litter boxes in one location may create access problems. These problems may include: guarding by another cat and physical challenges (e.g., stairs/distance) with getting to the litter box location.
Litter box style	Large	Boxes that are too small may be uncomfortable for cats to use, causing them to seek out other sites.
	Uncovered	Boxes that are covered may trap odors, creating an unpleasant environment and causing the cat to seek other toileting sites.
Litter	Clumping (sand-like) Unscented	Although individual preferences exist, the majority of cats prefer unscented clumping (finely particulate matter–similar to sand) litter.
Litter box hygiene	Daily litter box scooping Complete litter box cleaning/ change every 1 to 4 weeks	Cats tend to be fastidious and prefer clean toileting locations. Frequency of full box cleaning (wash/new litter) will depend on litter type; clumping type litters that allow owners to remove urine may require less frequent changes.
Scratching posts/pads	Multiple, sturdy, tall, prominently located	Scratching is a form of marking behavior. Encouraging scratch marking on appropriate targets may reduce the likelihood of other forms of marking and prevent destruction of household items.
Resting perches	Multiple, single cat sized, elevated, upholstered surfaces	Creative use of vertical space in the home can reduce inter-cat tension/aggression. Cats tend to prefer upholstered surfaces over slick surfaces but individual preferences may exist.
Feeding/water stations	Number of stations = number of cats	Providing adequate resources spread throughout the environment allows cats to self-segregate; this may help to reduce social tension in multi-cat households.
Play/social interaction	At least 2 to 3 daily short sessions (5 to 10 minutes)	Cat age and personality may affect type and duration of interaction but it is important to recognize that domesticated cats are social and will often benefit from play/interaction. Indoor-only cats can especially benefit from owner-initiated activity such as play with toys for overall stress reduction and exercise. Play activity also enhances the family-pet bond and is useful for overweight cats.

*Adapted from Neilson JC. FLUTD: When should you call the behaviorist? In: Proceedings. Hill's Symposium on Feline Lower Urinary Tract Disease, 2007: 20-28 (www.hillsvet.com/conferenceproceedings).

Despite evidence for effectiveness of nutritional management for dissolving struvite uroliths, many veterinarians still prefer to surgically remove uroliths because of perceptions that surgical management is more effective, is less expensive overall when considering monitoring and aftercare, controls clinical signs quicker and will not be associated with urethral obstruction as uroliths decrease in size, especially in male cats. Although surgical removal of uroliths has not been critically evaluated in cats, a retrospective study of 37 dogs and 29 cats with urinary bladder uroliths revealed that four cats (14%) and eight dogs (22%) had incomplete removal of uroliths by cystotomy in a veterinary teaching hospital (Lulich et al, 1993a; Lulich and Osborne, 2007).

Assess and Select the Food

Table 46-24 provides nutrient information about foods compared with recommended levels of key nutritional factors for dissolution of struvite uroliths. Generally the food that most closely matches the recommendations should be selected; however, only two foods[f,g] have published clinical evidence of effectiveness. Treatment with a struvite dissolution food is contraindicated in growing kittens, reproducing queens and

Table 46-23. Tips for increasing water consumption in cats.

Food
Feed moist food
Add small amount of water to moist food
Add warm water to dry food
Divide daily food amount into several smaller meals
Add flavor enhancers to food
- Low-sodium chicken or beef broth
- Clam juice
- Tuna juice (low sodium)

Water
Use fresh, clean water at all times (change at least once daily)
Try water from different sources
- Tap water
- Filtered water
- Bottled water
- Distilled water

Place ice cubes in water or provide cold water
Offer frozen cubes of water mixed with low-sodium tuna juice, etc.

Containers
Use non-reflective bowls for food and water
Use wide bowl so whiskers do not touch sides
Ensure ideal location of water and food bowls
- Quiet, draft-free environment (avoid noisy appliances, near vents)
- In areas where cats can escape if needed
- Not in same area as litter boxes
- On different levels of multi-floor house

Provide access to other sources of water
- Water fountains with circulating water
- Dripping faucet

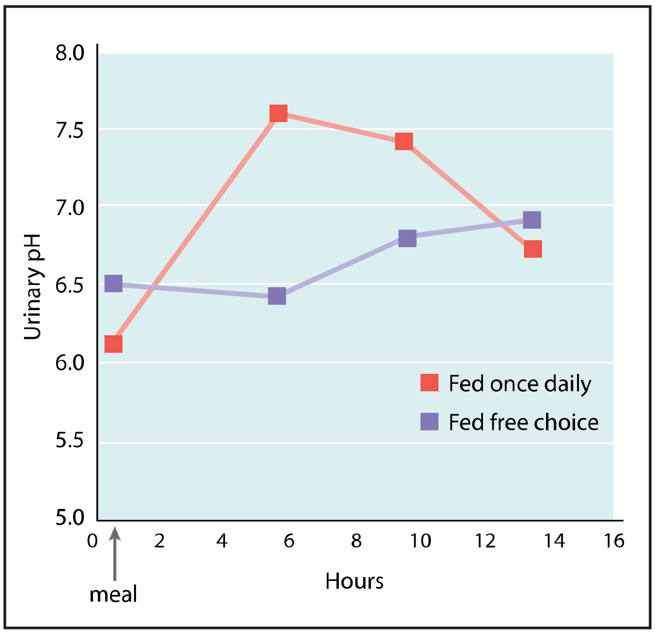

Figure 46-18. Mean urinary pH of cats fed a commercial food either free choice (i.e., ad libitum) or once daily. Note how once daily feeding results in a significant increase in urinary pH (i.e., postprandial alkaline tide). (Adapted from Taton DF, Hamar D, Lewis LD. Evaluation of ammonium chloride as a urinary acidifier in the cat. Journal of the American Veterinary Medical Association 1984; 184: 433-436.)

patients with metabolic acidosis or hypokalemia. In addition, struvite dissolution foods with increased amounts of sodium may not be ideal for patients with concomitant conditions including chronic kidney disease, hypertension or congestive heart failure.

Assess and Determine the Feeding Method

Cats with suspected struvite uroliths (usually <7 years of age, often with alkaline urinary pH, struvite crystalluria and/or radiopaque uroliths) can usually be transitioned to a dissolution food over a seven-day period. The method of feeding influences urinary pH values throughout the day and therefore may affect the success of the struvite dissolution protocol. When fed free choice, most cats will eat small amounts every few hours, resulting in a smaller but more prolonged alkaline tide than with meal feeding (**Figure 46-18**) (Taton et al, 1984). The smaller alkaline urinary pH excursions observed with free-choice feeding may improve dissolution of struvite uroliths and thus may be the preferred method of feeding. However, this has not been confirmed. Also, dry foods are most likely to be fed free-choice; nevertheless, feeding moist food is preferred for dissolution of struvite uroliths and managing most other types of uroliths and FIC.

If a UTI has been diagnosed, an appropriate antimicrobial drug should be administered for two to four weeks beyond removal or radiographic disappearance of uroliths. Although most cats do not have UTI, infection with urease-producing organisms may cause struvite uroliths in some cases and other bacteria may cause UTI secondary to uroliths in others.

Reassessment

During the time a dissolution food is being fed, cats should be reevaluated every two to four weeks. A thorough nutritional history should be collected, including amounts of all foods and supplements given; this is especially helpful when uroliths do not decrease in size as expected. Urinalysis is indicated to evaluate urinary pH and examine urine sediment for presence of abnormalities (e.g., crystalluria, pyuria). When interpreting pH of a spot or random urine sample, consider when the sample was collected relative to the time of eating. Samples obtained early in the morning, before food is offered, tend to be more acidic, whereas samples obtained within several hours of eating tend to be more alkaline (because of the postprandial alkaline tide). When evaluating effects of a food change on urinary pH, standardize the time of collection relative to the time of eating. For most accurate results, urinary pH should be measured using a pH meter. Urine culture should be done in cats with UTI to confirm the absence of infection during treatment with antimicrobial drugs and one week after completion of treatment to confirm eradication of UTI. Abdominal radiographs should be taken to evaluate number and size of uroliths compared with previous results. Nutritional management should be continued for one month beyond radiographic evidence of urolith(s) dissolution. If uroliths do not dissolve completely or decrease in size after two months of feeding a dissolution food exclusively, a different treatment (urolith removal) should be considered.

Figure 46-19 is an algorithm to assist in managing patients with struvite urolithiasis (Lulich, 2007a).

The rate of urolith recurrence has not been critically evaluated in cats. However, a recently published abstract described the rate of urolith recurrence in cats that had uroliths submitted for quantitative analysis at the Minnesota Urolith Center in 1998 (Albasan et al, 2006). Recurrence (defined as subsequent urolith submission) was detected in 2.7% of 1,821 cats with struvite uroliths; 0.2% of cats had a second recurrence. Mean time to initial recurrence was 27 months. Urolith recurrence was 1.6 times higher in females than males. Because some uroliths associated with recurrent episodes were likely not submitted for analysis, the actual recurrence rate for struvite uroliths was likely higher.

Table 46-24. Comparison of key nutritional factors in selected commercial veterinary therapeutic foods for dissolution of struvite uroliths in cats.*

Moist foods	Mg (%)	P (%)	Protein (%)	Na (%)	Urinary pH
Recommended levels	**0.04-0.09**	**0.45-1.1**	**30-45**	**0.3-0.6**	**5.8-6.2**
Hill's Prescription Diet s/d Feline	0.056	0.56	39.9	0.37	6.08
Medi-Cal Veterinary Diets Dissolution Formula	na	1.1	46.5	1.1	6.2
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	0.97	50.6	0.62	6.0-6.4
Royal Canin Veterinary Diet Dissolution Formula	0.052	1.0	49.9	1.21	5.9
Royal Canin Veterinary Diet Urinary SO in Gel	0.097	1.36	41.3	1.02	6.0-6.3
Dry foods	**Mg (%)**	**P (%)**	**Protein (%)**	**Na (%)**	**Urinary pH**
Recommended levels	**0.04-0.09**	**0.45-1.1**	**30-45**	**0.3-0.6**	**5.8-6.2**
Hill's Prescription Diet s/d Feline	0.059	0.77	34.4	0.4	5.9
Medi-Cal Veterinary Diets Feline Dissolution Formula	na	1.0	35.7	0.4	5.8
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	1.08	44.9	1.17	6.0-6.4
Royal Canin Veterinary Diet Urinary SO 33	0.065	0.88	37.1	1.45	6.0-6.3

Key: Mg = magnesium, P = phosphorus, Na = sodium, na = not available from manufacturer.
*Nutrients expressed on a dry matter basis unless otherwise stated.
**In general, moist foods should be fed to cats with FLUTD.

Table 46-25. Comparison of key nutritional factors in selected commercial veterinary therapeutic foods for decreasing risk of recurrence of struvite disease (uroliths or urethral plugs) in cats.*

Moist foods**	Mg (%)	P (%)	Protein (%)	Na (%)	Urinary pH
Recommended levels	**0.04-0.14**	**0.5-0.9**	**30-45**	**0.3-0.6**	**6.0-6.4**
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.052	0.68	43.8	0.32	6.35
Hill's Prescription Diet c/d Multicare with Seafood Feline	0.054	0.71	44.8	0.33	6.4
Hill's Prescription Diet r/d with Liver & Chicken Feline	0.075	0.62	37.5	0.29	6.25
Hill's Prescription Diet w/d with Chicken Feline	0.064	0.68	39.6	0.38	6.26
Iams Veterinary Formula Urinary S Low pH/S/Feline	0.088	0.75	41.8	0.26	na
Medi-Cal Veterinary Diets Feline Dissolution Formula	na	1.1	46.5	1.1	6.2
Medi-Cal Veterinary Diets Feline Preventive Formula	na	0.9	47.1	0.4	6.3
Medi-Cal Veterinary Diets Feline Reducing Formula	na	1.6	54.3	1.0	6.5
Medi-Cal Veterinary Diets Feline Urinary SO in Gel	na	1.2	43.5	1.1	6.4
Medi-Cal Veterinary Diets Feline Weight Control	na	1.1	40.0	0.5	6.6
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	0.97	50.6	0.62	6.0-6.4
Royal Canin Veterinary Diet Feline Control Formula	0.082	1.03	43.0	0.45	6.0-6.3
Royal Canin Veterinary Diet Feline Urinary SO in Gel	0.097	1.36	41.3	1.02	6.0-6.3
Dry foods	**Mg (%)**	**P (%)**	**Protein (%)**	**Na (%)**	**Urinary pH**
Recommended levels	**0.04-0.14**	**0.5-0.9**	**30-45**	**0.3-0.6**	**6.0-6.4**
Hill's Prescription Diet c/d Multicare Feline	0.06	0.65	36.1	0.35	6.30
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.061	0.65	34.6	0.33	6.35
Hill's Prescription Diet r/d Feline	0.073	0.81	36.9	0.35	6.38
Hill's Prescription Diet r/d with Chicken Feline	0.067	0.84	37.7	0.35	6.33
Hill's Prescription Diet w/d Feline	0.059	0.77	39.0	0.3	6.27
Hill's Prescription Diet w/d with Chicken Feline	0.068	0.86	39.9	0.35	6.22
Iams Veterinary Formula Urinary S Low pH/S/Feline	0.096	0.93	36.5	0.45	na
Medi-Cal Veterinary Diets Feline Dissolution Formula	na	1.0	35.7	0.4	5.8
Medi-Cal Veterinary Diets Feline Preventive Formula	na	0.9	33.4	0.4	6.1
Medi-Cal Veterinary Diets Feline Reducing Formula	na	1.2	41.8	0.3	6.1
Medi-Cal Veterinary Diets Feline Urinary SO 30	na	0.9	34.6	1.4	6.2
Medi-Cal Veterinary Diets Feline Weight Control	na	1.0	34.4	0.3	6.0
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	1.08	44.9	1.17	6.0-6.4
Royal Canin Veterinary Diet Feline Control Formula	0.065	0.65	33.7	0.71	6.0-6.3
Royal Canin Veterinary Diet Feline Urinary SO 33	0.065	0.88	37.1	1.45	6.0-6.3

Key: Mg = magnesium, P = phosphorus, Na = sodium, na = not available from manufacturer.
*Nutrients expressed on a dry matter basis unless otherwise stated.
**In general, moist foods should be fed to cats with FLUTD.

Box 46-8. Regulatory Claims Related to Feline Urinary Foods in the United States, Canada and the European Union.

The United States Food and Drug Administration, Center for Veterinary Medicine (FDA-CVM) has issued guidelines for pet-food companies to establish the following claims: "reduces urinary pH," "low magnesium" and "improves urinary tract health." The FDA-CVM suggests that submissions requesting permission to make "reduces urinary pH" or "improves urinary tract health" claims include supportive utility data demonstrating efficacy (i.e., the ability of the food to produce appropriately acidic urine compared with a non-acidifying control food) and safety data.

Foods with label claims such as "helps maintain urinary tract health" are low in magnesium and produce appropriately acidic urine. The FDA-CVM has promulgated guidelines for protocols to support urinary tract health claims. The guidelines focus on prevention of struvite urinary precipitates, but do not address the question of calcium oxalate precipitate formation.

Guidelines suggest safety studies for a minimum of six months. These studies should include physical examinations and the following observations: food consumption, body weight measurements, urinalyses (including sediment examinations), serum biochemistry and blood gas analyses and mineral (calcium, phosphorus, magnesium and potassium) balance studies. Foods claiming to promote urinary tract health and reduce urinary pH must be nutritionally complete and balanced, as demonstrated by the Association of American Feed Control Officials (AAFCO) feeding protocols. It is noteworthy that the "improves urinary tract health" claim focuses on documentation of safety, urine acidification and restricted dietary intake of magnesium and does not in any way address the issue of calcium oxalate urolith formation.

The guideline for a low-magnesium claim is a magnesium level guaranteed less than 0.12% dry matter, using the maximum magnesium and maximum water guarantee. The magnesium must also be less than 25 mg/100 kcal, with energy content based on the AAFCO-approved calculation method or an actual digestibility study. Analysis of multiple batches is required. The FDA-CVM does not allow the claim of "low ash" on cat food labels. Current scientific information does not demonstrate that ash per se is related to the incidence of lower urinary tract disease. Ash content can only be included in the guaranteed analysis of the food.

The Canadian Veterinary Medical Association (CVMA) Pet Food Certification Program has established guidelines for nutrient standards for magnesium-restricted/pH-controlling cat foods. These foods must meet the following requirements:

Magnesium levels must be no more than 0.1% and no less than 0.05%, dry matter basis.

Magnesium levels per 100 kilocalories (kcal) of metabolizable energy (ME) shall be no more than 20 milligrams.

The average resting urinary pH shall be 6.5 or less, and the average postprandial peak pH shall not exceed 7.0.

In July 1995, labeling of veterinary therapeutic foods in Europe (termed "dietetic pet foods") became strictly regulated (Chapter 9). European regulations require only certain indications for therapeutic foods, termed "Particular Nutritional Purposes." Indications permitted for feline lower urinary tract disease include: 1) dissolution of struvite uroliths, 2) reduction of struvite urolith recurrence, 3) reduction of oxalate urolith formation, 4) reduction of urate urolith formation and 5) reduction of cystine urolith formation. Essential nutritional characteristics of the corresponding foods and specific label declarations must be met.

The Bibliography for **Box 46-8** can be found at www.markmorris.org.

After dissolution or removal of struvite uroliths, further nutritional management is indicated to prevent recurrence. (See Feeding Plan for Prevention of Struvite Urolithiasis and Urethral Plugs.) If UTI with urease-producing bacteria was the cause of uroliths, controlling infections may prevent urolith recurrence; however, most uroliths in cats are either sterile or cause secondary infections. It is unknown how long struvite preventive foods should be fed. Struvite disease is more common in young- to middle-aged cats; however, as cats age, the risk of calcium oxalate urolithiasis increases. Cats eating struvite preventive foods should be monitored periodically for crystalluria and urinary pH values. If no episodes of struvite uroliths occur for several years, consider recommending a high-quality wellness food that avoids excessive magnesium and phosphorus, as cats get older. Cats should still be monitored periodically for occurrence of alkaline urinary pH, struvite crystalluria and urolith recurrence.

Struvite uroliths may recur months to years after removal or dissolution, particularly if preventive measures are not implemented (Osborne et al, 1990). Interpretation of recurrence of uroliths (of any mineral type) and interval until recurrence should be based on answering a number of questions (Lulich et al, 1993). 1) *Were all uroliths removed from the urinary tract at the time of surgery or other procedure?* Recurrence of uroliths following surgery is commonly attributed to failure of medical therapy to prevent urolith formation. However, this hypothesis is based on the premise that all stones were completely removed from the urinary tract before beginning preventive measures. Incomplete surgical removal of uroliths probably occurs more frequently than recognized, even when performed by experienced surgeons (Lulich et al, 1993a; Lulich and Osborne, 2007). 2) *Did nonabsorbable suture materials left exposed in the lumen of the urinary bladder during surgery provide a nidus for precipitation of crystalline material?* In 2005, the Minnesota Urolith Center analyzed uroliths from more than 32,000 dogs; nonmineral, foreign material was identified in uroliths from 96 dogs and 86 of these submissions contained a nidus of suture material (Lulich and Osborne, 2007). Uroliths from an additional 235 dogs contained a hollow cylindrical track consistent with formation around suture material. On the basis of these findings, approximately 1% of canine uroliths would be best prevented by more appropriate selection and placement of sutures. Similar data for cats have not been reported; however, it seems reasonable that inappropriate surgical techniques also could predispose to development of feline uroliths. 3) *What diagnostic methods were used to detect recurrence?* 4) *How often was the patient evaluated for recurrence?* 5) *Were recommendations to decrease likelihood of recurrence given and was the owner able to follow them?* 6) *Has infection with a urease-producing microorganism persisted or recurred?* Most uroliths in cats are not associated

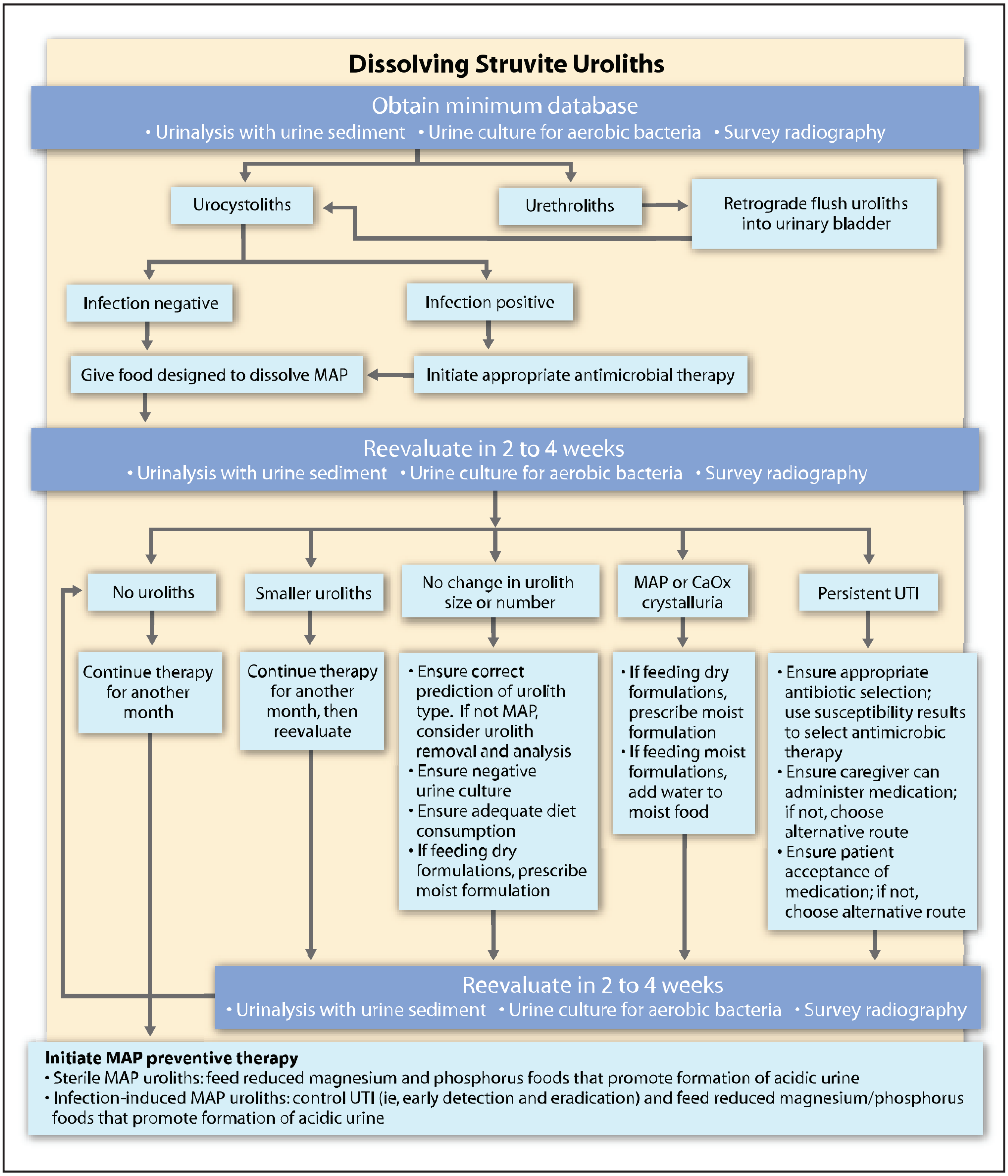

Figure 46-19. Algorithm for management and reassessment of cats with struvite urolithiasis. Key: MAP = magnesium ammonium phosphate (struvite), CaOx = calcium oxalate, UTI = urinary tract infection. (Adapted from Lulich JP. FLUTD: Are you choosing the right therapy? Part 1. Urolithiasis. In: Proceedings. Hill's Symposium on Feline Lower Urinary Tract Disease, 2007a: 29-36).

Table 46-26. Comparison of key nutritional factors in selected commercial veterinary therapeutic foods for decreasing risk of recurrence of calcium oxalate uroliths in cats.*

Moist foods**	Mg (%)	P (%)	Ca (%)	Protein (%)	Na (%)	Urinary pH
Recommended levels	**0.07-0.14**	**0.5-1.0**	**0.6-1.0**	**≥32**	**0.3-0.6**	**≥6.2**
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.052	0.68	0.72	43.8	0.32	6.35
Hill's Prescription Diet c/d Multicare with Seafood Feline	0.054	0.71	0.62	44.8	0.33	6.4
Iams Veterinary Formula Urinary O - Moderate pH/O	0.085	0.77	1.11	43.4	0.34	na
Medi-Cal Urinary SO in Gel	na	1.2	1.2	43.5	1.1	6.4
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	0.97	0.96	50.6	0.62	6.0-6.4
Royal Canin Veterinary Diet Urinary SO in Gel	0.097	1.36	1.02	41.3	1.02	6.0-6.3
Dry foods	**Mg (%)**	**P (%)**	**Ca (%)**	**Protein (%)**	**Na (%)**	**Urinary pH**
Recommended levels	**0.07-0.14**	**0.5-1.0**	**0.6-1.0**	**≥32**	**0.3-0.6**	**≥6.2**
Hill's Prescription Diet c/d Multicare Feline	0.06	0.65	0.74	36.1	0.35	6.3
Hill's Prescription Diet c/d Multicare with Chicken Feline	0.061	0.65	0.76	34.6	0.33	6.3
Iams Veterinary Formula Urinary O - Moderate pH/O	0.098	0.91	1.24	36.5	0.46	na
Medi-Cal Urinary SO	na	0.9	1.1	34.6	1.4	6.2
Purina Veterinary Diets UR Urinary St/Ox Feline Formula	0.07	1.08	1.1	44.9	1.17	6.0-6.4
Royal Canin Veterinary Diet Urinary SO 33	0.065	0.88	0.96	37.1	1.45	6.0-6.3

Key: Mg = magnesium, P = phosphorus, Ca = calcium, Na = sodium, na = not available from manufacturer.
*Nutrients expressed on a dry matter basis unless otherwise stated.
**In general, moist foods should be fed to cats with FLUTD.

Table 46-27. Stepwise approach for management of calcium oxalate urolithiasis in cats.*

1. Obtain baseline data (post-removal radiographs, complete urinalysis, serum concentrations of calcium, urea nitrogen and creatinine) to evaluate effectiveness of removal procedure, renal function and calcium homeostasis.
2. If the patient is hypercalcemic, correct underlying cause. If no cause is identified (i.e., idiopathic hypercalcemia exists) consider high-fiber foods and potassium citrate to decrease urine acidity.
3. If the patient is normocalcemic, consider foods with reduced oxalate, sodium and protein that do not promote formation of overly acidic urine (pH <6.2). Ideally foods should contain additional water and citrate and have adequate phosphorus and magnesium. Avoid excess vitamins C and D.
4. Reevaluate patient in two to four weeks to verify compliance with nutritional recommendations (urine specific gravity and pH) and amelioration of crystalluria (urine sediment examination). For most accurate results, urinary pH should be measured using a pH meter.
5. If calcium oxalate crystals or concentrated urine (specific gravity >1.030) persist, consider moist foods or additional water added to current food. If calcium oxalate crystals or aciduria persist (urinary pH <6.2), consider additional potassium citrate.
6. Reevaluate patient in two to four weeks to verify compliance with nutritional recommendation (urine specific gravity and pH) and amelioration of crystalluria (urine sediment examination). If calcium oxalate crystalluria persists, and patient is consuming a homemade food, consider vitamin B_6 supplementation (2 to 4 mg/kg every 24 hours).
7. After three to six months, reevaluate patient to verify compliance with nutritional recommendations, amelioration of crystalluria and lack of urolith recurrence (abdominal radiography). If no uroliths are present, continue present therapy and reevaluate in three to six months. If uroliths have recurred, consider nonsurgical urolith removal. Consider using voiding urohydropropulsion in females or male cats with a previously performed perineal urethrostomy. If unsuccessful, surgery can be considered if clinical signs referable to urocystolithiasis persist. If clinical signs are not present, continue therapy to minimize urolith growth.

*Adapted from Lulich JP. FLUTD: Are you choosing the right therapy? Part 1. Urolithiasis. In: Proceedings. Hill's Symposium on Feline Lower Urinary Tract Disease, 2007: 29-36.

with UTI; however, some cats will develop struvite uroliths associated with urease-producing organisms. 7) *Has an underlying anatomic defect gone uncorrected?*

Feeding Plan for Prevention of Struvite Urolithiasis and Urethral Plugs

Generally, appropriate nutritional management is the most important consideration for prevention of recurrence of struvite uroliths and urethral plugs.

Assess and Select the Food

Foods that are most similar to the key nutritional factor target ranges and/or have the best evidence for managing the patient's disorder should be selected. Information about content of many nutrients (e.g., magnesium, calcium, phosphorus and sodium) and target urinary pH ranges are not required on pet food labels. **Tables 46-19** and **46-25** provide lists of selected veterinary therapeutic foods marketed for prevention of struvite urolithiasis (and urethral plugs) and compare their key nutritional factor content to the recommended levels of key nutritional factors. The foods listed in **Table 46-19**, in addition to struvite-associated disease, are intended to co-manage FIC- and calcium oxalate-based FLUTD. These foods are compared to composite key nutritional factors for the aforementioned types of lower urinary tract disease. For foods under consideration that are not listed in **Tables 46-19** and **46-25**, contact the manufacturer or review published information to determine key nutritional factor content. For cats that have urethral plugs composed only of matrix or other substances (e.g., epithelial cells or mucus), feeding the moist form of the selected food is recommended.

Regarding urethral plugs, a struvite dissolution food (**Table 46-24**) may be appropriate for initial management (i.e., one to three months) after relieving obstruction. (See Feeding Plan for Struvite Urolith Dissolution, above.) However, such a food should not be fed long term because of risks associated with prolonged, excessive urinary acidification (urinary pH <6.0).

Several commercially available foods have claims for struvite prevention; however, only one has been evaluated in cats with urethral plugs. In a randomized, prospective study of cats with urethral plugs, effectiveness of feeding this food was compared with perineal urethrostomy alone and perineal urethrostomy plus the calculolytic food[f] (Osborne et al, 1991). During the one-year study, urethral obstruction was not observed in any group. This study did not include an untreated control group; however, recurrence rates for urethral obstruction in two other studies were 35 and 36% (Bovee et al, 1979; Gerber et al, 2007). Bacterial UTI occurred in 40 to 50% of cats that had perineal urethrostomies, but was not observed in cats managed by the calculolytic food alone. Several foods formulated for struvite prevention have been evaluated by measuring values for struvite saturation in healthy cats (Bartges et al, 1998; Abood et al, 2000; Devois et al, 2000; Xu et al, 2006).

Urinary tract health claims on pet food labels may be of some help in evaluating foods (**Box 46-8**). In the U.S., a food with a "low magnesium" claim contains a maximum of 0.12% DM magnesium or 25 mg magnesium/100 kcal ME.

Depending on the amount fed, treats and other supplements can significantly alter the key nutritional factor profile of the desired dietary regimen and may decrease the effectiveness of appropriately formulated therapeutic foods. Some commercial cat treats or foods, and processed human foods may have very high levels of magnesium or phosphorus and their effect on urinary pH is hard to predict. Most pet owners give their pets treats or supplement their pets' primary food with other foods, either another cat food or human food. Therefore, it is important for veterinary health care team members to educate owners about the importance of compliance to the successful outcome. This is especially true for cats that are at risk for urethral obstruction. Owners aware of the risks may be more willing to avoid feeding other foods or products and encourage their cats only to eat the recommended therapeutic food.

Assess and Determine the Feeding Method

Cats should be transitioned gradually to a food formulated to decrease occurrence of struvite crystalluria. The method of feeding influences urinary pH values throughout the day and therefore may affect success of the dietary management protocol. Ingestion of food stimulates secretion of acid by gastric parietal cells with subsequent secretion of bicarbonate into the blood in exchange for chloride ions. This alkali load transiently increases urinary bicarbonate and pH (i.e., postprandial alkaline tide) unless offset by absorption of acidifying ingredients. When offered food free choice, most cats will eat small amounts every few hours, resulting in a smaller but more prolonged alkaline tide than with meal feeding (**Figure 46-18**) (Taton et al, 1984). The smaller alkaline urinary pH excursions observed with free-choice feeding may reduce the likelihood of struvite precipitate formation, and thus may be the preferred method of feeding to prevent struvite associated disease; however, this has not be confirmed in clinical studies. Free-choice feeding may be associated with obesity; however, which in turn is a risk factor for lower urinary tract diseases in general. In addition, free-choice feeding is most likely to be done using dry food, and moist food is preferred for managing urolithiasis and FIC.

Based on information currently available, meal-feeding moist food would seem to be best for most cats with struvite disease because of increased water intake and reduced concentration of crystal-forming elements. However, less evidence supports this benefit compared with cats that have calcium oxalate uroliths. If meal feeding is associated with increased urinary pH throughout the day and significant struvite crystalluria or recurrent uroliths or urethral plugs, another feeding method should be considered (e.g., feeding dry food or feeding multiple small meals of moist food).

Reassessment

Cats eating struvite preventive foods should be monitored periodically for evidence of crystalluria and urinary pH values. If no episodes of struvite uroliths occur for several years, it would be appropriate to consider switching to a high-quality wellness food that maintains an appropriate urinary pH and avoids excessive magnesium and phosphorus.

Feeding Plan for Calcium Oxalate Urolithiasis

Calcium oxalate uroliths are not amenable to medical dissolution and must be removed by surgery, voiding urohydropropulsion, lithotripsy or other techniques. An alternative to cystotomy is voiding urohydropropulsion if urocystoliths are small enough to pass through the urethra (Lulich et al, 1993). Voiding urohydropropulsion is generally more successful in queens than in tomcats because the urethra is larger in females than in males. Voiding urohydropropulsion is usually ineffective in cats with uroliths lodged in the urethra. After urolith removal, medical protocols to minimize recurrence should be implemented. Goals of nutritional management include decreasing urine calcium and oxalate concentrations, promoting high concentrations of urolith inhibitors, decreasing urine acidity and decreasing urine specific gravity (i.e., urine dilution).

Assess and Select the Food

Several commercially available therapeutic foods are marketed for prevention of calcium oxalate uroliths in cats. No foods have been studied to determine if they prevent urolith recurrence and only one food[e] has been evaluated in cats with naturally occurring calcium oxalate uroliths (Lulich et al, 2004). In a study of 10 cats with confirmed calcium oxalate uroliths, urinary calcium oxalate saturation was measured before beginning the study and after feeding the therapeutic food. Using a cross-over design, half of the cats were randomly assigned to continue their regular food and the other half were assigned to eat the therapeutic food. After eight weeks, the foods were switched and fed for another eight weeks. Urinary calcium oxalate saturation values (i.e., activity product ratios and relative supersaturation values) were determined and compared between groups (regular vs. therapeutic food). Results revealed that hypercalciuria was a consistent abnormality in urolith-forming cats and urinary calcium oxalate saturation was significantly lower in cats fed the therapeutic food compared with regular food. This study concluded that feeding the therapeutic food decreased the risk of urolith recurrence.

Tables 46-19 and **46-26** list selected veterinary therapeutic foods marketed for prevention of calcium oxalate urolithiasis and compare their key nutritional factor content to the recommended levels. The foods listed in **Table 46-19** are also intended to co-manage FIC- and struvite-based FLUTD. These foods are compared to composite key nutritional factors for all three of these types of lower urinary tract disease. For foods under consideration that are not listed, contact the manufacturer or review published information to determine levels of key nutritional factors. Foods that are most similar to the key nutritional factor target ranges and/or have published evidence of efficacy for managing calcium oxalate urolithiasis should be selected. Owners of cats that form calcium oxalate crystals and uroliths should be cautioned about grocery brand foods with urinary tract health claims because these foods are formulated for healthy cats to avoid struvite crystals and uroliths. Feeding such foods may actually increase the risk of developing calcium oxalate uroliths. The standard of care for decreasing risk of calcium oxalate urolith recurrence is to feed moist food and encourage water intake (**Table 46-23**). In addition, owners should be advised to avoid giving treats with increased amounts of calcium or oxalate (**Tables 46-15** and **46-18**). These foods/products may increase urinary excretion of calcium and oxalate, which increases the risk for development of uroliths.

Therefore, veterinary health care team members need to educate owners about the importance of nutritional management in the treatment of cats with calcium oxalate disease, especially cats at risk of urethral obstruction. Increasing owners' awareness may lead to better compliance.

Assess and Determine the Feeding Method

Based on information currently available, meal feeding moist food is appropriate to manage cats with calcium oxalate uroliths. Moist foods increase water intake and reduce concentrations of crystal-forming elements. The method of feeding influences urinary pH throughout the day and therefore may affect success of managing cats with calcium oxalate urolithiasis. Although calcium oxalate crystalluria is not as pH dependent as is struvite crystalluria formation, management of urinary pH is still important. As discussed above, ingestion of food stimulates a postprandial alkaline tide, unless offset by acidifying ingredients in the food. When offered food free choice, most cats will eat small amounts every few hours, resulting in a smaller but more prolonged alkaline tide than with meal feeding (**Figure 46-18**) (Taton et al, 1984). Thus, it has been suggested meal feeding, rather than feeding multiple small meals per day (as in free-choice feeding), might lower the risk of calcium oxalate urolith formation because of the production of a more alkaline urinary pH (Bartges and Kirk, 2006).

Reassessment

Of cats with calcium oxalate uroliths submitted to the Minnesota Urolith Center in 1998 (n = 2,393), 169 (7.1%) had a recurrence (i.e., subsequent urolith submission), 15 (0.6%) had a second recurrence and two (0.1%) had a third recurrence (Albasan et al, 2006). Mean recurrence times were 23, 38 and 48 months, respectively. Urolith recurrence rate was not different between males and females. It is likely that uroliths from some cats with recurrences were not submitted for subsequent evaluation; therefore, the actual recurrence rate was probably higher. Further study is needed to better define recurrence rates for calcium oxalate uroliths in cats.

All cats should be monitored for recurrence, including urinalysis every three months to detect calcium oxalate crystalluria and diagnostic imaging every six months to detect uroliths. Serum calcium concentration should be monitored in cats with hypercalcemia. If uroliths recur, less-invasive procedures (e.g., voiding urohydropropulsion) are more likely to be effective when uroliths are smaller. **Table 46-27** summarizes the steps for managing cats with calcium oxalate urolithiasis. **Box 46-9** reviews other treatments for calcium oxalate urolithiasis

CONCLUSION

The most common forms of FLUTD include FIC, struvite disease (uroliths and urethral plugs) and calcium oxalate uroliths. Trends in occurrence of urolith types have changed in the past 25 years. Many risk factors have been identified for FLUTD, in general; however, additional study is needed to determine pathogenesis and show a cause-and-effect relationship. Although many treatments have been recommended for FIC, only a few have been evaluated by controlled, randomized clinical trials in cats with naturally occurring disease. When evaluating treatment, consider those options that have the highest level of evidence for effectiveness (**Tables 46-20** and **46-21**) (Roudebush et al, 2004; Forrester and Roudebush, 2007). Feeding moist food and recommending other methods to increase water intake are appropriate for the most common forms of FLUTD including FIC, urolithiasis and urethral plugs. In addition, implementing environmental enrichment and stress reduction is indicated for patients with FIC. Feeding a therapeutic food for one to two months is a very effective method for dissolving struvite uroliths in cats. Foods formulated to prevent recurrence of struvite uroliths or urethral plugs are indicated after urolith dissolution or removal of urethral plugs. Treatment for calcium oxalate uroliths involves urolith removal, followed by feeding moist food formulated to decrease risk of urolith recurrence. Cats with lower urinary tract disorders should be monitored periodically by performing urinalyses and diagnostic imaging to detect recurrence of their original disease, development of a different lower urinary tract disorder or occurrence of adverse events associated with therapeutic interventions. The therapeutic regimen can then be modified as needed.

ENDNOTES

a. Osborne CA, Lulich JP. Minnesota Urolith Center, University of Minnesota, St Paul, USA. Unpublished data. 2007.

b. Oakton pHTestr 1, Model 35624-00. Oakton Instruments, Vernon Hills, IL, USA.

Box 46-9. Additional Treatments for Calcium Oxalate Urolithiasis.

VITAMIN B_6

Deficiency of vitamin B_6 has been associated with increased urinary oxalate excretion; however, it has not been shown to cause calcium oxalate uroliths. Additional vitamin B_6 is unlikely to benefit cats eating most commercial foods; however, if a cat with calcium oxalate uroliths is being fed a homemade food, it would be appropriate to supplement with vitamin B_6 (2 to 4 mg/kg body weight orally once daily).

THIAZIDE DIURETICS

Thiazide diuretics are known to cause renal tubular reabsorption of calcium, resulting in decreased urine calcium excretion, which may decrease likelihood of calcium oxalate urolith recurrence. Thiazide diuretics have been used for treatment of calcium oxalate urolithiasis in people but no studies have been reported in cats with calcium oxalate uroliths. In a blinded, placebo-controlled crossover study performed with healthy cats, administration of hydrochlorothiazide suspension (1 mg/kg orally q12h) was associated with significantly decreased urinary saturation of calcium oxalate compared with placebo. For cats with recurrent calcium oxalate uroliths despite feeding a therapeutic food and increasing water intake, thiazide diuretics may be considered. Thiazide diuretics should not be used in cats with hypercalcemia.

POTASSIUM CITRATE

Increased urinary citrate may form soluble complexes with calcium, making it unavailable to form calcium oxalate uroliths. Citrate inhibits calcium oxalate crystal formation by promoting formation of alkaline urine and by forming complexes with calcium (**Figure 1**). When citrate complexes with calcium, ionic calcium concentration and urine saturation with calcium oxalate are reduced.

Hypocitraturia is reported to occur in 19 to 63% of human patients with calcium oxalate urolithiasis; however, frequency of hypocitraturia in cats with calcium oxalate urolithiasis is unknown. Changes in acid-base status influence renal handling of citrate. Metabolic acidosis virtually eliminates urinary citrate excretion by promoting citrate oxidation. Acidosis favors influx of citrate into renal mitochondria and inhibits efflux of citrate from mitochondria. Tubular and peritubular citrate uptake increases when cytosolic citrate concentration decreases. Increased reabsorption of citrate reduces urinary citrate excretion. The citrate in urine is the small quantity that escapes reabsorption. In metabolic alkalosis, urinary citrate increases because mitochondrial uptake and thus oxidation of citrate is reduced, cytosolic citrate concentration increases, reabsorption decreases and urinary excretion of citrate increases.

Thus, depending in part on the acid-base status of the patient, dietary citrate may have little effect on urinary citrate. Feeding up to 100 mg of citric acid/kg body weight to cats has been shown to have little effect on urine citrate concentrations. Effects of potassium citrate alone on urinary calcium oxalate saturation or urolith recurrence have not been evaluated in healthy cats or cats with calcium oxalate uroliths. One therapeutic food[a] containing potassium citrate was associated with decreased urinary calcium oxalate saturation in cats with calcium oxalate uroliths. Potassium citrate (50 to 75 mg/kg body weight orally q12h with food) should be considered in cats that have recurrent calcium oxalate uroliths despite using other measures (e.g., feeding moist food or therapeutic food, increased water intake).

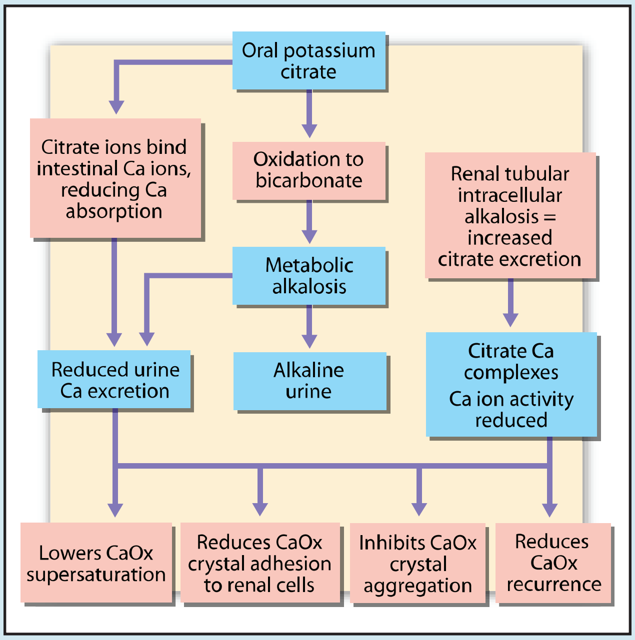

Figure 1. Schematic depicting the role of citrate in binding intestinal calcium (Ca) ions and reducing calcium absorption, promoting formation of alkaline urine and preventing calcium oxalate (CaOx) urolith formation.

ENDNOTE

a. Hill's Prescription Diet x/d Feline. Hill's Pet Nutrition Inc., Topeka, KS, USA.

The Bibliography for **Box 46-9** can be found at www.markmorris.org.

c. Feline Control pHormula Waltham Veterinary Diet. Waltham, Vernon, CA, USA.
d. Cystease. Ceva Animal Health, Chesam, United Kingdom.
e. Hill's Prescription Diet x/d Feline. Hill's Pet Nutrition Inc., Topeka, KS, USA.
f. Hill's Prescription Diet s/d Feline. Hill's Pet Nutrition Inc., Topeka, KS, USA.
g. Medi-Cal Dissolution Formula. Veterinary Medical Diets, Guelph, Ontario, Canada.

REFERENCES

The references for **Chapter 46** can be found at www.markmorris.org.

CASE 46-1

Obstructive Uropathy in a Cat

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Patient Assessment

A four-year-old, castrated male, mixed-breed cat was examined for acute dysuria, pollakiuria and stranguria. The cat had one previous episode of obstructive uropathy approximately 18 months earlier. No other historical problems were identified.

Physical examination revealed that the cat was depressed, lethargic and approximately 5% dehydrated. Temperature was normal. Heart and respiratory rates were increased. The cat weighed 6.4 kg and was considered overweight (body condition score 4/5). Abdominal palpation revealed a firm, painful and overly distended urinary bladder. A small plug of tan, gritty material was identified at the level of the external urethral orifice.

Analysis of a urine specimen collected by cystocentesis revealed moderately concentrated urine with a neutral pH, struvite crystalluria and findings typical of inflammation (i.e., hematuria, pyuria and proteinuria). Aerobic bacteria were not detected by quantitative urine culture. Results of a hemogram were within normal limits. A serum biochemistry profile revealed mild azotemia. Venous blood gas measurement identified a mild metabolic acidosis. Survey abdominal radiographs revealed increased amounts of intraabdominal fat and an overly distended urinary bladder.

Assess the Food and Feeding Method

The cat had been fed a dry commercial maintenance food free choice, which was supplemented with a small amount of moist commercial maintenance food (one tablespoon, once daily). The cat had unlimited access to fresh water.

Questions

1. What are potential causes of urethral obstruction in male cats?
2. What differences exist between uroliths and urethral plugs?
3. What are risk factors for formation of struvite crystals?
4. Can nutritional management dissolve urethral plugs?
5. What is the effectiveness of perineal urethrostomy vs. medical therapy for preventing recurrent urethral obstruction due to struvite-containing urethral plugs?

Answers and Discussion

1. Urethral obstruction may be caused by one or more intramural, mural or extramural abnormalities located at one or more sites. In a prospective study of urethral obstruction in 51 male cats, investigators identified crystalline-matrix urethral plugs in 59% of cats; urethroliths were identified in 12% of cats and a specific cause could not be identified in 29% of affected cats. In a prospective study of European cats, 45 of 67 male cats with signs of lower urinary tract disease had urethral obstruction; most common causes included feline idiopathic cystitis (FIC) (24 cats), uroliths (13 cats) and urethral plugs (eight cats). Other possible causes of urethral obstruction include sloughed tissue fragments originating from the bladder or urethra, acquired urethral strictures, prostatic lesions, urethral neoplasms, periurethral neoplasms, congenital urethral anomalies and functional urethral obstruction (e.g., reflex dyssynergia).
2. There are distinct physical and probable etiopathogenic differences between feline uroliths and urethral plugs; therefore, these terms should not be used synonymously. Uroliths are highly organized polycrystalline concretions composed primarily of minerals (organic and inorganic crystalloids) and smaller quantities of nonmineral matrix. In contrast, most feline urethral plugs are composed of relatively large quantities of matrix mixed with mineral crystals. However, some urethral plugs are composed primarily of matrix, some consist of sloughed tissue, blood and/or inflammatory reactants and a few are composed primarily of aggregates of crystalline minerals. In general, feline crystalline-matrix urethral plugs appear as cylindrical concretions that conform to the diameter of the urethra and vary from a few mm to several cm. They usually are soft, friable, easily compressed and have no visible organized external structure. Urethral plugs contain varying quantities of minerals in proportion to large quantities of matrix. Struvite is the most common mineral type identified in feline urethral plugs. However, a variety of different mineral types (e.g., calcium oxalate, ammonium urate, calcium phosphate) have been identified in urethral plugs of cats, suggesting that multiple risk factors are involved in their formation.

   The matrix component of feline urethral plugs is less well defined. Studies in cats and other species suggest that matrix is heterogeneous and may be composed of mucoproteins, albumin, globulins, cells (e.g., erythrocytes, leukocytes, epithelial cells and spermatozoa) and microorganisms (e.g., bacteria and viruses).

One hypothesis suggests that formation of matrix by infectious or inflammatory agents in cats with concomitant crystalluria of any type may lead to formation of matrix-crystal urethral plugs. Crystalluria per se is unlikely to cause production of large quantities of matrix because classic uroliths, which are composed of at least 90% crystalline material, contain relatively little matrix.

3. Risk factors associated with formation of struvite crystals found in urethral plugs are probably similar to those associated with formation of struvite uroliths. Factors of major therapeutic importance include nutritional factors affecting urine magnesium concentration and urinary pH and anything that predisposes to urinary tract infection with urease-producing microorganisms.
4. In general, the immediate need to remove urethral plugs within hours precludes attempts to induce their dissolution over a period of days or weeks. However, it is often possible to repulse urethral plugs into the urinary bladder lumen. Although urethral plugs contain markedly greater quantities of matrix than do uroliths, medical protocols that dissolve sterile struvite uroliths would probably also be effective for dissolving the struvite crystalline component of urethral plugs located in the urinary bladder lumen. However, such therapy may not result in dissolution of plug matrix. In addition, it must be emphasized that calcium oxalate, calcium phosphate and ammonium urate crystals are occasionally identified in some naturally occurring feline urethral plugs.

   Attempts to dissolve struvite crystals by promoting formation of acidic urine should not be initiated in cats with postrenal azotemia. The metabolic sequela of urethral obstruction, particularly severe metabolic acidosis, should be corrected before pharmacologic agents or foods designed to acidify urine are used.
5. Perineal urethrostomies can minimize recurrent obstruction of the penile urethra of patients unresponsive to nonsurgical therapeutic and prophylactic management. In a prospective study of 30 cats with struvite crystalline-matrix urethral plugs, perineal urethrostomy and nutritional management were equally effective in their ability to prevent recurrent urethral obstruction. However, 16 episodes of bacterial urinary tract infection developed in nine cats with perineal urethrostomies; bacterial urinary tract infections were not observed in cats treated only with nutritional management. Furthermore, staphylococcal-induced struvite urocystoliths developed in two cats with perineal urethrostomies. In another study of cats that had perineal urethrostomy, over half developed complications (urinary tract infection, stricture) or had recurrent clinical signs due to urolithiasis or FIC. These observations emphasize that perineal urethrostomies may be associated with significant short-term and long-term complications. Localization of the site(s) and cause(s) of urethral obstruction is especially important if urethrostomy is considered.

Progress Notes

To further characterize the composition of the urethral plug and identify potential etiopathologic factors, a portion of the urethral plug was obtained and submitted for light and electron microscopic examination and quantitative mineral analysis. Light microscopic evaluation of the urethral plug revealed that it was composed of numerous unorganized crystals, occasional white blood cells and large quantities of amorphous matrix (**Figure 1**). Electron microscopy did not reveal any specific etiologic agents. Subsequent quantitative mineral analysis revealed that the crystalline component of the plug was composed of 100% struvite.

Urethral patency was reestablished with a combination of procedures that included: 1) gentle massage of the distal urethra followed by gentle compression of the urinary bladder, 2) partial decompression of the bladder by cystocentesis and 3) flushing of the urethral lumen with sterile 0.9% saline solution. After urine flow was restored, particulate material in the urinary bladder was removed by lavage of the bladder lumen with sterile saline solution. Because the large quantity of urine precipitates in the bladder lumen represented a potential risk factor for reobstruction, a sterile indwelling red-rubber urinary catheter was placed and connected to a closed sterilized drainage system. Systemic fluid and acid-base imbalances associated with obstructive uropathy were corrected over a 24-hour period by intravenous administration of lactated Ringer's solution.

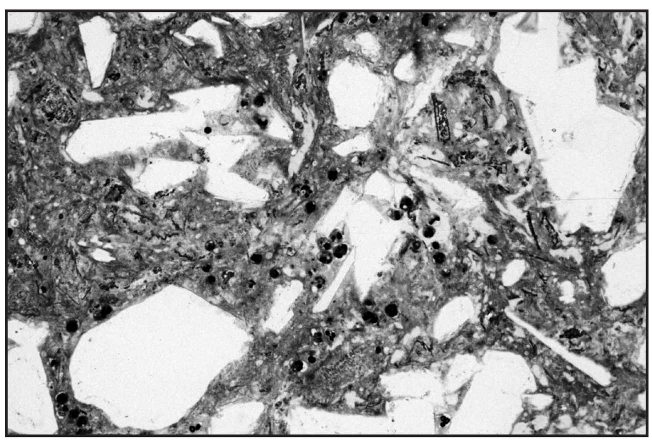

Figure 1. Photomicrograph of a urethral plug removed from a four-year-old, castrated male, mixed-breed cat with obstructive uropathy. Note spaces previously occupied by struvite crystals surrounded by large quantities of amorphous matrix containing white blood cells (toluidine blue stain; 100X original magnification).

Gross hematuria gradually subsided over 48 hours. The indwelling urinary catheter was removed and the cat was observed for signs of reobstruction. Aerobic bacteria were not detected on followup quantitative culture of urine collected via the indwelling catheter before its removal.

The cat was fed a commercial veterinary therapeutic food designed to promote dissolution of the struvite crystal component of the urethral plug (Prescription Diet s/d Feline[a]). When the cat was discharged from the hospital, its owner was instructed to feed the food in sufficient quantity to maintain stable body weight (approximately 320 kcal [1,339 kJ]; 2/3 cup). Analysis of a urine sample collected 20 days after initiation of nutritional therapy revealed a pH of 6.0 and no crystalluria. After approximately three weeks of calculolytic therapy, the food was changed to a commercial veterinary therapeutic food that has lower energy density, decreased fat, increased fiber, reduced magnesium concentration and that produces a normal acidic urine (Prescription Diet w/d Feline[a]). Therapeutic goals were to: 1) promote formation of acidic urine (pH 6.2 to 6.4) at approximately four to eight hours after feeding, 2) reduce or eliminate struvite crystalluria and 3) promote gradual weight reduction. Therapeutic efficacy was monitored by serial urinalyses and physical examinations. Over the next several months the cat lost approximately 1.2 kg and remained free of signs of lower urinary tract disease. The quantity of food was adjusted to maintain a stable body weight of 5 kg.

Endnote
a. Hill's Pet Nutrition, Inc., Topeka, KS, USA.

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CASE 46-2

Recurrent Urolithiasis in a Himalayan Cat
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Patient Assessment
A five-year-old, neutered male Himalayan cat was examined for a six-week history of pollakiuria, stranguria, gross hematuria and licking the perineal area. Multiple urocystoliths (bladder uroliths) had been removed one year earlier. The uroliths had been given to the owner at that time and were not submitted for analysis. The current clinical signs had not improved after treatment with an oral antimicrobial agent (sulfadiazine/trimethoprim).

Physical examination revealed a thin 3-kg cat (body condition score [BCS] 2/5) with a small and painful urinary bladder and erythematous penile mucosa. Evaluation of these problems included a complete blood count (normal), serum biochemistry profile (normal), urinalysis (red color, proteinuria, hematuria, pH = 6.5, no crystals visualized), aerobic urine culture (negative) and abdominal radiographs. Multiple radiodense uroliths (3 mm diameter) with rough edges were found in the urinary bladder. The owner had uroliths that had been previously removed, which were submitted for quantitative analysis. Results revealed the uroliths were composed of 100% calcium oxalate (monohydrate and dihydrate).

Assess the Food and Feeding Method

The cat was given a variety of commercial dry and moist cat foods before the urocystoliths were removed one year ago. After surgery, the food was changed to a commercial dry veterinary therapeutic food[a] formulated to avoid excessive magnesium and phosphorus and to allow production of normal acidic urine. These nutritional attributes are important for prevention of struvite crystalluria. This food was offered free choice.

Questions

1. Why were no crystals identified in urine from this patient?
2. What is the probable composition of the recurrent uroliths in this cat?
3. How should this cat be treated and how can urolith recurrence be minimized?

Answers and Discussion

1. Crystals were not seen in the urine sample because the urine was not supersaturated with crystal-forming substances at the time the sample was collected and examined. This finding suggests an absence of the typical combination of factors that lead to the initiation, nucleation, growth and aggregation of crystals. Some factors that influence the variable presence of crystals include time since the last meal, how concentrated or dilute the urine is, how the urine sample is handled after collection, fluctuations in urinary pH and differences between the food consumed at home vs. that in the hospital.
2. The urocystoliths are probably composed of calcium oxalate, based on the signalment (calcium oxalate occurs more commonly in neutered male, middle-aged cats with a higher prevalence in Burmese, Himalayan and Persian breeds) and clinical findings (i.e., aciduria, radiodense uroliths and analysis of the previous uroliths).
3. Medical protocols to promote dissolution of calcium oxalate uroliths in cats are currently unavailable. Urocystoliths small enough to pass through the urethra may be removed by voiding urohydropropulsion. Very small urocystoliths may be retrieved with the aid of a urinary catheter. At present, cystotomy is the only practical alternative for removing larger calcium oxalate uroliths. Following urolith removal, medical protocols should be considered to minimize urolith recurrence. In general, medical therapy should be formulated in a stepwise fashion, with the initial goal of reducing urine concentration of lithogenic substances.

   A food that provides adequate protein (>32% dry matter), avoids excessive calcium and sodium chloride and does not promote formation of overly acidic urine (urinary pH <6.2) should be considered to help minimize recurrence of calcium oxalate uroliths in this cat. Potassium citrate helps promote increased urinary pH and may inhibit formation of calcium oxalate crystalluria; it is present in some therapeutic urinary foods.[b,c] The food should not contain restricted or increased levels of phosphorus or magnesium. Excessive intake of vitamin D (which promotes intestinal absorption of calcium) and ascorbic acid (a precursor of oxalate) should be avoided by not offering vitamin supplements. The food should be adequately fortified with vitamin B_6 (pyridoxine) because pyridoxine deficiency may promote endogenous production and subsequent urinary excretion of oxalic acid. Most commercial foods contain more than adequate levels of pyridoxine; however, homemade foods might be deficient if they are not supplemented.

   Other preventive measures include increasing urine volume and maintaining less concentrated urine by feeding moist (canned) rather than dry food. Drugs (e.g., furosemide, glucocorticoids) that may increase hypercalciuria should be avoided. Hydrochlorothiazide diuretics may decrease urinary calcium oxalate saturation in healthy cats; however, there currently are no data to indicate their effectiveness in cats with calcium oxalate uroliths. Serial monitoring (e.g., radiographs, urinalyses, serum biochemistry profiles) should be performed every six months to detect underlying metabolic problems, and to aid detection of recurrent uroliths when they are small enough to be removed by nonsurgical techniques.

Progress Notes

Abdominal radiographs were reviewed to ensure that radiodense nephroliths were not overlooked. The urocystoliths were removed via cystotomy. Because the number of uroliths could not be determined from the pre-surgery radiographs, postsurgical radiographs were taken to confirm that all of the uroliths had been removed. Evaluating postsurgical radiographs is important because failure to remove all urocystoliths during surgery is possible and may result in the appearance of recurrence of clinical signs and uroliths despite preventive measures. A moist veterinary therapeutic food[b] that provided the appropriate nutritional benefits discussed above was prescribed; the nutritional benefits of this food currently are available in different food.[d] Because the cat was thin (BCS 2/5), the daily energy requirement (DER) was estimated to be 1.4 x the resting energy requirement at the ideal weight of 4 kg (DER = 265 kcal [1,109 kJ]). The owners were instructed to divide the amount of food supplying the DER into two daily feedings and monitor the food intake closely until optimal weight was achieved.

Serial monitoring consisted of periodic urinalyses (with emphasis on urine specific gravity, urinary pH, crystalluria and evidence of urinary tract infection), survey radiographs and serum biochemistry profiles (serum calcium and electrolytes). Initially, routine urinalyses were performed every two to four weeks and the owners were carefully interviewed to assess compliance with feeding recommendations.

Endnotes

a. Prescription Diet c/d Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.
b. Prescription Diet x/d Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.
c. Iams Veterinary Formula Urinary O Moderate pH/O/Feline, P&G Pet Care, Dayton, OH, USA.
d. Prescription Diet c/d Multicare Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.

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CASE 46-3

Struvite Urolithiasis in a Cat

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Patient Assessment

An eight-year-old, spayed female domestic shorthair cat was evaluated for pollakiuria of three days' duration. Although the cat was using the litter box, its caregivers suspected that it also was urinating in other locations in the house. Physical examination was unremarkable (body condition score 3/5) and the urinary bladder was small. The cat remained in the hospital until there was sufficient urine to collect for analysis.

Urine subsequently obtained by cystocentesis had a specific gravity of 1.043, pH of 6.5, hematuria (>200 RBCs/hpf) and struvite crystalluria. Survey abdominal radiographs revealed two radiopaque uroliths in the urinary bladder (**Figure 1**). Subsequent aerobic bacterial culture of the urine sample revealed no growth. With a tentative diagnosis of struvite urolithiasis, the attending veterinarian discussed treatment options with the owners including medical dissolution and surgical removal.

Assess the Food and Feeding Method

Before urolith diagnosis, the cat was fed a commercial moist food twice daily and a dry commercial maintenance food was available at all times. Water was available free choice.

Questions

1. What urolith types are most likely in cats and how does one determine their mineral composition?
2. What treatment should be recommended for cats with struvite uroliths?
3. What recommendations should be made to prevent struvite urolith recurrence?

Answers and Discussion

1. Approximately 90% of uroliths in cats are composed of either magnesium ammonium phosphate (struvite) or calcium oxalate. Using information from the history, signalment, urinalysis and diagnostic imaging, it is possible to estimate the mineral type. The textbook case of struvite uroliths involves a younger (<7 years), spayed female cat with slightly acidic to alkaline urine (pH >6.5), struvite crystalluria and round or disk-shaped radiopaque uroliths. Cats with calcium oxalate uroliths usually are older (>7 years), male, have acidic to neutral urinary pH, calcium oxalate crystalluria and radiopaque uroliths that may be small and/or have pointed edges. Some cats with uroliths may not have all findings (e.g., there may be no urine crystals) or there may be findings consis-

tent with both urolith types. Findings consistent with struvite uroliths in this cat include female gender, presence of struvite crystalluria and round, radiopaque uroliths whereas the age and urinary pH could occur with calcium oxalate uroliths. A definitive diagnosis requires quantitative urolith analysis, which is particularly helpful when there are mixed or compound uroliths. For this cat, one option would be to attempt nutritional dissolution therapy for four weeks; if the uroliths decrease in size or disappear, struvite urolithiasis is likely and treatment should be continued. If the uroliths do not decrease in size or they become larger, other treatment (e.g., physical removal of uroliths) is indicated because the uroliths are likely composed of another mineral type.

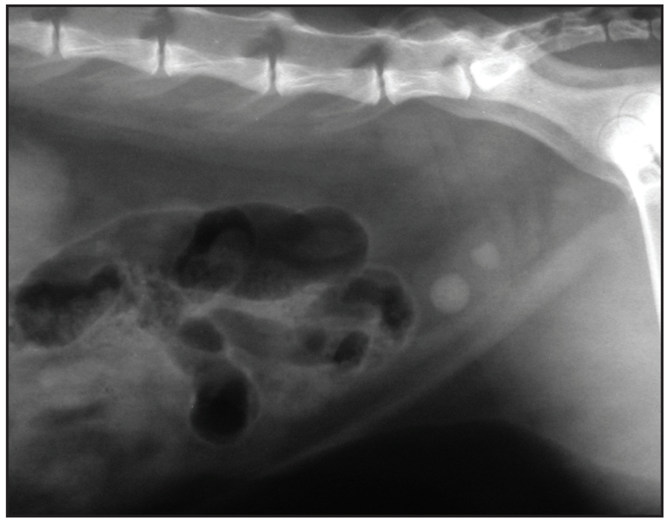

Figure 1. Lateral abdominal radiograph reveals two radiopaque uroliths in the urinary bladder.

2. At this time, the most common treatments for managing cats with struvite uroliths are surgical removal via cystotomy and medical dissolution with nutritional management. The choice between these options may depend on the clinician's preference and expertise as well as the pet owner's preferences. Many veterinarians prefer to surgically remove uroliths because they believe that surgical management is more effective, controls clinical signs quicker and will not be associated with urethral obstruction as uroliths decrease in size, especially in male cats. However, effectiveness of surgical removal of uroliths has not been critically evaluated in cats. A retrospective study including 20 cats with urinary bladder uroliths revealed that five cats (20%) had incomplete removal of uroliths by cystotomy in a veterinary teaching hospital. In the absence of appropriate studies, it should not be assumed that surgical management of uroliths is 100% effective. In addition, there have been no reported studies documenting the time required for resolution of clinical signs after surgical removal of uroliths or that urethral obstruction does or does not occur postoperatively.

   Medical management using dissolution foods[a,b] has been evaluated in two studies of cats with struvite uroliths. The mean time required for urolith dissolution was around four weeks; however, some cats had radiographic resolution of uroliths two weeks after beginning nutritional management. Urethral obstruction has not been reported to occur in male cats with struvite uroliths that were dissolved with nutritional management. In most cats, clinical signs are no longer evident within two weeks of beginning dissolution foods.

   In summary, when selecting treatment for cats with struvite uroliths it may help to ask and answer the following questions: 1) Which treatment is the least invasive?, 2) Which treatment would I prefer if I had uroliths? and 3) Which treatment is the most effective based on currently published evidence?

3. After dissolution or removal of struvite uroliths, nutritional management is indicated to decrease risk of urolith recurrence. Based on current evidence, foods used for prevention of struvite disease should avoid excessive protein, magnesium, phosphorus and sodium and should maintain a mildly acidic urinary pH. Cats eating struvite preventive foods should be monitored periodically for urinary pH values and evidence of crystalluria. The goal of treatment is to prevent occurrence of struvite crystalluria and maintain urinary pH $\leq$ 6.4.

Progress Notes

After considering treatment options and the owner's preferences, the veterinarian recommended a struvite dissolution fooda for this patient. The daily caloric requirement was calculated and divided into two meals. It was recommended that the patient return in two weeks for reevaluation to include physical examination, urinalysis and abdominal radiographs. During the first followup examination two weeks later, the patient was eating the prescribed food exclusively. Analysis of urine collected by cystocentesis revealed specific gravity = 1.034, pH = 6.0 and mild hematuria (7 RBCs/hpf); there was no pyuria, crystalluria or bacteriuria. Survey abdominal radiographs confirmed that uroliths were smaller (**Figure 2**); therefore, nutritional management was continued. Radiographic evaluation performed four weeks after initiation of the dissolution food revealed no visible uroliths (**Figure 3**). The dissolution food was prescribed for an additional month after which it was recommended that the patient be transitioned to a maintenance food with reduced magnesium and phosphorus to prevent struvite urolith recurrence.

Endnotes

a. Prescription Diet s/d Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.
b. Dissolution Formula, Medi-Cal Royal Canin, Guelph, ON, Canada.

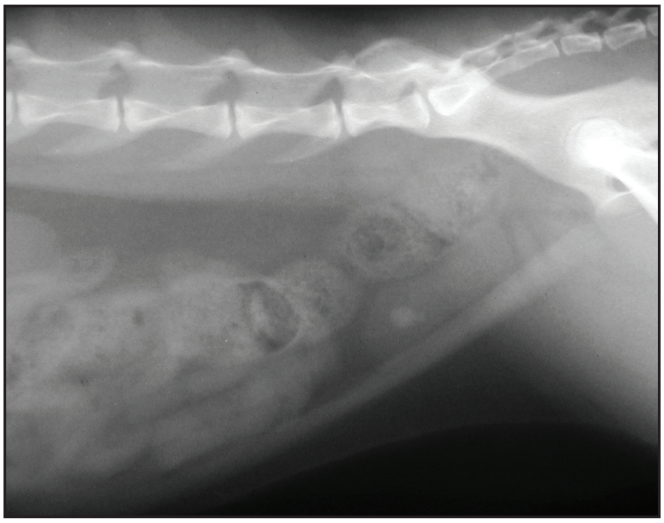

Figure 2. Radiographic image obtained two weeks after beginning nutritional management for struvite urolithiasis. Radiopaque uroliths have decreased in size.

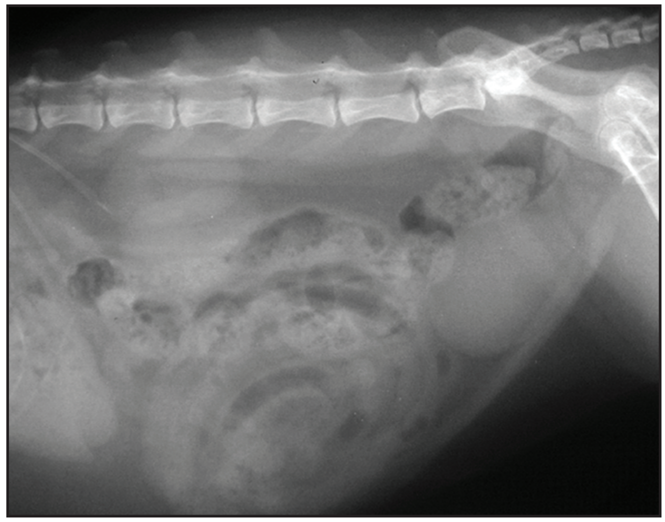

Figure 3. Radiographic image obtained four weeks after initiation of dissolution therapy reveals no evidence of uroliths. The struvite dissolution food should be continued for an additional four weeks to ensure that small uroliths (below the level of radiographic detection) are dissolved.

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CASE 46-4

Inappropriate Urination in a Cat

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Patient Assessment

A four-year-old, spayed female domestic shorthair cat was presented for evaluation of inappropriate urination that occurred intermittently over the past four to six months. The owner reported that the cat urinates in the litter box but also in various locations throughout the home (e.g., bathtub, laundry basket). For the past three days the owner also noted increased frequency of urination and the urine appeared pink. The cat lives indoors with two other cats that are healthy. Physical examination revealed a body weight of 5.5 kg and body condition score of 4/5.

Initial evaluation included a urinalysis and diagnostic imaging. Analysis of urine collected by cystocentesis revealed a red/hazy appearance with a specific gravity of 1.052. Dipstick analysis revealed a urinary pH of 6.0, 2+ protein and 3+ occult blood. There were numerous red cells and three to five white cells/hpf noted during urine sediment examination. Aerobic urine culture was negative for bacterial growth. Results of abdominal ultrasound and radiographs were normal. Based on all findings, feline idiopathic cystitis (FIC) was considered most likely.

Assess the Food and Feeding Method

Before the diagnostic evaluation the cat was fed primarily dry commercial food that was available at all times with occasional canned food as a treat. Water was available free choice.

Questions

1. What disorders are associated with inappropriate urination and why is it important to identify the underlying cause?
2. How is FIC diagnosed?
3. What is the most effective approach for controlling clinical signs in patients with FIC?

Answers and Discussion

1. Inappropriate urination (i.e., periuria) may occur as a result of behavioral and/or medical disorders. Any medical condition that causes inflammation of the lower urinary tract (e.g., FIC, urolithiasis, urinary tract infection) may cause urination outside the litter box. Behavioral periuria typically results from toileting problems or urine marking (spraying). Cats with toileting problems have elected to use an alternate location other than the litter box because they have an aversion to or preference for a particular substrate (e.g., litter) or litter box characteristics such as location, style and cleanliness. Cats with lower urinary tract diseases may develop secondary toileting problems that may persist after correction of the underlying medical disorder and this must be distinguished from primary behavioral periuria. Urine marking is a means of communication and often is characterized by expelling urine on vertical surfaces although cats may mark by depositing urine on horizontal surfaces from a squatting position. Finally, aging cats with osteoarthritis may urinate inappropriately in the absence of primary behavioral disorders or urinary tract diseases due to difficulty accessing the litter box (e.g., the sides are too high or the cat must travel up or down stairs to reach the litter box).

   Inappropriate elimination is the most common behavioral problem for which pet owners seek professional counsel. It also is a common reason why owners relinquish their cats to shelters. To prevent the negative impact of inappropriate urination on the pet-family bond, it is important to educate pet owners about potential causes of inappropriate urination so they seek help before relinquishing their cat. When medical causes are excluded, a veterinary behaviorist should be consulted so that appropriate evaluation and treatment can be recommended. This should be done sooner rather than later in the course of the disease, when the chances are greater for having a successful outcome with behavioral modification.
2. The presence of pollakiuria and hematuria indicates that inappropriate urination in this patient is probably due to a medical disorder of the lower urinary tract. In a young to middle-aged female cat, the most likely causes for these signs are FIC and struvite urolithiasis; less likely causes include uroliths of other mineral type (e.g., calcium oxalate, urate), urinary tract infection, anatomic anomalies and neoplasia. At a minimum, all cats with signs of lower urinary tract disease should have a urinalysis and diagnostic imaging performed. Selection of the initial diagnostic imaging procedure (i.e., plain abdominal radiographs or abdominal ultrasonography) may depend on equipment availability; however, using both modalities can be helpful. For radiographs, it is critical to include the entire urinary tract; otherwise, abnormalities such as urethral uroliths may be overlooked. On the basis of initial findings, additional tests such as urine culture and contrast urethrocystography may be indicated for some patients. FIC is diagnosed by excluding all other causes of lower urinary tract disease; therefore, thorough diagnostic evaluation is necessary.
3. A multimodal approach including nutritional management, environmental enrichment, pain management and in some cases, behavioral modification, is recommended to control clinical signs in patients with FIC. Many treatments have been suggested for managing affected cats; however, only a few have been evaluated in clinical studies. To date, the treatments that have been associated with improvement in patients with FIC are feeding moist food and implementing environmental enrichment. Gradual transition to moist food should be part of initial management. It is believed that increased urine volume associated with increased water intake results in dilution of inflammatory mediators in the urinary bladder of patients with FIC; however, other effects of feeding moist food (e.g., increased interaction with owners) cannot be excluded.

   Although being overweight or physically inactive has not been shown to cause urinary tract disease, both are risk factors for FIC. Recent research findings have confirmed that obesity is characterized by a state of systemic inflammation and other negative consequences such as insulin resistance. Therefore, to improve this cat's overall health, a weight-reduction program should be recommended with a goal of reaching ideal body weight and condition. This should include nutritional management and environmental enrichment (e.g., increased exercise and interaction with the owner).

Progress Notes

The owner was given additional information about environmental enrichment to help manage clinical signs of FIC and assist with achieving ideal body condition. A moist veterinary therapeutic food[a] was initially recommended until the cat achieved ideal body weight (4.5 kg). The resting energy requirement (RER) for ideal body weight was calculated as follows: $RER = 70(4.5)^{0.75} = 218$ kcal. In order to lose weight, it was initially recommended to feed approximately 175 kcal per day. The owners were instructed to transition the food change over seven days by feeding 0.75 can of the therapeutic food (87 kcal) twice daily and monitoring food intake closely until optimal weight was achieved. Body weight was measured every two weeks and recorded on a progress chart; the cat achieved ideal body weight five months later and was transitioned to another moist therapeutic food[b] formulated for management of cats with FIC. In order to maintain body condition, the owners were instructed to initially feed 0.75 can of the therapeutic food twice daily (147 kcal per can), which provided slightly less than the daily energy requirement (1.4 x RER) for the cat's ideal body weight. The owner was counseled that this amount of food was a starting point and that adjustments should be made as needed to maintain body weight.

Endnotes

a. Prescription Diet r/d Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.
b. Prescription Diet c/d Multicare Feline, Hill's Pet Nutrition, Inc., Topeka, KS, USA.

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