

BioChange

An innovative
treatment
for urinary
incontinence

biochange.life



CellFoamTM

Empowering nature to do what it does best

BioChange is harnessing the body's natural homeostasis capability during recovery from injury, disease, trauma or aging. Our platform technology is CellFoamTM, a foam scaffold designed to reconnect cells in a three-dimensional environment that facilitates complex synchronal tissue repair. This cutting-edge technology has proven to be safe and effective in long-term animal studies. It is currently commercialized for veterinary use and is on its way to its first clinical approval in humans, focused on the treatment of periodontitis. Near future applications include products for the aesthetic and neurology market.

BioChange

One platform.
Universal tissue scaffold.
Multi-organs repair.
Scalable. Affordable.



Protein based
foam scaffold
inspired by
embryonic ECM
(Extra Cellular Matrix)

VetFoamTM

**An innovative foam
scaffold designed
for the treatment
for urinary
incontinence
in female dogs**

BioChange



What is VetFoam™?

The clinical procedure

VetFoam™ provides long-lasting continence with minimal risk and naturally degrades within three months, while the therapeutic effect can last much longer.

The Technology

Injectable scaffold based on CellFoam™ technology.



BioChange

VetFoamTM

How VetFoamTM works?

- Fills and supports urethral tissue
- Forms a stable, supportive matrix that gradually degrades as tissue heals
- Demonstrates high success rates (87%) and can provide continence for up to three years in some cases

BioChange



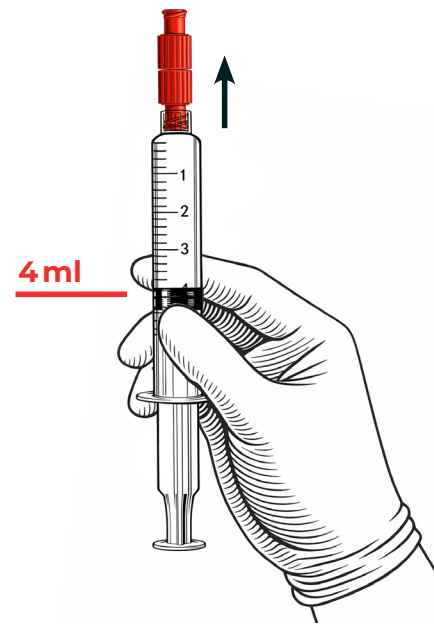
VetFoam™ preparation steps:

Work with gloves to keep the VetFoam™ syringe sterile.

Warm a sterile saline bag for the procedure to 37°C (for the cystoscope and mixing).

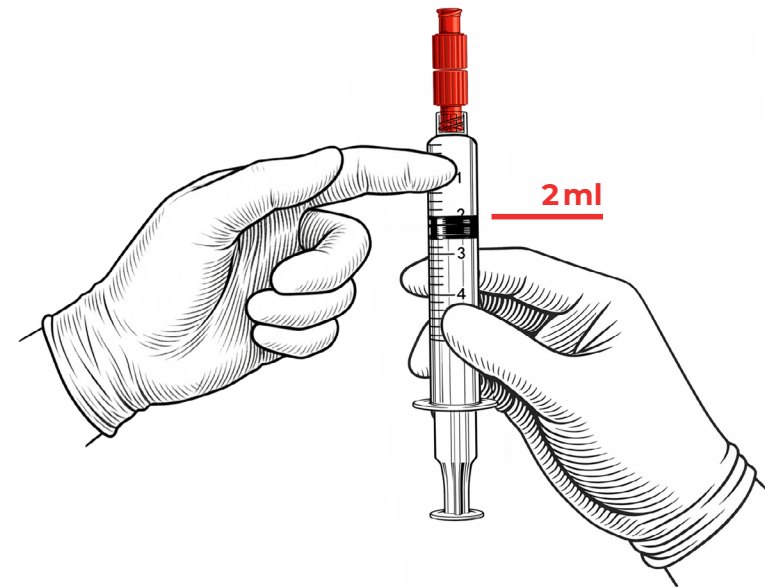
Avoid injecting VetFoam™ with the cystoscope temperature below 25°C.

- 1.** Open the aluminum package of the VetFoam™ powder syringe.

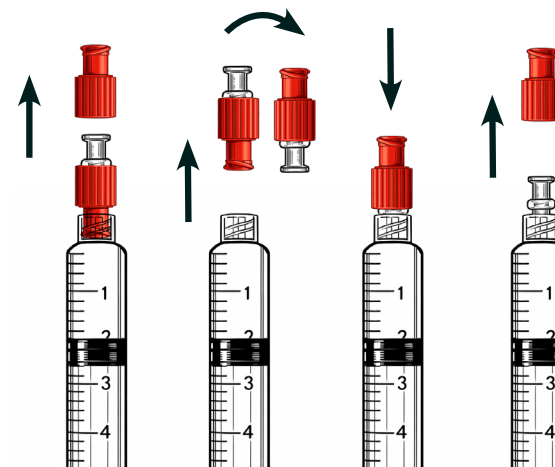


- 2.** Open slightly the red cap attached to the syringe with the powder so it is attached loosely to the syringe. Bring the plunger to the 4 ml line.

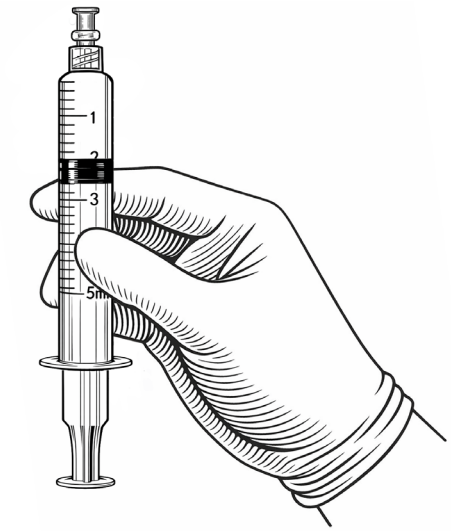
- 3.** Gently tap with your finger on the top part of the VetFoam™ syringe several times to release any powder aggregates. Bring the plunger up to the 2 ml line.



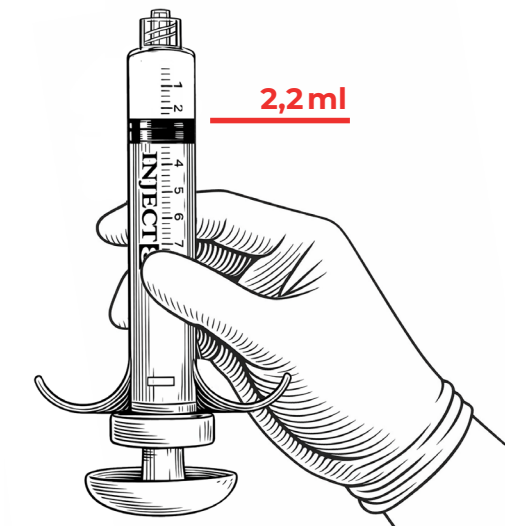
- 4.** Remove the red caps from the VetFoam™ syringe, and re-attach the luer connector to the VetFoam™ syringe.



- 5.** You now have the **VetFoam™ syringe** with a luer connector ready for mixing.



- 6.** Fill the **Wings syringe** with 2.2 ml sterile saline from the warm saline bag.



Final preparation steps:

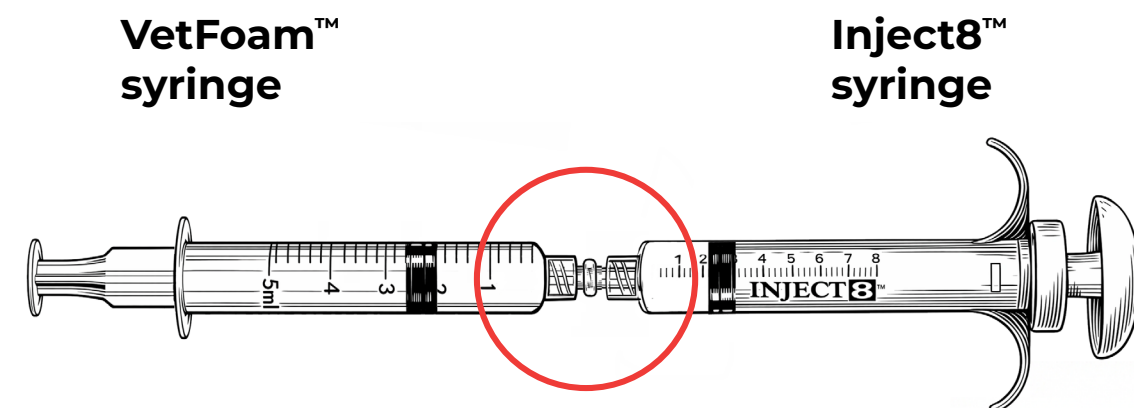
Start these steps when ready to inject.

UNDER THESE CONDITIONS, THE PROCEDURE TIME FRAME (FROM MIXING TO FINAL BULGE INJECTION) IS APPROXIMATELY 5 MINUTES.

The cystoscope should be at a temperature of 37°C.

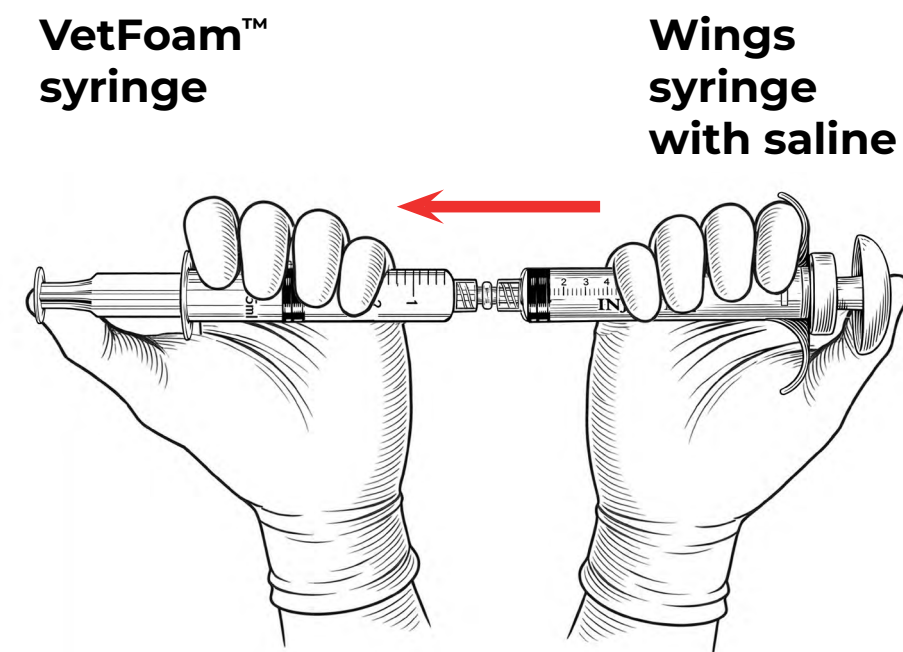
The dedicated needle for bladder injection (BONEE 1.7 mm needle – Coloplast) should be placed in the desired location.

- 7.** Connect the saline filled (2.2 ml) Wings syringe with the VetFoam™ syringe. Keep the two connected syringes horizontal until mixing.



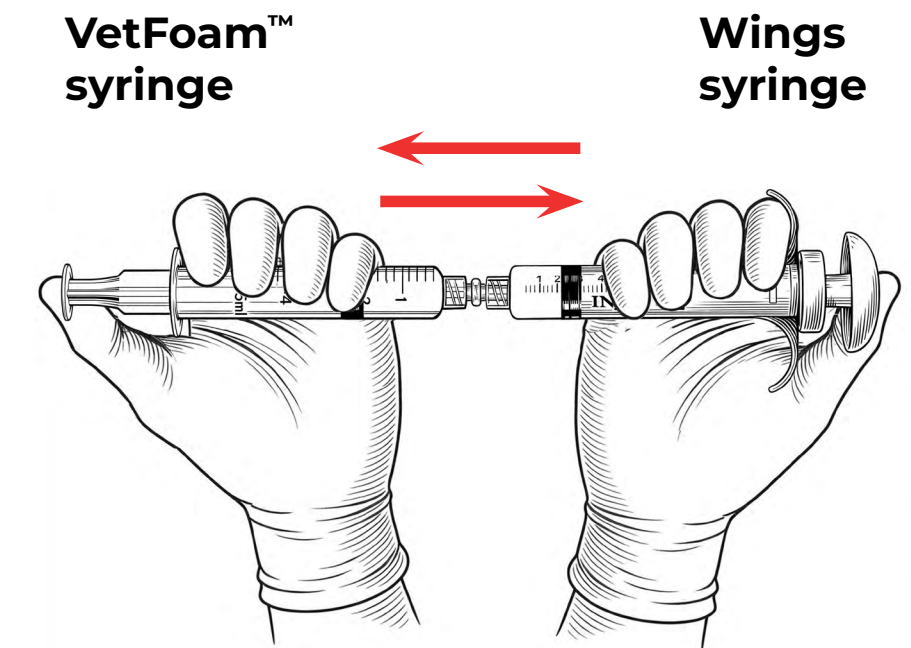
Mixing steps:

- 8.** Push the plunger of the Wings saline syringe fully into the powder-containing syringe.



- 9.** Push the plunger of the powder syringe **halfway** into the liquid syringe.

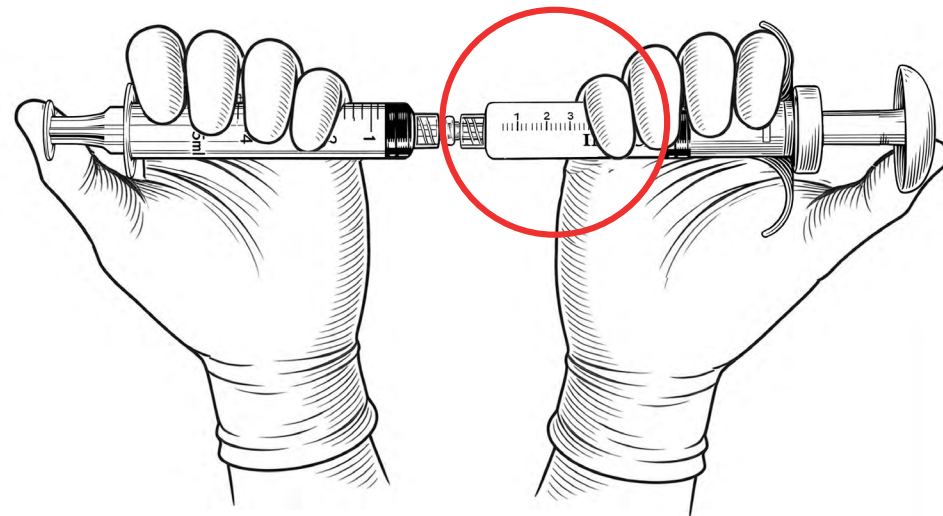
Repeat this halfway-mixing 4 times.



- 10.** Push the plungers **back and forth fully and rapidly** between the two syringes for **30 seconds** until a uniform foam forms.
After the final plunge, the foam should remain in the winged syringe.
Wait for 3-4 minutes.

**VetFoam™
syringe**

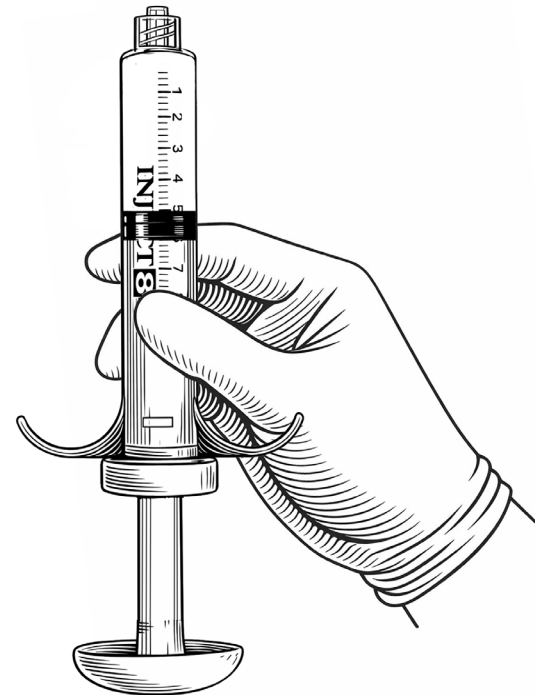
**Wings
syringe**



Mix it again back and forth rapidly 4 times.

- 11.** Disconnect the VetFoam™-containing winged syringe.

VetFoam™ in the winged syringe is now ready for injection.



Injection steps:

- 12.** Connect the Wings syringe (with VetFoam™) to the dedicated needle for bladder injection.
- 13.** Prefilling of BONEE needle (Priming) can be performed at room temperature before insertion.
- 14.** Inject 2-4 bulges into the submucosa of the proximal urethra.
Following each bulge injection, keep the needle in place for about 30 seconds, pull back and place it in the next desired bulge location.



Frequently Asked Questions

BioChange

Why should I treat my patient with VetFoam™?

VetFoam™ is a safe and effective novel agent, for the management of urinary incontinence in female dogs. In an independent study conducted by leading veterinary hospital, it showed high success rates (87%) following the first procedure with a mean continence duration of 11.1 months. It is a minimally invasive treatment with minimal risk of side effects.

Does one treatment of VetFoam™ guarantee long-term continence?

VetFoam™ shows high success rates (87%) in the management of urinary incontinence following the first procedure. Treatment efficiency and long term continence can vary between canine patients. In some cases, a single treatment lasted 3 years, in others repetitive treatments were required.

Is VetFoam™ safe for use?

VetFoam™ is a biomaterial made of natural materials. The product is sterile and is applied by trained personnel. It's safety for use in the treatment of urinary incontinence in female dogs was confirmed in a veterinary clinical study.

Is my patient too old / too young to get the VetFoam™ treatment?

VetFoam™ treatment is not age-dependent.

Is VetFoam™ a bulking agent? How does it work?

VetFoam™ has a bulking effect initially, but the main efficacy stems from an additive value of tissue remodeling encouragement. It is a scaffold with 3D structure which starts as flowable foam and solidifies within the target tissue, transforming into a supportive tissue graft. Once set in stable physical shape (within a few minutes), **VetFoam™** keeps its volume acting similarly to bulking agents. With time, the matrix degrades simultaneously with a natural buildup of new tissue that supports the therapeutic effect over time.

How do I use the VetFoam™?

VetFoam™ administration is under endoscopic guidance into the urethral sub-mucosa and can be done only by trained and certified Veterinarians. See IFU (information for use) document attached to the **VetFoam™** package.

Is VetFoam™ efficient in treating all urinary incontinence medical conditions?

VetFoam™ is known to be a safe and effective treatment for the management of urethral sphincter mechanism incompetence (USMI).

Evaluation of cross-linked gelatin as a bulking agent for the management of urinary sphincter mechanism incompetence in female dogs

[Click
to read
the full
article](#)

Dr. Hila Chen DVM, Dip. ECVIM **Dr. Anna Shipov DVM, Dip. ECVS** **Prop. Gilad Segev DVM, Dip. ECVIM**

Background:

Bulking agent implantation is a minimally invasive intervention for the management of urethral sphincter mechanism incompetence (USMI).

Hypothesis/objectives:

To evaluate the efficacy and safety of the novel bulking agent VetFoam for the management of urinary incontinence in female dogs diagnosed with USMI.

Animals:

Fifteen client-owned female dogs.

Methods:

Prospective study. Female dogs diagnosed with USMI, refractory, or unamenable to medical treatment were included. VetFoam™ was injected under endoscopic guidance into the urethral submucosa. Continence score was evaluated before and after the procedure and monthly thereafter.



Evaluation of cross-linked gelatin as a bulking agent for the management of urinary sphincter mechanism incompetence in female dogs

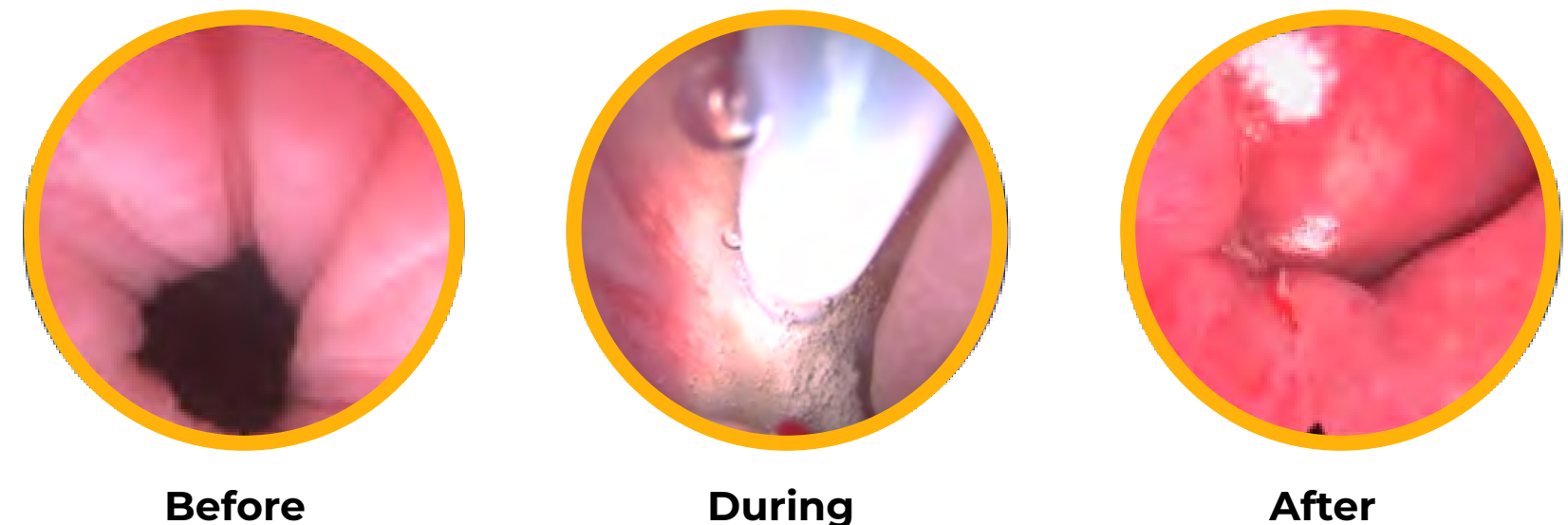
Dr. Hila Chen DVM, Dip. ECVIM **Dr. Anna Shipov DVM, Dip. ECVS** **Prop. Gilad Segev DVM, Dip. ECVIM**

Results:

Twenty-two injection procedures were performed in 15 dogs (5 dogs underwent >1 procedure). Median age of all dogs at the time of the procedure was 111 months (range, 18-180). Median continence score significantly increased after, compared with before bulking agent injection (1.5; range, 1.0-3.5 versus 4.0; range, 1.5-5 respectively; $P < .001$; effect size, 2.6). Continence was achieved in 13/15 (87%) dogs after the first procedure and in 7/7 (100%) repeated procedures. Overall, 20/22 (91%) procedures resulted in high (≥ 4) continence scores at time of first follow-up. Mean duration of continence was 11.1 months (SD, 10.7) after the first injection. One dog (7%) developed self-limiting stranguria, pollakiuria, and tenesmus while no other apparent adverse effects were recognized in the other dogs.

Conclusions and clinical importance:

VetFoam™ is an apparently safe, effective novel bulking agent, which can be used as an alternative for the management of USMI.



No adverse event has been reported during the past 7 years!

Diagnosing and Managing Urinary Incontinence in Canine Patients

Genna F. Atiee, DVM
DACVIM (SAIM)

Audrey Cook
BVM&S, MSc VetEd, MRCVS, DACVIM (SAIM), DECVIM-CA, DABVP (Feline)

**Click
to read
the full
article**

Abstract

Urinary incontinence can profoundly impact quality of life for dogs and their caretakers. This article provides an overview of the common causes of urinary incontinence and outlines a logical approach for evaluation and management of dogs with this condition.

Take-Home Points

- Urinary incontinence (UI) is a common condition in dogs and is particularly prevalent in older females.
- Most dogs with UI have a storage disorder, meaning that urine is not retained appropriately within the urinary bladder.
- Congenital defects such as ectopic ureter are the most common cause of UI in juveniles.
- Selection of an appropriate medical therapy requires differentiation of UI due to a storage disorder from UI due to a voiding disorder.
- Interventions—cystoscopic or surgical—may be necessary for the effective amelioration of some causes of UI.
- Prompt referral for specialized diagnostics or treatments, when indicated, is expected to improve long-term outcomes for affected patients.

Urinary incontinence (UI), defined as the passive and involuntary leakage of urine, must be differentiated from periuria (the conscious voiding of urine in inappropriate locations).¹ In some instances, complications related to UI such as urinary tract infection (UTI) can cause confusion, and care must be taken to establish a reliable clinical picture. The prevalence of UI in dogs is unclear, although it is well established that spayed female dogs are predisposed.²⁻⁶ The severity is variable, with clinical signs ranging from an occasional damp spot on bedding to persistent dripping throughout the day and night. However, even low-grade UI can impact patient wellbeing and cause substantial distress to caretakers^{2,3,7}; it is therefore important to promptly identify the cause and offer appropriate management options.

Case Example: Urinary Incontinence in a 5-Year-Old Dog

Genna F. Atiee, DVM
DACVIM (SAIM)

Audrey Cook
BVM&S, MSc VetEd, MRCVS, DACVIM (SAIM), DECVIM-CA, DABVP (Feline)

**Click
to read
the full
article**

History

A 5-year-old female spayed Doberman pinscher presented for additional management of urinary incontinence (UI). The owners reported that they first noticed small (hand-sized) wet spots on the dog's bedding about 4 months earlier. These were initially uncommon but became an every-other-day or daily occurrence. Leakage only seemed to occur when the dog was resting. There were no other changes in urinary habits, and the dog continued to void appropriately outside 4 to 5 times a day. This dog was spayed at 6 months of age, prior to her first heat, and was otherwise well. On initial evaluation by her primary care veterinarian approximately 3 months after UI was first noted, the dog's physical examination was unremarkable. A urine sample collected via cystocentesis had a specific gravity of 1.038 and pH of 6.5, with an unremarkable sediment examination. Based on these findings, the dog was presumptively diagnosed with urethral sphincter mechanism incompetence (USMI) and started on extended-release phenylpropanolamine at 2.1 mg/kg PO q24h. The owners noted some improvement in continence after 2 weeks but still routinely found wet spots on the bedding. Estriol was subsequently started at 2 mg PO q24h for 14 days, then 1 mg PO q24h, but appeared to provide minimal benefit and was subsequently discontinued. The dog was referred to an internist for further evaluation.

Diagnostic Findings

The dog's physical examination was unremarkable. There was no evidence of urine scald or perivulvular dermatitis. Results of a CBC and serum biochemical profile were unremarkable. Transabdominal ultrasonography showed normal kidneys and a mid-sized urinary bladder. No masses or stones were noted, and both ureteral openings appeared to be within the trigone. The dog was observed to urinate normally when outside and had a postvoid residual volume of 0.4 mL/kg. Findings on routine urinalysis were similar to those reported before, and a quantified urine culture was negative. The dog was anesthetized a few days later for cystourethroscopy performed with a 2.7-mm 30° rigid pediatric cystoscope with the patient in dorsal recumbency. The vestibule was unremarkable, but a vestibulovaginal septal remnant was noted spanning the vaginal opening and was ablated with a diode laser (**FIGURE A**).

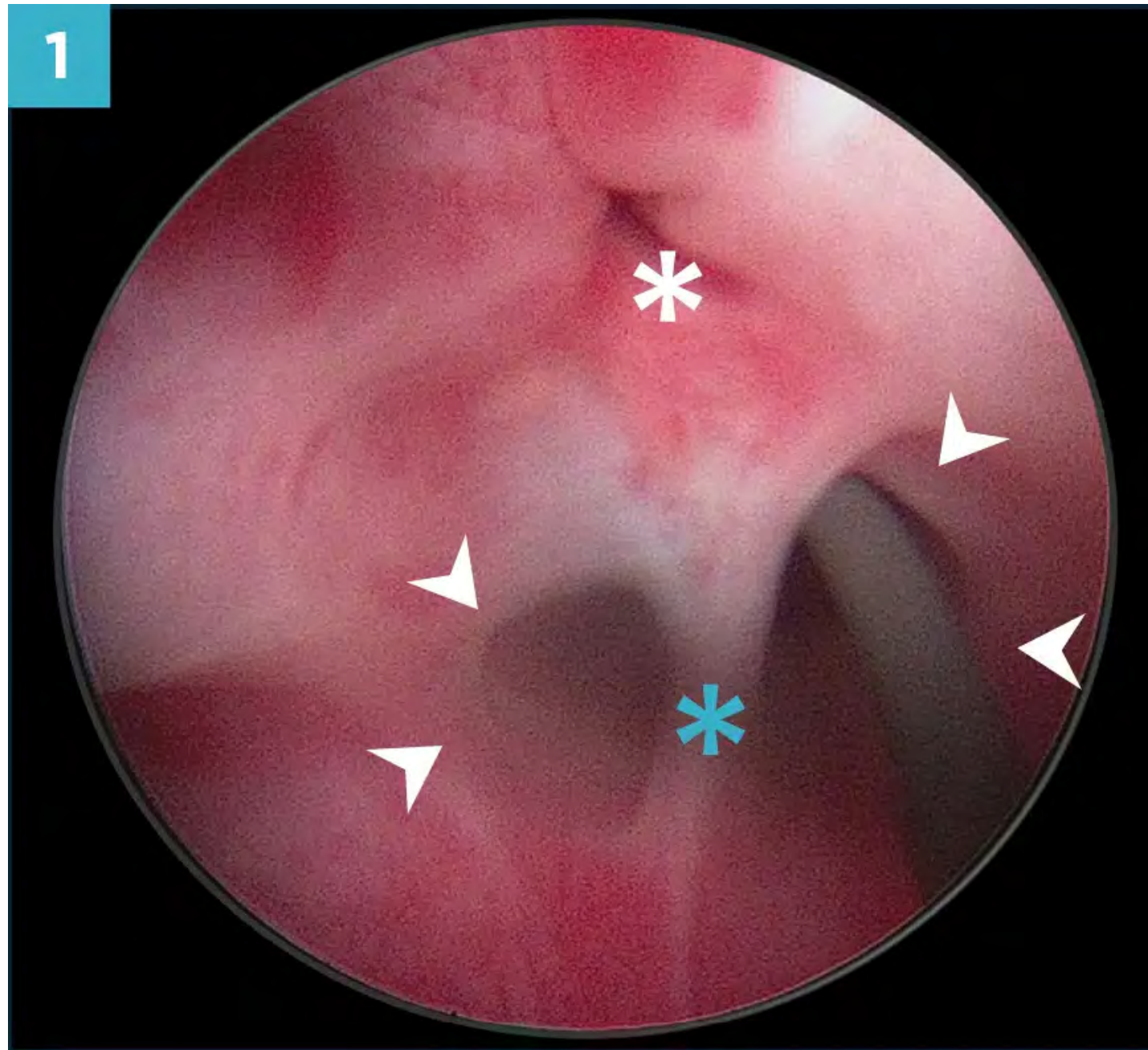


Figure A. Cystoscopic images of a 5-year-old spayed female Doberman pinscher with a 4-month history of intermittent urinary incontinence. The dog is in dorsal recumbency for the procedure. (1) A vestibulovaginal septal remnant (blue asterisk) spans the vaginal opening (arrowheads). A hydrophilic guidewire has been placed through the left side of the vaginal opening to enable the endoscopist to reliably differentiate a septal remnant from a bifid vagina. The urethral papilla is visible near the top of the image (white asterisk).

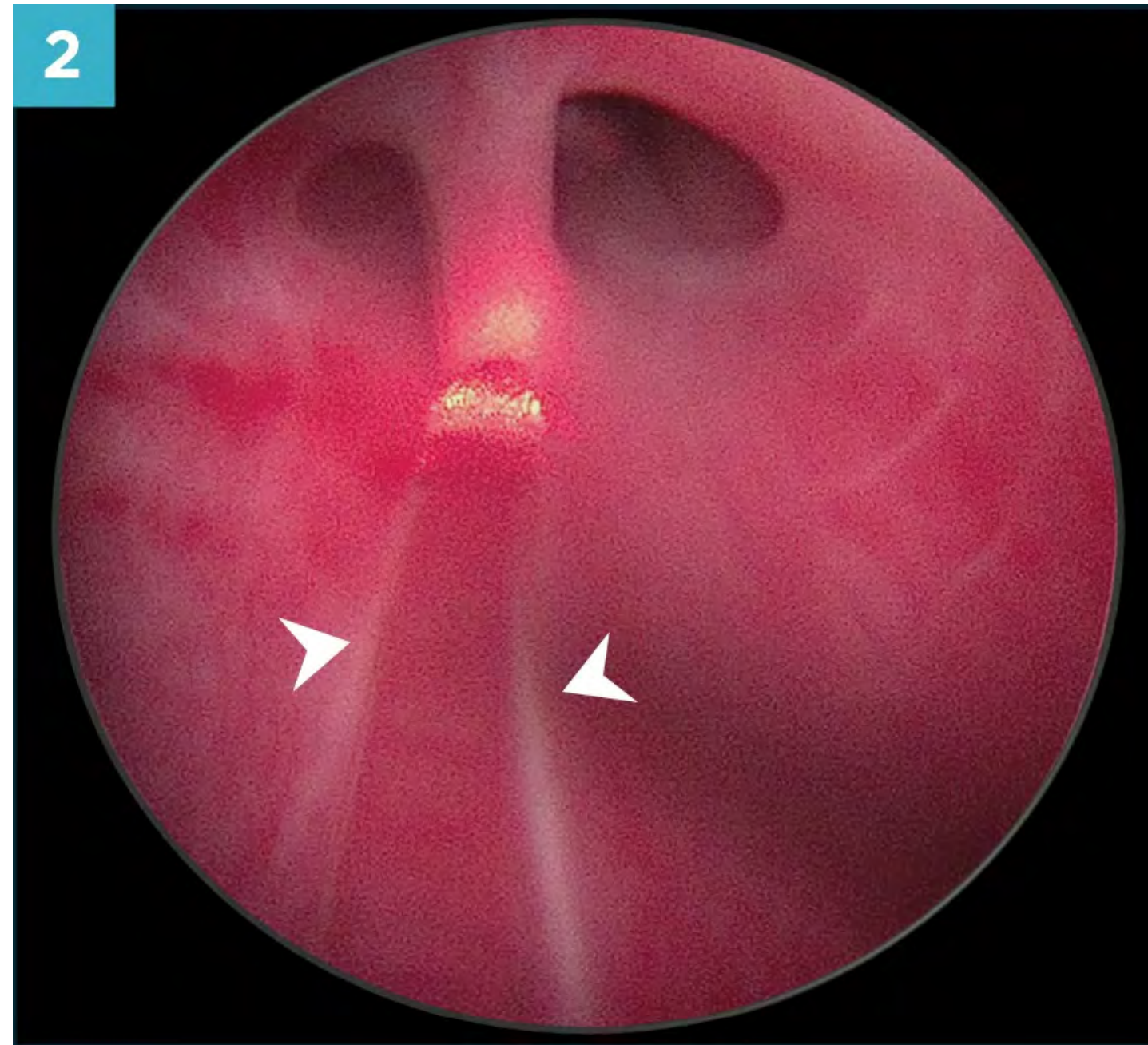


Figure A2. A diode laser (arrowheads) is used to bisect the vestibulovaginal

The urethral walls were smooth and pink; urethral length was somewhat shorter than expected at 7 cm. The trigone was clearly defined and was easily traversed with the cystoscope. The urinary bladder wall was unremarkable, with no stones or masses. Both ureteral openings were identified and appeared normal. A urethral bulking agent containing cross-linked porcine gelatin (**VetFoam™; BioChange, biochange.life**) was injected at 3 sites within the proximal urethra, approximately

1 cm caudal to the trigone. About 1.3 mL of bulking agent was injected at each site, with the 3 blebs positioned at regular intervals around the circumference of the urethra (FIGURE B). The dog was discharged with a 3-day course of carprofen (2 mg/kg PO q12h), and the owner was instructed to discontinue phenylpropanolamine. Four weeks postprocedure, the dog was fully continent and able to void comfortably.

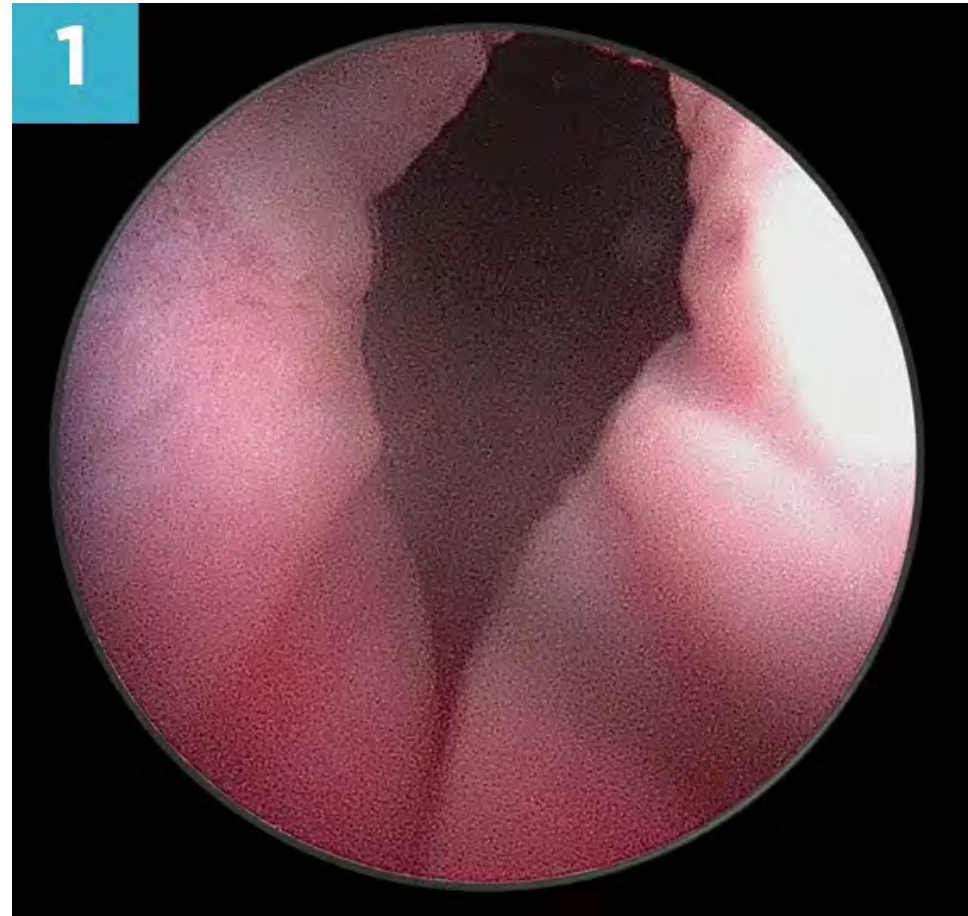


Figure B. Cystoscopic images of the same dog as in Figure A. (1) The transition from proximal urethra to urinary bladder on initial examination.

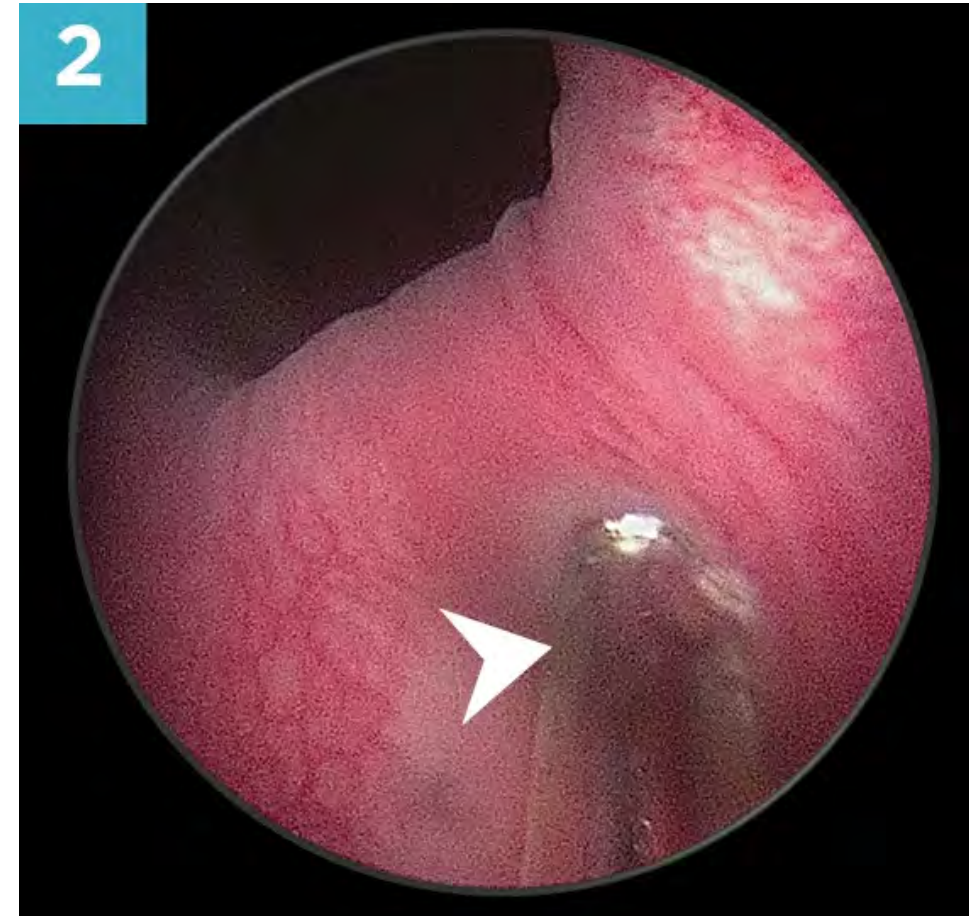


Figure B2. A 22-gauge flexible endoscopic needle (arrowhead) is positioned against the urethral mucosa approximately 1 cm caudal to the trigone.



Figure B3. Injection of cross-linked gelatin into the mucosa. A small white bleb (arrowhead) is evident.

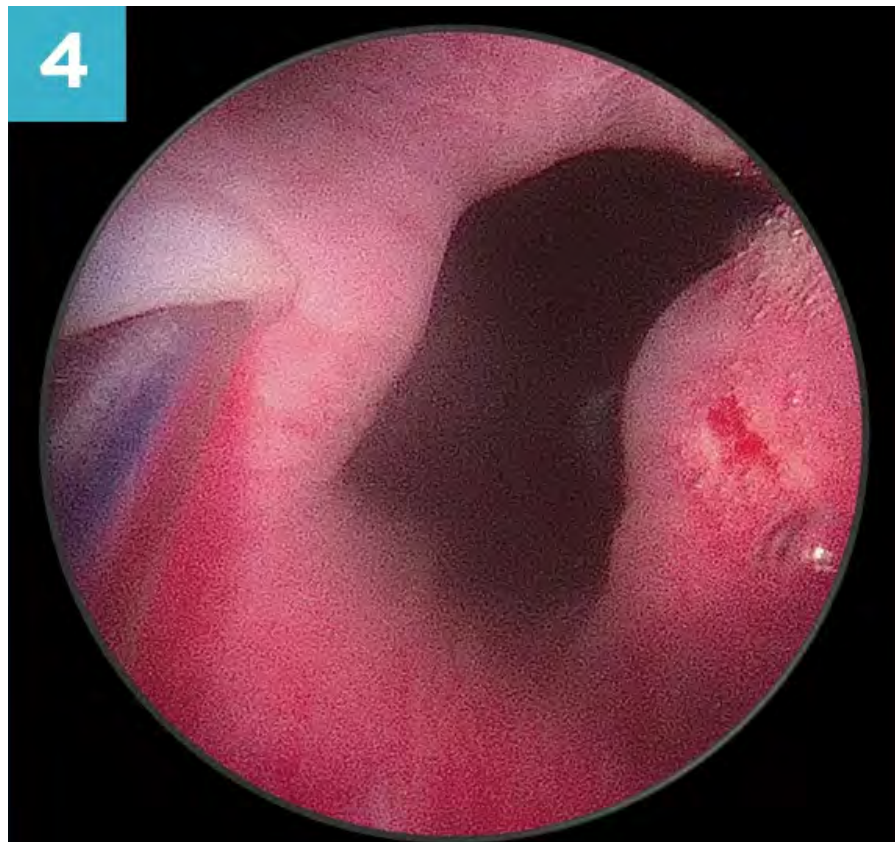


Figure B4. The second bleb is injected on the other side of the urethra; a small amount of hemorrhage is noted from the first bleb.



Figure B5. Large white bleb is evident at the end of the second injection.

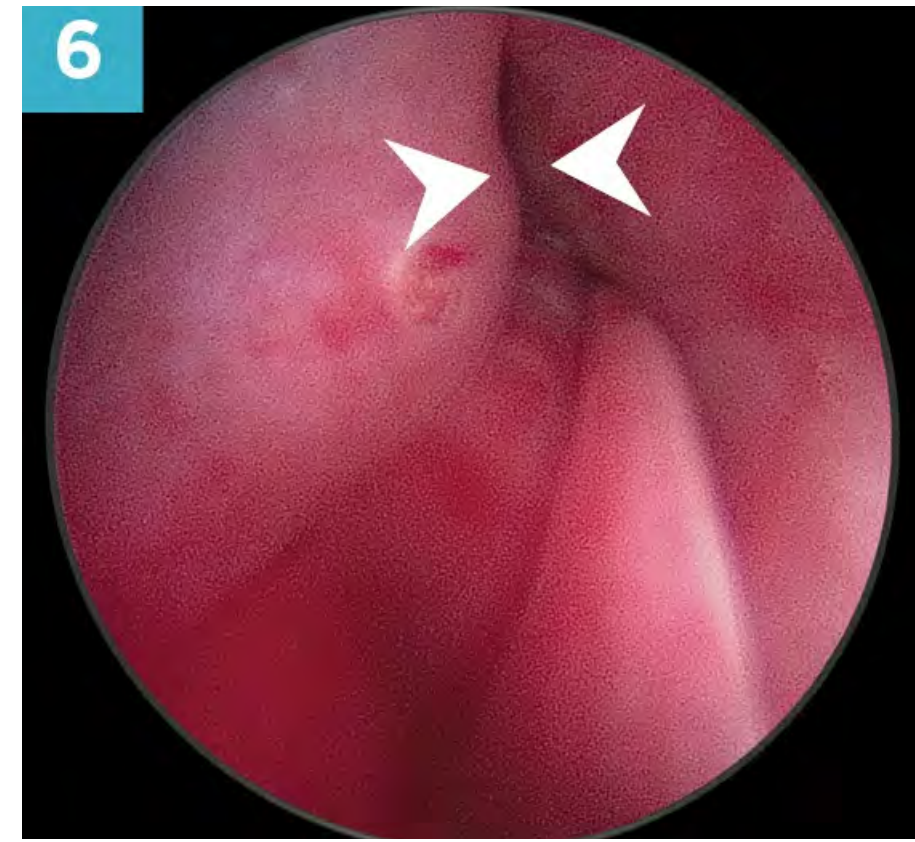


Figure B6. The appearance of the trigone at the end of the procedure; note that the urethral lumen (arrowheads) is now essentially occluded by expanded mucosa.

Discussion

This dog's history is very consistent with USMI. This case is likely due to a combination of diminished urethral tone secondary to ovariectomy and a somewhat short urethra. Although many dogs respond well to medical management, some experience adverse effects or have limited improvement. Urethral bulking agents are excellent options for female dogs with refractory USMI, with response rates greater than 90% reported.¹ Patients should be screened for UTI prior to administration of a bulking agent. As urethral bulking agents are delivered through a rigid scope, this treatment option is not routinely performed in males. However, bulking agents can be injected into the distal urethra with a rigid scope in large males or via a perineal approach in smaller

individuals. Vestibulovaginal septal remnants may be incidental and unrelated to lower urinary tract disease, but they sometimes distort the urethral papilla and have been associated with recurrent urinary tract infection.² The authors routinely ablate these during cystoscopic examinations in case they are contributing to clinical problems. The urethral bulking agent used in this case is expected to slowly dissipate within a year, at which time the incontinence may recur. In some patients, restarting phenylpropanolamine may be sufficient to achieve continence for a few more months. However, owners should be counseled that the procedure will likely need to be repeated for long-term maintenance of continence.

Ectopic Ureter

This condition can be unilateral or bilateral and is the primary cause of incontinence in juvenile dogs.¹ Affected animals usually drip urine continuously and often get severe urine scald. The abnormal ureteral opening(s) can be repositioned within the bladder through cystoscopic laser ablation or surgical reimplantation.²⁰⁻²² The latter option should be reserved for dogs with extramural ectopia; cystoscopic laser ablation is the superior option for dogs with intramural (tunnelling) ectopic ureters as complications are rare and the recovery time is brief. Unfortunately, some dogs with ectopic ureter remain incontinent after correction; this is often due to a concurrent short urethra and may improve with phenylpropanolamine.^{21,22}

Idiopathic Detrusor Instability

This condition—also known as hyperactive bladder — is characterized by involuntary bladder contractions despite minimal filling; affected dogs exhibit urinary urgency or dribble urine after voiding.^{1,3} Definitive diagnosis requires cystometry (see under IMAGING below), but it is reasonable to assess the response to drugs (**TABLE 1**) such as oxybutynin, an anticholinergic antispasmodic, if the clinical picture is consistent with this diagnosis and conditions such as UTI or urinary tract neoplasia have been reliably excluded.

Voiding Disorders

Dogs with UI due to a voiding disorder are unable to effectively empty the bladder, and PVRV is >3 mL/kg.¹ This condition is sometimes referred to as overflow incontinence, as urine leaks out when the storage capacity of the bladder is exceeded; this is routinely noted when the dog is resting. These dogs may attempt to urinate but only

pass dribbles or short spurts of urine.²³ In some cases, a small amount of urine may be forcibly ejected from the bladder when deliberate efforts to void are abandoned.

Patients with voiding disorders may again be broadly categorized as having non-neurogenic or neurogenic disorders (**FIGURE 1**).¹ Non-neurogenic issues are subcategorized as mechanical or functional; mechanical causes include urolithiasis, urinary tract neoplasia, urethral stricture, prostatic disease, bladder displacement, and extramural compression. Functional disorders include bladder atony or fibrosis and idiopathic functional outflow obstruction. Common neurogenic causes of voiding disorders include those affecting the T3 to L3 and S1 to S3 spinal regions, such as intervertebral disk herniation, ischemic myelopathy, and degenerative lumbosacral stenosis.^{24,25} Prognosis and treatment will depend on the underlying cause.

Bladder Displacement

Conditions such as perineal hernia can compromise urine voiding.^{26,27} Affected dogs are usually intact middle-aged males, and concurrent prostatomegaly may play a role. On digital rectal examination, there is often an obvious weakness within the pelvic canal; in severe cases, a bulge may be visible on either side of the anus. Urethral kinking with caudal displacement of the urinary bladder may occur in dogs of any sexual status and can cause severe compromise to micturition.²⁸ As the affected dog postures to urinate, the bladder moves caudally, and the urethra becomes compressed and occluded. Signs can be intermittent but tend to be more pronounced when the bladder is fully distended. This condition may be diagnosed using contrast cystourethrography and is addressed by surgically securing the cranial aspect of the bladder to the ventrolateral abdominal wall.

Idiopathic Functional Outflow Obstruction

This condition was traditionally referred to as detrusor–urethral dyssynergia or reflex dyssynergia and is due to failure of the bladder to contract and/or failure of the urethra to relax.¹ Affected patients are usually large-breed, middle-aged males, and clinical signs range from a narrowed and erratic urine stream to complete inability to void.²⁹⁻

³¹ Signs can wax and wane, and treatment may be delayed if owners fail to grasp the significance of changing urinary patterns. These dogs are particularly prone to secondary bladder atony, as long periods of incomplete emptying slowly stretch the wall and damage the connections between the detrusor fibers.

Treatments focus initially on urethral relaxation, with α -adrenergic blockers such as prazosin, tamsulosin, or phenoxybenzamine. Skeletal muscle relaxants such as dantrolene sodium, acepromazine, or a benzodiazepine may also be useful, particularly in males, as these agents reduce tone in the extensive urethralis muscle.¹ Concurrent detrusor atony may be subsequently addressed with bethanechol; if indicated, the authors introduce this drug 2 to 3 days after starting urethral relaxants.

Patient Evaluation

The first step in the evaluation of a patient with UI is to collect a detailed history, including duration of clinical signs, pattern(s) of incontinence, voiding behaviors, and response(s) to previous therapy. Patient signalment should be considered; UI in puppies is usually due to anatomic defects such as ectopic ureter, whereas UI in older dogs is more likely to be USMI or related to mechanical or functional obstruction.

On physical examination, careful attention should be paid to the appearance of the external genitalia and surrounding skin. Are the tissues inflamed or urine scalded? A digital rectal examination should be performed in all dogs, as abnormalities of the urethra or prostate may be noted. In older intact males, the structural integrity of the pelvic diaphragm should be carefully assessed. Urinary bladder size and tone should be noted, along with any signs of discomfort. A full neurologic examination should also be performed, including assessment of anal tone. It is also very helpful to observe the dog's behavior during micturition, including ability to effectively posture, and the strength of the urine stream. If necessary, the dog may need to be placed off-leash in a secured area to facilitate voiding. The PVRV should then be established to narrow the list of possible causes of UI.

Diagnostic Testing

Findings on routine urinalysis should be carefully evaluated. Pyuria and bacteriuria indicate UTI; this is most likely to be secondary to UI rather than the cause, although cystitis can exacerbate leakage or trigger urge incontinence in dogs with

mild USMI. A quantified urine culture should be performed if UTI is suspected and results used to guide therapy. Abnormal transitional epithelial cells or evidence of squamous metaplasia suggest obstructive conditions and indicate the need for imaging to evaluate urinary tract and prostatic anatomy. Poorly concentrated urine is not a reason for UI per se but will certainly affect the magnitude and frequency of leakage.

Results of a CBC and serum biochemical profile should be evaluated. Although these tests are unlikely to provide direct insight into the cause of UI, concurrent issues such as chronic kidney disease or endocrinopathy may exacerbate UI by driving polyuria and should be addressed as appropriate.

Imaging

Plain abdominal radiography can provide insight into the size and position of the kidneys, urinary bladder, and prostate (**FIGURE 2A**) and can reliably identify radiopaque uroliths. Readily apparent stones are usually calcium oxalate or magnesium ammonium phosphate (struvite); urate stones may sometimes be noted with high-quality imaging.^{32,33} In males, the perineal and penile urethra are best evaluated with the back legs pulled cranially (**FIGURE 2B**). Compressing the bladder with a paddle may facilitate the detection of small cystoliths (**FIGURE 2C AND 2D**).

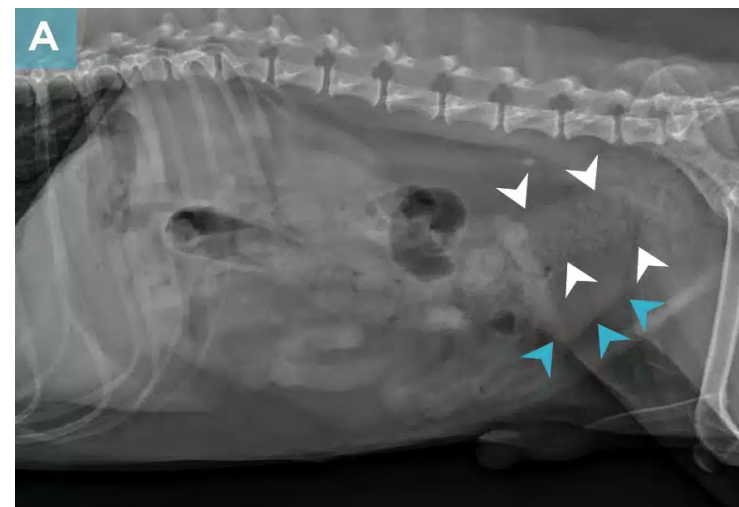


Figure 2. Right lateral abdominal radiographs of a 5-year-old bichon frise with a history of intermittent urinary incontinence (UI) attributable to a storage issue and characterized by small puddles voided while at rest. (A) Standard lateral abdominal image; the bladder (blue arrowheads) is small and is overlain by the colon (white arrowheads).



Figure 2B. The patient's hind legs have been pulled forward to allow for effective imaging of the prostatic, pelvic, and penile urethra.



Figure 2C. A large plastic spoon is used to compress the urinary bladder and displace the overlying colon dorsally.

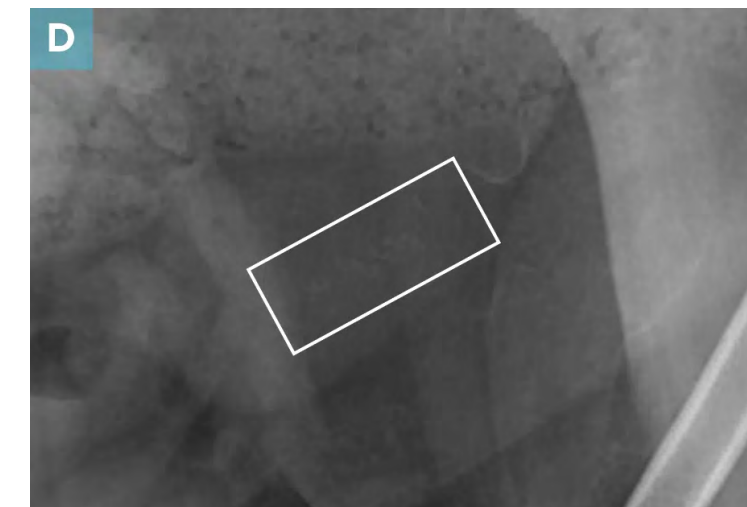


Figure 2D. Magnified view of the same image as C; more than a dozen tiny cystoliths are now visible (box). These stones were successfully removed with voiding urohydropropulsion and were found to be calcium oxalate. The dog's diet was adjusted to reduce the risk of stone recurrence, and UI was successfully managed with phenylpropanolamine.

Transabdominal ultrasonography allows for detailed evaluation of the kidneys, ureters, urinary bladder, proximal urethra, and prostate, as well as routine identification of masses, cysts, stones, and extraluminal compressive lesions. Although ureteral jets may be visualized using color Doppler ultrasonography, this imaging modality may not reliably identify an ectopic ureter and most experts prefer to rely on cystoscopy to establish or refute this diagnosis.^{1,34}

Contrast radiographic studies can be performed using standard radiography, fluoroscopy, or computed tomography. As a general rule, patients should be deeply sedated or fully anesthetized for these studies to ensure adequate image collection and minimize risk to personnel. The most appropriate modality will depend on the likely causes of UI in a particular patient. Retrograde positive-contrast cystourethrography is often the best choice for patients with signs suggestive of mechanical urethral obstruction; fluoroscopic contrast studies are particularly useful in dogs with fistulae or those with dynamic mechanical obstructions due to caudal displacement of the bladder.^{1,28} Computed

tomography with intravenous contrast administration allows more detailed evaluation of the anatomy without the hindrance of anatomic superimposition. This modality has superior diagnostic reliability for dogs with ectopic ureter than ultrasonography or traditional retrograde contrast studies but is still less sensitive than cystoscopy.³⁵

Cystourethroscopy, direct endoscopic visualization of the urethra and bladder, is highly informative in many instances, and is the most reliable way to identify or exclude urolithiasis, stricture, neoplasia, and ureteral ectopia **(FIGURE 3)**. General anesthesia is required for cystourethroscopy, and practitioners must be adequately trained. Rigid cystoscopy is routinely performed in females, whereas a flexible scope is required for males. Patient size must be considered, as the urethra must comfortably accommodate the scope. In males, it is prudent to pass an appropriately sized red-rubber catheter before scheduling cystourethroscopy to be sure that the scope will be able to traverse the distal urethra. If necessary, a minimally invasive perineal approach may be used in males to allow access to the pelvic and prostatic urethra with a rigid scope.³⁶

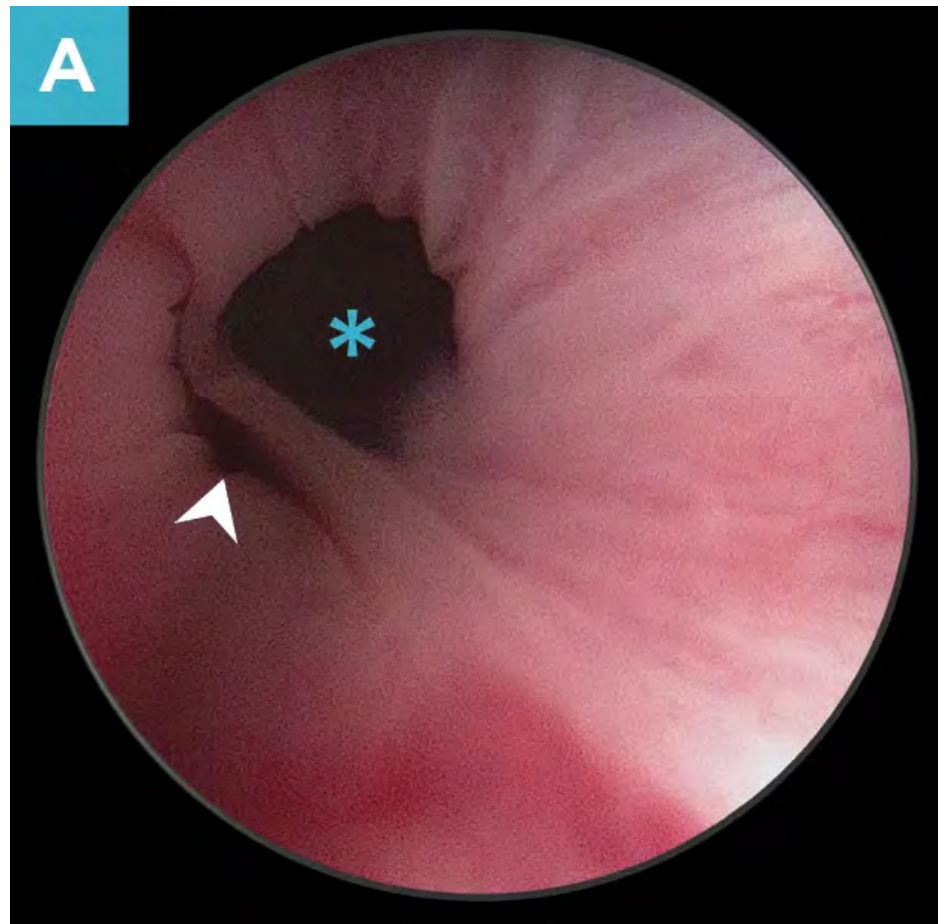


Figure 3. Cystoscopic images of a 6-month-old female intact goldendoodle with severe urinary incontinence, characterized by persistent dripping. The dog is in dorsal recumbency for the procedure. (A) The opening to an ectopic right ureter (arrowhead) is visible within the urethral lumen (asterisk).

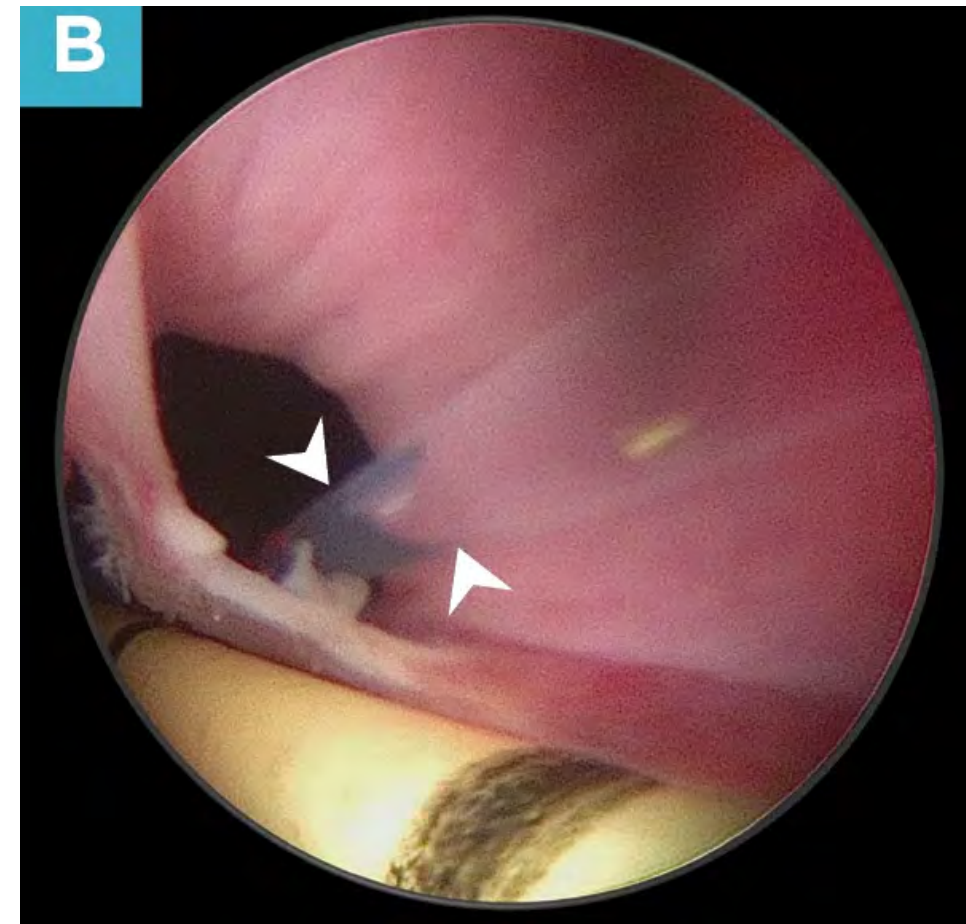


Figure 3B. A 5-Fr, yellow, open-ended ureteral catheter has been placed over a hydrophilic guidewire into the ectopic ureter. A diode laser fiber (arrowheads) is being used to cut the tissue between the ectopic ureter and the urethral lumen.

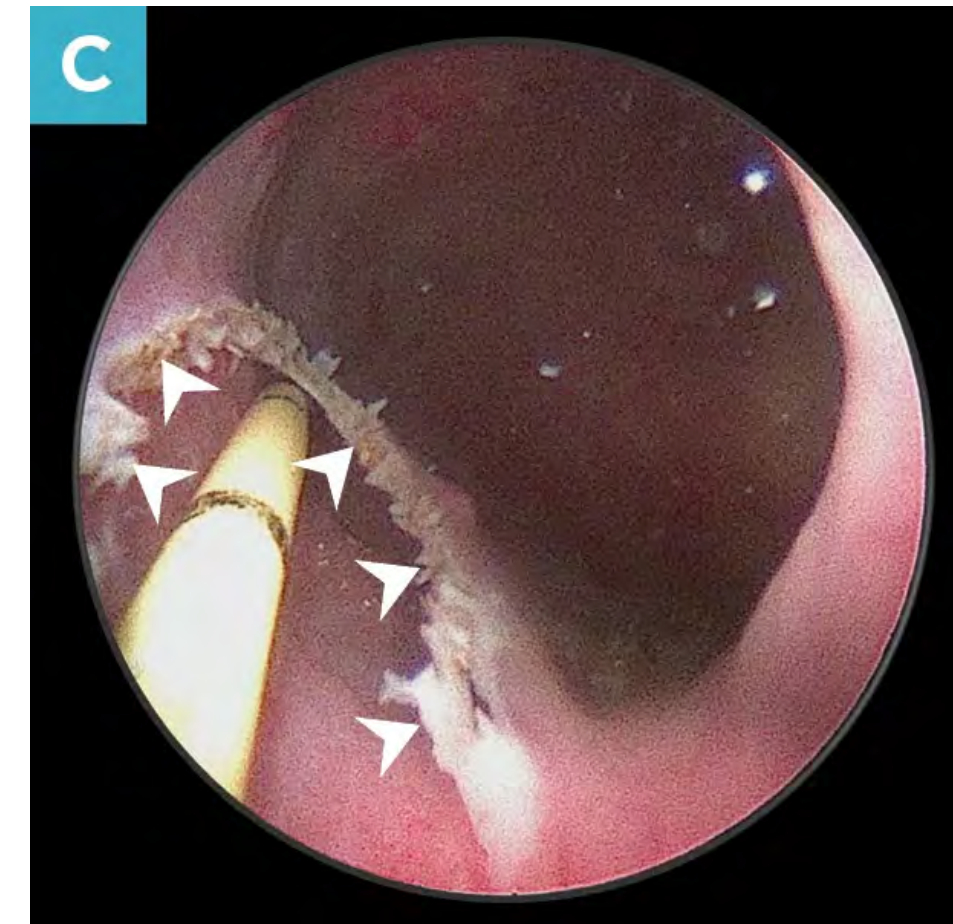


Figure 3C. The opening to the right ureter is now within the urinary bladder. The cut edges of the ureter are visible (arrowheads). Urine from the right kidney will now enter the urinary bladder. This dog was completely continent following this procedure.

Urodynamic studies such as cystometry and urethral pressure profiling are available at some referral centers and can provide specific information regarding lower urinary tract function.^{1,37} However, specialized equipment and standardized sedation/anesthesia protocols are necessary, and most clinicians feel that the benefits of performing these studies are limited. Cystometry determines the amount of fluid required to trigger involuntary detrusor contraction and is needed to confirm a diagnosis of detrusor instability or bladder fibrosis.¹

Urethral pressure profiling assesses the tone of the urethra and can confirm USMI.¹

Summary

It is essential to establish a diagnosis in a dog with UI so that appropriate tests and treatments are provided in a timely manner. Initial differentials are influenced by signalment, history, and urine characteristics and should be combined with determination of PVRV. Referral should be recommended for challenging or refractory cases.

Urethral tissue engineering for canine urinary incontinence

Hilla Chen¹, Keren Sinik², Shai Sherbo², Ishay Atar², Anna Shipov¹, Gilad Segev¹

¹The Veterinary Teaching Hospital, Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, P.O. Box 12, Rehovot, 761001, Israel

²BioChange Ltd. Hatnufa 4, Hi-Tech Park, Yokneam, 2066717, Israel

Introduction

Bulking agent implantation is a minimally invasive intervention for the management of urethral sphincter mechanism incompetence (USMI).

Disadvantages of medical therapy include the need for lifelong treatment, potential side effects and incomplete response in some dogs.

As bovine glutaraldehyde cross-linked collagen, the most studied bulking agent in veterinary medicine, has become unavailable in many countries, an alternative bulking agent is needed.

Aims

1. Evaluate VetFoam™'s effect in-vivo by histopathological examination after its injection to the subcutaneous and urethral tissue in a pig.
2. Evaluate VetFoam™'s clinical effect in female dogs with USMI.

Materials and methods

VetFoam™ and saline (control) were locally injected into the urethra and sub-cutaneous tissue of a pig.

Injection sites were sampled 15, 30, 60, 90 or 140 days (skin and urethra, respectively) post-injection.

Masked histopathological evaluation using semi-quantitative scoring method (grade 0–4) was used to describe collagenesis along with scaffold resorption.



Figure 1: Cystoscopic image of the urethra after the submucosal injection of VetFoam™. Bulges were injected 1-3 cm caudal to the trigone in a circumferential arrangement. Bulges were added to achieve at least 80% decrease in the urethral lumen diameter to allow adequate coaptation.

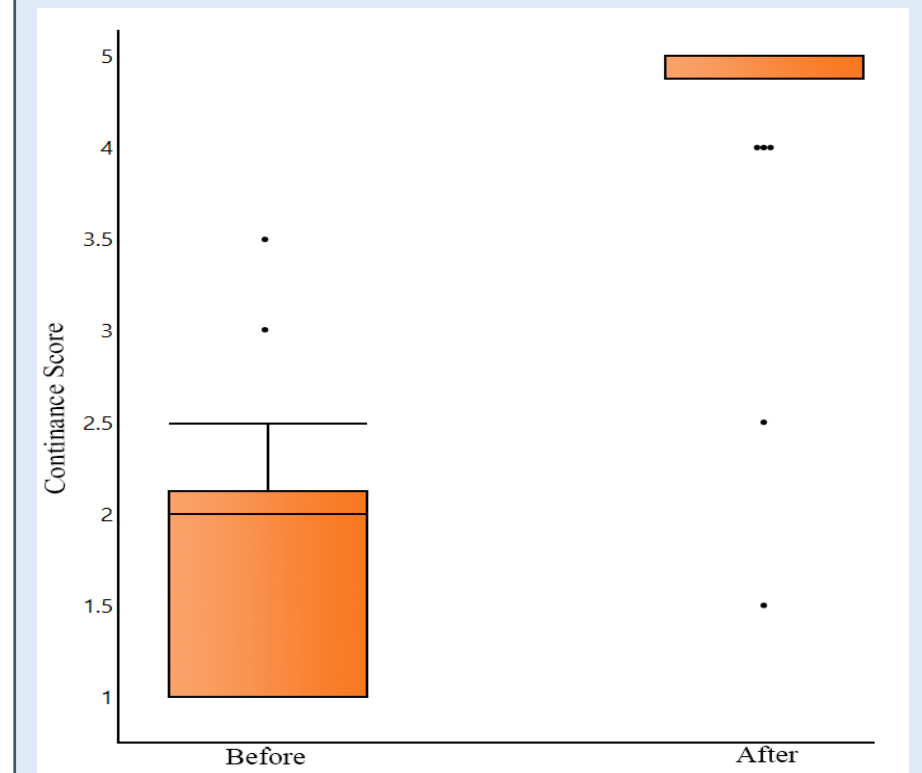


Figure 3: Continence scores of the dogs before and after bulking agent injection. Data are presented as box and whiskers. The box represents the 2nd and 3rd quartiles. The horizontal line within the box represents the median. The whiskers represent the range, and the circles indicate outlying data.

Urethral tissue engineering for canine urinary incontinence

Hilla Chen¹, Keren Sinik², Shai Sherbo², Ishay Atar², Anna Shipov¹, Gilad Segev¹

¹The Veterinary Teaching Hospital, Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, P.O. Box 12, Rehovot, 761001, Israel

²BioChange Ltd. Hatnufa 4, Hi-Tech Park, Yokneam, 2066717, Israel

For the clinical trial in dogs, 15 dogs diagnosed with USMI, refractory or unamenable to medical treatment were recruited.

1.6–2 ml of sterile saline was injected into a prepackaged syringe containing 500 mg VetFoam™ powder.

A flexible needle was used to inject 2–4 bulges (1–2 mLs in each bulge) into the urethral submucosa (Figure 1).

A continence score (CS), in a scale of 1–5 was assigned to each dog by the owners before and after the procedure and monthly thereafter.

The procedure was considered successful if CS was ≥ 4 at time of first follow up and the duration of continence was defined as the time during which the CS was ≥ 4 .

Results

Histopathology of porcine tissue showed new tissue formation within ~90 days, while the implanted scaffold was undetectable by that time.

Collagenesis grade was 3–4 in VetFoam™ injected tissue compared to 0 in control sites.

No inflammation, necrosis, cavity formation or edema were documented (Figure 2).

Twenty-two injection procedures were performed in 15 dogs (5 dogs underwent more than one procedure).

Overall, 20/22 (91%) procedures resulted in good continence scores (CS ≥ 4) at time of first follow-up.

Median post-procedural CS of dogs increased from baseline (1.5 vs 4, respectively, $P < 0.001$) (Figure 3), mean continence duration was 11.3 ± 11.0 months.

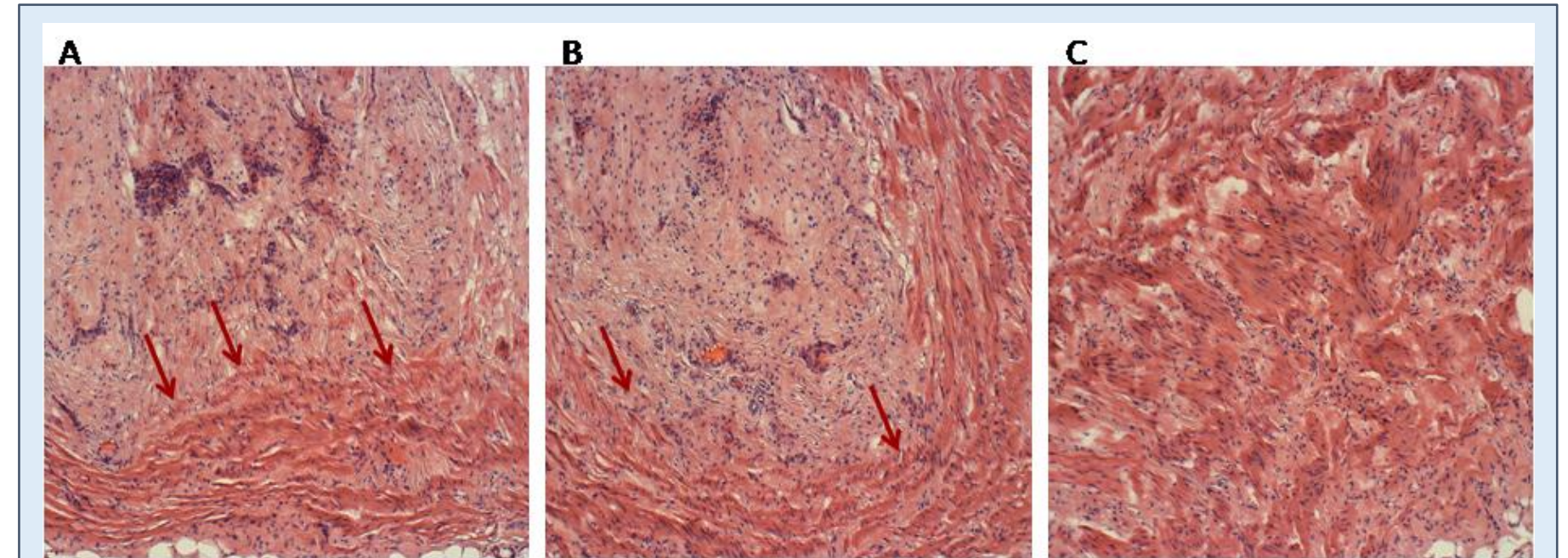


Figure 2: Histopathological evaluation of urethral tissue samples obtained 22 days after injection of VetFoam™ into the urethra of a pig. Collected tissues were fixed in 4% formaldehyde solution and stained with Hematoxylin & Eosin. Images A and B (40x) demonstrates presence of collagen without any inflammatory response, necrosis or cavity formation. Red arrows indicate the border between the collagen fibbers and pre-existing (normal) connective tissue. Image C - control - an area of healthy connective tissue.

Conclusions

VetFoam™ can be used as an alternative for the management of USMI.

It promotes collagenesis and thus has potential to maintain continence after its degradation.

The clinical effect demonstrated in dogs exceeded the time to full scaffold degradation, hence VetFoam™'s efficacy is likely the outcome of tissue remodeling, rather than of a bulking effect.

Evaluation of cross-linked gelatin as a bulking agent for the management of urinary sphincter mechanism incompetence in female dogs

Hilla Chen, Anna Shipov, Gilad Segev

Click
to read
the full
article

Abstract

Background:

Bulking agent implantation is a minimally invasive intervention for the management of urethral sphincter mechanism incompetence (USMI).

Hypothesis/Objectives:

To evaluate the efficacy and safety of the novel bulking agent VetFoam™ for the management of urinary incontinence in female dogs diagnosed with USMI.

Animals:

Fifteen client-owned female dogs.

Methods:

Prospective study. Female dogs diagnosed with USMI, refractory, or unamenable to medical treatment were included. VetFoam was injected under endoscopic guidance into the urethral submucosa. Continence score was evaluated before and after the procedure and monthly thereafter.

Results:

Twenty-two injection procedures were performed in 15 dogs (5 dogs underwent >1 procedure). Median age of all dogs at the time of the procedure was 111 months (range, 18-180). Median continence score significantly increased after, compared with before bulking agent

injection (1.5; range, 1.0-3.5 versus 4.0; range, 1.5-5 respectively; $P < .001$; effect size, 2.6). Continence was achieved in 13/15 (87%) dogs after the first procedure and in 7/7 (100%) repeated procedures. Overall, 20/22 (91%) procedures resulted in high (≥ 4) continence scores at time of first follow-up. Mean duration of continence was 11.1 months (SD, 10.7) after the first injection. One dog (7%) developed self-limiting stranguria, pollakiuria, and tenesmus while no other apparent adverse effects were recognized in the other dogs.

Conclusions and Clinical Importance:

VetFoam is an apparently safe, effective novel bulking agent, which can be used as an alternative for the management of USMI.



VetFoamTM

Veterinarians and owners share their experience

BioChange



Dr. Genna Fishgold Atiee, DVM

Texas University

VetFoam™ is a great option as it frequently results in drastically improves continence while reducing burden on the owner. Having lived with an incontinent dog myself, I can attest that dealing with constant accidents and medicating my dog changed our relationship and put stress on the entire household.



Tracy Hill, DVM

PhD, DACVIM (SAIM)

Senior Director of Ethos Scince

VetFoam is an excellent tool for managing urethral sphincter mechanism incontinence in dogs. In my practice VetFoam™ became my preferred option for youger to middle-aged dogs undergoing cystoscopy to screen for ectopic ureters.



Jonathan & Corinne

pet owners

In 2017, we noticed that our dog Manga was suffering from urinary incontinence. It was reflected in urine stains on her bed and also her fur was wet and smelled of urine. Our veterinarian referred us to an innovative treatment called VetFoam with high success rates at DVM Gilad Segev's clinic. After two days we saw a significant improvement in both her mood and urinary urgency!

BioChange



Try our
products

**We let
nature do
it's magic**

biochange.life

Info@biochange.life

VP Sales & Marketing – Hilit@biochange.life

