

INTERVENTIONAL ENDOSCOPY & ENDOUROLOGY SERIES: PART 2

This is the second of a 2-part series. Part 1 appears on page 89 of the October 2013 issue of *Clinician's Brief*.

Endourology: A New Way of Looking at Things

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Some of the most common interventional endoscopy techniques performed in veterinary medicine today involve the urinary tract.

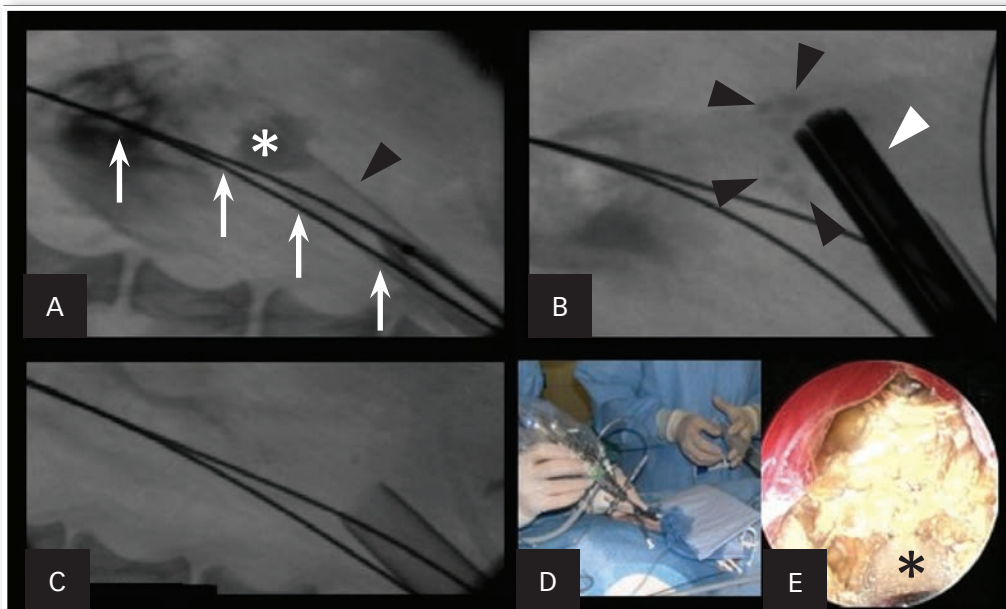
Urinary Interventions

Percutaneous Nephrolithotomy

This procedure is rarely necessary, as less than 10% of all nephroliths in dogs and cats become a clinical problem. In these patients, careful monitoring is the most appropriate course of action unless recurrent urinary tract infection, hydronephrosis,

worsening renal function, or nonpyelonephritis-associated pain or discomfort occurs. When these situations develop, traditional surgical options (eg, nephrotomy) can be met with complications and long-term morbidity. In a feline study looking at normal cats, a 10% to 20% decrease in glomerular filtration rate was noted in the kidneys that underwent nephrotomy.¹

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Percutaneous nephrolithotomy in a 3.1-kg female Yorkshire terrier with large nephroliths. Use of a percutaneous access kit under fluoroscopic guidance allows visualization of the large nephrolith (asterisk; A). The access sheath (black arrowhead) is inserted through the renal parenchyma over a dilation balloon. Two safety wires (white arrows) are present. The nephroscope (white arrowhead) is inserted through the sheath onto the stone with a lithotrite, breaking the large stone into fragments (black arrowheads; B). Fluoroscopic image after all stone fragments had been removed from the renal pelvis (C). The nephroscope being placed through the access sheath during percutaneous renal access (D). An endoscopic image of the nephrolith taken during lithotripsy (E). The lithotrite (asterisk) is seen through the working channel of the nephroscope.

In humans, less invasive methods (eg, extracorporeal shock-wave lithotripsy) have been shown to dramatically improve the preservation of renal function. Percutaneous nephrolithotomy (PCNL) can be markedly effective in removing all stone fragments in the calices. In addition, PCNL does not cause injury to the nephrons (Figure 1, previous page). Instead, the nephrons are spread apart with the use of a balloon dilation kit to allow a scope and intracorporeal lithotrite to remove the stone debris effectively. This has been shown in humans to be highly renal sparing and has been effective in the author's practice.

Ureteral Stenting

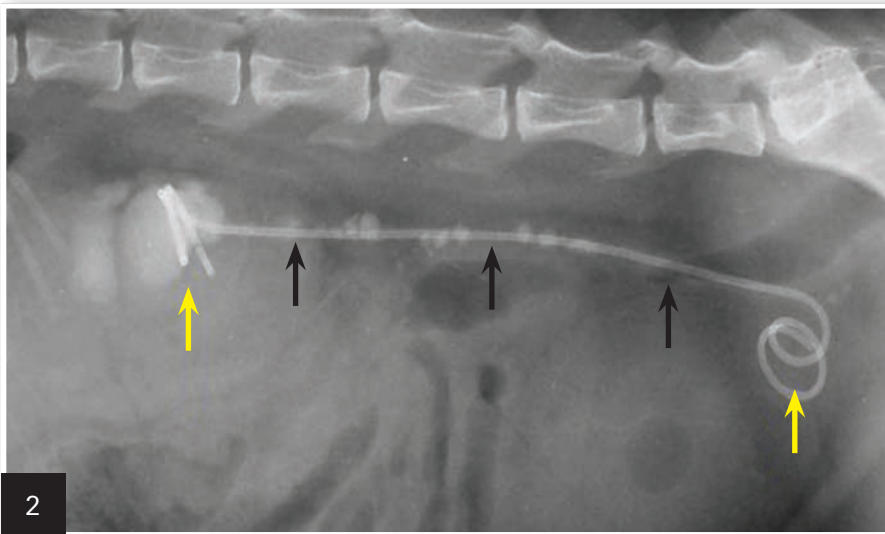
Ureteral stenting can divert urine through the ureteral lumen and into the urinary bladder, away from the renal pelvis. It can be a useful technique for treatment of a ureteral obstruction secondary to ureterolithiasis, ureteral or trigonal obstructive neoplasia, and ureteral strictures.

Passive ureteral dilation occurs after stent placement, resulting in dilation of the ureter between 4 and 8 times its normal diameter, which can improve the flow of urine, allow the passage of ureteroliths, or allow the passage of a flexible ureteroscope if necessary. In the author's practice, ureteral stents (Figure 2) have been placed in more than 300 dogs and cats, with a placement success rate exceeding 95%. It is typically performed endoscopically in dogs and surgically assisted in cats.

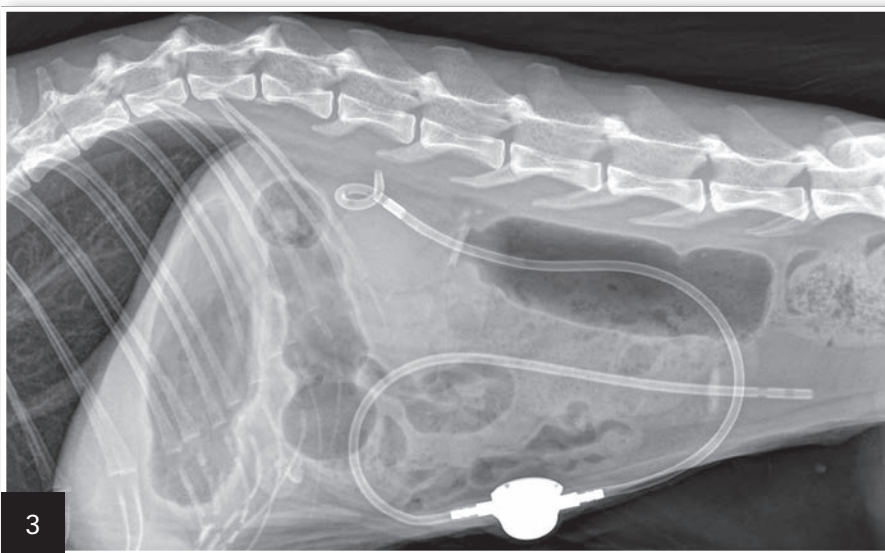
In dogs, ureteral stents are commonly associated with minimal perioperative morbidity and mortality and are a good alternative to the more invasive surgical technique. The long-term complications in cats are dysuria (5%–40%) and need for stent exchange (~20%). The irritation is likely attributable to presence of the distal pigtail of the stent that exits the ureterovesicular junction in the proximal urethra. Dysuria is uncommon after ureteral stenting in dogs. In the author's practice, ureteral stents have not been used in cats since development of the subcutaneous ureteral bypass (SUB) device.

Subcutaneous Ureteral Bypass Device

The use of SUB devices has become more common. They are typically used in feline patients with ureteral obstructions (Figure 3) and are preferred when compared with ureteral stenting in cats. An indwelling SUB device can be created using a cystostomy catheter and a combination locking-loop nephrostomy catheter. This device was modified after reports in



Lateral radiograph of a cat with a double pigtail ureteral stent (yellow arrows). The stent is placed next to the large number of ureteroliths (black arrows).



Lateral radiograph of a cat with a SUB device. The locking loop pigtail catheter connecting the subcutaneous shunting port is connected to a straight cystostomy catheter, allowing for a ureteral bypass.

PCNL = percutaneous nephrolithotomy,
SUB = subcutaneous ureteral bypass,
YAG = yttrium-aluminum-garnet

human medicine described a nephrostomy tube that could remain indwelling for longer periods.

The device has a subcutaneous shunting port that can be sampled and flushed as needed. In humans, a similar device has been shown to reduce complications associated with externalized nephrostomy tubes and improve quality of life.² SUB devices have been placed in more than 150 feline and canine patients in the author's practice with favorable results and are now the preferred treatment for feline ureteral obstructions. In dogs, the device is reserved for when stent placement fails. The perioperative complication rate associated with SUB devices has declined with the development of a commercially available device (<10%).

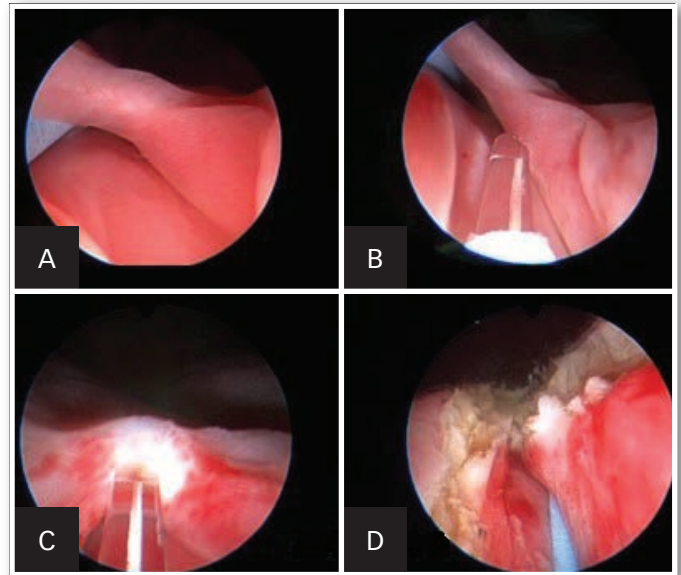
Cystoscopic-Guided Laser Ablation of Ectopic Ureters

In dogs, ectopic ureters are a common congenital anatomic deformity. The ureteral orifice is positioned distal to the bladder trigone within the uterus, vestibule, or vagina. More than 95% of ectopic ureters in affected dogs transverse intramurally and are candidates for the procedure. A laser is used to cut the intramural ectopic tunnel in this endoscopic procedure (Figure 4).

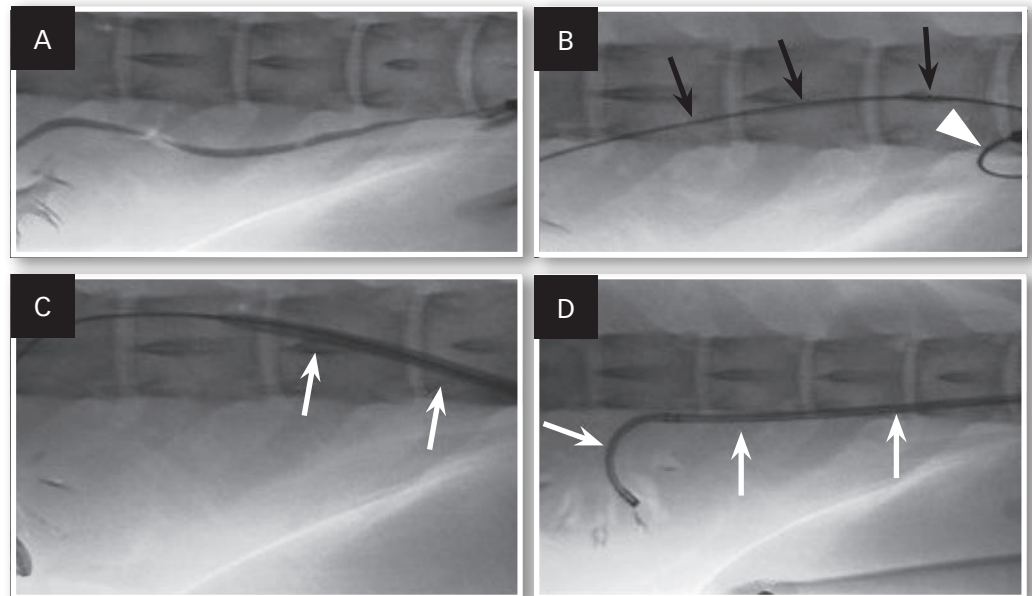
In the author's practice, more than 80 dogs (male and female) have successfully undergone endoscopic repair of ectopic ureters. This procedure is performed in conjunction with cystoscopy, fluoroscopy, and a diode or holmium: yttrium-aluminum-garnet (YAG) laser. This outpatient procedure is completed at the time of cystoscopic diagnosis of ectopic ureter, reducing the number of anesthesia events. A recent prospective study in the veterinary literature has shown promising results.³

Ureteroscopy
This procedure is possible in dogs that weigh more than 15 kg. It is mainly performed for the evaluation of idiopathic renal hematuria. Ureteroscopy can be difficult to perform

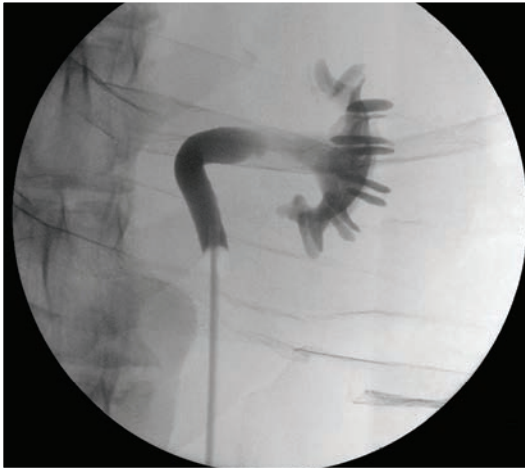
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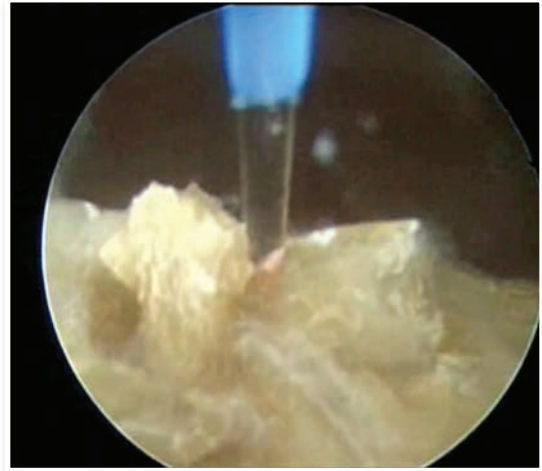
4 Endoscopic images during cystoscopic-guided laser ablation in a female dog with an intramural ectopic ureter. Guide wire in the ureteral lumen caudal to the trigone of the bladder (A). Laser fiber through the working channel of the endoscope before laser ablation (B). Laser fiber cutting the medial ureteral wall within the urethral lumen (C). The neoureteral orifice after cystoscopic-guided laser ablation (D).



5 Fluoroscopic images during retrograde ureteronephrosopy in a female dog. A rigid endoscope is placed in the urinary bladder (A). A catheter is advanced into the distal ureteral lumen for a retrograde ureteropyelogram. A guide wire (black arrows) is advanced through the ureter and into the renal pelvis, and an open-ended ureteral catheter (white arrowhead) is advanced over the wire (B). A ureteral dilation catheter (arrows) is advanced over the guide wire to ensure endoscopic passage (C). A flexible endoscope (arrows) is passed through the ureter and into the renal pelvis using fluoroscopic and endoscopic guidance (D).



6 Retrograde ureteropyelogram during sclerotherapy in a female dog with idiopathic renal hematuria in dorsal recumbency during cystoscopy and fluoroscopy.



7 Endoscopic image of a calcium oxalate stone in a female dog during laser lithotripsy.

through a normal ureteral orifice, as the ureteral opening in a normal dog is less than 2 mm and the smallest ureteroscope is approximately 2.7 mm. Ureteral access is obtained using cystoscopic visualization with fluoroscopy (Figure 5, previous page). Preplacement of a ureteral stent may allow the ureter to dilate enough for the ureteroscope to be passed more easily.

Essential (idiopathic) renal hematuria can occur when a focal area of bleeding occurs in the upper urinary tract. This can result in iron deficiency anemia (long-term), chronic hematuria, and clot formation or calculi formed because of clots, which can cause ureteral colic or signs of lower urinary tract disease.

In humans, angiomas, hemangiomas, and vascular malformations have been noted on ureteroscopy. These abnormalities can be cauterized using the ureteroscope. This procedure has been performed in a small number of dogs in the author's practice.

A more applicable procedure for essential renal hematuria is sclerotherapy for topical ureteral infusions (Figure 6). This has been performed in veterinary medicine and is most useful when the ureter is too small to allow ureteroscopic access.⁴

The procedure is performed with cystoscopic and fluoroscopic guidance in which a cauterizing sclerosing agent is carefully infused into the renal pelvis to stop the bleeding. The success rate is over 75%, and the procedure avoids the need for ureteronephrectomy. Between 25% and 33% of dogs will have bilateral

benign renal bleeding with this condition, so nephrectomy should be avoided when possible.

Laser Lithotripsy

This technique involves fragmentation of uroliths intracorporeally, which can be monitored with a flexible or rigid ureteroscope or cystoscope. The holmium:YAG laser has coagulation and cutting properties and causes fragmentation of the stones on contact. The energy, which is focused on the surface of the urolith, is directed using the cystoscope. The process is effective for cystic, ureteral, and urethral calculi of all types (Figure 7) and during PCNL when necessary for problematic nephroliths.

Percutaneous Cystolithotomy

Percutaneous cystolithotomy uses a rigid and flexible cystoscope and stone retrieval basket to remove stones from the bladder and urethra of male and female cats and dogs. The procedure is performed through a small incision in the abdomen at the level of the bladder apex. A small sheath is then advanced into the bladder lumen to allow for antegrade cystoscopy and stone retrieval with the stone basket. This fast, effective technique is typically performed outpatient and does not require laparoscopy (Figure 8).

Urethral Stenting for Malignant Obstructions

Malignant obstructions of the urethra can cause dysuria, marked discomfort, and azotemia. Approximately 10% of patients with transitional carcinoma of the prostate and/or

urethra have complete obstruction of the urinary tract, and more than 80% have dysuria. Radiation therapy and chemotherapy have been effective in slowing tumor growth, but a complete cure is rare. More aggressive therapy is indicated in cases of obstruction.

Some studies have described the use of transurethral resections, placement of cystostomy tubes, surgical diversionary procedures, and urethral laser procedures. These techniques rarely hold long-term promise, and cost is often a factor. In addition, many are associated with negative outcomes because of the need for manual urine drainage, increased morbidity, urinary frequency, and infection.

A reliable and safe alternative to establish urethral patency is placement of a self-expanding metallic stent by a transurethral approach with fluoroscopy (Figure 9). This outpatient

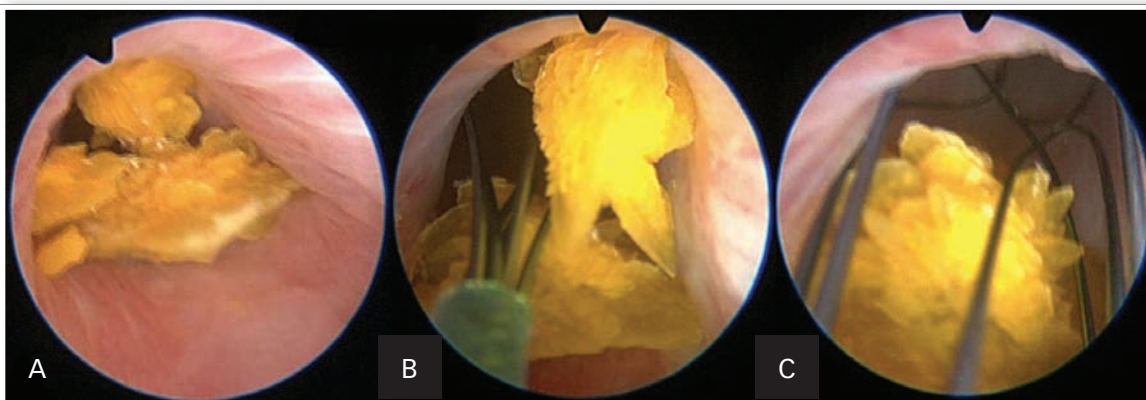
procedure is associated with good-to-excellent palliative outcomes in more than 95% of cases. It has been successful in both dogs and cats; however, approximately 25% of patients will exhibit some urinary incontinence after stent placement.

Urethral stenting has also been useful in patients with benign urethral strictures, granulomatous or proliferative urethritis, or reflex dyssynergia when traditional therapies have failed.

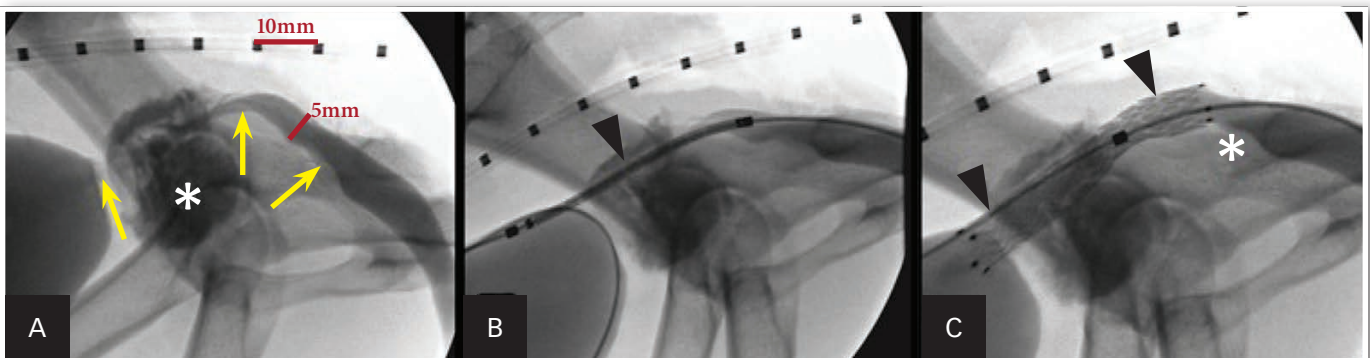
Transurethral Submucosal Bulking Agent Implantation

Transurethral submucosal bulking agent implantation using urethroscopy is indicated in patients with urethral sphincter mechanism incompetence if medical management has failed, is not tolerated, or is contraindicated. The procedure has a good overall success rate (>80%), but the average rate of maintaining urinary continence following this procedure has been shown to be 68% at 17 months, with potential indication for reinjections

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8 Endoscopic images of a dog with numerous calcium oxalate bladder and urethral stones during percutaneous cystolithotomy. Embedded stones within the urethral lumen (A). Stone basket entrapping the stones (B). Stone basket removing the stones (C).



9 Fluoroscopic images of a male dog during urethral stent placement for obstructive prostatic carcinoma (asterisk; A). Retrograde cystourethrography shows the obstructive lesion (arrows). A marker catheter is used to measure the urethral lumen diameter for stent sizing. A constrained urethral stent (arrowhead; B) is placed over a guide wire prior to deployment across the obstructive tumor. The deployed urethral stent (arrowheads; C) shows patency of the urethral lumen. There is still some tumor caudal to the stent (asterisk).

necessary thereafter.⁵ Varying materials have been used with variable success. Owners should be informed that this process can be cost-prohibitive and the benefits can be short-lived.

Looking Forward

Intraarterial Stem Cell Delivery for Chronic Kidney Disease

The use of autologous mesenchymal stem cells for the treatment of feline chronic kidney disease (CKD) is being investigated. At the author's practice, a fully funded, randomized, placebo-controlled study investigating the use of stem cells in feline patients with International Renal Interest Society (IRIS) stage 3 CKD that compares delivery of these cells intravenously and intraarterially to that of a placebo is currently underway.

This study will follow the patients for 3 years and assess systemic signs; blood pressure; glomerular filtration rate; and serum chemistry, ultrasonographic, and radiographic parameters. The same parameters will also be investigated in canine patients with glomerulonephritis/protein-losing nephropathy.

To date, with more than 75 intraarterial treatments having been performed in more than 30 patients, the procedure appears safe.

Intraarterial delivery involves placement of a catheter into the renal artery under fluoroscopic guidance via the femoral or carotid artery. This bypasses systemic circulation of the stem cells to ensure delivery directly into the renal capillary bed and allows higher engraftment rates, which have been shown in various animal models. To date, with more than 75 intraarterial treatments having been performed in more than 30 patients, the procedure appears safe. Efficacy is being investigated, but the results are promising.

Conclusion

Interventional endoscopy provides new alternatives to the treatment of certain conditions that are traditionally difficult to manage and can be considered when minimally invasive palliation is desired or other alternatives are not considered ideal. More treatments using these, or similar, noninvasive, image-guided therapies continue to become available for veterinary patients. ■ **cb**

See **Aids & Resources**, back page, for references & suggested reading.

CKD = chronic kidney disease

TRIFEXIS®

(spinosad + milbemycin oxime)

Chewable Tablets

Before using TRIFEXIS chewable tablets, please consult the product insert, a summary of which follows:

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Indications:

TRIFEXIS is indicated for the prevention of heartworm disease (*Dirofilaria immitis*). TRIFEXIS kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*), and the treatment and control of adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis* and *Toxascaris leonina*) and adult whipworm (*Trichuris vulpis*) infections in dogs and puppies 8 weeks of age or older and 5 pounds of body weight or greater.

Contraindications:

There are no known contraindications to the use of TRIFEXIS Chewable Tablets.

Warnings:

Not for human use. Keep this and all drugs out of the reach of children.

Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with spinosad alone, one of the components of TRIFEXIS Chewable Tablets (see **ADVERSE REACTIONS**).

Precautions:

Treatment with fewer than 3 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention (see **EFFECTIVENESS**).

Prior to administration of TRIFEXIS, dogs should be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with an adulticide to remove adult heartworms. TRIFEXIS is not effective against adult heartworms. While the number of circulating microfilariae may decrease following treatment, TRIFEXIS is not indicated for microfilariae clearance. Mild, transient hypersensitivity reactions manifested as labored respiration, vomiting, salivation and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Use with caution in breeding females. The safe use of TRIFEXIS in breeding males has not been evaluated. Use with caution in dogs with pre-existing epilepsy. Puppies less than 14 weeks of age may experience a higher rate of vomiting.

Adverse Reactions:

In a well-controlled US field study, which included a total of 352 dogs (176 treated with TRIFEXIS chewable tablets and 176 treated with an active control), no serious adverse reactions were attributed to administration of TRIFEXIS chewable tablets. All reactions were regarded as mild.

In some cases, dogs vomited after receiving TRIFEXIS. To ensure heartworm prevention, observe your dog for one hour after administration. If vomiting occurs within an hour of administration, redose with another full dose.

Reactions that occurred at an incidence >2% (average monthly rate) within any of the 6 months of observation are presented in the following table:

Average Monthly Rate (%) of Dogs With Adverse Reactions

Adverse Reaction	TRIFEXIS Chewable Tablets ^a	Active Control Tablets ^a
Vomiting	6.13	3.08
Pruritus	4.00	4.91
Lethargy	2.63	1.54
Diarrhea	2.25	1.54

^an=176 dogs

In the US field study, one dog administered TRIFEXIS experienced a single mild seizure 2½ hours after receiving the second monthly dose. The dog remained enrolled and received four additional monthly doses after the event and completed the study without further incident.

Following concomitant extra-label use of ivermectin with spinosad alone, a component of TRIFEXIS, some dogs have experienced the following clinical signs: trembling/twitching, salivation/rooling, seizures, ataxia, mydriasis, blindness and disorientation. Spinosad alone has been shown to be safe when administered concurrently with heartworm preventatives at label directions.

In US and European field studies, no dogs experienced seizures when dosed with spinosad alone at the therapeutic dose range of 13.5-27.3 mg/lb (30-60 mg/kg), including 4 dogs with pre-existing epilepsy. Four epileptic dogs that received higher than the maximum recommended dose of 27.3 mg/lb (60 mg/kg) experienced at least one seizure within the week following the second dose of spinosad, but no seizures following the first and third doses. The cause of the seizures observed in the field studies could not be determined.

For technical assistance or to report an adverse drug reaction, call 1-888-545-5973. Additional information can be found at www.TRIFEXIS.com.

Post-Approval Experience (March 2012):

The following adverse reactions are based on post-approval adverse drug event reporting. The adverse reactions are listed in decreasing order of frequency: vomiting, depression/lethargy, pruritus, anorexia, diarrhea, trembling/shaking, ataxia, seizures, hypersalivation, and skin reddening.

Effectiveness:

Heartworm Prevention:

In a well-controlled laboratory study, TRIFEXIS was 100% effective against induced heartworm infections when administered for 3 consecutive monthly doses. Two consecutive monthly doses did not provide 100% effectiveness against heartworm infection. In another well-controlled laboratory study, a single dose of TRIFEXIS was 100% effective against induced heartworm infections. In a well-controlled six-month US field study conducted with TRIFEXIS, no dogs were positive for heartworm infection as determined by heartworm antigen testing performed at the end of the study and again three months later.

Flea Treatment and Prevention:

In a well-controlled laboratory study, TRIFEXIS demonstrated 100% effectiveness on the first day following treatment and 100% effectiveness on Day 30. In a well-controlled laboratory study, spinosad, a component of TRIFEXIS, began to kill fleas 30 minutes after administration and demonstrated 100% effectiveness within 4 hours. In field studies conducted in households with existing flea infestations of varying severity, flea reductions of 98.0% to 99.8% were observed over the course of 3 monthly treatments with spinosad alone. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus as a direct result of eliminating the fleas.

Treatment and Control of Intestinal Nematode Infections:

In well-controlled laboratory studies, TRIFEXIS was ≥ 90% effective in removing naturally and experimentally induced adult roundworm, whipworm and hookworm infections.

NADA #141-321. Approved by the FDA

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