Urine for the Win

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Thank you

PRN PHARMACAL
Micturition

- Coordinated action between the sympathetic & parasympathetic
- Somatic nervous systems and central control centers
Micturition Disorders

- Dysfunction
  1. storage
  2. voiding of urine
- Disorders
  1. neurogenic
  2. non-neurogenic
Micturition Disorders

Neurogenic
- Lower motor neuron (Detrusor areflexia)
  - Urinary sphincter mechanism incompetence
- Upper motor neuron (Detrusor areflexia with sphincter hypertonus)
- Detrusor-urethral dyssynergia
- Dysautonomia

Non-neurogenic
- Functional
  - Detrusor overactivity
  - Urge incontinence
  - Idiopathic instability
  - Detrusor atony
  - Overflow incontinence
  - Primary
  - Secondary
  - Idiopathic urethral hypertonicity
- Overflow obstruction
- Outflow obstruction
- Mechanical
- Anatomical
  - Ectopic ureter(s)
  - Intrapelvic bladder
  - Urethrectal fistula
- Miscellaneous
  - Post-prostatectomy incontinence (dogs)
  - Post-perineal urethrostomy incontinence
  - Ureterovaginal fistula
Micturition Disorders

• Incontinence
  • failure of voluntary control
  • with constant/intermittent unconscious passage of urine

• Common issue for which owners bring their pet to the hospital

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Urinary Incontinence

- Urethral closure not a single anatomic sphincter
- Result of smooth muscle tone
  - Female dogs = entire urethra
  - Male dogs = proximal fourth of the urethra
Urinary Incontinence

- Urethral closure pressure > bladder pressure
  - urine remains in bladder until voluntary urination
- Bladder pressure increases above urethral closure pressure
  - incontinence
Owner Observations

- Pool of urine where they have been lying
- Dribbling urine while walking
- Perineal area of the pet is always wet
- Licking genital area excessively
- Perivulvar or peripreputial dermatitis
- +/- Concurrent urinary tract disease signs
History

- Determine UI vs. behavioral vs. systemic
- Awareness of urine passage
- PU/PD
- Time of onset
- Ability to void bladder
History

• Age of onset
• Reproductive status
• Age at neutering
• Current medications
• Hx - urinary tract disorders
• Observe the patient urinating
  • estimation of initial bladder volume
  • final bladder volume
Physical Examination

- Complete physical examination
- Rectal examination - careful palpation of the urethra
- Unable to posture normally?
  - neurologic evaluation
  - orthopedic evaluation
  - incomplete emptying of the bladder and UI
Urinalysis

- Urinalysis with sediment examination
- Leaking urine - worsened by UTI
- UI may predispose the patient to a UTI
- Bloodwork
  - Low urine-specific gravity
  - Dehydrated
Urethral Sphincter Mechanism Incompetence

- Acquired urinary incontinence
  - Neutered female dogs
  - Most common
- Reduction in the urethral closure
- Weakening of the urethral sphincter
- “Hormone-responsive urinary incontinence”
- “Idiopathic Incontinence”
- “Spay Incontinence”
Urethral Sphincter Mechanism Incompetence

Pathophysiology

- Multifaceted – beyond loss of estrogen
- Alterations
  - tissue structure
  - collagen content
  - estrogen receptors
  - follicle-stimulating hormone
  - luteinizing hormone concentrations
Urethral Sphincter Mechanism Incompetence

Pathophysiology
- anatomical conformation of the dog
- tail docking
- urogenital tract position
Other Causes

- Age – collagen content of urogenital tissues changes
- Decreased responsiveness of hormone receptors in the urethra
- Abnormal length of the urethra
- Abnormal anatomical position - urethra and/or urinary bladder
- Overweight & obesity
Prevalence

• Overrepresentation of breeds
  • German shepherd
  • Rottweiler
  • Doberman pinscher
  • Old English sheepdog
  • Boxer
  • English springer spaniel
  • Weimaraner
  • Irish setter
  • Giant Schnauzers
Prevalence of Urinary Incontinence

- Within 2–4 years of OVH
- Young or middle-aged dogs
- Weigh >20 kg
USMI

- USMI over time
- Frequency/severity - unbearable for O
- Urine leakage - sleeping or lying down
- Intra-abdominal pressure increases when dogs lie on their sides
- Increased parasympathetic (relative to sympathetic) nervous activity while sleeping
Management

Medical therapy
- Goal - increase urethral tone
- stimulating α-receptors - smooth muscle of urethra w/ α-agonists
- +/- number/sensitivity w/ estrogen compounds.
- estrogen - a trophic effect on periurethral tissues/vasculature
- incontinence may be reduced by improving urethral support
• $\alpha$-receptors = identified mediators of smooth muscle contraction & relaxation

• To increase urethral closure pressures - $\alpha_{1A}$ receptors in smooth muscle of urethra and bladder neck need to be stimulated

• Important part of resting urethral tone
α1-Agonists

- Common UI therapy
- Phenylpropanolamine (PPA) (Proin, prnpharmacal.com) = most widely used α-agonist for the treatment of UI
- FDA-approved
- PROIN® (phenylpropanolamine hydrochloride) Chewable Tablets
Side Effects

• Hypertension
  • lack of specificity of the agonists for LUT & stimulation of vascular smooth muscle

• Sympathetic Stimulation
  • Behavioral changes
  • Decreased appetite
Concurrent Disease

- USMI
- CKD
- Hyperadrenocorticism
- Protein-losing nephropathy
- PPA - judicious
- Monitor BP frequently
- Indirect systolic blood pressure prior to treatment
- Repeat 1 to 2 weeks
Concurrent Disease

- Observe for:
  - Restlessness
  - Aggression
  - Changes in sleep patterns
  - GI signs
- Alleviated = reduction in dose or frequency
PROIN® (phenylpropanolamine hydrochloride) Chewable Tablets

- **Proven** - FDA approved control of urinary incontinence due to USH
- **Precise** - Scored tablets three strengths for accurate dosing
- **Pet-Accepted** - Chewable, liver-flavored tablets dogs love
PROIN ER™
(phenylpropanolamine hydrochloride extended-release tablets)

• Convenient - Given with food, a single dose per day
• Innovative - Patented release technology provides controlled release that ensures steady absorption
• Easy to Administer - Chewable, liver-flavored tablets
• Easy to Prescribe - Four dosing strengths
• FDA Approved - FDA approved for control of urinary incontinence due to USH
Urethral Sphincter **Without** PROIN ER or PROIN

**Internal Urethral Sphincter**
PROIN ER™ And PROIN®

Increasing Urethral Sphincter Muscle Tone to Help Prevent Urinary Leakage
Phenylpropanolamine

• Continence rates 75% to 90%
• PROIN® - 98.1% owner satisfaction for the control of UI
Estrogen

- Treatment of incontinence
- Strengthen pelvic and periurethral tissues
- Enhances glandular function
- Impacts collagen strength
- Increases the number & sensitivity of α-receptors in the smooth muscle of the urethra.
Estrogen

- Well tolerated
- Alternative for female dogs
  - concurrent diseases - predispose them to hypertension
  - intolerant of α-agonist treatment
Diethylstilbestrol (DES)

- Synthetic, nonsteroidal estrogen
- 1938
- Reduce complications in pregnancies
- Manage a variety of conditions in women until 1971.
- Found to contribute to risk of cancer and birth defects
- Compounding pharmacies
Diethylstilbestrol (DES)

- Treat UI in dogs for more than 40 years.

Adverse effects of estrogens overall:
- Mammary swelling
- Vulvar swelling
- Attractiveness to males

Decreases with dose reduction.
Other Therapies

- Severe/Refractory Cases
  - Estrogen and PPA
  - Evidence supporting a synergistic increase in efficacy is controversial
- Injectable urethral bulking agents
  - increase the stretch in the sphincter muscle fibers
  - leading to an increased resting closure pressure in the urethra
- Surgical Intervention
Review

• Mechanisms of UI in dogs are multilayered
• Incontinence
  • inability to hold urine during bladder filling
  • inability to empty the bladder during active urination.
• Medical therapy
  • directed at the smooth muscle of the urethra
Prevention?

• Best management for UI = prevent it
• UI is most common in dogs that are spayed or neutered
  • the exact mechanism/relationship to estrogen is unclear
  • relationship of UI and age at spay = risk of UI increases if spayed ≤ 3 months
• Larger breeds (adult weight >15 kg)
  • decreased risk of UI with every month delay in OVH
  • larger the dog - more pronounced this alteration in risk
Communication

- Understands USMI
- Management
- Allow for questions
- Give written directions
- Contact information
Follow Up

- 2 days, 2 weeks, 2 months
- Ensure understanding
- Issues? Questions?
- Compliance
Questions?
Thank you
Micturition (urination) depends on the coordinated action between the sympathetic, parasympathetic and somatic nervous systems and central control centers. Disorders of micturition are a result of dysfunction in the storage or voiding of urine. Micturition disorders may be neurogenic or non-neurogenic. The failure of voluntary control of micturition, with constant or intermittent unconscious passage of urine is known as urinary incontinence. In small animal general practice, urinary incontinence is a common issue for which owners bring their pet to the hospital.1

Urinary incontinence (UI) in pets is a cause of increased visits to the veterinary hospital, especially when older pets are involved. There are several reasons why urinary incontinence may occur; therefore, it is imperative for veterinary teams to manage the patient based on an accurate diagnosis. Urethral closure is not accomplished by a single anatomic sphincter in the dog and cat. Rather it is mainly the result of smooth muscle tone along the entire urethra in female dogs and along the proximal fourth of the urethra in male dogs. Therefore, if the urethral closure pressure is greater than the bladder pressure, urine remains stored in the bladder until voluntary urination occurs. However, if bladder pressure increases above urethral closure pressure, the result is incontinence. Other types of incontinence include neurogenic incontinence, nonneurogenic incontinence, paradoxical incontinence, and miscellaneous incontinence.

Owners will report their pet leaving a pool of urine where they have been lying or dribbling urine while walking. Additionally, the owner will report, and the veterinary team will observe the perineal area of the pet is always wet. Another potential sign resulting from urine scalding is perivulvar or peripreputial dermatitis. Concurrent urinary tract disease signs may also be present.

**History, Exam, Diagnostics**

The veterinary technician plays an important role in helping the veterinarian with a diagnosis of UI. Performing an in-depth history is crucial when presented with a urinary incontinent pet.2 It is important to determine whether the issue is truly UI as opposed to behavioral conditions and/or systemic problems (e.g., polyuria, pollakiuria). Additionally, the veterinary team should establish that the animal truly is unaware of the passage of urine. If the patient presenting with UI has arisen in conjunction with increased water intake, disorders causing polyuria and polydipsia need to be ruled out. It is important for the veterinary team to determine the timing of the UI onset and the ability of a dog to empty its bladder. This information will aid in diagnosing the underlying cause.
The history should also include age of onset, reproductive status of the pet, age at neutering, current medication, and history of previous urinary tract disorders. A thorough physical and neurologic examination should be performed. Additionally, observing the patient urinating provides valuable information - including estimation of initial and final bladder volume.

A complete physical examination should be performed, including a rectal examination with careful palpation of the urethra. Finally, a neurologic and orthopedic evaluation should be conducted if the dog is unable to posture normally to urinate, as this can lead to incomplete emptying of the bladder and UI.\(^2\)

For all pets presenting with UI, a urinalysis with sediment examination should be performed. Leaking urine may be worsened by a urinary tract infection (UTI); on the other hand, UI may predispose the patient to a UTI. If the patient has a low urine-specific gravity and is considered to be dehydrated, the veterinary team should also perform bloodwork.\(^2\)

**Urethral sphincter mechanism incompetence (USMI)**

The most common cause of acquired urinary incontinence in neutered female dogs is urethral sphincter mechanism incompetence (USMI)\(^3\) - a reduction in the urethral closure due to weakening of the urethral sphincter.\(^4\) This condition has traditionally been referred to as “hormone-responsive urinary incontinence”. However, it is now believed that the pathophysiology is more multifaceted – beyond loss of estrogen. USMI is believed to include alterations not only in tissue structure, collagen content, and estrogen receptors;\(^3\); but alterations in follicle-stimulating hormone and luteinizing hormone concentrations as well.\(^3\,7\)

Other factors that may play a role in USMI development are: anatomical conformation of the dog, tail docking, urogenital tract position.\(^3\,7\,9\)

**Prevalence**

The risk of USMI increases in dogs that weigh >20 kg. In addition, there appears to be overrepresentation of certain breeds of dog when discussing prevalence of USMI. These breeds are: German shepherd, Rottweiler, Doberman pinscher, Old English sheepdog, Boxer, English springer spaniel, Weimaraner, and Irish setter.\(^3\) Urinary incontinence also has been reported to develop most often within 2–4 years of ovariohysterectomy (OVH).\(^3\,9\) UI typically develops in young or middle-aged dogs.\(^2\) Dogs typically develop USMI over time; thus, owners may not seek veterinary care until the frequency or severity of the incontinence becomes unbearable for the owner. Urine leakage while the dog is sleeping or lying down is common.\(^10\)

Intra-abdominal pressure increases when dogs lie on their sides; thus, this gives an indication why affected dogs have incontinence while sleeping. An additional reason may be increased parasympathetic (relative to sympathetic) nervous activity while sleeping.

**Management**

The first line of management in dogs with USMI is often medical therapy. The goal is to increase urethral tone by stimulating \(\alpha\)-receptors in the smooth muscle of the urethra with \(\alpha\)-agonists
and/or increasing the number and sensitivity of those receptors with estrogen compounds. Additionally, estrogen appears to have a trophic effect on the periurethral tissues and vasculature. Consequently, incontinence may be reduced by improving urethral support.

In many tissues, α-receptors are identified mediators of smooth muscle contraction and relaxation. To increase urethral closure pressures the α1A receptors in the smooth muscle of the urethra and bladder neck need to be stimulated. This is also an important part of resting urethral tone.

The α1-Agonists have been identified as the most commonly used UI therapy in veterinary patients. α-Agonists can be used in both genders of dogs and cats. Hypertension is the most serious adverse effects of which the veterinary team should be aware. Hypertension may occur because of the lack of specificity of the agonists for the lower urinary tract and stimulation of vascular smooth muscle. Additional adverse effects to watch for are behavioral changes and decreased appetite, as these are related to sympathetic stimulation.

Phenylpropanolamine (PPA) (Proin, prnpharmacal.com) is the most widely used α-agonist for the treatment of UI. This FDA-approved drug is commercially available in doses designed for use in dogs.

Contraindications = Hypertension, or a predisposition to hypertension (due to concurrent disease). Veterinary technicians should be aware that use of PPA in dogs with USMI and concurrent chronic kidney disease, hyperadrenocorticism, or protein-losing nephropathy, should be judicious and blood pressure should be monitored frequently. Veterinary team members should perform an indirect systolic blood pressure on every patient prior to treatment with PPA. This should be repeated after 1 to 2 weeks of therapy. Other potential side effects with PPA to watch for are: restlessness, aggression, changes in sleeping patterns, and gastrointestinal signs. These are also usually alleviated by a reduction in dose or frequency.

For decades, estrogen has been used for the treatment of incontinence. Estrogen helps to strengthen pelvic and periurethral tissues. Additionally, estrogen enhances glandular function, impacts collagen strength, and increases the number and sensitivity of α-receptors in the smooth muscle of the urethra. Estrogen is typically well tolerated and can be a good choice for female dogs with concurrent diseases that predispose them to hypertension, or that are intolerant of α-agonist treatment.

Diethylstilbestrol (DES) is a synthetic, nonsteroidal estrogen. It was first synthesized in 1938 and was used in the United States and around the world to reduce complications in pregnancies and manage a variety of conditions in women until 1971. At this time, DES was found to contribute to an increased risk of cancer and birth defects. DES is no longer available commercially and is only available to veterinarians through compounding pharmacies.
DES has been used to treat UI in dogs for more than 40 years. Adverse effects of estrogens overall are mammary and vulvar swelling and attractiveness to males. Often, these can be lessened with dose reduction.

UI in dogs is a common disorder, especially in older, female dogs. Veterinary technicians need to understand the disease condition and how to communicate with concerned owners regarding the disease and management of the disease. Knowledge of PPA and how it helps manage UI, specifically USMI is key to compliance and a better quality of life for the patient.

References


