Micturition refers to the process of storing and periodically voiding urine. Disorders of urine storage usually lead to urinary incontinence, whereas disruption of urine voiding leads to incomplete emptying, dysuria, or urine retention. Micturition is a complex integration of the central, sympathetic, parasympathetic, and somatic nervous systems, with resultant muscular activity. The two functional units of the lower urinary tract include the reservoir/pump (urinary bladder) and the continence/conduit (urethra). The urinary bladder and proximal urethra are composed of smooth muscle and are thus under autonomic nervous system control, while the distal urethra is composed of skeletal muscle and thus is under somatic nervous system control.

**Disorders of Micturition**

There are several different ways of classifying disorders of micturition. There are problems with storage and problems with voiding, the urination problem can occur with a full bladder or with an empty bladder, and the urination problem can be neurogenic or myogenic in origin. It is important to establish the status of the urinary bladder contractile force and the patency of the urethral outlet, to determine whether the disorder is primarily neurogenic or myogenic, and to identify the underlying etiology or contributing factors. In addition to the routine collection of historical information and performing a complete physical examination, a complete neurological examination and rectal palpation should be performed. Have the owners describe what the pet is doing and whether there is a good urine stream or not. If possible, observe urination or have the owners take a video of the pet urinating. Depending on the underlying disorder of micturition, additional diagnostic testing should always include a urinalysis and urine culture. Laboratory evaluation may include a complete blood count (CBC), biochemical analysis, and infectious disease testing. Abdominal imaging by survey radiography and possibly ultrasonography or contrast radiography should be considered. Cystoscopy or exploratory laparotomy may also be considered.

**Problems with Storage**

**Bladder overactivity.** Bladder overactivity occurs due to hyperexcitability of the storage phase. This results in inability to permit adequate bladder filling because of urgency. Patients have increased frequency of urination (pollakiuria) and inappropriate urination. Often urethral irritation or spasm is present. Examples of bladder hyperactivity include cystitis, urocystolithiasis, and chemical stimulation (cyclophosphamide). The treatment is to relax the bladder using antimuscarinic agents (propantheline, oxybutynin, tolterodine) and an antispasmodic agent (oxybutynin, flavoxate, tolterodine). These drugs decrease detrusor activity and have urethral antispasmodic effects. Other drugs, including tricyclic antidepressants such as imipramine and amitriptyline, may help with refractory incontinence by increasing urine storage. These may improve bladder storage by means of several mechanisms, including anticholinergic, alpha-adrenergic, and beta-adrenergic effects.

**Bladder atony.** Bladder atony may be due to neurogenic or myogenic causes. Bladder atony is associated with bladder overdistention, but the patient does not posture to urinate. The treatment is to stimulate bladder contraction. This should only be done if the urethra is also relaxed pharmacologically. Manage a large overdistended bladder with urinary catheterization. Pharmacologically, bethanechol is a parasympathomimetic with direct cholinergic activity that stimulates or augments smooth muscle contraction. Metoclopramide has been shown to stimulate canine ureteral smooth muscle in vitro and anecdotally to stimulate bladder contraction in human beings with bladder atony associated with diabetes mellitus. It appears to stimulate bladder contraction in some dogs and cats.

**Problems with Voiding**

**Increased outlet resistance.** Inability to void due to increased outlet resistance may occur because of mechanical problems (e.g., urethral obstruction from a stone or mass) or functional problems (e.g., urethral spasm or neurogenic). The treatment is to relieve the urethral obstruction or relax the urethra if neurogenic.

**Relieve the obstruction:** The urethral obstruction should be relieved by inserting a urethral catheter that may be left in place or performed intermittently or by repeated cystocentesis.

**Relax the urethra:** Urethral relaxation is accomplished by administering sympatholytic agents that antagonize alpha-adrenergic receptors (e.g., phenoxybenzamine, prazosin, tamsulosin). Tamsulosin is an effective drug that is...
administered once a day and builds up in prostatic and urethral smooth muscle tissue. Skeletal muscle relaxants (e.g., diazepam, dantrolene, baclofen) may relax the urethral skeletal muscle (external urethral sphincter); however, they have less effect than alpha-adrenergic blockers.

**Urethral stent:** In patients with urethral obstruction due to neoplasia, a urethral stent may be placed. Usually self-expanding metallic stents composed of nitinol are used. These are placed with fluoroscopic guidance. Most dogs are incontinent after placement, as many transitional cell carcinomas involve the entire length of the urethra.

**Low profile cystostomy catheter:** A low-profile cystostomy catheter is a mushroom-tipped catheter that is surgically implanted into the urinary bladder through the ventral abdominal wall lateral to midline. A cystectomy is also performed. The catheter sits just above the skin surface and contains 1 or 2 valves to prevent leakage. It provides urinary diversion; however, owners must empty the urinary bladder 2 to 3 times per day.

**Paradoxical incontinence:** Paradoxical incontinence occurs when there is outflow obstruction resulting in bladder overdistention. The increased bladder pressure results in “leaking” of urine through or around an obstruction. Usually the patient dribbles urine with a full bladder and is unable to void. It may be due to a functional or mechanical outflow obstruction and is often associated with bladder atony.

**Decreased outlet resistance:** Decreased urethral tone and outlet resistance results in incontinence, which may be neurogenic, myogenic, or anatomic in origin. The most common cause is urethral sphincter mechanism incompetency in female dogs.

**Ectopic ureters:** Normally, the ureters enter at the trigone; however, occasionally they may terminate distally. They may either be extramural (where the ureter bypasses its normal insertion and inserts into the urethra or vagina at a distal point) or, more commonly, intramural (where the ureter enters the bladder at the trigone but tunnels in the wall before opening). Extramural ectopic ureters are surgically corrected. Intramural ectopic ureters may also be surgically corrected; however, laser ablation of the medial wall results in better continence (85% vs. 65%).

**Urinary incontinence:** Urinary incontinence refers to the unconscious release of urine and is most often due to urethral sphincter mechanism incompetency (USMI). It is uncommon in male dogs and male and female cats, but may occur in up to 20% of spayed female dogs. Usually urination while awake is normal.

**Treatment:** Pharmacologically, the treatment for urinary incontinence is to stimulate the urethral smooth muscle resulting in increased tone of the internal urethral sphincter. Administration of sympathomimetics (e.g., alpha agonists: phenylpropanolamine) results in continence in 85% to 90% of patients. Once-a-day treatment may be as effective as three-times-a-day administration and is associated with fewer side effects. Estrogen replacement therapy (estriol, diethylstilbestrol, Premarin) may increase alpha-adrenergic receptor responsiveness and improve urethral vascularity and other mucosal characteristics. It is safe and reasonably effective (40% to 65%); however, estriol (Incurin) is reported to have a 93% excellent response rate. Gonadotropin releasing hormone (GnRH) analogs have also been used. In ovariecetomized dogs, chronically unsuppressed FSH and LH release (due to lack of negative feedback) may contribute to urinary incontinence. Administration of GnRH analogs paradoxically reduces FSH and LH over time. It was found effective in 12/13 dogs in one study, and in another study 9/23 dogs were continent from 70 to 575 days, with another 10/23 having partial response; however, the 23 dogs also responded to PPA.

There are also several potential nonpharmacological treatments for patients with USMI that are unresponsive to pharmacological therapy. Urethral bulking involves injection of an agent submucosally in the proximal urethra via cystoscopy. It is thought to create artificial urethral cushions, improving urethral closure (coaptation). It may also function as central filler volume, increasing the length of smooth muscle fibers and the closure power of the internal urethral sphincter. There are no bulking agents available for use in veterinary medicine. Historically, glutaraldehyde cross-linked collagen was used, but it has been withdrawn from market. A study with polydimethylsiloxane has promising results. An artificial sphincter/urethral occluding device is similar to a blood pressure or vascular cuff that is placed surgically around the proximal urethra with a loose fit. A tube connects the device with a subcutaneously implanted injection port, providing a means to increase pressure within the device and therefore urethral pressure in the area of the internal urethral sphincter. Continenice rates are high; however, they may require adjustment over time. Although surgical techniques (e.g., slings, plication, culposuspension) are available, long-term continence rates are low.
**Reflex dyssynergia.** Reflex dyssynergia refers to an incoordination between bladder contraction and urethral relaxation. The patient usually postures normally, and initiates a good stream, but then the stream stops and yet the animal continues to posture and attempt to void. Treatment involves relaxing the urethra as described. If the bladder does not completely empty despite urethral relaxation, then add a bladder stimulant.

**Feline Lower Urinary Tract Disease**
Lower urinary tract disease is common in cats between the ages of 1 and 10, whereas in dogs the prevalence increases with advancing age. In cats more than 10 years old, bacterial urinary tract infection is the most common type, whereas in young cats, idiopathic lower urinary tract disease occurs most commonly. Urinary tract infections and urolithiasis has been discussed previously in this conference; therefore, this discussion will focus on feline idiopathic cystitis (FIC).

**What is FIC?** Currently, there are two hypotheses concerning FIC. One hypothesis is that a viral infection is present. A gamma-herpesvirus, a calicivirus, and a retrovirus have been isolated from urine and from tissues from cats with naturally occurring FIC. Viral particles have been observed in plugs recovered from cats with matrix-crystalline urethral plugs. The other hypothesis is that FIC represents neurogenic inflammation. Cats with idiopathic lower urinary tract disease have a decreased urinary glycosaminoglycan concentration and similar light microscopic changes to interstitial cystitis. FIC may represent a central nervous system problem, because cats with FIC appear to have dysregulation of the sympathetic nervous system. There is sympathetic nervous system activation without activation of the hypothalamic-pituitary-adrenal axis for counter-regulation. Corticotrophin releasing factor is released without an appropriate increase in cortisol (adrenocortical hypoplasia). This may result in tissue inflammatory response, increased epithelial permeability, and pain. The origin of neurogenic inflammation may be a developmental disorder.

**Clinical signs of lower urinary tract disease.** Cats with lower urinary tract disease present with similar clinical signs, including, but not limited to, pollakiuria, hematuria, stranguria, and inappropriate urination.

**Diagnostic testing with lower urinary tract signs.** The CBC and biochemical analysis are normal unless urethral obstruction is present. Urinalysis reveals hematuria; however, pyuria and bacteriuria may be present with UTI. The urine culture is negative unless UTI is present. Abdominal radiography and ultrasonography may be normal unless uroliths are present. In cats with FIC, cystoscopy reveals small pinpoint hemorrhages called glomerulations, and bladder wall biopsy often reveals submucosal edema, mucosal ulceration, possible submucosal inflammation, and possible fibrosis. FIC is a diagnosis of exclusion.

**Treatment of Lower Urinary Tract Disease**

**Urethral obstruction.** Urethral obstruction may occur from uroliths or urethral plugs. Matrix-crystalline urethral plugs are found only in male cats, and approximately 84% of matrix-crystalline plugs contain a mineral component, with struvite being the most common mineral present. Uroliths have been discussed previously. Urethral obstruction results in dehydration, azotemia, metabolic acidosis, hyperphosphatemia, hyperkalemia, and eventually death. Treatment involves rehydration, relieving the urethral obstruction, and managing hyperkalemia. After the urethral
obstruction is relieved, an indwelling urinary catheter may be required. If a catheter is inserted, use a closed collection system, do not administer antimicrobial agents, and do administer urethral relaxants (alpha-adrenergic blockers).

Nonobstructive idiopathic lower urinary tract disease. There have been dozens of proposed treatments for cats with lower urinary tract disease, but very few have undergone evaluation in a randomized controlled clinical trial.

Antimicrobial agents: Unless a UTI is present, administration of an antimicrobial agent is not warranted.

Urinary tract antiseptics and analgesics: Methenamine and methylene blue are not indicated in cats, as they may induce metabolic acidosis and Heinz body anemia. Phenazopyridine is an over-the-counter preparation available for use by women with recurrent vaginitis and cystitis that causes Heinz body anemia in cats.

Smooth muscle and skeletal muscle relaxants: Many cats with FIC have urge incontinence and inappropriate urination. Propantheline, an anticholinergic agent, minimizes force and frequency of uncontrolled detrusor contractions and may be beneficial in some cats; however, one study did not document a benefit. Phenoxybenzamine and prazosin are sympatholytic agents that decrease urethral tone and spasm and may help some cats. Diazepam and dantrolene are skeletal muscle relaxants that may decrease tone and spasm of the distal urethra.

Anti-inflammatory and analgesic agents: Glucocorticoids have been used to decrease inflammation; however, studies have shown no benefit in cats with FIC. They are contraindicated in cats with urethral obstruction or those that have indwelling urinary catheters because they increase the risk of UTI. Nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease inflammation and pain; however, they are contraindicated with azotemia and dehydration. Buprenorphine and Torbugesic do not have anti-inflammatory properties, but do decrease pain and appear to make cats with FIC more comfortable.

Amitriptyline: Amitriptyline is a tricyclic antidepressant that 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. The goal is to find a dose that will have a calming effect.

Glycosaminoglycans (GAGs): Cats with FIC have decreased concentrations of GAGs in their urine. GAGs may have a protectant role at the mucosal-urine interface. Two controlled studies failed to show a difference in clinical signs between a GAG 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.

Clomipramine and fluoxetine: These drugs are used for urine spraying and marking behavior. They appear to modify behavior and may have some analgesic effects.

Pheromones: Feline facial pheromones may calm a cat; however, in one study of cats with FIC, no benefit was found.

Multimodal environmental modification (MEMO): Cats do not respond to force, are territorial, and like to be in control of their environment. Minimizing stress and conflict may help some cats with FIC. Litter boxes and food should be away from noise and distractions. Cats like to climb, hide, scratch, and hunt; therefore, vertical and horizontal space should be provided. One food dish, water bowl, and litter pan should be available for each cat in the household with one additional of each. Additional information can be found at the Indoor Cat Initiative (see vet.ohio-state.edu/indoorcatt.htm).
**Treatment for Cats with Lower Urinary Tract Disease**

**YOUNG CAT, FIRST EPISODE**

**Urethral obstruction**
- Unobstruct
- Radiographs, UA (other lab work?)
- Indwelling catheter?
- Torbugesic?
- Diet change (likely)?
- Antibiotics (pericatheterization)?
- MEMO?
- If persists or recurs: diagnostics

**No urethral obstruction**
- Urinalysis (minimum)
- MEMO
- Torbugesic?
- Diet change? (Likely, usually stones or plugs)
- If persists or recurs:
  - Do additional diagnostics
  - Diet?
  - Amitriptyline?
  - Glycosaminoglycans?

**OLD CAT, FIRST EPISODE**

**Urethral obstruction**
- Unobstruct
- Radiographs, UA (other lab work?)
- Indwelling catheter?
- Torbugesic?
- Diet change (likely)—stones or plug?
- Others?
- Antibiotics (pericatheterization)
- If persists or recurs: diagnostics

**No urethral obstruction**
- Diagnostics
- MEMO
- Torbugesic?
- Diet change? (Likely, urolithiasis, calcium oxalate)
- If persists or recurs:
  - Do additional diagnostics
  - Torbugesic as needed
  - Diet?
  - Amitriptyline?
  - Glycosaminoglycans?

**References**
