The Minnesota Urolith Centre has analysed uroliths from cats for more than two decades (FIGURE 1). During this period we have observed substantial increases in the number of cats with calcium oxalate (CaOx) uroliths (FIGURE 2). For example, in 1981 quantitative mineral analysis was performed on uroliths from 69 cats; only one cat had a urolith composed of CaOx. In 2001 uroliths were analysed from 6185 cats; approximately 3,500 cats (55 per cent) had uroliths composed of calcium oxalate. In 2004 we analysed almost 9,000 uroliths from cats; the percentage of CaOx and magnesium ammonium phosphate (MAP) uroliths were approximately equal (FIGURE 3).

The exact aetiologic cascade of events which have lead to the increased prevalence of CaOx uroliths in cats is unknown. Hypotheses ranging from excessive diet-induced urine acidification to an ageing feline population have been implicated. This manuscript will discuss the associations between feline CaOx urolithiasis and several risk factors, and novel therapies to eradicate and prevent urolith recurrence.

WHAT RISK FACTORS HAVE BEEN ASSOCIATED WITH CALCIUM OXALATE UROLITHIASIS?

Figure 1. The distribution of feline urolith submissions to the Minnesota Urolith Centre between 1981 and 2004 (n=64,588).
The impact of urine acidification

Results of epidemiologic studies support the hypothesis that diets designed to minimise MAP urolith formation may have inadvertently increased the occurrence of CaOx uroliths. Several biologic phenomena provide plausible explanations for this association. Whereas diet-mediated urine acidification enhances the solubility of MAP crystals in urine, dietary acids promote CaOx crystalluria by inducing hypercalciuria. This association between aciduria, acidaemia and hypercalciuria may be explained by the fact that acidaemia promotes mobilisation of carbonate and phosphate from bone to buffer hydrogen ions. Concomitant mobilisation of bone calcium may result in hypercalciuria. In addition, metabolic acidosis in dogs, humans, and rats resulted in hypocitraturia. If consumption of dietary acids precursors is associated with hypocitraturia in cats, it may increase the risk of CaOx uroliths because citrate is an inhibitor of CaOx crystal formation.

The impact of age

In a retrospective study of feline CaOx uroliths from 922 cats, only three were less than one year old. Ninety-seven per cent of affected cats were more than two years old. These observations are interesting because conditions promoting urine acidity have been identified as a risk factor for CaOx urolith formation and the urine pH of young cats has been reported to be lower than that of adult cats consuming the same diet. If acidic urine is an important risk factor for CaOx, a reasonable question would be why CaOx uroliths are uncommon in immature cats in which urine is normally acidic. The answer is likely to be related to a combination of risk factors associated with calcium oxalate urolithiasis, including the concentrations of minerals, non-mineral crystallization inhibitors and promoters, and the quantity of urine produced. There is likely no simple cause-and-effect relationship between a single risk factor and CaOx urolithiasis.

In a case-control study comparing the age of 7,895 cats with CaOx uroliths that were submitted to the Minnesota Urolith Centre between 1981 and 1997 to the age of 150,482 cats admitted to veterinary colleges in North America, cats at greatest risk for developing CaOx uroliths were between seven and less than ten years of age. Cats in this age group were 67 times more likely to form uroliths than cats of one to two years of age. The mean age of cats with CaOx uroliths was 7.5 ± 3.3 years. 59 per cent were male and 41 per cent were female. In contrast, cats at highest risk for developing magnesium ammonium phosphate uroliths were between four years and less than seven years of age; 42 per cent were male and 58 per cent were female. These comparisons are clinically important because they emphasise the need to monitor cats receiving diets that promote urine acidification because as cats get older the risk for CaOx urolithiasis increases.

The impact of hypercalcaemia

During the last decade hypercalcaemia has been increasingly recognised in cats. Urolithiasis has been observed in approximately 15 to 35 per cent of cats with increased blood calcium concentration. Hypercalcaemia is a risk factor for CaOx urolith formation because excesses in ultra-filterable calcium parallel excesses in urine calcium excretion and concentration. In turn, increased urine calcium concentration promotes CaOx precipitation. In a
retrospective study, urolith recurrence abated and hypercalcaemia resolved when cats were fed a high fibre diet.12

The impact of kidney disease

The increase in occurrence of CaOx uroliths in cats has been associated with a parallel increase in occurrence of CaOx uroliths found in their kidneys and ureters. In fact, there has been a 10-fold increase in the frequency of upper tract uroliths diagnosed in cats evaluated at veterinary teaching hospitals in North America during the past 20 years.9 Between 1981 and 2003, the Minnesota Urolith Centre analysed nephro-ureteroliths from 1599 cats. 70 per cent had uroliths composed of CaOx. By contrast, only eight per cent were composed of MAP (FIGURE 4). While enrolling cats with renal failure into a clinical trial, we were unexpectedly surprised to recognise that 65 per cent of the first 20 participants had radiographic evidence of nephroliths or ureteroliths. This finding emphasises the importance of CaOx prevention and control in cats to minimise potential life-threatening renal failure.

Is kidney disease a cause or consequence of urolith formation? Hyperoxaluria may be the common link between the two processes. One current hypothesis proposes that excessive oxalate damages kidney tubules.16 The damaged tubules become mineralised and serve as a nidus for calcium oxalate precipitation (epitaxy). By increasing urine saturation, hyperoxaluria also promotes precipitation of calcium. In turn, CaOx uroliths of sufficient size can block the ureter promoting kidney failure.

MANAGING LOWER TRACT UROLITHS IN CATS

Detection of uroliths is not always justification for their management. The need for urolith removal and the type of therapy depends on the effects of the urolith on the patient (asymptomatic, recurrent infection, dysuria, urinary obstruction), the characteristics of the urolith (composition, size, contour, and location) (TABLE 1), the familiarity with removal techniques (TABLE 2) and availability of specialised equipment to the veterinarian. For example, with additional training and newer technological advances (cystoscopy and lithotripsy), surgical urolith removal is becoming less desirable for both the patient and client. The following describes several novel methods of urolith management that are much less invasive than surgery.

Medical dissolution

Medical therapy to dissolve CaOx uroliths in cats has yet to be developed. However, uroliths composed of magnesium ammonium phosphate (struvite) can be dissolved medically with a high degree of

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Radiographic density compared to soft tissue</th>
<th>Surface contour</th>
<th>Shape</th>
<th>Approximate size</th>
</tr>
</thead>
<tbody>
<tr>
<td>CaOx</td>
<td>+++ to ++++</td>
<td>Spiculated to smooth</td>
<td>Faceted to round</td>
<td>2–4 mm</td>
</tr>
<tr>
<td>Sterile MAP</td>
<td>++ to +++</td>
<td>Smooth</td>
<td>Round or disk</td>
<td>2–7 mm</td>
</tr>
<tr>
<td>Infection MAP</td>
<td>+ to +++</td>
<td>Smooth</td>
<td>Round to faceted</td>
<td>2–7 mm</td>
</tr>
<tr>
<td>Urate</td>
<td>– to ++</td>
<td>Smooth</td>
<td>Round to oval</td>
<td>2–4 mm</td>
</tr>
<tr>
<td>CaP</td>
<td>++ to ++++</td>
<td>Smooth</td>
<td>Round to faceted</td>
<td>2–4 mm</td>
</tr>
<tr>
<td>Cystine</td>
<td>– to +++</td>
<td>Smooth</td>
<td>Round to faceted</td>
<td>2–4 mm</td>
</tr>
<tr>
<td>Silica</td>
<td>++ to ++++</td>
<td>Radial</td>
<td>Projections</td>
<td>2–4 mm</td>
</tr>
</tbody>
</table>

Table 1. Predicting mineral composition of uroliths based on radiographic appearance.

Most nephro-ureteroliths are composed of CAOX; MAP is rare. CAOX = calcium oxalate; CaP = calcium phosphate; MAP = magnesium ammonium phosphate.
Typically, sterile struvite uroliths dissolve in two to four weeks with diets that provide reduced quantities of magnesium and phosphate and promote acidification of urine. When formation of struvite stones results from urinary tract infection caused by urea-splitting bacteria, dissolution time is typically longer. When managing infection-induced struvite uroliths, remember that in addition to special diets, appropriate antimicrobials are necessary throughout the entire period of dissolution. It is important to recognise that uroliths located in the urethra are less likely to dissolve because they are not continually surrounded by urine that is under-saturated for magnesium ammonium phosphate. Therefore, urethroliths need to be flushed back into the urinary bladder and their position periodically monitored to improve success of dissolution therapy.

**Voiding uro-hydropropulsion**

We developed a non-surgical method of removing uroliths from the bladder. We named this procedure voiding uro-hydropropulsion (TABLE 3). This technique is designed to take advantage of

---

**TABLE 2**

<table>
<thead>
<tr>
<th>Method</th>
<th>Suitable application</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Least invasive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous voiding</td>
<td>Small (&lt; 3 to 5 mm), asymptomatic urocystoliths</td>
<td>Patients with uroliths larger than the urethral lumen may develop urethral obstruction. Concomitant UTI should be eradicated</td>
</tr>
<tr>
<td>Medical dissolution</td>
<td>Sterile struvite and infection-induced struvite. Also see our website: <a href="http://www.cvm.umn.edu/depts/minnesotaurolithcenter/home">http://www.cvm.umn.edu/depts/minnesotaurolithcenter/home</a></td>
<td>Sterile struvite uroliths dissolve within weeks. Large infection induced struvite stones may take two to three months to dissolve</td>
</tr>
<tr>
<td>Voiding Uro-hydropropulsion (VUH-Table 3)</td>
<td>To evacuate small to moderate size urocystoliths (&lt;2 to 4 mm) of any composition</td>
<td>Not suitable for male cats unless they have a perineal urethrostomy. Not suitable for patients with a urethral obstruction. Not ideal for patients that have recently undergone bladder surgery. Eradicate urinary infection prior to performing VUH</td>
</tr>
<tr>
<td>Stone basket retrieval</td>
<td>Urocystoliths smaller than (&lt;3 to 5 mm) the distended diameter of the urethra</td>
<td>Not suitable for male cats unless they have a perineal urethrostomy. Performed during cystoscopy. Stone retrieval baskets are delicate and break easily</td>
</tr>
<tr>
<td>Intracorporeal lithotripsy (laser, ultrasonic, or ballistic)</td>
<td>Urocystoliths in females</td>
<td>Performed during cystoscopy. The urethra of the male cat will rarely accommodate cystoscopy equipment to perform lithotripsy</td>
</tr>
<tr>
<td>Extracorporeal shock wave lithotripsy (ESWL)</td>
<td>Nephroureteroliths</td>
<td>The ability to perform ESWL without damaging feline kidneys is controversial. Newer generation lithotriptors may prove safer</td>
</tr>
<tr>
<td>Cystotomy</td>
<td>Urocystoliths or uroliths lodged in the urethra</td>
<td>Consider retrograde urohydropropulsion of urethroliths prior to urethral surgery. Cystotomy fails to remove all uroliths in 15–20 per cent of cases</td>
</tr>
<tr>
<td>Ureterotomy</td>
<td>Clinically active ureteroliths</td>
<td>High degree of surgical skill required when performed on cats. Surgery performed on dilated ureters has been associated with greater success than normal sized ureters</td>
</tr>
<tr>
<td>Nephrostomy</td>
<td>Nephroliths</td>
<td>Some reduction in kidney function should be anticipated following surgery</td>
</tr>
</tbody>
</table>

Table 2. Methods of urolith removal.
the effects of gravity on urolith position in the urinary bladder and the dilation of the urethral lumen that occurs during the voiding phase of micturition. Voiding uro-hydropropulsion permits safe and rapid removal of small urocystoliths of any mineral composition from cats. Special equipment is not required. In some cats, uroliths can be removed without anaesthesia.

Successful urolith removal by voiding uro-hydropropulsion depends on selecting patients with urocystoliths that are small enough to completely pass through the distended normal urethra. Because the diameter of the distal portion of the urethral of male cats is narrower than the urethral diameter of female cats, voiding uro-hydropropulsion is generally more successful in females. The largest urolith we have removed from a female cat was five millimetres in diameter, while the largest urolith removed from a male cat was only one millimetre in diameter. Urocystoliths larger than one millimetre in diameter can be removed from male cats that had a perineal urethroscopy.

In addition to urolith size, urolith contour may influence the success of urocystolith removal. Smooth round uroliths usually pass through the urethral lumen more readily than do irregularly shaped uroliths of similar size. Therefore, appropriate caution should be used when considering voiding urohydropropulsion to remove sharp-edged urocystoliths that are approximately five millimetres in diameter from female cats.

**Basket retrieval of uroliths**

Retrieving uroliths cystoscopically with a stone basket is ideal for removing small stones from the urinary bladder (FIGURES 5 to 7). It is a relatively simple technique. It can be performed in patients who recently had a cystotomy in which all stones were not completely evacuated. Its limitation, however, is that stones must be small enough such that they can be pulled through the urethra. A variety of stone baskets are available to facilitate this technique (Stone Retrieval Grasping Forceps, Boston Scientific, Natick MA and N-Circle® Nitinol Tipless Stone Extractor, Cook Urologic Inc, Spencer, IN).

**Intracorporeal lithotripsy**

Several forms of energy (electrohydraulic, ultrasonic, and ballistic) can be delivered through a cystoscope to fragment uroliths in the bladder and urethra of cats. Each device has its advantages and disadvantages. Because of the versatility of laser lithotriptor and the author’s familiarity with laser lithotripsy, the remaining discussion applies to Holmium:YAG laser lithotripsy in companion animal practice for the fragmentation of urocystoliths and urethroliths.

The term ‘laser’ is an acronym for ‘Light Amplification by Stimulated Emission of Radiation’. A laser is a device which transmits light of various frequencies into an extremely intense, small, and nearly non-divergent beam of monochromatic radiation in the visible region with all the waves in...
Lasers are capable of mobilising immense heat and power when focused in close range.

Use of laser energy for intracorporeal lithotripsy is a relatively new concept. In 1968, investigators first reported in vitro fragmentation of uroliths with a ruby laser. However, because fragmentation of stones was associated with generation of sufficient heat that would likely damage adjacent tissues, it could not be used to treat patients. Likewise, use of carbon dioxide laser energy was considered to be unsuitable for clinical use because it could not be delivered through non-toxic fibres. However, in 1986 researchers using a 504 nm pulsed-dye laser successfully and safely treated human patients with uroliths. The Holmium:YAG laser is the newest device available for clinical lithotripsy.

The mechanism of stone fragmentation with the Holmium:YAG laser is mainly photo-thermal, and involves a thermal drilling process rather than a shock-wave effect. Holmium:YAG laser energy is transmitted from the energy-generating crystal to the urolith via a flexible quartz fibre. To achieve optimum results, the quartz fibre tip must be guided with the aid of a cystoscope so that it is in direct contact with the surface of the urolith. After uroliths have been sufficiently shattered such that they are small enough to pass through the urethra, fragments can be removed using a stone basket or voiding uro-hydropropulsion.

**MANAGING UPPER TRACT UROLITHS IN CATS**

The high occurrence of upper tract uroliths composed of CaOx pose unique management problems. This is especially true because a method to promote medical dissolution of CaOx uroliths has not yet been developed. The problems are magnified in cats with chronic renal failure since partial or total obstruction of just one ureter with a urolith may precipitate an acute onset of a uraemic crisis, so-called ‘acute-on-chronic’ renal failure. Although in concept surgical removal of upper tract uroliths may decrease the magnitude of renal dysfunction, ureteral surgery has been associated with significant risks, especially irreparable iatrogenic damage to the ureters and kidneys.

Factors likely to influence the migration of uroliths through the ureter include 1) the size and shape of uroliths; 2) inherent areas of narrowing of the ureteral lumen, 3) hydrostatic pressure of urine proximal to the urolith and, 4) ureteral spasm, inflammation, and oedema at the site of the urolith.

Although some of these factors can be modified such that ureterolith migration is enhanced, prospective studies are needed to determine which factors are important and which therapies are effective and safe for cats. For example, increasing the hydrostatic pressure proximal to the uroliths appears to be an important factor facilitating their passage through the ureter.\(^{1,14,17}\) This hypothesis is based on studies in rabbits evaluating ureteral transit time of two millimetres artificial concretions with and without holes.\(^{14}\) Average transit time for concretions with holes was 29 days compared to five days for concretions without holes. These results provide the basis for providing intravenous or subcutaneous isotonic fluid administration to promote the passage of stones in cats. Administration of osmotic diuretics (e.g., mannitol) and loop diuretics (e.g., furosemide) may also beneficially increase proximal ureteral hydrostatic pressure by augmenting urine volume. However, to avoid adverse renal effects, cats should be adequately hydrated prior to, during, and following diuretic administration. Likewise, monitoring (e.g., body weight, central venous pressure) is important to ensure that patients do not become morbidly over-hydrated. In addition to increasing urine output, administration of medication to decrease ureteral spasm, oedema and inflammation improved stone expulsion rate and decreased expulsion time in humans with distal ureteral stones.
The urgency for surgical intervention depends on:
- the degree and progression of renal dysfunction,
- the potential for renal recovery,
- the potential for urolith migration through the ureter,
- the presence of infection or uncontrollable pain, and
- anticipated risks associated with surgery.
If renal failure has abruptly deteriorated such that electrolyte abnormalities are persistent and life threatening, intervention to improve glomerular filtration by relieving urinary obstruction should be considered if they cannot be controlled by less invasive measures such as fluid replacement, haemodialysis or peritoneal dialysis. Although placement of nephrostomy tubes may appear as a logical and feasible method of temporarily bypassing the obstruction, maintaining nephrostomy tube position, seal and patency for longer than 24 hours is often technically difficult. In addition to severe unresponsive azotaemia, if infection and pain cannot be appropriately managed, surgical ureterolith removal should be considered. As consequence of the high risk of irreparable ureteral damage associated with ureterotomy, ureterolith removal is not indicated if 1) ureteroliths are migrating through the ureter, 2) azotaemia is resolving; 3) the associated kidney is non-functional, or 4) ureteral surgery is attempted by surgeons unfamiliar with appropriate techniques.

**MINIMISING CALCIUM OXALATE UROLITH RECURRENCE**

Although formation of CaOx uroliths is associated with a complex and incompletely understood

<table>
<thead>
<tr>
<th>TABLE 3</th>
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</thead>
<tbody>
<tr>
<td>1. Anaesthetise the patient</td>
</tr>
<tr>
<td>2. Attach a three-way stopcock to end of the urinary catheter</td>
</tr>
<tr>
<td>3. Fill the urinary bladder</td>
</tr>
<tr>
<td>4. Position the patient such that the spine is approximately vertical</td>
</tr>
<tr>
<td>5. Agitate the bladder</td>
</tr>
<tr>
<td>6. Express the urinary bladder</td>
</tr>
<tr>
<td>7. Repeat steps two through six</td>
</tr>
<tr>
<td>8. Medical Imaging</td>
</tr>
</tbody>
</table>

Table 3. Performing voiding uro-hydropropulsion.
A sequence of events, several key factors are evident. Cats with CaOx uroliths are hypercalciuric compared to normal cats. Results of epidemiological studies support the hypothesis that urine-acidifying diets designed to minimise MAP urolith formation may have inadvertently increased the occurrence of CaOx uroliths. By inducing hypercalciuria, dietary acids promote CaOx crystalluria. If consumption of dietary acids precursors is associated with hypocitraturia in cats, it may also increase the risk of CaOx uroliths because citrate is an inhibitor of CaOx crystal formation. Deficiencies in vitamin B6 promote excessive urine oxalate excretion and therefore, should be avoided. In addition, cats fed diets with low protein, potassium, or moisture were at increased risk for CaOx urolith formation.

Crystal formation and subsequent crystal growth are a reflection of urine supersaturation for CaOx. Therefore, therapy that reduces urine calcium concentration and urine supersaturation with calculogenic substances should minimise urolith recurrence. Controlled studies to evaluate the efficacy of dietary modification in reducing the recurrence of feline CaOx uroliths have not been reported. Diets with high moisture content are preferred over dry formulations because the diuresis associated with increased fluid intake minimises the concentration of calculogenic substances in urine and promotes more frequent evacuation of urinary crystals that may form.

Following urolith removal, medical protocols should be considered to minimise urolith recurrence or to prevent further growth of uroliths remaining in the urinary tract. In general, medical therapy should be formulated in a step-wise fashion (see below), with the initial goal of reducing urine concentration of calculogenic substances in urine and promotes more frequent evacuation of urinary crystals that may form.

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non-surgical urolith removal. We do not recommend voiding urohydropropulsion in male cats unless a perineal urethrostomy was performed previously. If unsuccessful, surgery can be considered if clinical signs referable to urocystolithiasis are persistent. If clinical signs are not present, continue therapy to minimise urolith growth.

- Prescription diet Feline x/d™, Hills Pet Nutrition, Inc. Topeka, Kansas.

REFERENCES