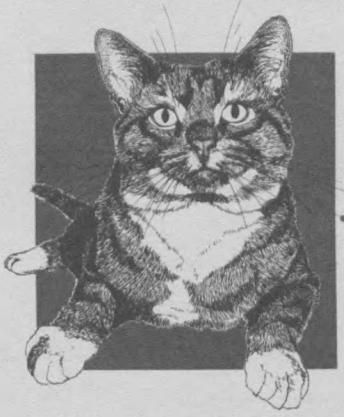

Cornell Feline Health Center

Veterinary News

Fall 1985

Part 1: Understanding FUS

The feline urologic syndrome (FUS) is widely accepted as being the occurrence of varying combinations of dysuria, hematuria, marked crystalluria, and/or urethral obstruction in male and female cats. This combination of signs is occasionally referred to as feline urolithiasis, feline cystitis, feline urethritis, lower urinary tract disease of the cat, and feline urethral obstruction. Although different names and definitions have been applied to FUS, in reality FUS is a synonym for lower urinary tract disease which may be complicated by renal dysfunction. If accurate, FUS may result from fundamentally different causes that may be single, multiple, and interacting, and/or unrelated in male and female cats (Table 1). FUS is not a diagnosis.

The following discussion summarizes the latest relevant information that supports the idea that the FUS is induced by different causes. Thus, FUS requires different approaches to its treatment and prevention depending on the specific cause of the FUS.

Causes of Urethral Obstruction

Urethral obstruction may be caused by a variety of different lower urinary tract diseases in cats (Table 2). In the past, most individuals have considered urethral plugs to be the major cause of urethral obstruction, hence, FUS. Consequently, controversy has focused on whether urethral obstruction and urethral plugs are initiated by a virus or diet-related factors. Numerous articles pertaining to the viral or dietary-related etiology and pathogenesis of urethral obstruction have been written to support these theories. Only recently have investigators broadened their ideas as to what are the cause(s) of urethral obstruction in male and female cats.

Recent radiographic studies of the urethras and urinary bladders of male cats with naturally occurring urethral obstruction admitted to the University of Minnesota Veterinary Teaching Hospital have revealed that urethral obstruction may be associated with urethral plugs, true uroliths, strictures caused by connective tissue, disease of the prostate gland, and extraluminal masses that have compressed the urethral lumen. Clinical experience and anatomic studies have indicated that the penile urethra is the most common site of urethral obstruction. Therefore, surgical removal of the penile urethra has been recommended to prevent the recurrence of urethral obstruction. No doubt, this approach is helpful in the majority of cats with urethral obstruction. However, special radiographic studies (contrast urethrocystograms) of the urethras and

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urinary bladders of male cats with naturally occurring urethral obstruction in the Minnesota study revealed that partial or total urethral obstruction occurs at sites other than, or in addition to, the penile urethra. These observations also suggest that surgical procedures designed to minimize obstruction of the distal urethra of male cats by amputating the penis may be partially or totally ineffective in some cats. Persistence of unrecognized concomitant abnormalities may contribute to what is perceived to be a recurrent nature of lower urinary tract disease.

The higher rate of occurrence of urethral obstruction in male cats has been explained anatomically by the length of the male urethra being longer than the female urethra and that the diameter of the penile urethra is much smaller than the diameter of the postprostatic and preprostatic urethra. To date, naturally occurring and experimentally induced urethral plugs have only been reported in intact and castrated male cats with lower urinary tract disease. It has been implied that a cell-associated virus causes lower urinary tract disease in male and female cats. However, experimental induction of FUS in female cats with cell-associated virus has not yet been fully evaluated.

If viruses are capable of inducing lower urinary tract disease in male and female cats, why have urethral plugs only been identified in male cats? Investigators at University of Minnesota speculate that special secretory glands found only in the postprostatic urethra of male cats produce at least a part of the mucus matrix that contributes to the formation of urethral plugs. The glands' secretory activity may be enhanced by viral infections or other pathogenic stimuli, thus, causing urethral plugs and not true uroliths. Lack of urethral plug formation in viral infected female cats may be hypothesized to be related to the absence of similar periurethral mucus secreting glands. They emphasize that this hypothesis is only speculative at the present time; and it requires further study.

What are urethral plugs?

Urethral plugs found in male cats are typically soft, paste-like, compressible, mineral matrix material that may assume a cylindrical shape when forced out of the external urethral orifice. The urethral plugs are composed of varying quantities of minerals (crystals) and matrix. Quantitative mineral analysis of 184 male feline urethral plugs from male cats submitted to the University of Minnesota by practitioners revealed that 79% (146) were composed of 100% struvite crystals; 15% (27) were composed primarily (greater than 80%) of struvite crystals; less than 1% (1) was composed primarily of calcium phosphate; and less than 1% (1) was composed of calcium oxalate. The infrequency with which non-struvite minerals were recognized in urethral plugs suggest that

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they are not of great clinical importance. However, they do suggest that any type of crystal may become trapped in the plug matrix and that the matrix plays an important primary role in the formation of urethral plugs. The crystals then play a secondary role in urethral plug development.

The specific composition and origin of the matrix in urethral plugs have not been identified. Also it has not been established whether or not matrix components of different plugs are consistently similar. However, studies show that most urethral plugs are composed of matrix and crystalline material containing a similar type of as yet unidentified matrix.

What role does diet play?

Recently, investigators have reported convincing data concerning experimental production of struvite uroliths in cats consuming stone-forming (calculogenic) diets. However, the relationship of calculogenic diets to formation of urethral plugs is not clear. Although dietary ingredients could contribute to the mineral (crystalline) component of urethral plugs, it is difficult to comprehend how they could influence the production of the matrix component of urethral plugs.

How do infectious agents influence urethral obstruction?

Viruses, bacteria, mycoplasmas, and ureaplasmas have been implicated as causes of urethral obstruction (FUS) in male cats. Some investigators suggest viruses are more likely to cause urethral plugs in male cats than to cause the struvite uroliths that are encountered in either male or female cats. However, the general consensus is that the role of viruses as causative agents in naturally occurring urethral obstruction (FUS) remains unsolved, and the search for viral pathogens must continue.

Results of clinical investigations of lower urinary tract disease performed at many institutions indicate that the initial episode usually occurs in absence of significant numbers of detectable urine bacteria. When bacterial urinary tract infection has been confirmed, it frequently occurred as a secondary, or complicating, rather than a primary cause of urethral obstruction. Despite these observations, one should not exclude the possibility that primary bacterial infection plays a role in at least an occasional cat with urethral obstruction. Therefore, routine screening quantitative urine culture prior to the administration of diagnostic or therapeutic agents is recommended. Mycoplasmas and ureaplasmas have been isolated from the genitourinary tract of cats. However, preliminary efforts to isolate these organisms from urine of naturally occurring lower urinary tract disease have been unsuccessful. Further studies are desirable, because mycoplasmas and ureaplasmas are difficult to isolate and grow once they have been removed from the body.

Can there be mechanical causes for FUS?

On occasion, the urethral lumen of male cats can become obstructed by tissue sloughed from the mucosal lining surface of the lower urinary tract as result of inflammatory disease or malignant tumor. Although this form of urethral plug leading to urethral obstruction is uncommon, it represents one form of lower urinary tract disease that could be labeled FUS.

Diagnosis

In addition to an appropriate history and physical examination, complete urinalyses and possibly quantitative urine cultures performed on samples obtained by cystocentesis should be obtained routinely. Survey and contrast radiography may be required to aid in localization of problems in addition to identifying the underlying cause(s) of persistent or recurrent clinical signs (Table 1). Localization of the site(s) and cause(s) of persistent or recurrent urethral obstruction is especially important if urethral surgery is being

considered. Cats showing signs of renal dysfunction caused by lower urinary tract disease should be evaluated with the aid of complete blood counts and blood chemistry profiles (especially serum creatinine and electrolytes). Analyses of uroliths and possible urethral plugs should be done routinely. Any tissue removed surgically should be submitted for evaluation by light microscopy.

Management of Urethral Obstruction

Complete urethral obstruction produces a predictable set of abnormalities characterized by depression, vomiting, dehydration, azotemia, hyperphosphatemia, acidosis, and hyperkalemia. Fundamentals of management for urethral obstruction are straight-forward. They chronologically are 1) correct deficits and excesses of fluid volume, acid-base balance, and electrolytes; 2) restore and maintain urethral patency; 3) anticipate postobstructive diuresis and manage fluid and electrolyte therapy appropriately; 4) continue diuresis until uremia and azotemia resolve; and 5) verify that the cat can voluntarily micturate effectively.

TABLE 1. Possible Causes of Lower Urinary Tract Disease in Cats

- Urolithiasis (stones)
  - Magnesium ammonium phosphate (struvite)
  - Calcium oxalate
  - Calcium phosphate
  - Ammonium urate
  - Uric acid
  - Matrix
  - Other
- Infection
  - Bacteria
  - Yeasts and fungi
  - Mycoplasma?
  - Viruses?
  - Parasites
- Congenital Defects
  - Urachal anomalies
  - Urethral deformities
  - Others?
- Trauma
  - External blunt trauma
  - Indwelling urinary catheters
  - Others
- Neoplasms (tumors)
  - Bladder tumors
  - Urethral tumors
  - Genital tumors
    - Prostate
    - Uterus
    - Vagina
  - Others
- Neuromuscular Disorders
  - Neurogenic urethral obstruction (reflex dyssynergia)
  - Atonic bladder
  - Others
- Idiopathic (Unknown) Disorders

The most immediate threat to life in complete urethral obstruction is hyperkalemia. Laboratory determination of serum potassium concentration may be useful if the result is available quickly. However, electrocardiogram is often more useful because results are more rapidly available and because it provides information about the physiologic effects of hyperkalemia, whatever its numerical value. Intravenous administration of calcium, a physiologic antagonist of the myocardial effects of excess potassium, can be used if serious arrhythmias occur before other therapeutic modalities can reduce the hyperkalemia.

Relief of urethral obstruction can be accomplished satisfactorily in a variety of ways. Regardless of how it is done, it is imperative to avoid or minimize injury to the urethra. Trauma-induced injury to the urethra causes swelling associated with submucosal inflammation that may encroach on the urethral lumen and impair effective micturition or promote reobstruction. In time, urethral injury can contribute to stricture formation or generalized fibrosis, hence, increasing the risks of recurrence. All instrumentation of the lower urinary tract should be performed with sterilized equipment, lubricants, and solutions and with aseptic technique.

Some have advocated routinely using indwelling urinary catheterization for the first few hours or days following relief of obstruction to insure urethral patency. Indwelling urethral catheters have been shown to cause tissue injury, infection, or both even in normal male cats.

Although the chances of immediate reobstruction are sufficient in some cats to justify indwelling catheterization, this is clearly not always the case. Some cats can be satisfactorily managed without indwelling catheterization. Indications for use of an indwelling catheter include: 1) inability to restore a urine stream of normal caliber; 2) abundance of debris which cannot be lavaged or aspirated from the lower urinary tract; 3) evidence of detrussor muscle hypotony (atonic bladder); and 4) intensive care of critically ill cats when urine formation rate is continuously monitored as a guide to fluid therapy requirements. Routine use of indwelling catheters as a matter of convenience or as an alternative to regular observation of the cat should be abandoned for better standards of care.

Bacterial urinary tract infections should be managed by eliminating the infections by appropriate antimicrobial therapy. It is undoubtably wise to avoid feeding calculogenic diets to cats, particularly those cats with a known predisposition to urethral obstruction. The non-calculogenic diet, which contains equal to or less than 20 mg of magnesium/100 Cal. metabolizable energy, 0.1% of magnesium in its dry matter, or 5% ash in the dry matter of a dry or soft-moist food, should be fed exclusively for 2 to 3 months to dissolve the struvite crystals that occur in the urethral plugs. Urinary acidifiers should not be given when special non-calculogenic diet (eg. Prescription Diet Feline s/d® - Hill's) is being fed. After 2 to 3 months a non-calculogenic diet providing 20 mg of magnesium/100 Cal. or less should be fed indefinitely to prevent recurrence.

For cats that have never been affected with urethral obstruction, feeding a low magnesium diet is unnecessary unless the disease is of particular concern. For all cats, encouraging exercise and frequent micturition, preventing obesity, decreasing confinement, keeping the litter box clean and easily available, and always having palatable water readily available

TABLE 2. Possible Causes of Urethral Obstruction in Male Cats

Primary Causes	Perpetuating Causes	Iatrogenic Causes[a]
Intraluminal Plugs (matrix and crystals) Uroliths Sloughed tissue (uncommon)	Intraluminal Sloughed tissue Inflammatory cells and red blood cells (clots) Overproduction of mucoprotein	Tissue damage Reverse flushing solutions Catheter trauma Catheter-induced foreign body reaction Catheter-induced infection
Mural[b] or Extramural Neoplasms Strictures Anomalies Reflex dyssynergia	Mural[b] Inflammatory swelling Muscular spasm Strictures	Postsurgical dysfunction
Combinations	Combinations	Combinations
Other?	Other?	Other?

[a]Iatrogenic means disorders induced by individuals involved in diagnosis and treatment of diseases.
[b]Mural is derived from the Latin word *muralis*, pertaining to wall.

assist in preventing urethral obstruction (FUS).

Perineal urethrostomy undeniably reduces the risk of urethral obstruction for male cats, but it is no more a cure for FUS than is any particular medical strategy. For cats with recurrent urethral obstruction, urethrostomy generally provides freedom from the most life-threatening and expensive consequences of the problem. It does not always prevent the occurrence of lower urinary tract disease. ■

Acknowledgment: The tables have been reprinted with permission from Kal Kan Forum 4:1, 1985.

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Part II, in the next issue, will present information on urinary calculi.

Is Feline Leukemia Transmissible to Man?

(Adapted from article by Tim Byers, MD, MPH)

When feline leukemia virus (FeLV) was first discovered in 1964 by William Jarrett and his coworkers, it was thought that viruses like FeLV spread only vertically by genetic means.[1,2] However, Oswald Jarrett and his coworkers reported in 1969, that natural field isolates of FeLV replicate well in normal human embryonic lung cells.[3] Since 1969, there have been other reports of the growth of FeLV in human cells.[4,5] Consequently, those reports, together with the observation that FeLV is spread contagiously among cats, has lead to the fear that FeLV may be able to induce disease in people and be a contributing cause of cancer among veterinarians.[6,7] This article briefly reviews the epidemiologic findings of cancer among veterinarians and the arguments against FeLV being transmitted from cat to man, resulting in FeLV-induced cancer.

Studies of Cancer in Veterinarians

Veterinarians are frequently exposed to FeLV-infected cats as a part of their occupation. Since 1966, there have been several reported studies on the cause of death in veterinarians, each with conflicting results.

A study of 390 white, male, Missouri veterinarians and 486 mostly white, male, Illinois veterinarians showed no statistically significant differences in the occurrence of cancer deaths compared to the general Missouri and Illinois population.[8,9] However, an excess of skin melanomas in 1,722 white, male, California veterinarians was reported in another study.[10] The number of deaths from leukemia and lymphoma in the California and Missouri studies was comparable to their general populations.

Gutensohn and her coworkers in 1980 reported that Matanowski had found an 80 percent increase in the occurrence of lymphoid tumors among 19,000 U.S. veterinarians who died 45 years of age or over as compared to physicians and the general U.S. population. No conclusion as to the cause of this increased risk of lymphoid tumors in veterinarians was possible, however.

In another study in 1980, Blair and Hayes also found a significantly increased occurrence of leukemia and Hodgkin's disease in 1,551 white, male, veterinarians who were in clinical practice.[12] In an expanded study, Blair and Hayes reported in 1982 on the causes of death among 5,016 white, male, veterinarians identified from obituary listings in the JAVMA.[13] Proportions of deaths were significantly increased for cancers of the lymphatic and hematopoietic system, colon, brain, and skin, with fewer cases of lung cancer. Recently, Kinlen found no excess of deaths from leukemia or other cancers among 3,440 Great Britain veterinary surgeons over a 25-year period.[14]

The reason for the differences in findings among the various cancer mortality studies is not clear. It may be relevant, however, that some studies do not ascertain all deaths in a defined population but consist of a proportionate analysis of death such as expressed in the obituary columns of the JAVMA. Therefore, the proportionate mortality from certain causes can be inflated if other diseases have a reduced mortality. Another possible bias is differential reporting to the JAVMA of deaths from cancer compared with deaths from other causes. Of course, many studies of mortality among veterinarians are too small for detailed analysis of different cancers.

The question also arises as to how frequent are the veterinarians in the mortality cancer studies exposed to FeLV-infected cats. The leukemias and lymphomas in these studies are not limited to small animal practitioners but include large animal practitioners, laboratory workers, meat inspectors, and regulatory veterinarians who have limited or no exposure to FeLV-infected cats. Therefore, mortality cancer studies do have their limitations.

Serologic Studies of Humans Exposed to FeLV

Several studies have examined human sera for evidence of either current or past FeLV infection by testing for antibodies to FeLV, antigens of FeLV, and the FeLV-associated tumor-specific antigens (FOCMA).[15-24] Although earlier studies suggested that FeLV antigens may be found in human sera, a recent study by Sordillo and coworkers failed to duplicate these findings.[25] The sera of 192 adults and 47 children affected with leukemias, lymphomas, and soft tissue sarcomas were found not to have even a trace amount of FeLV antigen, FeLV antibody, or FOCMA antibody. In addition, no detectable FOCMA antigen was found on the membranes of bone marrow cells in a subset of these patients.

Concluding Remarks

It is difficult to evaluate the conflicting results of the epidemological studies in humans. However, most studies do support the idea that FeLV does not infect people. In addition, investigators state that FeLV and its potential of inducing disease or cancer in man and other animals needs further study. Whether FeLV may infect persons who may be uniquely susceptible to FeLV (eg. immunosuppressed persons or fetuses in utero) is questionable. Therefore, it is prudent that further investigations on the possibility of cat to man transmission of FeLV continue and to minimize one's exposure to FeLV, especially individuals who may be vulnerable to infections.

(continued on page 8)

The Will Is the Way

The old adage "If there is a will there is a way" has new meaning when contemplating estate planning. Consider the client who has a very deep attachment for their pet and they want to provide a perpetual fund that will benefit all cats. The will is the way which can best express a client's concern for animal health and welfare. Monies received from estates are applied towards our feline health studies and educational programs.

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Present Research on Cancer & Veterinarians

Investigators at the University at Buffalo, State University of New York are presently conducting a study of proportional cancer incidence among veterinarians in New York State. Their preliminary findings do not indicate a significant increase of leukemias or lymphomas. ■

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