Prevalence of lower urinary tract disease is more common in cats between 1 and 10 years of age; whereas in dogs, the prevalence increases with advancing age.

* In cats >10 years of age, bacterial urinary tract infection is most common
* In young cats, idiopathic lower urinary tract disease is most common

Figure. Causes of lower urinary tract disease in cats from 6 studies.
What is Feline Idiopathic Cystitis (Idiopathic Feline Lower Urinary Tract Disease)?

- Currently, there are 2 hypotheses concerning FIC
  - **Viral hypothesis**
    - A gamma-herpesvirus, a calicivirus, and a retrovirus have been isolated from urine and tissues from cats with naturally occurring idiopathic lower urinary tract disease
    - Reproducible clinical evidence that viruses cause naturally occurring disease is scarce
    - Viral particles have been observed in plugs recovered from cats with matrix-crystalline urethral plugs
  - **Neurogenic inflammation hypothesis**
    - Similar in some respects to hypothesis for interstitial cystitis in women
    - Cats with idiopathic lower urinary tract disease have decreased urinary glycosaminoglycan concentration and similar light microscopic changes to interstitial cystitis
    - This may represent a central nervous system problem
      - In cats with FIC, there appears to be a dysregulation of the sympathetic nervous system
      - sANS activation w/o activation of hypothalamic-pituitary-adrenal axis for counter-regulation
        - ↑CRF release w/o appropriate ↑ cortisol (adrenocortical hypoplasia)
        - ↑ tissue inflammatory response
        - ↑ epithelial permeability
          - Fluorescein studies
        - ↑ neuron firing ->pain (nitric oxide?)
        - “flare-ups” of signs with stress
  - **Developmental disorder (Pandora Syndrome)**
    - Early age adverse experience (?)
      - Queen stress -> cortisol suppression of adrenal development in kittens
    - Other organ system problems

Clinical signs of feline lower urinary tract disease

- Causes of lower urinary tract disease in cats present with similar clinical signs including, but not limited to:
  - Pollakiuria
  - Hematuria
  - Stranguria
  - Dysuria
  - Inappropriate urination
  - +/- Urethral obstruction

Diagnostic testing for cats with lower urinary tract signs

- **CBC and biochemical analysis** are normal unless urethral obstruction is present
- **Urinalysis** reveals hematuria
  - Pyuria and possibly bacteriuria present, if UTI
  - Crystalluria may be present with plugs or stones
- **Urine culture** is negative unless a UTI is present
- **Abdominal radiography** and **ultrasonography** may be normal
  - A large bladder may be found with urethral obstruction
  - Uroliths may be observed or “sand”
  - Urinary bladder wall may be thickened on ultrasound
- **Cystoscopically**, small pin-point hemorrhages (glomerulations) are found and occasionally larger mucosal ulceration
  - These can be found with other diseases of the lower urinary tract
- **Bladder biopsy** often reveals submucosal edema, mucosal ulceration, possible submucosal inflammation, possible fibrosis
  - May be observed with other diseases of the lower urinary tract
We routinely biopsy the bladder wall for histopathologic examination and aerobic and anaerobic bacterial culture.

Idiopathic disease is a diagnosis of exclusion.

TREATMENT OF LOWER URINARY TRACT DISEASE

Urethral obstruction
- Obstruction may occur from uroliths or from matrix-crystalline urethral plugs
  - Matrix-crystalline plugs have been found only in male cats
  - Approximately 80% of matrix-crystalline plugs contain a mineral component
  - Struvite is present in 80% of these
  - Urethral plugs have not been observed to occur in dogs
  - Uroliths occur in both dogs and cats

Consequences of urethral obstruction
- Consequences of urethral obstruction
  - Early in course of urethral obstruction
    - May not be clinically evident
    - Stranguria, pollakiuria, and inability to urinate may be present
    - Patient may appear uncomfortable and/or have behavior changes
  - As obstruction progresses, clinical signs increase in severity
    - Cat may sit in litter box attempting to urinate or dog may attempt urination and pass only few drops; owners often mistake this sign as constipation
    - As urine retention continues, post-renal azotemia and uremia develops
      - Depression, lethargy, moribund state
      - Vomiting due to uremia
      - Bradycardia and collapse due to hyperkalemia
      - Halitosis due to uremia
      - Death may occur in 72-96 hours after complete obstruction
  - If urethral obstruction is relieved, patient is likely to recover
  - The most common abnormalities associated with obstructive uropathy include: dehydration, hyperkalemia, metabolic acidosis, and post-renal azotemia

Dehydration
- Fluid therapy is very important in obstructive uropathy because of dehydration and for circulatory support
- Remember the 3 components of fluid therapy
  - Amount for rehydration
    - % dehydrated x BWkg = L for rehydration
  - Maintenance
    - Typically 1 ml/lb/hour (2.2 ml/kg/hour)
  - On-going losses
    - Measure or estimate
    - Some recommend ½ maintenance fluid requirements
- You should review types of fluid and routes of administration that are acceptable for managing patients with obstructive uropathy

Hyperkalemia
- Management of hyperkalemia with obstructive uropathy is similar to management of hyperkalemia occurring with acute renal failure
- Re-establishing urethral patency and fluid therapy is often all that is required as long as arrhythmias are not present
• Arrhythmias (bradycardia -> sinoatrial arrest -> ventricular escape beats) typically do not occur until the serum potassium is > 8 mEq/L
• Death occurs with potassium concentration exceeds 12-13 mEq/L
• 3 ways to decrease plasma/blood potassium concentration
  (1) Dilute and excrete – fluid therapy or dialysis
  (2) Transcellular shift
    • Glucose
    • Insulin
    • Insulin and glucose
    • Bicarbonate
  (3) Counteract effect of hyperkalemia at sino-atrial node
    • Calcium gluconate

Re-establishing urethral patency

- Male dogs – retrograde urohydropropulsion
  ➢ Technique for retropropulsion of uroliths or urethral plugs lodged in the urethra back into the urinary bladder
  ➢ General idea is to “lubricate” the urethra to facilitate retrograde passage of urethroliths
  ➢ Uroliths may move back into the urinary bladder with lubrication alone
  ➢ If uroliths remain in the urethra, then they are moved into the urinary bladder by creating a high pressure behind the uroliths.
  ➢ Uroliths are in essence “shot” out of the urethra into the urinary bladder

  ➢ Description of technique

1. Make dilute sterile lubricant solution by mixing 1 part sterile lubricant with 1 part sterile water. This can be done by putting 15 ml of sterile lubricant in a 35 ml syringe, attaching a 3-way stopcock, and putting 15-20 ml of sterile fluid in a second 35 ml syringe. Attach syringes to the 3-way stopcock, squirt the sterile solution into the lubricant, squirt the sterile lubricant-fluid solution back into the empty syringe, and repeat several times Alternatively, 10 ml of sterile lubricant may be added to a 20-30 ml of sterile fluid in a 35 ml syringe, turned upright, and the lubricant allowed to suspend in the fluid by waiting 15 minutes or so.
2. Sedate/anesthetize animal
3. Insert lubricated urethral catheter to site of obstruction
4. Infuse sterile lubricant-fluid solution to lubricate the urethra. Sometimes, this is all it will take.
5. Attach a syringe with sterile fluid to the urethral catheter
6. Have someone do a rectal and occlude the urethra through the rectum
7. Occlude distal penile urethra and infuse sterile fluid under pressure.
8. When the urethra is distended (can feel through the rectum), release occlusion in the pelvic urethra. If uroliths are repulsed into the bladder, you should feel a “popping” sensation, and the person doing the rectal can often feel the uroliths “fly by”.
9. Believe it or not, in some dogs, this procedure can be done without chemical restraint
10. Uroliths that are amenable to this procedure:
    • usually easy to perform if urate or cystine
    • often works with struvite
    • little more difficult with calcium oxalate because of surface texture
    • procedure will not work if uroliths are embedded in the urethral mucosa or if there is a stricture proximal to the uroliths.

- Adequate sedation/relaxation is important for this technique to be successful
- Complications
  ➢ Uncommonly occur
  ➢ Urethral rupture rarely occurs and is associated with using a stiff catheter, with an area of urethral necrosis, or an undiagnosed urethral rent
  ➢ Iatrogenic bacterial urinary tract infection may occur and can be prevented by Clinical signs are related to urethral obstruction and post-renel azotemia/uremia
**Male cats**

- Male cats may be obstructed with uroliths or matrix-crystalline urethral plugs
- In male cats, heavy sedation or anesthesia is required
- Position male cats in lateral or dorsal recumbency – dorsal is best
- **Massage distal urethra** while compressing the urinary bladder may dislodge the plug
- Perform **cystocentesis** in order to obtain a diagnostic sample and to decompress the bladder. Do not remove all of the urine so that the bladder can be palpated. A potential complication is urine extravasation, which is uncommon if the procedure is performed correctly.

  - **To remove a larger volume of urine in a dog,** attach a 22G, 1 ½ inch needle to an extension set, a 3-way stopcock, and 60ml syringe. Insert the needle into the bladder and withdraw a syringe of urine. Turn the stopcock to close to the patient but open to the side port and squirt the urine in the syringe into a bowl. Turn the stop cock to open to the patient and withdraw another syringe. This allows removal of a large quantity of urine without performing multiple sticks into the urinary bladder.

- Urethral patency can be re-established by retrograde flushing the urethra

**Make every effort to protect the patient from iatrogenic complications associated with catheterization of the urethra (especially trauma, and urinary tract infection with bacteria).**

- Strive to use meticulous aseptic "feather-touch" technique.
- Use only sterile catheters.
- Perform a cystocentesis for a diagnostic sample and to relieve back pressure
- Cleanse the penis and prepuce with warm water prior to catheterization.

- Select the shortest Minnesota olive tipped feline urethral catheter* or a Tom Cat catheter (such as a Slippery Sam) for initial catheterization of the urethra.
- Coat the olive tip with sterile aqueous lubricant.
- Prior to insertion of the catheter into the external urethral orifice, the extended penis should be displaced dorsally until the long axis of the urethra is approximately parallel to the vertebral column.
- Carefully advance the catheter to the site of obstruction. If necessary, replace the short olive tipped Minnesota needle with a longer one. Record the site of suspected obstruction, since this information may be of value when considering use of muscle relaxants, and/or when considering urethral surgery to prevent recurrent obstruction. **CAUTION:** Do not mistake resistance induced by curvature of the feline male urethra for a site of obstruction. In addition, never use excessive force when advancing the catheter.

- Next, a large quantity of physiological saline or lactated Ringer’s solution (as much as several hundred ml) should be flushed into the urethral lumen, and allowed to reflux out the external urethral orifice. When possible, the catheter may be advanced toward the bladder. As a result of this maneuver, the obstructed urethral plugs may be gradually dislodged and flushed around the catheter and out of the urethral lumen. Application of steady but gentle digital pressure to the bladder wall after the urethra has been flushed with physiological saline or lactated Ringer’s solution may result in expulsion of a urethral plug urolith from the urethral lumen. Excessive pressure should not be used because it may result in: 1) trauma to the bladder, 2) reflux of potentially infected urine into the ureters and renal pelves, and/or 3) rupture of the bladder wall.

- If the technique outlined is unsuccessful; it may be necessary to attempt repulsion of suspected urethral plugs or uroliths back into the bladder lumen by occluding the distal end of the urethra around the olive tip of the catheter before injecting fluid into the urethra. By preventing reflux of solutions out of the external urethral orifice, this maneuver will tend to dilate the urethral lumen. If the obstruction persists, an attempt may be made to gently advance the suspected plug or urolith toward the bladder. **Excessive force should not be used.**

- On occasion it is advantageous to allow the reverse flushing solution to soften the obstructing urethral plugs (this technique is ineffective for most uroliths) before attempting to propel them back into the bladder. Allowing lapse of several hours between attempts to remove firmly lodged plugs by reverse flushing has been effective.

**Minnesota feline olive tipped urethral catheters are available from EJAY International, Inc., P.O. Box 1835, Glendora, California 91740.**
Female dogs and cats
- More difficult to unobstruct, but fortunately urethral obstruction does not occur commonly
- Often the urolith can be palpated in the urethra via digital rectal examination and the urolith can be moved back into the bladder
- A catheter can be used to push the urolith back into the bladder after anesthetizing or heavily sedating the dog or cat
- If you can visualize the urolith at the urethral orifice in the vestibule, do not grab the stone and pull the stone out. This often results in serious trauma

If the cat is difficult to unobstruct, then it can be managed by cystocentesis and the procedure tried again later or until a more aggressive approach is tried
- Perineal urethrostomy is often recommended; however, it should not be done unless a good work up has been done
  - A urethrostomy can be not be corrected at a later date
  - It is important to make sure that the part of the urinary tract that is removed is in fact the cause of the problem
  - Short term complications include urine leakage and hemorrhage
  - Long term complications include stricture formation and bacterial urinary tract infection
  - Incidence of bacterial urinary tract infection increases from 1-2% to 35-50% depending on the technique and skill of surgeon
  - Furthermore, a perineal urethrostomy does not address the underlying reason(s) for obstruction; therefore, the cat may continue to have lower urinary tract signs

Aftercare once urethral patency is re-established
- Re-establishing urethral patency is not the end point
  - Remove as much of the urine as possible once the cat is un-blocked
  - The bladder may need to be “rinsed” if there is a lot of particulate matter and/or mucous present in the urine
    - Use sterile crystalloids or water; do not use glucose containing solutions
    - Do not infuse antibiotics, anti-spasmodics, anesthetics, or acidifiers into the bladder
    - Glucocorticoids are not indicated as they increase risk of infection
    - Systemic antibiotics may be administered if an indwelling urinary catheter is not inserted
  - Anti-spasmodics (urethral relaxants) may help, but there is little data that they in fact do help
    - In order to relax the urethra, an alpha-antagonist is administered
    - Phenoxybenzamine or prazosin can be used
    - Some people administered a skeletal muscle relaxant; however, diazepam has minimal effect on the urinary tract
  - An indwelling urethral catheter may be required
    - Indications for an indwelling urethral catheter include
      - Difficulty in un-obstructing the patient
      - A large amount of particulate matter and/or mucous despite flushing of the urinary bladder
      - When there is a high likelihood of re-obstruction
      - If detrusor atony is present

Management of an indwelling urethral catheter
- An indwelling urethral catheter should be considered on an individual case basis
  - Severely ill patients
  - If difficult to catheterize
  - Poor urine stream post obstruction
  - Detrusor atony (atonic bladder)
- A urethral catheter should be connected to a closed collection system
• **Management**
  - **Systemic antibiotics** should not be administered unless given for some other reason
    - The risk of bacterial urinary tract infection decreases with antibiotic administration
    - However, when an infection occurs, the organism has a high degree of resistance
    - Furthermore, the bacterial organism may invade the upper urinary tract resulting in chronic pyelonephritis
  - **Anti-inflammatory agents** – such as an NSAID – may be beneficial as long as renal function is good
  - With an indwelling catheter, a urethral relaxing agent (alpha blocker) is administered to minimize catheter-induced urethral trauma and irritation
  - With bladder atony, a drug to stimulate bladder contraction, parasympathomimetic, is administered

• **Catheter-associated UTI**
  - Occurs in 50-80% of catheterized patients
  - Prophylactic antibiotics decrease incidence, but increase likelihood of resistance or of an unusual organism
  - Prevention:
    - Use as clean to aseptic technique as possible
    - Physically separate patients with indwelling catheters from others
    - Wear gloves and wash hands between patients
    - Replace catheters when damaged or dirty
  - Typically, an indwelling urinary catheter is maintained for 2 to 3 days
    - This is not a hard and fast rule, however
    - Decision to remove the catheter should be based on the progress of the patient, appearance of the urine, and likelihood that the tight junctions of the detrusor muscle have re-established
  - Remove if catheter is non-patent, damaged, or contaminated

• **Post-obstructive diuresis** must be addressed
  - Due to back pressure from the obstructive uropathy being transmitted to the upper urinary tract, a heavy diuresis may develop when the obstruction is relieved
  - This may be as much 2.4 L per day (most cats urinate 30-40 ml per day)
  - It is important to adjust fluid intake to match urine output so that dehydration does not occur

• **Cystostomy catheters** may be inserted and used long term
  - These may be mushroom-tipped catheters or low-profile catheters
  - Allows for long term, indefinite use

**Non-obstructive idiopathic feline lower urinary tract disease**
- There have been dozens of proposed treatments for cats with lower urinary tract disease; very few have undergone evaluation in a randomized controlled clinical trial

• **Antimicrobial agents**
  - Often administered
  - Bacterial urinary tract infection is an uncommon cause of lower urinary tract disease in cats <10 years of age occurring in <1% of such cats
  - If a bacterial infection was present, then the cat would have a diagnosis of bacterial cystitis and not idiopathic lower urinary tract disease
  - Their use is not indicated in cats without a proven bacterial urinary tract infection

• **Urinary tract antiseptics**
  - **Methenamine** and **methylene blue** are not indicated in cats with idiopathic lower urinary tract disease
  - They may cause side effects such as metabolic acidosis (methenamine) or Heinz body anemia (methylene blue)
  - Since bacterial urinary tract infections are uncommon in young cats, they are not recommended

• **Urinary tract analgesics**
• **Phenazopyridine** is an over the counter preparation available for use by women with recurrent vaginitis/cystitis
  • In cats, phenazopyridine causes Heinz body anemia and should not be used

• **Smooth muscle and skeletal muscle relaxants**
  • Many cats with idiopathic lower urinary tract disease have urge incontinence and inappropriate urination
  • **Propantheline**, an anticholinergic agent, minimizes force and frequency of uncontrolled detrusor contractions, but has negligible effect on urethral tone
    • It may be beneficial in some cats
    • However, one study could not document a benefit
  • **Phenoxybenzamine** and prazosin are sympatholytic agents that decrease urethral tone and spasm
    • Clinical data is lacking as to their efficacy with idiopathic feline lower urinary tract disease
    • I use for a short time in some cats that strain frequently or that had a urethral obstruction especially if an indwelling urinary catheter was inserted
  • **Diazepam** and **dantrolene** are skeletal muscle relaxants that may decrease tone and spasm of the distal urethra
    • Diazepam has minimal effect on urethral tone
    • Dantrolene is more effective
    • Clinical studies are lacking as to efficacy of these drugs in cats with idiopathic lower urinary tract disease
    • I do not usually use

• **Anti-inflammatory agents**
  • **Glucocorticoids**
    • Have been used historically to decrease inflammation
    • Several studies have shown no benefit
    • They are contraindicated in cats with urethral obstruction or those that have indwelling urinary catheters
      • Risk of urinary tract infection increases in cats with indwelling urethral catheters that receive glucocorticoids
      • Some cats develop pyelonephritis
  • **Non-steroidal anti-inflammatory agents**
    • There are no clinical studies demonstrating safety or efficacy of use of these drugs in cats with idiopathic lower urinary tract disease

• **Amitriptyline**
  • A tricyclic antidepressant
  • May have analgesic properties, stabilize mast cells, and decrease inflammation
  • In one uncontrolled study, 9 of 15 cats with idiopathic lower urinary tract disease improved with amitriptyline
  • One controlled study of cats with active lower urinary tract disease showed no benefit and cats receiving amitriptyline had a higher incidence of recurrence of lower urinary tract signs
  • Goal is to find a dose that will have a calming effect on the cat

• **Glycosaminoglycans**
  • Cats with idiopathic lower urinary tract disease have decreased concentrations of glycosaminoglycans in their urine
  • Glycosaminoglycans may have a protectant role at the mucosal-urine interface
    • Two controlled studies, failed to show a difference in clinical signs between a glycosaminoglycan and placebo in cats with idiopathic lower urinary tract disease

• **Dietary modification**
  • In cats with matrix-crystalline plugs or with struvite crystalluria, feeding a “struvite preventative” diet may have some benefit
• In one study of cats with idiopathic lower urinary tract disease, cats fed a canned diet had fewer recurrences than those fed a dry diet
  • However, there were more drop-outs in the canned group for unexplained reasons
  • If added back in – no difference between diet groups
  • These cats were fed “struvite preventative” diets
  • There is a new diet high in omega-3 fatty acids and antioxidants that has been shown to decrease recurrences by 89% in a randomized controlled L-clinical trial
• L-tryptophan and alpha-casozepine
  • Shown to decrease stress responses in cats
  • Alpha-casozepine is available as Zylkene
• Clomipramine and Fluoxetine
  • Used for urine spraying / marking behavior
  • Modifies behavior may have some analgesic effects
  • Not studied for FIC
• Pheromones
  • Sprays and diffusers
  • May calm a cat down
  • 1 study of cats with FIC – no benefit
• Multi-modal environmental modification (MEMO)
  • Cats do not respond to force
  • Cats are territorial and ‘in control’
  • Litter boxes and food should be away from noise and distractions
  • Cats like to climb, hide, scratch, and hunt – vertical and horizontal space
  • Cats are clean and self-grooming
  • Cats are active at night
  • 1+1 rule – 1 food dish, 1 water bowl, and 1 litter box per cat plus 1 extra
    • Indoor Pet Initiative: https://indoorpet.osu.edu/
How do I treat cats with lower urinary tract disease?

- **First episode, urethral obstruction, young cat**
  - Unobstruct
  - Radiographs, UA (other lab work?)
  - Indwelling catheter?
  - Torbugesic?
  - Diet change (likely)?
  - Antibiotics (peri-catheterization)
  - Environmental and behavioral modification?
  - If persists or recurs, do additional diagnostics

- **First episode, no urethral obstruction, young cat**
  - Urinalysis (minimum)
  - Torbugesic?
  - Diet change (likely)? – usually crystal-related disease (either stones or plugs)
  - If persists or recurs
    - Do additional diagnostics
    - Consider
      - Diet?
      - Amitriptyline?
      - Pentosan polysulfate?
      - Environmental and behavior treatment

- **First episode, urethral obstruction, older cat**
  - Unobstruct
  - Radiographs, UA (other lab work?)
  - Indwelling catheter?
  - Torbugesic?
  - Diet change (likely)
  - Stones?
    - Struvite: infection vs. non-infection
    - Calcium oxalate
    - Matrix-crystalline plug?
  - Others?
  - Antibiotics (peri-catheterization)

- **First episode, no urethral obstruction, older cat**
  - Diagnostics
  - Torbugesic?
  - Diet change? Most likely – urolithiasis most likely cause (especially calcium oxalate)
  - If persists or recurs
    - Torbugesic as needed
    - Diet?
    - Amitriptyline?
    - Pentosan polysulfate?
    - Environmental and behavior treatment