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Contents

A FEW WORDS FROM THE EDITOR
BW Parry 4

CASE REPORTS
Bacterial endophthalmitis secondary to pyelonephritis in a cat 5
Boo G, Whittaker C, Caruso K, Smith J

Disseminated intravascular coagulation following stereotactic radiotherapy of a nasal tumour in a Labrador retriever 12
Carey B, Malikides N, Cook E, Dill-Macky E, Morgan E

Metastatic Sertoli cell tumour in a dog treated with surgery, and metronomic cyclophosphamide and toceranib phosphate 21
Hawkes C, Thomson MJ, O’Connell K, Morgan EJ

Management of a skin wound associated with use of an electronic anti-barking collar in a dog 32
Walmsley D, Day SK, Nash K

ABSTRACTS 42

GUIDELINES FOR AUTHORS 62

The Australian Veterinary Practitioner is the official journal of the Australian Small Animal Veterinarians. The AVP is an independently refereed clinical journal, published four times per year to further the clinical and educational interests of veterinary practitioners and students throughout Australia. The AVP is abstracted by: Biological Abstracts; CAB International; Current Contents (Agriculture etc); First Move - Veterinary Librarian; Index Veterinarius; Science Citation Index; Small Animal Practice; Veterinary Bulletin; Veterinary Reference Service; VIN. Guidelines for authors can be found at https://www.ava.com.au/library-resources/library/ava-scientific-journals/contribute-to-a-journal/

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A few words from the editor

Well, not quite the start to 2022 and the Chinese Year of the Tiger that any of us had envisaged! While recent years have seen fires and pestilence (in the form of COVID), we’ve now had floods for an extraordinarily extensive stretch of the east coast, and Japanese encephalitis virus making itself felt further south than ever before. Probably not enough to convert a climate-change skeptic to a ‘true believer’, but certainly sufficient to consolidate the views of those already in the climate change camp. And to add to the world’s woes, there is a war in the Ukraine that has no justification and is causing a humanitarian crisis. It is enough to make one wonder where it will all end.

Amidst all of this doom and gloom, remember to do what you can, wherever you are. Reach out to your friends. Ask “R U OK?” There are plenty of ways to do it, but some of the best involve picking up the ‘phone or chatting over a cuppa. Take a little time for yourself and for them.

In this issue:

**Boo, Whittaker, Caruso and Smith**, from the Eye Clinic for Animals in Artarmon, describe a domestic shorthair cat that was presented to them with a 3-week history of acute vision loss. How can such a case link aqueocentesis to renal ultrasonography? It’s an interesting case, even if you don’t have an ophthalmological bent. Read about their diagnostic trip around the body on pages 5-11.

**Carey, Malikides, Cook, Dill-Macky and Morgan**, at the Animal Referral Hospital in Sinnamon Park, were referred a cryptorchid male Swiss shepherd dog with acute abdominal discomfort. Abdominal ultrasonography revealed a mid-abdominal mass. “A Sertoli cell tumour”, I hear you say! Well, yes, but what if post-operative monitoring revealed metastasis to the regional lymph nodes? What then?! How about metronomic chemotherapy? What’s that? Could it result in remission? For how long? Go to pages 21-30 to learn more.

**Walmsley, Day and Nash**, from the University of Queensland Small Animal Hospital, report on a Cavoodle bitch that was presented to them for management of an extensive and severe skin wound that resulted from the prolonged use of an electronic anti-barking shock collar. Read how they managed this rather nasty wound and the case outcome on pages 32-40 (and consider your stance on the use of these devices).

I hope that you find these articles stimulating. If you’re a general practitioner and have had an interesting case of your own, let’s share it with your colleagues. If you’re in referral practice and have a case series or study that your peers would find interesting, let’s get it in print. The current instructions to authors are printed on pages 62-63. Don’t be discouraged if you have not written a scientific paper before; drop me an email at editor.avp@ava.com.au and we shall work on it together.

Regards, Bruce

**Professor emeritus Bruce W. Parry**
Bacterial endophthalmitis secondary to pyelonephritis in a cat

Boo G,* Whittaker CJG, Caruso KA, Smith JS

Eye Clinic for Animals, 63 Herbert Street, Artarmon, NSW 2064, Australia

ABSTRACT A 9-year-old domestic shorthair cat was presented with a 3-week history of acquired bilateral heterochromia and acute vision loss. Ophthalmic examination revealed bilateral uveitis, ulcerative keratitis and ocular hypertension in the right eye. Cytology of an aqueocentesis sample was consistent with bacterial infection. Complete blood count and biochemical analysis of the blood revealed an inflammatory leukogram, mild azotaemia and increased hepatocellular enzymes. Abdominal ultrasonography revealed marked hydronephrosis of the left kidney and left ureteral dilation with hyperechoic foci. Urine culture and sensitivity revealed *Escherichia coli* cystitis. The owner elected to pursue conservative treatment. The cat regained vision in the left eye 3 weeks later and was improving clinically. Unfortunately, the cat died 3 months later.

The present case highlights the need to consider systemic diseases as major differential diagnoses for bilateral uveitis in cats. Bacteraemia can disseminate to the eye, causing endophthalmitis.

KEYWORDS bacteraemia, cat, *Escherichia coli*, endophthalmitis, pyelonephritis, uveitis

ABBREVIATIONS OD, oculus dexter (right eye); OS, oculus sinister (left eye); OU, oculus uterque (both eyes)

* Aust Vet Pract 52 (1): 5-11, 2022

CLINICAL FEATURES

A 9-year-old female spayed domestic shorthair cat was presented to the ophthalmology service with a 3-week history of bilateral acquired heterochromia. The cat had suffered acute vision loss a few days prior to presentation. The cat had lost weight in the previous 6 months, despite having a good appetite. Prior treatment by the referring veterinarian included oral amoxicillin-clavulanic acid and topical neomycin sulphate, polymixin B sulphate, prednisolone and sulfacetamide (Amacin; Jurox Pty Ltd, Rutherford, NSW).

On admission to our hospital the cat weighed 3.55 kg, was lethargic and had dull mentation. Physical examination did not reveal other abnormalities. On ophthalmic examination, the right eye (culus dexter; OD) lacked a menace response and dazzle reflex, and there was an axial superficial corneal ulcer. There was marked aqueous flare, hyphaema and hypopyon OD. There were multifocal areas of dense melanosis in the iris and posterior synechiae OD (Figure 1). There were multifocal coalescing areas of hyporeflectivity and increased pigmentation in the tapetum OD.
The intraocular pressure (TonoVet, Jorgensen Labs, Loveland, CO, USA) was 36 mmHg OD (Reference range: 10-25 mmHg).

The left eye (oculus sinister; OS) lacked a menace response but retained a good dazzle reflex.

There was diffuse hyphaema and hypopyon, precluding examination of the lens, posterior segment and fundus (Figure 2). The intraocular pressure was 7 mmHg OS.

Sonography of the left eye was performed because anterior segment pathology precluded posterior segment examination. However, it did not reveal any retinal detachments or vitreous haemorrhage. Hyphaema and hypopyon, seen on slit lamp examination, were also seen on ultrasound as hyperechogenic foci in the anterior chamber (Figure 3).

Aqueocentesis of both eyes (oculus uterque; OU) was performed under general anaesthesia, with smears and 0.15 mL of aqueous humour sent for cytological analysis. While awaiting the latter results, a single dose of 1 mg/kg methylprednisolone sodium succinate (Solu-medrol, Pfizer Australia Pty Ltd, West Ryde, NSW), was given intravenously. Topical dorzolamide...
hydrochloride 2%/timolol maleate 0.5% (Cosopt, Merck Sharp & Dohme Pty Ltd, South Granville, NSW) 8-hourly OD and chloramphenicol/polymycin B sulphate (Opticin; Troy Lab Pty Ltd, Glendenning, NSW) 8-hourly OU were commenced.

Cytology of the aqueocentesis samples revealed bacterial rods and coccobacilli. Degenerate neutrophils, some of which had coccobacilli within their cytoplasm, were also seen (Figure 4). Unfortunately, cultures could not be performed as the sample was lost.

A complete blood count showed marked leukocytosis, marked neutrophilia with a left shift, and monocytosis. Lymphopenia was also evident. Serum biochemistry analysis revealed mild azotaemia, hypokalaemia, and mild increase in hepatocellular enzymes, creatine kinase, cholesterol and triglyceride (Table 1). Urinalysis from a cystocentesis sample revealed large numbers of leukocytes, erythrocytes and bacteria (Figure 5). The urine specific gravity was 1.014.

On Day 2 of hospitalisation, blood samples were collected for aerobic and anaerobic bacteriologic cultures. Cephazolin (Cephazolin Alphapharm, Alphapharm Pty Ltd, Millers Point, NSW) 22 mg/kg every 8 hours for 3 days, was commenced.

An abdominal ultrasound revealed marked hydronephrosis in the left kidney with some sediment (Figure 6). The left ureter was dilated up to 5 mm in diameter with a small focus of mineralised material in the lumen (Figure 7). The right renal pelvis was also dilated to 5.3 mm in diameter (Figure 8). Osmotic diuresis was induced with a loading dose of 0.5 mg/kg mannitol (Osmitrol Intravenous infusion, Baxter Healthcare Pty Ltd, Old Toongabbie, NSW) given over 30 min, followed by a constant rate infusion at 1 mg/kg/min. Prazosin (APO-Prazosin, Apotex Pty Ltd, Macquarie Park, NSW, Australia) 0.25 mg, was also administered orally every 8 hr for one day. Urine culture revealed a heavy growth of *Escherichia coli* which was susceptible to ampicillin/amoxicillin, cephalexin, enrofloxacin, cefovecin, marbofloxacin, sulphna/trimethoprim and amoxicillin-clavulanic acid.

During the first 72 hours of hospitalisation, ophthalmic findings did not differ from initial presentation. The owner declined surgical treatment such as nephrectomy, ureteral stenting and subcutaneous ureteral bypass and opted to treat the cat conservatively with renal decompression. A sonography-guided percutaneous aspiration was performed under general anaesthesia, removing 15 mL of purulent fluid from the left kidney. Also at this time, tissue plasminogen activator (Actilyse, Boehringer Ingelheim Pty Ltd, North Ryde, Australia) was injected intracamerally in both eyes.

### Table 1: Serum biochemistry analysis (showing only abnormal results)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Units</th>
<th>Result</th>
<th>Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium</td>
<td>mmol/L</td>
<td>3.5</td>
<td>3.7-4.9</td>
</tr>
<tr>
<td>Urea</td>
<td>mmol/L</td>
<td>18.1</td>
<td>3.0-10.0</td>
</tr>
<tr>
<td>Creatinine</td>
<td>µmol/L</td>
<td>235</td>
<td>40-190</td>
</tr>
<tr>
<td>AST</td>
<td>U/L</td>
<td>62</td>
<td>1-60</td>
</tr>
<tr>
<td>ALT</td>
<td>U/L</td>
<td>213</td>
<td>1-80</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>U/L</td>
<td>269</td>
<td>&lt;261</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>mmol/L</td>
<td>6.5</td>
<td>2.4-5.2</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>mmol/L</td>
<td>1.7</td>
<td>0.1-0.6</td>
</tr>
</tbody>
</table>
On Day 4, the patient was discharged on the following treatment plan: weekly renal decompression; topical dorzolamide hydrochloride 2%/timolol maleate 0.5% three times a day OD, chloramphenicol/ polymycin B sulphate four times a day OU, and ofloxacin (Ocuflox eye drops, Allergan Australia Pty Ltd, Gordon, NSW) 1 drop four times a day OU; and oral amoxicillin-clavulanic acid (Amoxyclav, Dechra Veterinary Products (Australia) Pty Ltd, Somersby, 50 mg twice a day.

Aerobic and anaerobic bacteriologic cultures of the blood were negative. Scant leukocytes were seen on Gram stain of the renal fluid, but aerobic and anaerobic bacteriologic cultures of renal fluid were negative.

The cat was re-presented 17 days later. The owner reported that the cat had regained vision and was bright, alert and responsive. Ophthalmic examination revealed marked improvement in both eyes. There was reduction of aqueous flare, hyphaema and hypopyon in both eyes. The intraocular pressure OD had reduced from 36 mmHg to 9 mmHg. The left eye had regained a menace response. The axial superficial corneal ulcer OD was still present. The right eye still lacked a menace response and dazzle reflex. There were significant posterior synechia OD. There were multifocal to coalescing areas of hyporeflectivity in the tapetum OD. The intraocular pressure was 7 mmHg OS.
Another abdominal ultrasound was performed, showing a hydronephrotic left kidney, similar to the previous scan. The left ureter measured up to 5 mm in diameter and the distal portion of the left ureter had a tortuous appearance. No discrete ureteral calculus was identified. The right renal pelvis measured 2.5 mm in width. There was decreased corticomedullary distinction in the right kidney and the caudal pole was shrunken. Culture of the renal fluid collected by percutaneous aspiration and urine collected by cystocentesis yielded no bacterial growth.

The cat was discharged on the same treatment plan as previously but unfortunately did not return for follow up. The cat died suddenly 3 months after the initial presentation. A necropsy was not performed.

DISCUSSION

Uveitis, inflammation of the uveal tract of the eye, is a potentially blinding disease. The underlying causes of uveitis in cats include trauma, corneal ulceration, penetrating wounds, infections, lens-induced, neoplastic or idiopathic.\(^1,2\) The most common causes of feline uveitis include *Toxoplasma gondii*, feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), feline infectious peritonitis virus (FIP), *Bartonella henselae*, cryptococcosis and idiopathic causes.\(^2,3\) Independent of the underlying aetiology, aqueous flare, hypopyon, hyphaema, miosis, iritis, keratic precipitates and chorioretinitis are manifestations of uveitis.\(^1,2\) Posterior synechiae, cataract formation, retinal degeneration, retinal detachment and glaucoma are common sequelae to uveitis.\(^1\)

Underlying systemic diseases ought to be ruled out to direct specific therapy to the aetiology. Thorough history, physical examination and a minimum database (complete blood count, serum biochemistry and urinalysis) are essential. Outdoor cats should also be tested for *Toxoplasma gondii*, FIV and FeLV.

Bacterial endophthalmitis is uncommonly reported in veterinary medicine and includes two cases in cats,\(^4,5\) two cases in dogs,\(^6,7\) and five cases in horses.\(^8,10\) The pathogenesis of bacterial endophthalmitis involves initial intraocular bacterial penetration with subsequent dissemination to the posterior segment of the eye. Bacterial proliferation then triggers aggressive intraocular inflammatory responses.\(^11\) Host inflammatory processes (e.g. breakdown of blood-ocular barriers, complement production, cytokine elaboration, and leukocyte chemotaxis) and bacterial virulence factors (e.g. lipopolysaccharide and secretory toxins) contribute to the rapid and dramatic damage to the intraocular tissues.\(^12\)

Aqueous humour cytology is often poorly diagnostic in cases of non-neoplastic anterior uveitis.\(^13,14\) In one paper, the aqueous humour of 27 of 39 cats with anterior uveitis did not have neoplasia as the cause, and 4 of those 27 aqueous samples were predominated by neutrophilic inflammation.\(^13\) Only two out of the latter 4 cases were found to have septic foci in other parts of the body. In another study, a definitive cause for anterior uveitis was not found by cytologic assessment of aqueous humour alone.\(^14\) When the results of all diagnostic tests were considered, the cause of anterior uveitis was not found in 60% of the feline cases.\(^14\)

In the present report, the finding of phagocytosis of coccobacilli in the aqueous humour was diagnostic for bacterial endophthalmitis. In the absence of a penetrating corneal injury, it prompted further investigation, with aerobic and anaerobic cultures of the blood and renal fluid. Therefore, aqueocentesis was an extremely useful diagnostic tool that was employed early in the diagnostic process and guided our therapeutic options.
The findings of leukocytosis, due to neutrophilia with left shift, was consistent with a marked systemic inflammatory response. The findings of azotaemia, poorly concentrated urine and large numbers of *E. coli* in the urine sample and severe hydronephrosis were supportive of a diagnosis of pyelonephritis. All these findings, coupled with the findings of bacterial endophthalmitis, were strongly suggestive of bacteraemia, even though blood culture and renal fluid culture results were negative. In 292 cats presented with signs of sepsis in a retrospective study, only 23% of the blood cultures were positive. The most frequently isolated bacteria were Enterobacteriaceae, obligate anaerobic species, *Staphylococcus* species and *Streptococcus* species. In another study, *E. coli* was isolated in one-third of the animals. The lack of a positive result could be explained by the fact that shedding of bacteria into the bloodstream is usually intermittent, even in the most serious septicaemias. Furthermore, the number of organisms/mL of blood is usually low. In human studies, it has been demonstrated that the volume of blood taken for blood culture is the most important factor in determining the sensitivity of blood culture. Thus, the limited amount of blood that can be taken from a cat may have reduced the chance of a positive blood culture in the present case. In addition, the prior use of oral antibiotics may have resulted in a false-negative result for both blood and renal fluid cultures. In a study in rats, the detection rate of *E. coli* bacteraemia was reduced from 100% to 0% at 25 and 55 min after *E. coli* challenge, when intravenous antibiotics were administered concurrently. Polymerase chain reaction tests afford a significantly higher detection rate than blood culture at clinically significant antibiotic levels, and could be a useful adjunctive tool in diagnosing bacteraemia.

In humans, endogenous bacterial enophthalmitis is rare, but *E. coli* is one of the more commonly isolated Gram-negative organisms in blood culture, with many patients having an extraocular focus of infection. In feline studies, *E. coli* was found to be one of the most common Gram-negative isolate in cats with occult lower urinary tract infections. Risk factors significantly associated with increased odds of urinary tract infections were urinary incontinence, transurethral procedures, urogenital surgery, gastrointestinal disease, decreased body weight and decreased urine specific gravity. Renal disease and lower urinary tract anatomic abnormalities also contributed to urinary tract infections. In the present case, the cat had a 6-month history of weight loss. Risk factors, such as diabetes, were excluded. Unfortunately, testing for FIV and FeLV infections was declined by the owner. Therefore, they cannot be ruled out as a predisposing cause.

In the present case, the corneal ulcer in the right eye may have been sustained due to trauma or may have been an incidental finding. Ulcers can cause reflex iridocyclitis, however, this is unlikely to have been the situation in the present case, because there was endophthalmitis rather than anterior uveitis. In addition, the unilateral nature of the corneal ulceration does not correlate with the bilateral presentation of endophthalmitis.

**CONCLUSION**

The treatment plan in the present case was aimed at treating the suspected underlying cause, namely the ureterolith, pyelonephritis and cystitis, and the resultant bacteraemia and bacterial endophthalmitis. The cat showed a positive response to medical management of the ureterolith. Repeat ultrasound failed to show the presence of a mineralised calculus seen on the first ultrasound. The cat also responded to
systemic antibiotics, as urine culture results were negative post-antibiotic therapy, and she regained vision in her left eye.

The case illustrates the importance of ruling out systemic causes of uveitis and the potential usefulness of aqueocentesis as a diagnostic tool.

A limitation of the present report is the lack of culture results of the aqueous humour. A positive culture of the same isolate as the bacteriuria would have been more conclusive.

Nevertheless, to the authors’ knowledge, the present case is the first to describe ureterolithiasis, pyelonephritis, and cystitis due to *E. coli*, together with bacterial endophthalmitis in a cat.

**CONFLICTS OF INTEREST**

No conflicts of interest are declared.

**REFERENCES**

Disseminated intravascular coagulation following stereotactic radiotherapy of a nasal tumour in a Labrador retriever

Carey BL,* Malikides N, Cook EK, Dill-Macky E, Morgan E

Animal Referral Hospital, 532 Seventeen Mile Rocks Road, Sinnamon Park, QLD 4073, Australia

ABSTRACT A 10-year-old, male, castrated Labrador retriever was presented to the Animal Referral Hospital for evaluation of a sinonasal mass causing facial deformity. Computed tomography (CT) and histopathological evaluation identified the presence of a large, primarily unilateral, sinonasal malignant neoplasm (suspected carcinoma), extending past the cribriform plate. The dog underwent a course of stereotactic radiotherapy (SRT), three fractions totalling 24 Gray (Gy) over three days. One month later, the dog was re-presented with epistaxis. A coagulation profile identified disseminated intravascular coagulation (DIC). A repeat CT showed significant remission of the sinonasal mass. Despite medical treatment, the DIC persisted for 17 days, at which time the dog collapsed, suffered a respiratory arrest and was humanely euthanised (44 days after SRT).

The present case report documents that DIC may occur following SRT, and clinicians should be mindful of this possibility.

KEYWORDS disseminated intravascular coagulation, dog, nasal tumour, stereotactic radiotherapy

ABBREVIATIONS aPTT, activated partial thromboplastin time; CBC, complete blood (cell) count; CT, computed tomography; DIC, disseminated intravascular coagulation; Gy, Gray; HCT, haematocrit; PCV, packed cell volume; PT, prothrombin time; SRT, stereotactic radiotherapy; TPP, total plasma protein concentration; TT thrombin time

Aust Vet Pract 52 (1): 12-20, 2022

The availability of stereotactic radiotherapy (SRT) in veterinary practice has increased over the past ten years.1 Stereotactic radiotherapy uses collimators that are highly conformal, allowing accurate doses to be administered to specific areas, including structures with differing shapes. This high conformity allows administration of high fractional doses with a rapid dose drop-off, thus reducing the dose to adjacent normal tissues and minimising acute and late radiation effects.1,2

In the past six years, there have been three studies describing the use of SRT for canine sinonasal tumours.3-5 Two other studies have investigated the use of stereotactic radiosurgery.6,7 Several mild, acute (weeks to months), as well as multiple late-term (months to years) adverse effects were noted following therapy.3,7

Investigations into SRT collimation have shown variation in radiation treatment protocols and contouring.8 These inconsistencies mean that both the total radiation dose received and the total area of tissue targeted could vary from case to case, making prediction of an individual animal’s
response difficult. It is therefore plausible that other adverse effects could occur following SRT. For example, changes in coagulation parameters (specifically D-dimers) have been observed in humans following both partial and total body radiation.9

The present report describes the use of SRT in a dog with a sinonasal mass (suspected carcinoma), that subsequently developed DIC.

**CASE REPORT**

**Day 0**

A 10-year-old male, castrated Labrador retriever was presented to the referring veterinarian for blepharitis and purulent ocular discharge. A mass was visible overlying the frontal sinus. A complete blood count (CBC), performed at an external laboratory, was within reference limits. The haematocrit (HCT), total plasma protein concentration (TPP), neutrophil count and platelet count are shown in Table 1. The dog had been seen four months earlier because of signs of sneezing and epistaxis.

**Day 6**

The dog was referred to our hospital. Physical examination identified a 4 x 3 cm, raised protrusion overlying the frontal sinus and left submandibular lymphadenomegaly. Thick, serosanguinous fluid was observed draining from the right nostril. Full body computed tomography (CT) identified an invasive, predominately left-sided, nasal soft-tissue mass (Figure 1A) extending into the right nasal cavity, left frontal sinus, left retrobulbar tissue and left calvarium through the cribiform plate, with rostral left frontal lobe white matter oedema (modified Adams stage 4).10 Left lateral mandibular and left retropharyngeal lymphadenomegaly (2.57 cm in height) were also noted. The thorax and abdomen were within acceptable limits.

Fine needle aspirates of the mass were performed. A specialist pathologist identified severe neutrophilic to mixed inflammation and malignant neoplasia. The neoplasm was suspected to be a carcinoma, as there were rafts of cells with variably defined cell borders, negligible blue-grey cytoplasm, and round to ovoid nuclei with stippled chromatin and mildly conspicuous multiple nucleoli. Histopathological diagnosis was not pursued as the physical examination, imaging findings and cytology were strongly supportive of an intranasal carcinoma. In addition, the dog’s owner was extremely concerned and elected to immediately proceed with radiation therapy. Treatment with amoxicillin/clavulanic acid (Amoxyclav, Dechra Veterinary Products, Somersby, NSW, Australia; 14 mg/kg orally every 12 hr) and prednisolone (Pred-X 20, Dechra Veterinary Products; 0.55 mg/kg orally every 24 hr) was commenced for an indefinite period.

**Days 18-20**

The dog underwent a course of SRT (via volumetric modulated arc therapy) targeting the nasal cavity and frontal sinus, and the left cervical lymph nodes. A radiation oncologist was consulted for radiation planning and approval, and SRT was performed off-site at a human facility. A gross tumour volume of 199.8 cm³ (nasal cavity) and 16.8 cm³ (lymph nodes) was calculated. This resulted in a planning target volume of 249.5 cm³ for the nasal cavity and 33.3 cm³ for the cervical lymph nodes. The dog received one 8 Gray (Gy) fraction daily for three days in a row, representing a total dose of 24 Gy.

The same anaesthetic protocol was used for each fraction. The dog received dexamethasone (Dexapent, Troy Laboratories, Glendenning, NSW; 0.05 mg/kg intravenously) and butorphanol (Butorgesic, Troy Laboratories; 0.1 mg/kg intravenously) prior to induction with propofol (Propofol-Lipuro, Braun Australia, Bella Vista, NSW; 3.3 mg/kg intravenously). A size 12 cuffed endotracheal tube was used, and the dog was maintained on oxygen
and isoflurane. The dog was positioned in ventral recumbency. Each anaesthetic lasted approximately 15 minutes and there were no reported adverse events. The dog was hospitalised overnight following the first and second fractions and was discharged home a few hours after receiving the third fraction. While in hospital, there were no seizures observed and a normal appetite was maintained. Upon discharge, amoxicillin/clavulanic acid and prednisolone were continued at the same dose. The owner was instructed to feed soft food, avoid bathing the dog and monitor for seizure activity.

The major organs at risk from the SRT were the eyes, lenses and brain. Each lens had a mean exposure of approximately 4 Gy and each eye had a mean exposure of approximately 8 Gy. The Gy exposure to the brain varied due to the presence of cribriform penetration. The exposure ranged from 24.6 Gy adjacent to the cribriform plate to 2.9 at the more distal (normal) aspects of the brain. Overall, the brain had a mean exposure of 9.8 Gy.

**Day 39**

The dog was returned for a scheduled recheck. The owner reported that there had been no nasal discharge and the lump between the dog’s eyes had resolved. These findings were confirmed on physical examination. A mild pyrexia (39.3 °C) was noted, but no other abnormalities were found. No blood tests were performed, and the dog was scheduled for another recheck in two weeks.

Figure 1. Computed tomography of the nasal mass. (A) Day 6, before, and (B) Day 50, after stereotactic radiation therapy.
Day 47 (approximately one month after finishing SRT)

The dog was presented for right-sided epistaxis. It was reported that the dog had otherwise been clinically well. On examination, vital signs were within normal limits, but a blood clot in the right nare and mucohaemorrhagic discharge from the left nare were found. Clinical pathology showed a moderate anaemia and hypoproteinaemia, a mild neutrophilia with no left shift and a moderate thrombocytopenia. A biochemical panel was unremarkable. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were unreadably high (Table 1). Consequently, there was concern that the dog may have developed DIC.

The dog was given an intravenous transfusion of fresh frozen plasma (Caniplas, Plasvacc, Rigby, QLD; 400 ml). He was also started on intravenous fluids (Plasmalyte, Baxter Healthcare, Old Toongabbie, NSW; 3 ml/kg/hr for seven days), tranexamic acid (Xgen Pharmaceuticals, Horseheads, NY, USA; 20 mg/kg intravenously every 8 hr for two days), vitamin K1 (Koagulon, International Animal Health Products, Blacktown, NSW; 2.5 mg/kg subcutaneously every 12 hr for five days), amoxycillin/clavulanic acid (14 mg/kg orally every 12 hr for seven days), prednisolone (0.4 mg/kg orally every 24 hr for seven days) and maropitant (Cerenia, Zoetis, Rhodes, NSW; 1 mg/kg intravenously every 24 hr for seven days). Overnight the PCV decreased to 0.17 L/L, and 450 ml whole blood was collected (Terumo single blood bag CPDA-1) from a DEA 1.1 positive in-hospital donor and immediately administered intravenously over four hours. The dog’s PCV increased to 0.24 L/L a few hours post-transfusion. After this treatment, epistaxis ceased, but bilateral mucopurulent nasal discharge, bilateral periorbital alopecia and mucopurulent ocular discharge were noted.

Day 48

In-hospital PT and aPTT were still markedly prolonged (Table 1).

Day 49

PCV and TPP were improved, but in-hospital PT and aPTT were still markedly prolonged (Table 1).

Day 50

The dog developed signs of lethargy, anorexia and increased respiratory effort. PCV was stable and TPP was within reference limits. Blood was submitted to an external laboratory for a CBC and coagulation profile. Salient results were a mild reduction in HCT and a mild neutrophilia. Platelets were clumped but appeared to be reduced on blood smear. The PT and aPTT were within reference limits, however, the thrombin time (TT) was prolonged, and there was hypofibrinogenaemia (Table 1). The normalisation of the PT and aPTT was considered to reflect differences in methodologies for the tests (also reflected by the differences in their reference values) and the variable results that are possible in an animal with ongoing DIC.

Thoracic radiographs showed a bronchointerstitial pulmonary pattern with a dorsocaudal distribution. Abdominal ultrasound identified two thrombi in the portal vein. A repeat CT of the head, thorax and abdomen showed only a small amount of residual soft tissue within the nasal cavity, mild reduction in height of the left retropharyngeal lymph node (2.57 cm to 2.4 cm) and unchanged osteolysis and frontal lobe involvement (Figure 1B) compared to the original CT on Day 6. There were multifocal peripheral pulmonary alveolar/interstitial lesions. The portal venous thrombus was confirmed, and an infarct was noted in the left kidney. The diagnostic and clinical findings therefore indicated concurrent pulmonary, portal and renal thromboembolic disease as well as pulmonary haemorrhage.
Although fibrin/fibrinogen degradation products and D-dimer concentrations were not measured, the clinical findings and laboratory results (Table 1), and the combination of overt haemorrhage (hypocoagulability) and thrombus formation (hypercoagulability), were considered strongly supportive of a diagnosis of DIC. To reduce platelet aggregation, clopidogrel (Plavix, Sanofi-Aventis, Macquarie Park, NSW; 2.2 mg/kg orally every 24 hr) was commenced.

**Day 51**
The dog appeared brighter and was eating well, although the increased respiratory effort continued. In-hospital clinicopathological results demonstrated ongoing coagulopathy and a slight reduction in PCV (Table 1).

**Day 52**
The dog was hyporexic and the PCV decreased throughout the day from 0.22 L/L to 0.18 L/L. A transfusion of packed red blood cells (300ml, compatible crossmatch) was administered. Monitoring of PCV and TPP was performed, and the PCV increased to 0.30 L/L a few hours after the transfusion.

**Day 53**
The dog’s respiratory effort and appetite had improved. The PCV had decreased slightly, and there were marked increases of in-hospital PT and aPTT. Blood was submitted for a CBC and coagulation panel. This showed a moderate neutrophilia, clumped platelets, although they appeared reduced on blood smear, an prolonged PT, normal aPTT and prolonged TT (Table 1). Clopidogrel was consequently discontinued, due to the subjective reduction in platelet numbers. Thoracic radiographs were repeated to investigate an ongoing, mildly increased respiratory effort. A dorsocaudal alveolar pulmonary pattern was noted, which was not considered to be significant.

**Day 54 (seven days after presentation)**
The dog’s PCV remained at 0.27 L/L and an in-hospital platelet count was approximately $60 \times 10^9/L$. The dog’s demeanour and respiration were considered sufficiently stable to warrant discharge from hospital, and treatment with amoxycillin/clavulanic acid and prednisolone was continued.

**Days 56-57**
The dog was rechecked daily and was reported to be bright and eating well at home. The owner expressed no concerns. On Day 56, PCV was slightly reduced to 0.25 L/L, but remained stable on Day 57 at 0.26 L/L. There was ongoing thrombocytopenia and increasing neutrophilia (Table 1). Schistocytosis, acanthocytosis and target cells were noted on smears. A coagulation panel, submitted on Day 57, showed that PT, aPTT and TT were significantly increased, and fibrinogen was undetectable.

**Day 59 (five days after discharge)**
The dog was presented to our emergency service for hypoxemia and epistaxis. The dog had developed mild pyrexia (39.3°C). There was ventral abdominal petechiation and bruising of the penis. The anaemia had stabilised, while schistocytosis, neutrophilia and thrombocytopenia remained present. Changes consistent with infarcts in both renal cortices were identified on abdominal ultrasonography. The portal thrombus also remained visible. Thoracic radiographs showed improvement in the bronchointerstitial and alveolar pulmonary patterns compared to previous radiographs (on Day 53).

**Day 60**
Coagulation times remained significantly prolonged, and fibrinogen remained below the limit of detection (Table 1).
Day 61

The dog’s PCV decreased overnight from 0.24 L/L to 0.21 L/L and the TPP was now 50 g/L (compared to 63 g/L on Day 60). Transfusions with fresh frozen plasma (Caniplas, Plasvacc; 200 ml) and whole blood from a compatible crossmatch in-hospital donor (Terumo single blood bag CPDA-1) were administered intravenously. The PCV was only 0.23 L/L following the blood transfusion and there was ongoing epistaxis. As a result, both transfusions were repeated within 12 hr.

Day 62

The dog’s pyrexia had increased to 40.2 °C. Peripheral limb oedema developed. Haematology showed continued anaemia with schistocytosis, neutrophilia and clumped platelets. The PT, aPTT and TT were prolonged, but less so than on Day 60 (Table 1).

Day 63

The pyrexia persisted. The anaemia was similar to Day 62, but the hypoproteinaemia was worsening. A coagulation panel showed PT was slightly prolonged, but aPTT could not be measured. The laboratory noted that the reason for this was unclear but was not due to a prolonged result.

Day 64 (five days following the second presentation)

The anaemia and thrombocytopenia had worsened. Mean blood pressure decreased from 78 mmHg to 54 mmHg. The dog collapsed, suffered a respiratory arrest and was humanely euthanised. No necropsy was performed.

DISCUSSION

Traditional fractionated radiotherapy (daily fractions over a 3-4 week period) has previously been considered the standard of care for canine nonlymphomatous neoplasms, due to improved median survival times compared with chemotherapy and/or surgery. However, the development of new technology has allowed for more targeted radiation. The use of SRT, for canine sinonasal neoplasia, has been shown to provide a median survival time ranging from 8.5-19.3 months, which is similar to that of fractionated radiation (10.4-19.1 months), but with fewer anaesthetic sessions required and no increase in adverse side effects. As a result, SRT is becoming more widely accepted as a treatment option for these neoplasms.

Nevertheless, when using both methods of radiotherapy for sinonasal neoplasms, numerous adverse events have been noted that are not directly related to the effect on the tumour. When using SRT, mild and acute (weeks to month) toxicities have included mucositis, alopecia, and ocular toxicities, while late-term (months to years) side effects have included leukotrichia, cataracts, alopecia, chronic rhinosinusitis, seizures, oronasal fistulae, nasocutaneous fistulae, osteonecrosis and fungal rhinitis. Finally, both venous thrombosis and DIC have been reported in dogs following radiation therapy. It is important to note that, in general, these studies were retrospective case series in which the prevalence of potential adverse outcomes following SRT were determined, and that no causal relationships or statistical associations were established.

There are many conditions that can result in DIC. The most common causes in dogs are neoplasia, sepsis and systemic inflammation. Other conditions that have preceded and possibly triggered the development of DIC include burns, vasculitis, shock and partial and whole-body radiation.
Research in humans has shown that partial body radiation can alter proteins and activate the coagulation cascade, inducing changes in haemostasis.\textsuperscript{17,18} It is plausible, therefore, that the SRT may have promoted the pathophysiological conditions and inflammatory cascade that led to the development of DIC. This is supported by evidence showing continued radiation-induced alteration in protein profiles up to a month following treatment.\textsuperscript{18} The mechanism by which radiation can activate the coagulation cascade and potentially result in progression to DIC is unknown, although there are multiple hypotheses. These include the production of free radicals and reactive oxygen species or the initiation of inflammation and resultant release of cytokines (e.g. tissue factor).\textsuperscript{9,19}

Following irradiation, there is evidence of monocyte activation and neutrophil margination, indications of an acute inflammatory response.\textsuperscript{20} It is suspected that this inflammatory response is due to radiation-induced apoptotic cells rather than due to irradiation itself.\textsuperscript{20} Additionally, if there is failure to remove these apoptotic cells (which can occur when there are large numbers of dying cells in a short timeframe), they can progress to necrotic cells, which is another well-known initiator of an inflammatory response.\textsuperscript{20} However, as supported by emerging evidence in the human literature, even partial radiation has been shown to induce changes in protein profiles and cause upregulation of the inflammatory cascade.\textsuperscript{17,18}

This could then lead to the initiation of DIC. It is possible that, in addition to radiation effects, the destruction of the tumour itself might have also increased cell apoptosis and resultant necrotic tissue, thus triggering a local inflammatory response and activation of the coagulation cascade.\textsuperscript{19,20} It has been shown that radiation-induced inflammation can persist for months,\textsuperscript{19} which might explain the delayed onset of DIC in the present case.

Solid nasal tumours \textit{per se} have been linked to the development of DIC in dogs.\textsuperscript{21} Furthermore, a human study has shown that neoplasia often leads to activation of coagulation, with the prevalence of DIC in patients with solid tumours at approximately 7%.\textsuperscript{22} Although it is not possible to determine precisely when DIC developed in the present case, there were no overt indications of DIC, before SRT. The dog had a normal CBC and an absence of thrombi on the whole-body CT scan on Day 6. Additionally, the repeat CT (following radiation) showed only a small amount of residual soft tissue in the nasal cavity. The extra-axial lesion in the frontal lobe remained unchanged. These findings suggested that neoplasia per se was unlikely to be involved with the events that precipitated DIC, as the tumour bulk was significantly reduced. However, even though the dog was apparently well on Day 39, there was a mild pyrexia present. It is possible that a coagulopathy may have been present as a ‘low-grade’ disorder prior to re-presentation with epistaxis on Day 47. Therefore, neoplasia cannot be completely excluded as a concurrent, or even primary, cause of DIC in the present case.

Other less common triggers of DIC were reasonably excluded as follows. Firstly, there was no evidence of systemic inflammation. This was supported by the repeat CT, which was performed on Day 50, three days after DIC was first diagnosed. There was no evidence of inflammation at the site of the nasal tumour or elsewhere in the body (e.g. pancreatitis, effusions). Additionally, there was no evidence of a neutrophilic left-shift until Day 56, suggesting an absence of an inflammatory stimulus at the initial diagnosis of DIC on Day 47. A diagnosis of sepsis was considered unlikely, as the dog was clinically well at the time of presentation and was not hypoglycaemic, hyperthermic or hypothermic. Furthermore, there was no obvious source of infection. As of Day 47, there had been no nasal discharge noted at home. Lastly an intravenous catheter was last used approximately a month prior to the dog's presentation with signs of DIC.
In conclusion, while neoplasia per se may have played a role in the development of DIC in the present case, SRT cannot be ruled out as a contributing factor. The resultant tumour debulking and remission, the induction of changes in protein profiles and upregulation of the inflammatory and coagulation cascades may mechanistically explain the initiation of DIC.

While SRT is an important component in the management of sinonasal neoplasia, veterinary practitioners should be aware that DIC may be a potential complication. The present case highlights the importance of closely monitoring animals after SRT, particularly as early diagnosis of DIC may lead to improved prognosis and reduced costs of treatment.

ACKNOWLEDGEMENTS

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest related to the publication of this paper.

REFERENCES


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Table 1: Summary of clinicopathological results and blood products administered

aPTT activated partial thromboplastin time, CNR could not read (no result obtained, unclear reasons), FFP fresh frozen plasma, HCT haematocrit, PCV packed cell volume, PT prothrombin time, TT thrombin time, TPP total plasma protein, WB whole blood
Metastatic Sertoli cell tumour in a dog treated with surgery, and metronomic cyclophosphamide and toceranib phosphate

Hawkes CIK,* Thomson MJ, O’Connell K, Morgan EJ

Animal Referral Hospital, 532 Seventeen Mile Rocks Road, Sinnamon Park, QLD 4073, Australia

ABSTRACT A 4-year-old cryptorchid male Swiss shepherd dog was presented to a referral hospital with acute onset of restlessness and abdominal discomfort. Abdominal ultrasonography revealed a 5.61-cm x 7.23-cm hypoechoic mid-abdominal mass, suspected to be a neoplastic abdominal left testis. The dog underwent a coeliotomy with orchiectomy and a histopathological diagnosis of a Sertoli cell tumour (SCT) was made. Post-operative monitoring and cytological interpretation revealed metastasis to the left lumbar aortic lymph node 96 days later. The dog was commenced on metronomic cyclophosphamide and toceranib phosphate. Six months later the dog underwent lymphadenectomy of the affected lymph node. Disease recurrence was reported three months post-lymphadenectomy. The dog displayed intermittent, progressive disease and developed thrombocytopenia 17 months after diagnosis of metastatic disease. Despite cessation of chemotherapy, he developed neutropenia, thrombocytopenia and non-regenerative anaemia, consistent with myelotoxicosis, and was euthanized 23 months after initial diagnosis.

The incidence of metastatic SCT is low in dogs, and there are currently no defined criteria for optimal treatment. This is the first report, to the authors’ knowledge, of a metastatic SCT treated with metronomic cyclophosphamide and toceranib phosphate in the palliative setting.

KEYWORDS dog, metastatic Sertoli cell tumour, metronomic chemotherapy

ABBREVIATIONS CBC, complete blood count; CT, computed tomography; LLALN, left lumbar aortic lymph node; MTD, maximally tolerated dose; PDGFR, platelet derived growth factor receptor; RR, reference range; SCT, Sertoli cell tumour; Tregs, Regulatory T cells; VEGFR2, vascular endothelial growth factor receptor; VCOG-CTCAE, Veterinary Cooperative Oncology Group - common terminology criteria for adverse events.

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Sertoli cell tumours (SCT) represent between 8-16% of testicular tumours in dogs, with an incidence of metastasis of less than 15%. One of the greatest risk factors for development of SCT is cryptorchidism. SCT may be associated with hyperoestrogenism and affected dogs can display clinical signs such as symmetrical flank alopecia, hyperpigmentation and feminization. Dogs with SCT displaying feminization demonstrate significantly higher serum estradiol concentrations than those without SCT or those with SCT but without signs of feminization. Feminization is also more common in dogs with an abdominal or an inguinal neoplastic testis, as opposed to a scrotal one.

Treatment for SCT generally involves bilateral orchiectomy and ongoing monitoring for signs of feminization or bone marrow hypoplasia, which could indicate metastatic disease or oestrogen toxicity. There is very little published veterinary literature regarding treatment of metastatic SCT, thus defined criteria for management, and the benefit of adjuvant therapy is unknown. Two cases of dogs with metastatic SCT treated with cisplatin have been described, with survival times of 7 months and > 31 months.

Metronomic chemotherapy is defined as continuous (daily) oral administration of low dose, minimally toxic chemotherapy. Unlike traditional maximally tolerated dose chemotherapy (MTD), where rapidly dividing cells are the target, vascular endothelial cells that support tumour growth have become one of the important targets of metronomic chemotherapy. Inhibition of pro-angiogenic factors, such as vascular endothelial growth factor receptor (VEGFR2), platelet derived growth factor receptor (PDGFR), and modulation of the immune response via regulatory T cell (Tregs) inhibition are key theoretical goals of metronomic chemotherapy.

The present report describes a dog with SCT that developed lymph node metastasis and was treated with lymphadenectomy, and metronomic cyclophosphamide and toceranib phosphate. The dog had an overall survival time of 23 months and metastatic disease was managed for 20 months.

**CLINICAL FEATURES**

A 4-year-old, cryptorchid male Swiss shepherd dog presented to the Animal Referral Hospital, Sinnamon Park, for assessment following acute onset of restlessness, non-productive retching and straining to defecate. On physical examination the right testis was palpable and subjectively atrophied within the scrotum, however, the left testis was not palpable within the scrotum or inguinal region. A right lateral abdominal radiograph revealed a soft tissue opacity in the ventral mid-abdomen resulting in dorsal displacement of the bladder. A complete blood (cell) count (CBC) and serum biochemistry panel were performed. Abnormalities were a mild leukocytosis (23.0 x 10^9/L [reference range (RR) 5.1-16.8 x 10^9/L]) characterized by a mature neutrophilia (19.7 x 10^9/L [RR 3.0-11.6 x 10^9/L]) and monocytosis (1.4 x 10^9/L [RR 0.2-1.1 x 10^9/L]).

A midline coeliotomy was performed by a board-certified surgical oncologist and a large mid-abdominal mass was visualized and identified as the left testis. The spermatic cord was strangulated and testicular
torsion was present. An untorsed segment was identified and ligated. No further intra-abdominal abnormalities were noted on thorough examination. The free fluid observed by ultrasonography was not apparent during surgery. The para-aortic lymph nodes appeared macroscopically normal, but sampling was not performed. The right testis was removed via a pre-scrotal approach and modified open-castration technique. The patient made an uneventful recovery from anaesthesia and was discharged two days post-operatively. The surgery sites healed without complication.

A board-certified anatomical pathologist reported the histopathology and described tubular structures and confluent sheets consisting of pleomorphic round to spindloid cells, occasionally palisading around tubular margins. These cells contained medium to large, frequently hyperchromatic, nuclei and scant to ample, sometimes lightly vacuolated, eosinophilic cytoplasm. There were < 5 mitotic figures per 10 high power (400x) fields and neoplastic cells were confined to within the testicular capsule. The histopathological interpretation was intratesticular SCT (Figure 1).

Three months post-surgery the dog was presented for re-examination after developing generalized mild alopecia. Blood was collected for a CBC, serum biochemistry panel and total thyroxine concentration. All the latter results were unremarkable. Repeat abdominal ultrasonography revealed two discrete, enlarged and hypoechoic, left lumbar aortic lymph nodes (LLALN), measuring 1.82 cm x 3.19 cm and 2.48 cm x 2.46 cm. Fine-needle aspirates of the LLALN were performed. Cytology was interpreted by a board-certified clinical pathologist. There were rafts of ovoid to polygonal cells, with moderate anisocytosis and anisokaryosis. Some individual cells displayed a central round nucleus, one-to-two prominent nucleoli, coarsely stippled chromatin, and a small-to-moderate amount of light blue cytoplasm, often containing discrete clear vacuoles indicative of lipid. The cytological interpretation was a malignant neoplasm consistent with metastatic SCT (Figure 2).

It was recommended that the dog undergo lymphadenectomy, followed by adjuvant chemotherapy; either MTD or metronomic cyclophosphamide and toceranib phosphate. The owners elected to try neoadjuvant metronomic chemotherapy and assess the response.

Twelve days later (3.5 months post-surgery) the dog was commenced on 150 mg (2.71 mg/kg) toceranib phosphate (Palladia, Zoetis Australia Pty Ltd, Rhodes, NSW) orally on Monday, Wednesday and Friday, and 20 mg (13.7 mg/m²) cyclophosphamide (Cyclophosphamide, Bova Compounding, Caringbah, NSW) orally on Tuesday, Thursday, Saturday and Sunday. Furosemide (0.72 mg/kg; Lasix, Sanofi-Aventis Australia Pty Ltd, Macquarie Park, NSW) was administered orally with cyclophosphamide to reduce the risk of sterile haemorrhagic cystitis.

Figure 1
Histopathology image of intratesticular Sertoli cell tumour. Hematoxylin and eosin stain, 40 x magnification.
A CBC was performed 10 days after commencing metronomic chemotherapy, which revealed a mild neutropenia (2.7 x 10^9/L [RR 3.0-11.6 x 10^9/L]). The latter neutropenia is classified as grade one, according to the Veterinary Cooperative Oncology Group - common terminology criteria for adverse events (VCOG-CTCAE). The dog was clinically well, with no clinically obvious side effects of the chemotherapy at this time.

Over the subsequent 6 months, the dog was monitored monthly by clinical examination, haematology and urinalysis (and sometimes serum biochemistry). The CBC at each presentation were within reference limits. The neutropenia noted 10 days after commencing treatment had resolved two weeks later. An abdominal ultrasound examination was performed every 8 weeks; and intermittently progressive lymphadenopathy was reported. Lymphadenectomy was regularly discussed with the owners.

Nine months post-surgery, the dog was still clinically well and the LLALN measured 4.95 cm x 5.76 cm and 2.33 cm x 3.91 cm, with a third hypoechoic LLALN in the chain measuring 1.25 cm x 3.02 cm.

At 9.5 months post-surgery (6 months after initiating chemotherapy), the dog underwent a full body computed tomography scan (CT) followed by lymphadenectomy. The CT revealed marked lumbar aortic lymphadenomegaly with heterogenous contrast enhancement (Figure 3). A midline coeliotomy was performed by a board-certified surgical oncologist and an incision was made in the caudo-dorsal peritoneum to allow entry into the retroperitoneal space. Blunt dissection around the capsule of each enlarged lymph node was performed and three lymph nodes were subsequently removed. No other gross abnormalities were appreciated or reported within the abdomen or retroperitoneal space. The abdomen was closed routinely, and the patient recovered well and was discharged the following day. Histopathology of the lymph nodes was interpreted by a board-certified anatomical pathologist and confirmed metastatic SCT. The same cyclophosphamide and toceranib phosphate protocol was recommenced, 14 days post-lymphadenectomy.

Four weeks after lymphadenectomy, the dog was clinically well, although losing weight.
A CBC was within reference limits and no abnormalities were detected on abdominal ultrasonography, indicating clinical remission. The dose of toceranib phosphate was reduced to 130 mg (2.45 mg/kg) orally on Monday, Wednesday and Friday, because of the post-surgical weight loss.

Two months after lymphadenectomy, the dog was presented for pelvic limb lameness, which the owner mentioned had occurred twice previously. Orthopaedic examination revealed 2/5 lameness in the left pelvic limb, with no appreciable joint swelling or pain elicited on palpation. Treatment with toceranib phosphate was temporarily discontinued, because lameness is a known adverse effect of toceranib. The lameness rapidly resolved and toceranib phosphate was recommenced one week later.

Three months after lymphadenectomy, the dog developed generalized alopecia and reduction in coat quality. A CBC and urinalysis were within reference limits. Abdominal ultrasound revealed multiple hypoechoic LLALN; two adjacent to the aorta measuring 0.81 cm x 1.59 cm and 0.42 cm x 0.64 cm, and two intermuscular nodules in the ventrolateral inguinal region. Fine needle aspiration biopsies of the intermuscular nodules were performed. Smears were stained with Diff-Quik and examined by a medical oncologist at 400x magnification. Cytology revealed a population of neuroendocrine appearing cells, with vacuolated cytoplasm, marked anisokaryosis and multiple prominent nucleoli. This was consistent with metastatic SCT and progressive disease. The recommendation was made to the owners to consider surgery or adjunctive palliative radiation therapy, however, due to financial constraints and the guarded prognosis, they opted to continue with the current protocol.

Four weeks later (4 months after lymphadenectomy), the dog’s body weight had increased and the dose of toceranib phosphate was increased to 150 mg (2.62 mg/kg). The dog continued to be monitored closely for the next 5 months and retained an excellent quality of life as assessed by the owners and the attending clinicians.

At 9.5 months after lymphadenectomy, a further progression in the size of the metastatic LLALN was detected on ultrasonography (now 2.50 cm x 3.20 cm, 1.11 cm x 2.46 cm and 2.49 cm x 2.72 cm). Eight weeks later (11.5 months after lymphadenectomy), in-house CBC revealed thrombocytopenia (51 x 10^9/L [RR 148-484 x 10^9/L]). However, platelet clumps were evident on a blood smear and the number

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**Figure 3**

Post-contrast CT images of dorsal (A) and sagittal (B) planes with a soft tissue window. There is marked enlargement of the lumbar aortic lymph nodes (white arrows), with heterogenous contrast enhancement, consistent with tumour metastasis.
of platelets was assessed as appropriate to continue chemotherapy. The dog’s LLALN had increased substantially in size in this period (the largest of which now measured 4.59 cm x 6.80 cm). Treatment options were discussed with the owners at length; surgery and radiation therapy were declined, and the goals of care remained as palliation and slowing the progression of disease.

Four weeks later (12.5 months after lymphadenectomy), the dog was presented for pollakiuria. Urinalysis revealed trace proteinuria and 3+ haematuria on dipstick examination. The dog was treated with 25.4 mg/kg cephalexin orally, twice daily, for 5 days (Cephalexin, Apex Laboratories Pty Ltd, Somersby, NSW) pending results of urine culture. The latter revealed a moderate growth of *Haemophilus haemoglobinophilus*. The pollakiuria improved following antimicrobial therapy.

In the following 10 weeks, the dog had several further episodes of haematuria, which were not investigated. Potential causes of the haematuria included recurrent urinary tract infection or haematuria secondary to thrombocytopenia.

At the time of the above pollakiuria, the largest LLALN now measured 5.89 cm x 8.97 cm. An in-house CBC revealed a marked thrombocytopenia (14 x 10⁹/L [RR 148-484 x 10⁹/L]), however, moderate numbers of clumps and macroplatelets were present on examination of blood smear. It was decided to replace cyclophosphamide with chlorambucil in the treatment protocol and to closely monitor the platelet count. Chlorambucil (Leukeran, Aspen Pharmacare Australia Pty Ltd, St Leonards, NSW) was given orally at a dose rate of 3.92 mg/m² on Tuesday, Thursday, Saturday and Sunday.

Ten weeks later (15 months after lymphadenectomy; 22 months after initial surgery), the dog was lethargic, had developed multiple episodes of haematuria, and had developed bilateral elbow pressure sores. The dog had a grade one neutropenia according to VCOG-CTCAE (1.7 x 10⁹/L [RR 3.0-11.6 x 10⁹/L]) and grade four thrombocytopenia (2 x 10⁹/L [148-484 x 10⁹/L]) and was started on 16.6 mg/kg amoxicillin clavulanic acid (Curam Duo Forte; Sandoz Pty Ltd, Macquarie Park, NSW) orally twice a day. Metronomic chemotherapy was discontinued.

At 22.5 months after initial surgery, the dog had a grade one non-regenerative anaemia (haematocrit 0.30 L/L [RR 0.37-0.55 L/L]) and a grade three neutropenia (0.8 x 10⁹/L [RR 3.0-11.6 x 10⁹/L]). This haematocrit decreased to 0.20 L/L over the next two weeks, by which time the dog had become lethargic and had developed intermittent haematuria. The haematological findings were considered consistent with bone marrow suppression.

At this time, 23 months after initial surgery (20 months after the detection of metastatic disease), the owners were offered and declined further surgery, palliative radiation therapy and MTD chemotherapy. They decided that the dog’s quality of life had deteriorated to a point where they requested euthanasia for their pet.

**DISCUSSION**

Sertoli cell tumours are rare in humans, accounting for 0.4-1.5% of testicular tumours with a metastatic rate of 10-20%. The most frequently reported sites of metastasis are the retroperitoneal para-aortic lymph nodes, lungs and bones. When metastatic disease is present in human patients, the prognosis is guarded, with a reported median survival time of 20 months. In humans, the risk factors for metastatic spread of SCT include patient age, tumour diameter, extension into the spermatic cord, presence of necrosis, a high mitotic index and angiolymphatic invasion. Treatment most commonly involves...
Case Report

orchiectomy with or without retroperitoneal lymphadenectomy, if lymphatic invasion is suspected or metastatic disease is confirmed. No specific adjuvant therapy is considered standard of care at this time, leading to challenges with decision making in these patients. Radiation of metastasis has been reported in 13 cases; 12 of which subsequently developed progressive disease. Reported chemotherapy agents used in the treatment of human SCT include cisplatin, vinblastine, bleomycin, etopside, doxorubicin and cyclophosphamide.

In contrast, SCT are the third most common tumour of canine testes, representing 8-16% of tumours and with an incidence of metastasis of <15%. Cryptorchidism is considered a major risk factor for the development of SCT in dogs <10 years of age, with reports of up to 68% of SCT deriving from an inguinal or abdominal testis. Some of the prognostic factors applied to human SCT that are associated with an increased likelihood of metastasis were present in the histopathology report of the tumour of the present case, for example, the presence of necrosis and the large size of the tumour. However, there was a lack of angiolymphatic invasion or extension into the spermatic cord. Hence direct extrapolation from the human literature may not be appropriate and more research needs to be conducted regarding indicators of metastasis of canine SCT.

There are few reports in the veterinary literature regarding treatment options for dogs with metastatic SCT. The use of MTD, using cisplatin, was reported in two dogs. The first underwent surgical resection of a mass associated with the serosa of the left kidney, which was histopathologically diagnosed as a metastatic SCT. The latter dog received 60 mg/m² adjuvant cisplatin every three weeks for five treatments and was still alive at 31 months, with no ultrasonographic or radiographic evidence of recurrence or metastasis. The second dog had gross hepatic and splenic metastases and received two doses of 60 mg/m² cisplatin at a three-week interval, following a splenectomy and liver biopsies. Chemotherapy was then discontinued, and the dog died 7 months after the first dose of cisplatin.

Angiogenesis is regarded as a hallmark of cancer and is fundamental for ongoing tumour progression. The vascular endothelial cells divide at considerably lower rates than the associated neoplastic cells, and so are poorly affected by standard chemotherapy. Furthermore, whilst tumour cells are genetically unstable and have a high mitotic rate, allowing them to develop resistance to chemotherapeutic agents, this would not be anticipated for endothelial cells. Mouse xenograft models have demonstrated how cyclophosphamide, used at doses approximately one-third of the MTD, could be antiangiogenic; and by inducing apoptosis of endothelial cells, apoptosis of cyclophosphamide resistant tumour cells would follow.

Metronomic cyclophosphamide has an immunomodulatory action through inhibition of Tregs. Tregs play a role in inhibiting the anti-tumour response of the immune system. A once daily oral dose of metronomic cyclophosphamide (15 mg/m²) was demonstrated to reduce tumour blood vessel density and the absolute numbers and percent of circulating Tregs within grades one and two soft tissue sarcomas in dogs.

The present case was switched from metronomic cyclophosphamide to metronomic chlorambucil. Metronomic chlorambucil has been demonstrated to inhibit migration of vascular endothelial precursors as well as vasculogenesis. Chlorambucil has also been shown to be well tolerated in dogs and have antitumour effects when used against a variety of neoplasms in a metronomic fashion (4 mg/m² daily).
Toceranib phosphate is an inhibitor of multiple tyrosine kinase receptors found on the surface of tumour cells and blood vessels; including VEGFR2, PDGFR and Kit.\textsuperscript{10,19} VEGF and VEGFR2 are important for tumour angiogenesis via promotion of endothelial cell survival.\textsuperscript{19} One study showed that plasma VEGF concentrations, which can be considered a surrogate biomarker of VEGFR2 inhibition, were significantly increased in dogs treated with 2.4-2.75 mg/kg toceranib phosphate every second day.\textsuperscript{10} As such, toceranib phosphate has been investigated for its efficacy against a number of neoplasms.\textsuperscript{20}

The present case was treated with oral toceranib phosphate at 2.71 mg/kg on Monday, Wednesday and Friday. He experienced three episodes of left pelvic limb lameness, which resolved with a brief withdrawal of toceranib phosphate. Muscle pain, resulting in lameness of varying degree, has been reported in dogs treated with 2.5-2.75 mg/kg toceranib phosphate every other day.\textsuperscript{10} All of the latter cases of lameness resolved with analgesia, rest, or reduction of the drug dose. The weight loss observed in our patient may have been secondary to toceranib phosphate-induced, or post-surgical, inappetence.

Combination toceranib phosphate and metronomic cyclophosphamide has been demonstrated to be well tolerated in dogs diagnosed with various neoplasms. Toceranib phosphate has been shown to selectively reduce circulating Tregs, and addition of metronomic cyclophosphamide can help maintain this response and have further immunomodulatory effects by triggering release of interferon gamma.\textsuperscript{21}

The dog in the present report had no gross evidence of metastatic disease at the time of initial surgery, but was later diagnosed with metastases to LLALN via fine needle aspiration biopsy. He was displaying clinical signs associated with hyperoestrogenism at this time, namely generalized alopecia. Oestrogen myelotoxicosis can occur in dogs with SCT, even after castration, and is typically an indicator of metastasis and carries a grave prognosis.\textsuperscript{22} In contrast, a recent study evaluating outcomes of seven dogs with bone marrow suppression secondary to SCT found a more favourable outcome, with 4/7 dogs alive 12 months after surgery. It is worth noting that none of the latter dogs had evidence of metastatic disease, and all were treated with surgical excision of the primary tumour alone.\textsuperscript{23}

The pancytopenia that eventually occurred in the present case was likely caused by myelotoxicity, either due to hyperoestrogenism, or less likely chemotherapeutic agents. Differentiation of these causes would have required measurement of serum estradiol concentration, which was not performed.

Many studies have evaluated the haematological toxicity of long-term metronomic cyclophosphamide use in dogs, and neutropenia and thrombocytopenia were
not reported features of such use.\textsuperscript{11,24-26} One theory for the lack of thrombocytopenia is the platelet sparing effect of cyclophosphamide.\textsuperscript{27} Chlorambucil has also not demonstrated significant myelosuppression when used in a metronomic fashion, with only one report of a dog displaying anaemia, thrombocytopenia and neutropenia after 20 months of continuous treatment. These dyscrasias resolved after cessation of chlorambucil.\textsuperscript{18}

Any haematological toxicity of toceranib phosphate is usually low grade, with grade one neutropenia and anaemia more common than grade two (using the VCOG-CTCAE grading system) and thrombocytopenia being rare and grade one if present.\textsuperscript{10} Furthermore, when neutropenia was observed it often occurred in the initial weeks of therapy, before resolving. The latter was the situation in the present case. In those dogs whose neutropenia did not resolve, it did not worsen with continued treatment.\textsuperscript{10}

The LLALN drain the lymph vessels of the testes. They are a series of small (1-2 mm) nodes which lack a consistent pattern of organization. They are poorly defined from the surrounding adnexa and adipose tissue and so can be very difficult to identify during exploratory laparotomy or by ultrasonography. This likely explains the recurrence of lymphadenomegaly (caused by metastases to the lymph nodes) after the initial lymphadenectomies. There also appeared to be metastasis to muscles of the hind limb.

There is a paucity of published information regarding treatment of metastatic SCT. This leads to challenges in clinical practice; including selection of the most effective treatment, how to slow the progression of disease and how to manage the owner’s expectations. Metastatic SCT is often a terminal condition in human patients; with the majority developing progressive disease despite surgery, chemotherapy and radiation therapy.\textsuperscript{15} In the present case, metronomic cyclophosphamide and toceranib phosphate was offered as a palliative treatment option in the face of metastatic disease, to attempt to slow the progression of the disease through their combined antiangiogenic and immunomodulatory mechanisms of action. Further investigations are necessary regarding VEGF expression, microvessel density, and the role Tregs may play in canine SCT.

**CONCLUSION**

Metastatic SCT are rare in dogs and there is no current standard of care for management of this disease. There are many limitations when interpreting case reports, not least the lack of a control population. In the present case, the dog lived for 23 months from the initiation of treatment (20 months with grossly evident metastatic disease), and the owner repeatedly reported that their pet’s quality of life was excellent until shortly before elective euthanasia. This outcome was comparable to other reported cases of canine SCT which received MTD chemotherapy with cisplatin. Detection of bone marrow suppression occurred only in the last three months of life and the associated clinical signs were ultimately the reason for euthanasia.

Metronomic chemotherapy is being used with increasing frequency in veterinary medicine and provides the opportunity to improve the prognosis of animals with naturally occurring cancer.

The present report demonstrates that surgery, combined with metronomic cyclophosphamide and toceranib phosphate therapy, are a palliative treatment option for metastatic canine SCT.

**ACKNOWLEDGEMENTS**

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CONFLICTS OF INTEREST
The authors declare no potential conflicts of interest.

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Management of a skin wound associated with use of an electronic anti-barking collar in a dog

Walmsley DW,* Day SK, Nash KJ

UQ Vets Small Animal Hospital, University of Queensland, Gatton, QLD 4343, Australia

ABSTRACT A 3-year-old entire female Cavoodle was presented for wounds on the ventral neck region following prolonged application of an electronic anti-barking shock collar (EABSC). It was concluded likely that pressure from prolonged device-tissue contact time, in combination with shear forces, resulted in local inflammation, tissue damage, and superficial infection. Staging and management were guided by the National Pressure Injury Advisors Panel clinical practice recommendations. The injury was classified as a Stage II pressure injury, characterised by partial-thickness skin loss with exposed dermis. Conservative management was therefore deemed a suitable treatment strategy. Microbial culture yielded growth of *Staphylococcus pseudintermedius* and *Acidovorax temperans*.

Treatment abided by the principles of moist wound healing, with management adjusted for each phase of wound healing. Complete secondary intention wound healing was achieved by Day 18, with a satisfactory clinical and cosmetic outcome.

To the authors’ knowledge, this is the first case report describing management of a pressure injury associated with the use of an EABSC in a dog.

The welfare implications of EABSC are discussed.

KEYWORDS animal welfare, electronic anti-barking shock collar, pressure injury

ABBREVIATIONS EABSC, electronic anti-barking shock collar; ECMA, Electronic Collar Manufacturers Association; NPIAP, National Pressure Injury Advisors Panel

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into electronic collar use by the Companion Animal Welfare Council concluded that sound arguments are available both for and against the use of EABSC, however, the investigation also found there was inadequate evidence to reach strong conclusions about their safety and efficacy.⁷ Recent studies, specifically evaluating electronic collars, including EABSC, demonstrated inferior or equivalent efficacy when compared with other training methods.⁶⁻⁹ All three of the latter studies found that electronic collars negatively impacted animal welfare. Additional reported negative consequences of electronic collars include alterations in physiologic parameters, undesired behavioural responses, and signs of stress, fear and pain.⁴⁻⁷ Despite these findings, proponents of EABSC maintain that they can be utilised successfully for behavioural modification without negative welfare implications when used appropriately.¹⁰

Physical injury associated with the use of EABSC has been reported. Pressure necrosis of tissue in direct contact with or adjacent to the dermal electrodes of the EABSC has been reported and is suspected to be a result of local inflammation and tissue necrosis from prolonged device-tissue contact.¹¹⁻¹² Manufacturer guidelines recommend time-limited use of EABSC for this reason.¹² Despite this, there are several anecdotal reports of pressure necrosis associated with EABSC.¹² To the authors’ knowledge, pressure injury associated with the use of EABSC, with subsequent moist dermatitis and infection and its corresponding management is yet to be described in detail in the literature. The latter is the subject of the present report.

CASE DESCRIPTION

History and Examination

A 3-year-old entire female Cavoodle (weighing 4 kg) was presented to the university veterinary teaching hospital for assessment of wounds on the ventral cervical region. According to the owner, an EABSC had been applied to the animal approximately 14 days prior, while the dog was under the care of the owners’ friends. Upon returning into the owners’ possession, wounds emitting a pungent odour were noted on the ventral cervical region under the EABSC. The owners were informed that the EABSC had remained in place for the duration of their departure. Previously, the EABSC had been used only sporadically. The EABSC was removed and discarded, and the dog was transported immediately for veterinary assessment.

Upon presentation, the patient was bright and haemodynamically stable. Physical examination revealed a moist, erythematous and malodourous wound on the ventral neck (Figure 1A). Venous blood gas measurements, packed cell volume, and total protein were within reference limits. Abdominal and thoracic focused assessment with sonography for trauma were unremarkable.

Management

The patient was heavily sedated with medetomidine hydrochloride (7.5 μg/kg, Illium, Troy Animal Healthcare Pty Ltd, Glendenning, NSW) and methadone (0.1 mg/kg; Illium, Troy Animal Healthcare Pty Ltd) intramuscularly and the ventral aspect of the cervical region was clipped. An approximately 8 x 15 cm dirty, highly exudative (purulent), erythematous, partial thickness abrasive wound, extending along the midline from the caudal aspect of the mandibular rami to just caudal to the larynx was apparent (Figure 1A). An approximately 2 x 1.7 cm dirty, mildly exudative, erythematous partial thickness puncture wound, with exposed dermis, was identified just lateral to the larynx on the right side. The position of this puncture wound was consistent with the likely location of an EABSC electrode (Figures 1A and 2). A swab of the exudative material at the surface of the wounds was submitted for aerobic and anaerobic microbial culture and sensitivity.
Figure 1 Digital images demonstrating the progression of wound healing by secondary intention healing from presentation (Day 0) to complete wound closure (Day 18). White arrow (1A) depicts the likely site of one of the device’s electrodes. Abbreviations: m, morning; e, evening.
<table>
<thead>
<tr>
<th>Day</th>
<th>Phase of healing</th>
<th>Wound size</th>
<th>Wound characteristics</th>
<th>Primary contact layer</th>
<th>Systemic treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Inflammatory</td>
<td>15 cm x 8 cm</td>
<td>Highly exudative (purulent)</td>
<td>Silver sulfadiazine&lt;sup&gt;a&lt;/sup&gt;, Allevyn&lt;sup&gt;b&lt;/sup&gt;</td>
<td>IVFT, Methadone IV TID, Amoxi/Clav IV BID</td>
</tr>
<tr>
<td>1m</td>
<td>Inflammatory</td>
<td>15 cm x 8 cm</td>
<td>Highly exudative (purulent), superficial tissue sloughing</td>
<td>Allevyn</td>
<td>IVFT, Methadone IV TID, Amoxi/Clav IV BID, Meloxicam SC SID</td>
</tr>
<tr>
<td>1e</td>
<td>Inflammatory</td>
<td>15 cm x 8 cm</td>
<td>Moderately exudative (purulent), superficial tissue sloughing, angiogenesis</td>
<td>Allevyn</td>
<td>IVFT, Methadone IV TID, Amoxi/Clav IV BID, Meloxicam SC SID</td>
</tr>
<tr>
<td>2m</td>
<td>Inflammatory/ Proliferation</td>
<td>14 cm x 7 cm</td>
<td>Mildly exudative (serosanguinous), angiogenesis, granulation tissue formation, epithelialisation apparent</td>
<td>Honey&lt;sup&gt;d&lt;/sup&gt;, Cutilin&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Methadone IV BID, Amoxi/Clav PO BID, Meloxicam PO SID</td>
</tr>
<tr>
<td>2e</td>
<td>Proliferation</td>
<td>13.5 cm x 6.5 cm</td>
<td>Minimally exudative (serosanguinous), healthy granulation bed, epithelialisation, tissue contraction</td>
<td>Honey, Cutilin</td>
<td>Methadone IV BID, Amoxi/Clav PO BID, Meloxicam PO SID</td>
</tr>
<tr>
<td>3d</td>
<td>Proliferation</td>
<td>13 cm x 6 cm</td>
<td>Minimally exudative (serosanguinous), healthy granulation bed, epithelialisation apparent</td>
<td>Honey, Cutilin</td>
<td>Amoxi/Clav PO BID, Meloxicam PO SID</td>
</tr>
<tr>
<td>7</td>
<td>Proliferation</td>
<td>7.5 cm x 4 cm</td>
<td>Epithelialisation and contraction, no discharge</td>
<td>-</td>
<td>Amoxi/Clav PO BID, Meloxicam PO SID</td>
</tr>
<tr>
<td>12</td>
<td>Proliferation / Maturation</td>
<td>4.5 cm x 2 cm</td>
<td>Epithelialisation and contraction, no discharge</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>18</td>
<td>Maturation</td>
<td>Healing Complete</td>
<td>Healing complete</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> Flamazine, Smith & Nephew Pty Ltd  | <sup>b</sup> Allevyn, Smith & Nephew Pty Ltd  | <sup>c</sup> Amoxicillin/Clavulanic Acid  | <sup>d</sup> PAW Manuka Wound Gel, Blackmores Pty Ltd  | <sup>e</sup> Cutilin, Smith & Nephew Pty Ltd

m, morning; e, evening; d, patient discharged for at-home management; IV, intravenous; IVFT, intravenous fluid therapy; PO, orally; SID, once daily; BID, twice daily; TID, thrice daily
Low-pressure, high-volume irrigation was performed using 0.9% sodium chloride, and the surrounding tissue was cleaned with dilute aqueous chlorhexidine scrub (Dechra Veterinary Products (Australia) Pty Ltd, Somersby, NSW). The smaller puncture wound was probed and was not associated with subcutaneous dead-space. The wound was dressed with topical silver sulfadiazine (Flamazine, Smith & Nephew Pty Ltd, Mount Waverley, VIC) and covered with a non-adhesive, non-occlusive, highly absorbent hydrocellular foam dressing (Allevyn, Smith & Nephew Pty Ltd). Orthopaedic padding (Soffban Synthetic 7.5 cm x 2.7 m, BSN Medical Australia, Mulgrave, VIC), conforming bandage (Easifix conforming retention bandage 7.5 cm x 1.75 m, BSN Medical Australia), and cohesive bandage were then applied circumferentially around the neck.

The patient was hospitalised overnight, on intravenous fluid therapy (Lactated Ringer’s solution, 2.5 mL/kg/hr), intravenous methadone (0.1 mg/kg every 4-6 hr) and intravenous amoxicillin/clavulanic acid (20 mg/kg every 8 hr; Juno Pharmaceuticals Pty Ltd, Cremorne, VIC), and was transferred to the surgical service the next day for ongoing management.

On evaluation by the surgical service, the dog was bright and haemodynamically stable. She was sedated with medetomidine hydrochloride (2.5 μg/kg) and methadone (0.2 mg/kg) intramuscularly and a comprehensive skin and tissue assessment was performed, adapted from guidelines provided by the National Pressure Injury Advisors Panel (NPIAP). The wounds were highly exudative (purulent), painful on manipulation, and remained erythematous and malodourous (Figure 1B; Table 1). The wound was classified as a Stage II pressure injury as per the NPIAP staging system and was characterised by partial-thickness skin loss with exposed dermis. Low-pressure, high-volume irrigation was repeated using 0.9% sodium chloride, and the surrounding tissue again cleaned with dilute aqueous chlorhexidine scrub. Given the significantly exudative nature of the wound, it was elected to not apply a topical primary contact layer at this time, to reduce the risk of peri-tissue maceration. A non-adhesive, non-occlusive, highly absorbent hydrocellular foam dressing contact layer was applied directly over the wounds. Orthopaedic padding, conforming bandage, and cohesive bandage were reapplied circumferentially around the neck with ~50% overlap. Meloxicam (0.1 mg/kg subcutaneously every 24 hr; Ilium, Troy Laboratories Australia Pty Ltd) was added to the treatment. Due to the highly exudative nature of the wound, twice daily bandage changes were recommended until improvement in exudate production was achieved. That evening (Day 1), the wounds were moderately exudative with no significant change to the wound characteristics (Figure 1C; Table 1), and the bandage was replaced as previously described.

Following overnight incubation, microbial culture results identified growth of *Staphylococcus pseudointermedius* and a Gram-negative bacillus. The latter was later identified via matrix-assisted laser desorption/ionisation (MALDI) time-of-flight (TOF) mass spectrometry as *Acidovorax temperans*. Both bacteria were susceptible to amoxicillin/clavulanic acid.
On Day 2 of hospitalisation, the wound remained mildly exudative (serosanguinous) with evidence of angiogenesis and the initial formation of healthy granulation tissue with epithelialisation (Figure 1D; Table 1). The puncture wound appeared to demonstrate further healing. In-house cytology of the serosanguinous discharge from the primary wound was negative for bacteria. The wound was irrigated and, given the significant reduction in wound-related discharge, medical-grade honey (PAW Manuka Wound Gel, Blackmores Pty Ltd, Warriewood, NSW) was applied as the primary contact layer to enhance granulation tissue formation and promote further epithelialisation. A non-occlusive, low-adherent, absorbent dressing (Cutilin, Smith & Nephew Pty Ltd) was then applied and the bandage replaced as previously described. As the dog was eating and drinking, intravenous fluid therapy was discontinued, and she was transitioned to oral meloxicam (0.1 mg/kg, Norbrook Laboratories Australia Pty Ltd, Tullamarine, VIC) and oral amoxicillin/clavulanic acid (15 mg/kg, Dechra Veterinary Products Pty Ltd). The dog was increasingly comfortable with wound manipulation and no longer required sedation for dressing and bandage changes. That evening, the wound bed displayed the formation of further healthy granulation tissue, with ongoing epithelialisation and visible tissue contraction (Figure 1E; Table 1). The use of honey as the primary contact layer was continued.

Wound assessment on Day 3 of hospitalisation showed minimal serosanguinous discharge, with the formation of more granulation tissue and epithelialisation. The wound diameter measured ~2 cm (length) x 2 cm (width) smaller compared to the size at initial presentation. Following the application of the Manuka honey, a non-occlusive, low-adherent, absorbent dressing was applied as the primary contact layer, followed again by intermediary and outer layers (Table 1). The dog was stable and comfortable and no longer required daily bandage changes, due to minimal exudate production, so she was discharged with the oral medication continuing and with the bandage in situ.

The dog was presented four days following discharge (Day 7 from presentation) for reassessment. Significant wound epithelialisation and contraction was apparent, with the wound size was approximately half that of the time of initial presentation and with ~90% wound epithelialisation (Figure 1F; Table 1). Bandaging was discontinued and subsequent examinations at Day 12 (Figure 1G) and Day 18 (Figures 1H-I) showed further wound contraction and complete wound healing, respectively (Table 1). The owners were pleased with the cosmetic outcome at that time. The patient was lost to follow-up thereafter.

DISCUSSION

The use of EABSC in Australia is regulated under individual state/territory governing bodies. At the time of publication, Australian Capital Territory, New South Wales and South Australia have all banned the use of EABSC in domestic animals, with the remaining states/territories implementing certain restrictions on their use. Use of EABSC is banned completely in many European countries, with other countries relying on primary legislation and supporting guidelines to govern the proper use of electronic training products. The Australian Veterinary Association position statement on EABSC is that “behaviour-modifying collars that use electric shock should not be used on animals and should
be banned”, with recommendations against the use of collars utilising citronella or other nontoxic substances.\textsuperscript{16} This position is similar to that of the European Society of Veterinary Clinical Ethology,\textsuperscript{1} which strongly opposes the use of electronic collars in dog training and has urged all European nations to take a stance on this matter. A shift in the ethological paradigm has placed an increased emphasis on reward-based training as first recourse, with coercive methods that inhibit the expression of a behaviour without addressing its cause being considered not effective in the long-term and possibly causing undue stress to the animal, ultimately impacting their welfare.\textsuperscript{1}

One area of concern regarding EABSC is the reported inconsistent delivery of the electrical stimulus. Impedance between patient tissue and electrode contact points significantly affects the voltage and current delivered by the EABSC and can vary considerably and randomly.\textsuperscript{2,6,7} Other factors, including tissue moisture, device positioning, and individual animal variance, may affect the animal’s sensitivity to electrical stimuli and overall device consistency.\textsuperscript{2} Owner understanding and compliance with the manufacturer’s guidelines for the use of EABSC may also limit the device’s efficacy and safety.\textsuperscript{6} According to the Companion Animal Welfare Council, the safety and instructional information provided to owners varies considerably between manufacturers of EABSC and may be insufficient to enable inexperienced users to use these products safely.\textsuperscript{7} To combat this, the Electronic Collar Manufacturers Association (ECMA) have established a code of practice towards setting the minimum standards required for use of these devices.\textsuperscript{12} The ECMA recommend EABSC be worn for a maximum of 12 hours per day to reduce the risk of developing EABSC-associated pressure injury.\textsuperscript{12} Despite these guidelines, pressure injury is anecdotally reported to be a relatively common consequence of the use of EABSC.\textsuperscript{11,12}

Sustained pressure from EABSC, in combination with shear forces, leads to tissue ischaemia, devitalisation, necrosis, and deformation.\textsuperscript{17-19} Pressure injury, defined as localised damage to the skin and underlying soft tissue over a bony prominence or related to a medical or other device, occurs when force results in an external pressure greater than both arterial capillary filling pressure and venous capillary outflow pressure, prohibiting blood flow and leading to local tissue hypoxia.\textsuperscript{14,18} Shear and friction forces may also affect local capillary beds and are thought to contribute to tissue hypoxia.\textsuperscript{14,18} Disruption of the skin barrier may lead to secondary infection. The wound depicted in the case is considered to have likely developed from a combination of prolonged device-tissue contact time and shear frictional forces of the device on the neck, resulting in local inflammation, tissue damage, and subsequent superficial infection and moist dermatitis. This conclusion is based on the location of the most severely affected areas under the likely position of the dermal electrodes. Subsequent exudation and tissue maceration was likely exacerbated by self-trauma.

In humans, quantitative and qualitative deep tissue biopsy of pressure wounds for microbiological analysis (Gram stain and culture) is recommended to aid in the establishment of treatment protocols.\textsuperscript{17} In this regard, one study showed that concordance of microbial identification between superficial swabs and deep tissue culture was only 22% for advanced pressure injury in humans, with polymicrobial burden significantly higher for swabs than deep
tissue biopsy. This is potentially due to the inclusion of commensal microorganisms and environmental contaminants. Deep tissue culture was not performed in the present case due to financial constraints. Superficial swabs identified *Staphylococcus pseudintermedius* and *Acidovorax temperans*, likely representing a non-pathogenic commensal and an environmental contaminant, respectively. Thus the culture results may not have provided a true representation of the bacterial burden in the wound.

Conservative management of pressure injuries in humans is typically recommended for Stage I and II pressure injuries only, with treatment aimed at achieving a moist wound environment that facilitates the healing process by preventing dehydration, promoting angiogenesis and collagen synthesis, and breaking down necrotic tissue. In the present case, we followed the NPIAP guidelines and the principles of moist wound healing in our clinical decision making.

Silver sulfadiazine has been recommended for use during the inflammatory phase of wound healing. It was discontinued in the present case as it was the authors’ opinion that excessive production of exudate combined with a topical dressing might increase the risk of further peri-tissue maceration. Topical ointments were avoided until wound exudation had decreased markedly, at which time a combined Manuka Honey and natural wax and oils based ointment was utilised as the primary contact layer to expediate wound healing through early, robust epithelialisation, as per results observed by others, using a comparable product. We also felt justified in discontinuing topical silver sulfadiazine when cytological examination of the discharge on Day 2 showed no evidence of bacteria. The clinical efficacy of a non-adhesive, non-occlusive, highly absorbent hydrocellular dressing is well described. Despite the severity of the wound at presentation, the treatment protocol followed in the present case resulted in complete tissue healing by Day 18.

**CONCLUSION**

The present report illustrates a successful outcome of conservative management of a superficial infection and moist dermatitis in a dog following the prolonged use of an EABSC. It highlights the potential for tissue injury with the use of such devices. Prolonged use of EABSC is at odds with the ECMA code of practice recommendations and, potentially, the device manufacturer’s instructions for use.

To the authors’ knowledge, this is the first case report describing the management of a superficial infection and moist dermatitis following prolonged use of an EABSC in a dog. This emphasises the significant risks of both psychological and physical suffering to dogs associated with the use of these products.

**CONFLICTS OF INTEREST AND SOURCES OF FUNDING**

No funding or other financial support was received for this paper. There is no financial or other conflict of interest of any author related to a company or product used in the report.

**REFERENCES**


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Abstracts

These Abstracts have been sourced from the following journals: Journal of the American Veterinary Medical Association, Journal of Exotic Pet Medicine, Journal of Feline Medicine and Surgery, Journal of Veterinary Internal Medicine, Journal of Small Animal Practice, Journal of Veterinary Diagnostic Investigation, Veterinary Surgery and New Zealand Veterinary Journal. With the exception of the first few abstracts, they are arranged by species (Cat, Dog and Exotics) and then broad subject area.

GENERAL

Human allergy to cats: A review for veterinarians on prevalence, causes, symptoms and control
Sparkes AH

Human allergy to cats: A review of the impact on cat ownership and relinquishment
Sparkes AH

Pre-surgical hand preparation in veterinary practice
Crosse KR

The objective of this paper is to review the evidence for different methods of surgical hand preparation applicable to veterinary practice. Surgical hand preparation is an essential step in performing surgery as a veterinarian. Recommended protocols and products for surgical hand preparation have varied since its inception in the late 1800s. Many factors must be considered when assessing the efficacy, safety, and users’ compliance with any available product. Traditional scrub methods employing chlorhexidine gluconate or povidone-iodine have been compared to alcohol-based rub protocols with respect to immediate and prolonged efficacy, safety, compliance, requirements for theatre furniture, cost and water usage. Although much of the comparative data has been generated in human medical facilities, extrapolation of the data to veterinary surgery is appropriate. Considerations for veterinary practice are specifically discussed. Overall, the benefits of alcohol-based rubs indicate that this should be the preferred method of pre-surgical hand preparation for veterinarians in all types of practice.

Diagnostic utility of canine cerebrospinal fluid preserved by 10% buffered formalin
Montaños Sancho I et al.

Objectives: To examine the diagnostic utility of canine cerebrospinal fluid samples collected into tubes containing ethylenediaminetetraacetic acid (EDTA) with and without the addition of 10% buffered formalin analysed within 6 to 20 hours.

Materials and Methods: Inclusion criteria were dogs presenting to a referral hospital with neurological signs and having cerebrospinal fluid analysis performed. Samples were submitted to an external laboratory in tubes containing ethylenediaminetetraacetic acid as paired-samples; one with the addition of one drop of 10% buffered formalin and the other without formalin. Cytology report, total nucleated cell counts, and protein concentration were reviewed. Three different categories of cell preservation were defined: diagnostic, non-diagnostic and unclassified. Each sample was included in one of these categories depending on cytological features, and the diagnostic
quality between samples was compared. Samples were further divided in two groups depending on protein concentration using 50 mg/dL as cut-off value and the diagnostic quality between samples was compared.

**Results:** 254 samples from 127 dogs were included. 47% of samples without formalin were non-diagnostic, 46% diagnostic and 6% unclassified. In the formalin group, 2% samples were non-diagnostic, 92% diagnostic and 6% unclassified. Samples with formalin preservation were statistically more likely to be diagnostic than samples without formalin preservation. In both protein groups (≥50 and <50 mg/dL) formalin samples were statistically more likely to be diagnostic as well.

**Clinical significance:** The addition of one drop of 10% formalin is a simple, widely available method which can help to improve the accuracy of cytological assessment in canine cerebrospinal fluid by preserving cellular morphology when analysis is performed within 6 to 20 hours.

**CATS**

**Clinical Pathology**

*Effects of handling and storage on potassium concentration in plasma and serum samples obtained from cats*

**Domenegato BM et al.**

*JAVMA* 260: 187-193, 2022;
https://doi.org/10.2460/javma.20.09.0530

**Objective:** To compare potassium concentrations in feline plasma and serum samples analyzed promptly after collection or after 20 to 28 hours of refrigerated storage.

**Animals:** 41 cats.

**Procedures:** A venous blood sample was obtained from each cat. Aliquots were placed in 2 tubes without anticoagulant (blood was allowed to clot to derive serum) and 2 tubes with heparin (to derive plasma). One serum and 1 plasma sample were kept at room temperature and analyzed within 60 minutes after collection (baseline); the other serum and plasma samples were analyzed after 20 to 28 hours of refrigerated storage. At both time points, serum and plasma potassium concentrations were measured.

**Results:** Median baseline serum potassium concentration (4.3 mmol/L) was significantly higher than median baseline plasma potassium concentration (4.1 mmol/L). The median difference between those values was 0.4 mmol/L (95% CI, 0.2 to 0.5 mmol/L). Compared with their respective baseline measurements, the median serum plasma concentration (4.8 mmol/L) and median plasma potassium concentration (4.6 mmol/L) were higher after 20 to 28 hours of refrigeration.

**Clinical relevance:** Results indicated that with regard to potassium concentration in feline blood samples, clotting or refrigerated storage for 20 to 28 hours results in a significant artifactual increase. Detection of an unexpectedly high potassium concentration in a cat may represent pseudohyperkalemia, especially if the blood sample was placed in a no-additive tube, was stored for 20 to 28 hours prior to analysis, or both.

**Endocrinology**

*Insulin glargine 300 U/ml for the treatment of feline diabetes mellitus*

**Linari G et al.**

*J Fel Med Surg* 24: 168-176, 2022;
https://doi.org/10.1177/1098612X211013018

**Objectives:** The study aimed to evaluate the efficacy and safety of insulin glargine 300 U/ml (IGla-U300) in cats with variable duration of diabetes mellitus (DM).
Methods: Thirteen client-owned cats with DM completed a prospective clinical trial. Four cats were highly suspected of hypersomatotropism and excluded from the insulin efficacy evaluation. All cats were treated with Igla-U300 SC at a starting dosage of 0.5 U/kg q12h and fed with a low carbohydrate diet. Cats were monitored for 8 weeks with a once-weekly at-home 16 h blood glucose curve (BGC) and a questionnaire evaluating the presence of DM-related clinical signs. In-clinic evaluations, including serum fructosamine measurement, were scheduled within 3 days of the first, third, sixth and eighth BGC. Glycemic variability was assessed by calculating the SD of each BGC.

Results: Excluding four cats suspected of hypersomatotropism, at the time of the eighth BGC, improved or absent polyuria, polydipsia, polyphagia, weight loss, lethargy and improved or normal general demeanor were reported in 8/9 (88%), 8/9 (88%), 7/9 (77%), 7/9 (77%), 7/9 (77%) and 8/9 (88%) cats, respectively. Two cats achieved remission after 29 and 53 days. Another two cats went into remission after the end of the study (days 82 and 96). All cats that achieved remission were newly diagnosed diabetics. Median (range) serum fructosamine concentration significantly decreased when comparing the time of enrollment (604 [457–683] µmol/l) with the eighth week of treatment (366 [220–738] µmol/l) (P = 0.02). In all 13 cats, biochemical hypoglycemia (blood glucose <60 mg/dl; <3.3 mmol/l) was detected in 13/104 (12.5%) BGCs, while clinical signs suggesting hypoglycemic episodes were not reported. Glycemic variability was significantly lower at the fifth BGC when comparing cats that achieved remission with cats that did not achieve remission (P = 0.02).

Conclusions and relevance: Igla-U300 seems effective and safe for the treatment of feline diabetes, but more long-term and comparative clinical trials are needed.

Evaluation of hemostasis in hyperthyroid cats

Keebaugh AE et al.

Background: Hyperthyroid cats might have a predisposition to arterial thrombus formation. The mechanism for thrombogenesis currently is unknown but could be associated with systemic hypercoagulability as seen in hyperthyroid humans.

Objective: Our purpose was to evaluate markers of hemostasis in hyperthyroid cats compared to healthy cats, and in hyperthyroid cats before and after radioactive iodine treatment (RIT).

Animals: Twenty-five cats with hyperthyroidism and 13 healthy euthyroid cats ≥8 years of age.

Methods: Prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen concentration, antithrombin (AT), D-dimers, thrombin-antithrombin complexes (TAT), von Willebrand Factor antigen (vWF:Ag), and activity of factors VIII and IX were measured. An echocardiogram was performed in all cats. Hemostatic markers and echocardiogram were evaluated again 6 to 9 months after successful RIT in 7 cats.

Results: Hyperthyroid cats had higher fibrinogen concentration (P < .0001), AT activity (P < .0001), and vWF:Ag concentration (P = .01) than healthy control cats with all results decreasing significantly post-RIT. Hyperthyroid cats were not more likely to be in a hypercoagulable state than euthyroid cats (P = .08). Serum T4 concentration was not a predictor of a hypercoagulable state (P = .53).

Conclusions and clinical importance: Hyperthyroid cats have evidence of altered hemostasis that does not appear to be solely attributable to cardiac abnormalities, but no evidence of a hypercoagulable state. Findings
suggest altered hemostasis resolves after RIT. Hyperthyroid cats could have endothelial dysfunction as indicated by increased vWF:Ag which could potentiate thrombogenesis.

**Kidney**

**Appetite-stimulating effects of once-daily omeprazole in cats with chronic kidney disease: Double-blind, placebo-controlled, randomized, crossover trial**

*Spencer A et al.*


**Background:** Cats with moderate to advanced chronic kidney disease (CKD) often display clinical signs such as vomiting and decreased appetite, and frequently receive omeprazole or other acid suppressants despite a lack of evidence to support their use.

**Hypothesis/Objectives:** To evaluate the effect of once-daily PO omeprazole on appetite in cats with CKD. We hypothesized that omeprazole would improve subjective appetite assessments in cats with CKD.

**Animals:** Fourteen client-owned cats with International Renal Interest Society (IRIS) stage 2 or 3 CKD and hyporexia.

**Methods:** Cats were prospectively enrolled in a multi-institutional, double-blinded, randomized, crossover study to evaluate the effect of a 14-day trial of once-daily PO omeprazole (1 mg/kg) or placebo (lactose gel capsule) on vomiting frequency and appetite. A daily log was completed by the owner during all treatment and rest periods to assess appetite using a subjective, qualitative, and 5-point scoring system. Mixed model analyses of variance were performed to determine if average daily percentage food consumed or appetite score, as measured by subjective owner assessment, differed between treatments.

**Results:** Compared to placebo, a negligible but statistically significant difference in percentage of food consumed was observed between treatments (P = .04) with once-daily omeprazole treatment resulting in a 2.7% increase in food consumption compared to placebo. No significant difference, however, was found in appetite score, body weight, or serum creatinine concentration between treatments.

**Conclusions and clinical importance:** Once-daily omeprazole does not markedly increase appetite in cats with CKD and should not be used as a first-line treatment in the absence of evidence of gastrointestinal ulceration.

**Serum feline pancreatic lipase immunoreactivity and trypsin-like immunoreactivity concentrations in cats with experimentally induced chronic kidney disease**

*Xenoulis PG et al.*


**Background:** Serum feline pancreatic lipase immunoreactivity (fPLI) and trypsin-like immunoreactivity (fTLI) concentrations are commonly used in cats for the evaluation of pancreatic disease. The effect of kidney disease on these tests in cats are unknown.

**Objective:** To investigate the effect of experimentally induced chronic kidney disease (CKD) on serum fPLI and fTLI concentrations.

**Animals:** Surplus serum samples from 20 cats with CKD experimentally induced for an unrelated project and a group of healthy control cats.

**Methods:** Serum fTLI and fPLI concentrations were compared between groups.

**Results:** Mean (±SD) serum fTLI concentrations in 20 cats with CKD (117.8 ± 63.6 μg/L) were significantly higher
Abstracts

than those in healthy cats (n = 32; 46.9 ± 17.5 μg/L; P < .0001). Serum fTLI concentrations in cats with CKD were above the upper limit of the reference interval in 13 of 20 cats (65%). Serum fPLI concentrations were not significantly different between cats with induced CKD (n = 18; 8.6 μg/L; range, 5.4-9.9 μg/L) and healthy cats (n = 41; 7.4 μg/L; range, 5.0-15.2 μg/L; P = .12). All cats with experimentally induced CKD had serum fPLI concentrations within the reference interval.

Conclusions and clinical importance:
Decreased renal function has a clinically relevant impact on serum fTLI concentrations and potentially could interfere with a diagnosis of exocrine pancreatic insufficiency (EPI). Serum fPLI concentration was not affected by experimentally induced CKD and thus serum fPLI may be used for the diagnosis of pancreatitis in cats with kidney disease. Additional studies are needed to verify these results in cats with naturally occurring CKD.

Liver

Clinical features, concurrent disorders, and survival time in cats with suppurative cholangitis-cholangiohepatitis syndrome

Center SA et al.
JAVMA 260: 212-227, 2022;
https://doi.org/10.2460/javma.20.10.0555

Objective: To characterize clinical features, comorbidities, frequency of bacterial isolation, and survival time in cats with suppurative cholangitis-cholangiohepatitis syndrome (S-CCHS).

Animals: 168 client-owned cats with S-CCHS.

Procedures: Data were prospectively (1980 to 2019) collected regarding clinical features, comorbidities, bacterial infection, illness duration, and treatments. Variables were evaluated for associations with survival time.

Results: Median age of cats was 10.0 years, with no breed or sex predilection observed. Common clinical features included hyporexia (82%), hyperbilirubinemia (80%), lethargy (80%), vomiting (80%), jaundice (67%), weight loss (54%), and hypoalbuminemia (50%). Comorbidities included extrahepatic bile duct obstruction (53%), cholelithiasis (42%), cholecystitis (40%), and ductal plate malformation (44%) as well as biopsy-confirmed inflammatory bowel disease (60/68 [88%]) and pancreatitis (41/44 [93%]). Bacterial cultures were commonly positive (69%) despite prebiopsy antimicrobial administration in most cats. Of surgically confirmed choleliths, diagnostic imaging identified only 58%. Among 55 cats with “idiopathic pancreatitis,” 28 (51%) were documented to have transiting choleliths, and 20 had pancreatic biopsies confirming pancreatitis. Cholelithiasis (with or without bile duct obstruction) and cholecystectomy were associated with survival advantages. Survival disadvantages were found for leukocytosis, ≥ 2-fold increased alkaline phosphatase, and hyperbilirubinemia. Cholecystoenterostomy had no survival impact. Cats with ductal plate malformations were significantly younger at diagnosis and death than other cats. Chronic treatments with antimicrobials, S-adenosylmethionine, and ursodeoxycholic acid were common postbiopsy.

Clinical relevance: S-CCHS in cats was associated with bacterial infection and various comorbidities and may be confused with pancreatitis. Surgically correctable morbidities (ie, cholecystitis, cholecystocholelithiasis) and cholecystectomy provided a significant survival advantage.
Cholecystectomy in 23 cats (2005-2021)

Simpson M et al.

Objective: To describe the clinical presentation, treatments, and long-term outcomes following cholecystectomy in cats.

Study design: Clinical retrospective study.

Animals: Twenty-three client-owned cats.

Methods: Medical records of all cats undergoing cholecystectomy between 2005 and 2021 at a single referral hospital were retrospectively reviewed. No cats were excluded. An owner questionnaire assessed long-term outcomes.

Results: Vomiting, jaundice, and abdominal pain were the most common clinical signs; median duration of signs was 4 days (range 1-21). Cholelithiasis was the major indication for cholecystectomy followed by cholecystitis. Intraoperative hypotension and postoperative anemia were commonly encountered. Nine cats required a postoperative blood product transfusion. Cardiopulmonary arrest and death occurred in five cats. Eighteen cats (78.3%) survived to discharge. Long-term follow up (>60 days) was available for 16 cats at a median of 1003 days (range 81-4995). Fifteen cats survived over 6 months with eight cats (44.4%) surviving over 3 years. The most common short-term and long-term postoperative complication was vomiting. Owners assessed postoperative outcome as excellent in all cats and quality of life as excellent or good.

Conclusion: The most common indication for cholecystectomy was cholelithiasis. Perioperative complications were commonly encountered. Perioperative mortality rate was 21.7%. Long-term owner evaluation of clinical outcome was considered excellent.

Clinical significance: Cats undergoing cholecystectomy for non-neoplastic causes can have a favorable prognosis for recovery and quality of life. Concurrent extrahepatic biliary duct obstruction is not a contraindication for cholecystectomy provided that patency of the common bile duct is restored.

Pain Management

2022 ISFM Consensus Guidelines on the Management of Acute Pain in Cats

Steagall PV et al

Practical relevance: Increases in cat ownership worldwide mean more cats are requiring veterinary care. Illness, trauma and surgery can result in acute pain, and effective management of pain is required for optimal feline welfare (ie, physical health and mental wellbeing). Validated pain assessment tools are available and pain management plans for the individual patient should incorporate pharmacological and non-pharmacological therapy. Preventive and multimodal analgesia, including local anaesthesia, are important principles of pain management, and the choice of analgesic drugs should take into account the type, severity and duration of pain, presence of comorbidities and avoidance of adverse effects. Nursing care, environmental modifications and cat friendly handling are likewise pivotal to the pain management plan, as is a team approach, involving the cat carer.

Clinical challenges: Pain has traditionally been under-recognised in cats. Pain assessment tools are not widely implemented, and signs of pain in this species may be subtle. The unique challenges of feline metabolism and comorbidities may lead to undertreatment of pain and the development of peripheral and central sensitisation. Lack
of availability or experience with various analgesic drugs may compromise effective pain management.

**Evidence base:** These Guidelines have been created by a panel of experts and the International Society of Feline Medicine (ISFM) based on the available literature and the authors’ experience. They are aimed at general practitioners to assist in the assessment, prevention and management of acute pain in feline patients, and to provide a practical guide to selection and dosing of effective analgesic agents.

**Refinement of the Feline Musculoskeletal Pain Index (FMPI) and development of the short-form FMPI**

**Enomoto M et al.**

*J Fel Med Surg 24 (2): 142-151, 2022; https://doi.org/10.1177/1098612X211011984*

**Objectives:** The aim of this study was to investigate the reliability and responsiveness of the Feline Musculoskeletal Pain Index (FMPI) using the collective results of multiple clinical studies and iteratively refine the FMPI for future use.

**Methods:** Data were compiled from previously conducted studies involving client-owned cats with degenerative joint disease (DJD) and which used the FMPI. The reliability of the FMPI was assessed using the data from the initial visits of those studies. For the assessment of responsiveness of the FMPI, only placebo-controlled studies that used analgesic treatments were included. Treatment groups from each study were combined and categorized as ‘placebo’ group and ‘analgesic’ group. Then, the mean change from baseline in score of each FMPI item and across all items within and between these groups were assessed. Based on the results of the reliability and responsiveness of the FMPI, stepwise elimination was used to remove the items that were least able to distinguish between the placebo and analgesic groups. Finally, after the stepwise elimination, a proposed new FMPI-short form (FMPI-sf) was constructed and its reliability was reassessed using the data sets described above. Individual and combined data sets of the studies were also used to compare the responsiveness of the original FMPI and the FMPI-sf.

**Results:** The data from 180 cats from four studies were included. The original FMPI had a reasonable reliability, but low/no responsiveness. The elimination process of FMPI items refined the responsiveness of the instrument while maintaining its reliability. When the responsiveness was compared between the original FMPI (17 items) and the FMPI-sf (nine items), the treatment effect between groups was always greater when the FMPI-sf was used.

**Conclusions and relevance:** The proposed FMPI-sf may be able to better distinguish between placebo and analgesic effects in cats with DJD.

**Reproduction**

*J Fel Med Surg 24 (3) 2022*

Issue with articles on feline reproduction and neonatology.

**Trauma**

**Distribution of mortality patterns in cats with naturally occurring trauma: A Veterinary Committee on Trauma registry study**

**Hickey MC et al.**


A greater understanding of the prognostic variables that affect the timing of death for cats with trauma may help clinicians select treatments and monitoring plans. This
study investigated the mortality rate and its distribution pattern in a large population of cats to identify variables associated with the timing of trauma-related deaths. Clinical data was retrieved from the Veterinary Committee on Trauma database to determine mortality rates and timing of deaths, defined as early death (ED; <1 day post-presentation) or delayed death (DD; ≥1 day post-presentation). Multivariable logistic regression analyses were performed to identify characteristics and interventions that best predicted timing of death.

Overall mortality rate for 6703 feline trauma patients with complete records was 17.2%, with 7.6% due to natural death and 92.3% due to euthanasia. Among the subset of 543 cats with trauma that died after presentation or required euthanasia due to a grave prognosis (representing an 8.1% mortality rate), EDs were more common (71.7%) than DD and the cause of death was not significantly associated with the timing of death. Clinical pathology parameters were unable to identify animals more likely to die or to require euthanasia due to a poor prognosis during hospitalisation. Factors that were significantly different for cats with ED vs. DD included the median cumulative results for the Modified Glasgow Coma Scale (MGCS) score and the Animal Trauma Triage (ATT) score, the presence of spinal trauma, administration of blood products and undertaking surgical procedures. An increased likelihood of DD rather than ED was associated with the administration of blood products (odds ratio [OR], 3.959; P = 0.019) vs. not, performing a surgical procedure (OR, 6.055; P < 0.001) vs. not, and a cumulative MGCS of 15−17 or 18 (OR, 1.947 and 3.115; P = 0.031 and P = 0.01, respectively) vs. a cumulative MGCS ≤11.

DOGS

Endocrinology

Utility of a corticotropin-releasing hormone test to differentiate pituitary-dependent hyperadrenocorticism from cortisol-producing adrenal tumors in dogs

Tanaka S et al.


Background: Hyperadrenocorticism (HAC) is a common endocrine disorder in dogs; however, there are no reports on the use of the corticotropin-releasing hormone test (CRHT) to differentiate between pituitary-dependent hyperadrenocorticism (PDH) and cortisol-producing adrenal tumors (CPATs), both causative of HAC.

Objectives: To evaluate the usefulness of CRHT as a tool to differentiate between PDH and CPAT in dogs and to determine the reference intervals for CRHT in healthy, PDH, and CPAT dogs.

Animals: Dogs diagnosed with PDH (n = 21), CPAT (n = 6), and healthy beagle dogs (n = 33).

Methods: This prospective study included dogs with a definitive diagnosis of PDH and CPAT and healthy beagle dogs, in which CRHT was performed, were prospectively evaluated. We investigated the correlations of CRHT (endogenous adrenocorticotropic hormone [ACTH] concentration, endogenous ACTH concentration [EAC], and poststimulation ACTH concentration [PAC]) with pituitary-to-brain ratio (PBR) (in PDH) and with indices of adrenal ultrasonography (smaller and larger adrenal gland dorsoventral thickness in PDH and CPAT).

Results: For EAC, the area under the curve (AUC) was 0.95, with a cutoff value of 26.3 pg/mL (sensitivity: 90.62%, specificity: 87.50%). The AUC for PAC was 0.96 with a cutoff value of 54.5 pg/mL (sensitivity: 100.00%, specificity:
66.67%). The 95% reference interval for CRHT in healthy (control) dogs ranged 5.00 to 79.8 pg/mL (1.10-17.57 pmol/L) for EAC, and 1.92 to 153.42 pg/mL (0.42-33.78 pmol/L) for PAC. There was no significant correlation between PBR and CRHT, nor adrenal size and CRHT.

Conclusions and clinical importance: CRHT appears to be a rapid and reliable test for differentiating PDH from CPAT in dogs.

Gut

Identification of a canine coronavirus in Australian racing Greyhounds

Craig S. Smith CS et al.


Coronavirus infection can cause a range of syndromes, which in dogs can include mild-to-severe enteritis that generally resolves rapidly. Fatalities can occur from coinfection with other pathogens, including canine parvovirus. Between late December 2019 and April 2020, canine coronavirus (CCoV) was detected in Australian racing Greyhounds that displayed signs of gastrointestinal disease. The CCoV was genotyped using high-throughput sequencing, recovering 98.3% of a type IIb CCoV, generally thought to cause a mild but highly contagious enteric disease. The Australian CCoV was almost identical (99.9%, whole-genome sequence) to another CCoV associated with an outbreak of severe vomiting in dogs in the United Kingdom at the same time (December 2019–March 2020).

Advances in the diagnosis of acute pancreatitis in dogs

Cridge H et al.


In the last 20 years, the diagnosis of pancreatitis has become more frequent as a result of improved diagnostic modalities such as abdominal ultrasound examination, advanced imaging, and immunoassays for the measurement of pancreatic lipase. Our aim is to provide a state-of-the-art overview of the clinical diagnosis of acute pancreatitis (AP) in dogs with a particular focus on pancreatic lipase assay validation and clinical performance, in addition to advanced imaging modalities. We also discuss the potential indications for cytology and histopathology in dogs with suspected AP.

Heart

Prevalence of sudden cardiac death in dogs with atrial fibrillation

Borgeat K et al.


Background: Atrial fibrillation (AF) is associated with increased risk of sudden cardiac death (SCD) in humans, independent of secondary risk factors such as thrombogenic disorders. In dogs, SCD is described in a number of heart diseases, but an association between AF and SCD is unreported.

Hypothesis: (a) A higher proportion of dogs with AF will experience SCD, and (b) SCD will be associated with complex ventricular arrhythmias.

Animals: One-hundred forty-two dogs with AF, and 127 dogs without AF.

Methods: Retrospective, multicenter, case-control study. Dogs included in the AF group were compared to a control group of dogs in sinus rhythm, matched for echocardiographic diagnosis. Descriptive statistics were used to identify proportions of each group suffering SCD, compared using chi-squared testing. Risk factors for SCD in dogs with AF were evaluated at the univariable and multivariable level using binary logistic regression. Significance was P < .05.
**Results:** A significantly higher proportion of dogs with AF suffered SCD than dogs in the control group (14.8% vs 5.5%; P = .01). Younger age at diagnosis, larger left atrial size, and a history of syncope all were independent predictors of SCD in dogs with AF ($\chi^2$, 16.3; P = .04).

**Conclusions and clinical importance:** Atrial fibrillation was associated with a higher prevalence of SCD in dogs. A history of syncope may be a useful predictor of SCD risk.

**Liver**

**Postattenuation neurologic signs after surgical attenuation of congenital portosystemic shunts in dogs: A review**

*Mullins RA et al.*


The development of postattenuation neurologic signs (PANS) is a poorly understood and potentially devastating complication after surgical attenuation of congenital portosystemic shunts in dogs. Postattenuation neurologic signs include seizures but also more subtle neurologic signs such as depression, behavioral changes, tremors, and twitching. They most commonly occur within 7 days postoperatively and are typically unrelated to hyperammonemia, hypoglycemia, or electrolyte disturbances. This narrative review summarizes the findings of 50 publications from 1988-2020 that report occurrence of PANS. While most published reports included only dogs affected by postattenuation seizures (PAS), others included dogs with any form of PANS. Overall, PANS (including PAS) affected 1.6%-27.3% of dogs, whereas incidence of PAS ranged from 0%-18.2%. The etiology of PANS remains unknown; however, several theories have been proposed. Risk factors include preoperative hepatic encephalopathy, increasing age, and possibly certain breeds and extrahepatic shunt morphology. There is increasing evidence that prophylactic antiepileptic drugs do not prevent PANS. Treatment is centered around controlling neurologic signs with antiepileptic drugs and providing supportive intensive care. The 30-day survival rate in studies that included a minimum of four dogs affected by PANS was 0%-100% (median, 50.0%) and 0%-75.0% (median, 37.5%) for those with PAS. Mortality associated with PANS was typically related to occurrence of generalized seizure activity. Prognostic factors positively associated with short-term survival included having a history of preoperative seizures and development of focal seizures only. If affected dogs survived to discharge, survival for several years was possible, and the majority of neurologic signs manifested as part of the phenomenon of PANS appeared to resolve.

**Protein C and comparative biochemical changes in dogs treated with percutaneous transvenous coil embolization of congenital intrahepatic portosystemic shunts**

*Sunlight C et al.*


**Objective:** To evaluate protein C (PC) activity after intrahepatic portosystemic shunt (IHPSS) percutaneous transvenous coil embolization (PTCE) in dogs; to identify if PC is associated with clinical status after intervention, and to compare PC with standard biochemical values.

**Study design:** Retrospective case series.

**Animals:** Forty-seven client-owned dogs with IHPSS undergoing PTCE.

**Methods:** Records were reviewed for preoperative and postoperative PC, hematocrit (HCT), mean corpuscular volume (MCV), albumin (ALB), and blood urea nitrogen (BUN). Ultimate clinical status was classified
as excellent, fair, or poor, based on ongoing medical management and the presence of clinical signs. Intrahepatic portosystemic shunt was considered to be completely or incompletely occluded intraoperatively based on angiography.

**Results:** Postoperative PC activity increased in 37/47 (78.7%) dogs with a mean increase of 8.7% ± 2.1%. Ultimate postoperative clinical status was excellent in 16/43 (37.2%), fair in 19/43 (44.2%), and poor in 8/43 dogs (18.6%). No association was detected between preoperative PC (46.8% ± 1.8%) and ultimate clinical status but mean postoperative PC (75.7% ± 1.4%), HCT, MCV, ALB, and BUN were higher in dogs with excellent clinical status. Postoperative PC activity was higher when shunts were completely occluded (96.3% ± 10.9%), which was a finding associated with excellent status.

**Conclusion:** Postoperative, but not preoperative, PC activity was higher in dogs with better ultimate clinical status. Similar trends were noted in standard hematological and biochemical values. Complete occlusion of shunts was associated with a higher postoperative PC and superior ultimate clinical status.

**Clinical significance:** Postoperative PC may provide valuable information about the success of PTCE for IHPSS as it relates to the ultimate status and the need for additional procedures.

**Long-term outcome and quality of life of dogs that developed neurologic signs after surgical treatment of a congenital portosystemic shunt: 50 cases (2005–2020)**

**Carrera AE et al**

JAVMA 260: 236-334, 2022;
https://doi.org/10.2460/javma.20.11.0606

**Objective:** To determine survival time and quality of life of dogs that developed postattenuation neurologic signs (PANS) after surgical treatment of a single congenital portosystemic shunt and survived at least 30 days and identify whether neurologic signs present at the time of discharge would resolve or reoccur.

**Animals:** 50 client-owned dogs.

**Procedures:** Medical records were retrospectively reviewed, and follow-up data relating to neurologic signs and seizure activity were obtained. Owners were asked to complete a questionnaire related to the presence of neurologic signs, including seizures, and their dog’s quality of life.

**Results:** Thirty of the 50 (60%) dogs had postattenuation seizures with or without other nonseizure neurologic signs, and 20 (40%) had neurologic signs other than seizures. Neurologic signs had fully resolved by the time of discharge in 24 (48%) dogs. Signs resolved in 18 of the remaining 26 (69%) dogs that still had PANS other than seizures at the time of discharge. Seizures reoccurred in 15 of the 30 dogs that had postattenuation seizures.

Twenty-seven of 33 (82%) owners graded their dog’s long-term (> 30 days after surgery) quality-of-life as high. Forty-five (90%) dogs survived > 6 months. Most (29/43 [67%]) neurologic signs (other than seizures) present at the time of hospital discharge resolved.

**Clinical relevance:** Findings highlighted that survival times of > 6 months and a high QOL can be achieved in most dogs with PANS that survive at least 30 days. Most neurologic signs other than seizures resolved within 1 month postoperatively. Half of the dogs with postattenuation seizures had a reoccurrence.
Hypertrophic osteodystrophy is an uncommon orthopaedic disease that affects young, growing dogs. Aetiology is currently unknown; however, several unproven etiologies have been theorised in the literature including canine distemper virus, previous vaccination, hereditary causes and auto-immune disorders. Affected animals often present with varying degrees of lameness, lethargy, pyrexia and/or distal metaphyseal swelling of affected limbs. An index of suspicion is based on clinical signs. Confirmation is obtained with radiographs of the affected limb(s) by the presence of a "double physis," or a radiolucent line that is parallel to the physis. Treatment varies depending on degree affected, but generally consists of anti-inflammatory steroids, pain medications, gastrointestinal support, nutritional management and appropriate supportive care. Critically affected patients require intensive monitoring and more aggressive supportive care for prevention of life-threatening sequelae. Prognosis is very favourable with mildly and moderately affected patients, but good to guarded in severely affected patients.

**Study design:** Systematic review.

**Methods:** Google Scholar and Pubmed databases were searched for studies evaluating postoperative CCLD rehabilitation interventions from 1990 until March 2020 per the international Prospective Register of Systematic Reviews (PROSPERO). Each study was assigned a level of evidence score from I to IV and a risk of bias (RoB) score by 2 reviewers, and by a third reviewer, when consensus was not reached.

**Results:** Nineteen studies met the inclusion criteria. Twelve comprised randomized, controlled trials (Level II), 6 were nonrandomized or nonblinded (Level III), and one was retrospective (Level IV). Nine studies had high RoB scores. Sixteen studies yielded positive results. Therapeutic exercise had the most studies with positive results but all had high RoB. Cold compression therapy had 3 supporting studies (2 Level II, low RoB). Extracorporeal shockwave yielded 2 positive Level II studies (low-moderate and high-moderate RoB) and photobiomodulation had 1 positive study (Level II, low RoB) with objective outcomes. A negative outcome was noted in 1 photobiomodulation study. There was 1 supporting study on electrical stimulation and there was none on low-intensity pulsed ultrasound.

**Conclusion:** This systematic review supports the use of rehabilitation interventions in recovery of postoperative CCLD in dogs; however, many studies had a high risk of bias.

**Clinical significance:** There is a lack of class I level evidence in veterinary rehabilitation. This study supports therapeutic exercise and cold compression therapy for postoperative CCLD rehabilitation. Existing studies on other modalities are limited and demonstrate conflicting results.
Outcome of rest with or without bandaging for treatment of carpal flexural contracture deformities in puppies: 47 puppies and 75 joints (2000–2018)

**Petazzoni M et al**
JAVMA 260: 320-325; https://doi.org/10.2460/javma.20.10.0556

**Objective**: To review outcome of dogs with carpal flexural contracture deformities treated with rest alone or with rest and bandaging.

**Animals**: 47 dogs (75 joints).

**Procedures**: Medical records of dogs with unilateral or bilateral carpal flexural contracture deformities were reviewed, and dogs were grouped according to deformity severity grade (graded on a scale from 1 to 3) at the time of diagnosis. Two treatment groups were compared: rest only and rest with a modified Robert-Jones bandage. All dogs were reevaluated weekly until recovery (ie, resolution of the deformity and lameness).

**Results**: All dogs responded to conservative management, with all dogs regaining full extension of the antebrachiocarpal joint and ambulating normally at the time of the final visit. Mean ± SD time from initial diagnosis to recovery (ie, resolution of the deformity and lameness) was 2.9 ± 2.2 weeks (median, 2 weeks; range, 1 to 9 weeks). For dogs with grade 1 or 2 severity, mean time to recovery did not differ significantly between treatment groups. For dogs with grade 3 severity, however, mean time to recovery was significantly shorter for dogs treated with rest and bandaging than for dogs treated with rest alone.

**Clinical relevance**: Results suggested that conservative management (rest alone or rest and bandaging) was a successful treatment option for puppies with carpal flexural contracture deformity and that bandaging resulted in a shorter time to recovery for dogs that were severely affected.

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Neurology

Retrospective evaluation of the relationship between admission variables and brain herniation in dogs (2010–2019): 54 cases

**Jiwoong Her J et al.**

**Objective**: To document the admission systolic blood pressure (SBP), heart rate (HR), and modified Glasgow coma scale (MGCS) score in dogs with and without brain herniation and to determine their relationship with brain herniation.

**Design**: Retrospective study between 2010 and 2019.

**Setting**: University veterinary teaching hospital.

**Animals**: Fifty-four client-owned dogs with brain herniation and 40 client-owned dogs as a control group, as determined on magnetic resonance imaging.

**Interventions**: None.

**Measurements and main results**: SBP, HR, MGCS score, and outcome were extracted from medical records. MGCS score was retrospectively calculated based on initial neurological examination in dogs with adequate available information. Dogs with brain herniation had a significantly higher SBP (P = 0.0078), greater SBP–HR difference (P = 0.0006), and lower MGCS score (P < 0.0001) compared to control dogs. A cutoff value of an SBP ≥ 178 mm Hg, SBP–HR ≥ 60, and MGCS score ≤ 14 each provides a specificity of 90%–98%. A combination of an SBP > 140 mm Hg and HR < 80/min provided 24% sensitivity and 100% specificity to diagnose dogs with brain herniation (P < 0.0001).

**Conclusions**: A high SBP, a greater difference between SBP and HR, a combination of higher SBP and lower HR, and a low MGCS score were associated with brain herniation.
in dogs presenting with neurological signs upon admission. Early recognition of these abnormalities may help veterinarians to suspect brain herniation and determine timely treatment.

**Comparison of serum creatine kinase and aspartate aminotransferase activity in dogs with Neospora meningoencephalitis and noninfectious meningoencephalitis**

**Jones BS, Harcourt-Brown T**


**Background:** Creatine kinase (CK) and aspartate aminotransferase (AST) activity can be increased with myositis associated with Toxoplasma and Neospora infection in dogs.

**Hypothesis/Objectives:** Serum activity of CK and AST can be used as a rapid screen for predicting positive serology in meningoencephalitis caused by Toxoplasma gondii or Neospora caninum in dogs compared to dogs with noninfectious meningoencephalitis.

**Animals:** Eighty dogs with meningoencephalitis based on magnetic resonance imaging and cerebrospinal fluid analysis.

**Methods:** Retrospective case-control study. Serological cutoffs (≥1:800 immunofluorescence for Neospora and ≥1:400 IgG or ≥1:64 IgM or both for Toxoplasma) categorized dogs as infected (n = 21, all neosporosis) or noninfected (n = 59). Activities of CK and AST between infected and noninfected groups were compared using a Mann-Whitney U test and receiver operating characteristic curve analysis.

**Results:** No dogs were diagnosed with toxoplasmosis. Serum CK and AST activities were significantly increased (P < .001) in dogs with positive serology for Neospora (CK: median, 1334 U/L; range, 281-3633 U/L and AST: median, 124 U/L; range, 59-333 U/L) compared to noninfectious cases (CK: median, 215 U/L; range, 69-683 U/L and AST: median, 36 U/L; range, 19-139 U/L). A CK cutoff of 485 U/L had 95.24% sensitivity and 96.61% specificity with a negative predictive value of >99%. An AST cutoff of 57 U/L had 94.44% sensitivity and 85.71% specificity with an estimated negative predictive value of 99%.

**Conclusions and clinical importance:** High serum CK and AST activity can increase suspicion for neosporosis while awaiting serological tests for dogs with meningoencephalitis.

**Poisoning**

Retrospective analysis of hops toxicosis in dogs (2002-2014): 71 cases

**Alexandra Pfaff A et al.**


**Objective:** To describe a population of dogs with hops toxicosis, including clinical signs observed, treatments performed, patient outcome, and overall prognosis. Clinical findings and treatment interventions were evaluated for their potential effects on outcome. This study also aims to review hops toxicosis and treatment options.

**Design:** Retrospective observational study.

**Setting:** Poison Control Center.

**Animals:** Seventy-one dogs presenting for hops ingestion.

**Interventions:** None.
Measurements and main results: Records of 71 dogs with known hops ingestion from the ASPCA – Animal Poison Control Center (ASPCA-APCC) database and the Tufts University medical record system were reviewed. Fifty-nine (77%) of the dogs survived. The most common clinical signs on presentation were hyperthermia and tachycardia, with presenting temperatures and heart rates significantly higher in nonsurvivors. There was no significant difference between survivors and nonsurvivors in regard to signalment. Time to presentation was shorter in survivors (5.0 vs 5.5 h; P < 0.0001). The median amount of hops ingested was higher in nonsurvivors (2 vs 2.5 oz; P < 0.0001). Hops ingestion caused hyperthermia in 96% (68/71) of dogs. The median time to death in the nonsurvivor group was 10.7 hours (2-30 h). None of the decontamination, cooling, or treatment measures (dantrolene, cyproheptadine, sedatives) evaluated in this population were associated with improved survival. After adjusting for cooling, time to presentation, and dantrolene administration, every degree of elevation in temperature was associated with a 78% increased chance of death. All dogs that survived to discharge had complete resolution of clinical signs.

Conclusions: Hops toxicosis can result in significant hyperthermia, tachypnea, and tachycardia. Seventy-seven percent of dogs survived with intensive treatment. Continued education of the potential for hops toxicosis is advised.

Objectives: To describe clinical cases of aspiration pneumonitis and pneumonia in dogs, which were successfully managed without antimicrobials.

Materials and Methods: Retrospective case review of dogs presenting to a referral teaching hospital between February 2014 and February 2021. Cases were included when a clinical diagnosis of aspiration pneumonopathy was made (requiring one or more of the following: radiographic evidence of an aspiration pneumonopathy, endotracheal airway sampling consistent with aspiration and/or a positive endotracheal airway sample culture) which was not treated with antimicrobial therapy.

Results: Fourteen cases were identified of which nine had respiratory signs including increased respiratory rate or effort (n=8), arterial hypoxaemia (n=2), or a clinician-determined requirement for oxygen therapy (n=4). Where haematology was performed, five of nine displayed a normal neutrophil count with toxic changes, three displayed neutrophilia and one displayed neutropenia with toxic changes. Endotracheal airway sample cytology in four cases revealed neutrophilic inflammation with bacteria, plant material, yeasts and unidentified foreign material. Where respiratory signs were present, these resolved within 12 to 36 hours.

Clinical significance: In this case series, immunocompetent dogs sustaining aspiration events, even with classical evidence of pneumonitis or pneumonia, have been managed successfully without antimicrobials. Radiography alone cannot be used to determine the requirement for antimicrobials. Better characterisation of the pathogenesis and clinical trajectory of aspiration pneumonopathy is required, which may enable a reduction in inappropriate antimicrobial prescriptions.
Bacterial infection in dogs with aspiration pneumonia at 2 tertiary referral practices

Howard J et al.
https://doi.org/10.1111/jvim.16310

Background: In dogs, antimicrobial drugs are widely prescribed for aspiration pneumonia (AP) despite poor documentation of bacterial infection in AP (b-AP) using bronchoalveolar lavage fluid (BALF) analysis. Interpreting discordant cytology and culture results is challenging, contributing to lack of a criterion standard, and highlighting differences between veterinary and human medical criteria for b-AP.

Objectives: Determine how many dogs with AP had BALF collection and differences in diagnosis of b-AP using veterinary vs human medical criteria. Report findings of noninvasive markers (e.g. fever, band neutrophilia, radiographic severity score) in dogs with and without b-AP.

Animals: Retrospective cohort study of client-owned dogs (n = 429) with AP at 2 university veterinary hospitals. Twenty-four dogs met enrollment criteria.

Methods: Inclusion criteria were radiographic diagnosis of AP, ≥1 risk factor, CBC findings, and BALF cytology and culture results. Veterinary medical b-AP criteria were cytology findings compatible with sepsis with or without positive culture, or cytology findings not consistent with sepsis and positive culture (≥1.7 × 103 cfu/mL). Human medical b-AP criteria required culture with ≥104 cfu/mL or > 7% cells with intracellular bacteria on cytology.

Results: Only 24/429 dogs met all enrollment criteria; 379/429 dogs lacked BALF collection. Diagnosis of b-AP differed using veterinary (79%) vs human (29%) medical criteria. Fever, band neutrophils and high radiographic scores were noted in dogs with and without b-AP.

Conclusions and clinical importance: Lack of routine BALF collection hampers definitive recognition of bacterial infection in AP. Differences in dogs meeting veterinary vs human medical definitions for b-AP and usefulness of noninvasive markers warrant further study to improve understanding of the role of bacteria in AP.

Laryngeal paralysis secondary to cervical bite injuries in five dogs

Picavet PP et al
NZ Vet J 70: 109-118, 2022;
https://doi.org/10.1080/00480169.2021.1951865

Case histories: Medical records of a veterinary hospital in Belgium were reviewed for dogs (n = 5) that presented between 2016 and 2019 with laryngeal paralysis secondary to bite wounds to the cervical region received while fighting with other dogs. The time elapsed between the trauma and presentation was from a few hours up to 5 days.

Clinical findings and treatment: Bilateral laryngeal paralysis was identified in three dogs and unilateral laryngeal paralysis in two dogs via endoscopic assessment of laryngeal function. The primary concomitant lesions included tracheal injury in 3/5 dogs and oesophageal injury in 1/5 dogs. One dog with bilateral laryngeal paralysis was treated medically as no signs of dyspnoea were present. Surgical management was elected in 4/5 dogs based on evaluation of their clinical status and lesions revealed by endoscopic examination of upper gastrointestinal and respiratory tracts. Dogs underwent surgical procedures that were determined to be appropriate for treatment of the lesions identified on clinical examination, diagnostic imaging, and endoscopy. The cervical region was explored through a ventral midline approach in 2/4 cases, to close tracheal perforations. Temporary tracheostomy was performed in 2/4 cases. Procedures to correct brachycephalic airway obstructive
syndrome were performed in 2/4 cases. Cricoarytenoid lateralisation was performed in 2/4 dogs. Dogs were hospitalised for 2–10 days and received antimicrobial therapy before surgery and for 2–3 weeks after surgery. Physical examination and respiratory function were normal in 3/5 dogs 4–6 months after discharge. Information regarding outcomes for two cases was obtained from the owners by telephone assessment 1–6 months after surgery. The owner of each dog reported the respiratory function to be excellent.

**Diagnosis:** Uni- or bilateral, transient or permanent laryngeal paralysis with concomitant oesophageal, tracheal, or laryngeal lesions following cervical dog bite injuries diagnosed by endoscopic examination of upper gastrointestinal and respiratory tracts.

**Clinical relevance:** This case series describes the diagnosis and management of dogs with laryngeal paralysis secondary to cervical dog bite injuries. To the authors’ knowledge, this is the first published report documenting bilateral laryngeal paralysis secondary to cervical dog bite injuries. Clinicians should be aware of this pathology and the importance of investigating laryngeal function in dogs presenting with cervical bites, particularly those with inspiratory dyspnoea. Upper airway and digestive endoscopy are recommended for complete assessment of cervical traumatic injuries.

**Skin**

**Outcome of superficial brachial axial pattern flaps used to close skin defects in dogs: 16 cases (1996-2019)**

**E. Villedieu E et al.**


**Objectives:** To report the complication rate, type of complications and outcome of the superficial brachial axial pattern flap when used for closure of skin defects in dogs.

**Materials and Methods:** Medical records of dogs treated with a superficial brachial axial pattern flap for closure of a skin defect were reviewed. Information regarding signalment, reason for axial pattern flap use, skin flap size, flap healing, postoperative complications and need for revision surgery was collected.

**Results:** Sixteen dogs were included in the study. Indications for the superficial brachial axial pattern flap included closure following tumour removal (15/16, 94%) and management of a non-healing wound on the olecranon (1/16, 6%). Postoperative complications occurred in all dogs and included partial dehiscence (7/16, 44%), partial flap necrosis (6/16, 38%), seroma formation (5/16, 31%), flap oedema (3/16, 19%) and complete flap necrosis (2/16, 13%). Eight flaps (50%) healed without open wound management or additional surgery. Five dogs required open wound management without additional surgery, and three dogs (19%) required revision surgery.

**Clinical significance:** Use of the superficial brachial axial pattern flap was associated with a high rate of complications. Most complications were managed without additional surgery and all wounds eventually healed, in some cases after prolonged open wound management.

**CATS AND DOGS**

**Infection rate treating radial and ulnar fractures using bone plate fixation without antibiotic prophylaxis**

**Schmökel H et al.**


**Objectives:** To evaluate the effectiveness and complication rate of a 1.5- and 2.0-mm
titanium locking plate for the treatment of radial and ulnar fractures in small dog breeds and cats without peri-operative antibiotic prophylaxis in a prospective case series.

**Materials and Methods:** Medical records and radiographs of closed radial and ulnar fractures treated using internal fixation with a 1.5- or 2.0-mm titanium locking plate without antibiotic prophylaxis were collected prospectively. Patients were clinically followed up until radiographical fracture healing was complete.

**Results:** Thirty-two fractures in small breed dogs and cats with an average bodyweight of 3.9 kg met the inclusion criteria. The follow-up time radiographically and clinically was 4–35 weeks. All fractures showed radiographical fracture union, and all patients had a good clinical outcome. The superficial infection rate in this case series was 0%; the deep infection rate involving the implant/bone was 3.1%.

**Clinical significance:** The novel 1.5- and 2.0-mm titanium locking plate system was successfully used to treat simple closed radial and ulnar fractures in small breed dogs and cats without peri-operative antibiotic prophylaxis, resulting in good clinical outcome and a low infection rate.

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**Retrospective evaluation of the prognostic utility of plasma lactate concentration and serial lactate measurements in dogs and cats presented to the emergency room (January 2012 – December 2016): 4863 cases**

**Saint-Pierre LM et al.**


**Objective:** To determine the prognostic significance of plasma lactate concentration, plasma lactate clearance, and delta lactate in dogs and cats presented to an emergency room (ER).

**Design:** Retrospective study.

**Setting:** University teaching hospital.

**Animals:** A total of 8,321 animals with a plasma lactate concentration measured with 4,863 presenting to the ER and 1,529 dogs and 444 cats having a measurement within 4 hours of admission.

**Interventions:** None.

**Measurements and main results:** Plasma lactate concentration of dogs and cats presented to a university teaching hospital was retrospectively evaluated. Of dogs and cats with a plasma lactate concentration measured within 4 hours of admission to the ER, hyperlactatemia was common, and the prevalence of hyperlactatemia for dogs 78% (361/462) and cats 67% (78/116) was highest when evaluated within the first 30 minutes following admission. The distribution of patient’s plasma lactate concentration was significantly higher in non-survivors compared to survivors at all time points evaluated (P < 0.001). Both lactate clearance (P = 0.010) and delta lactate (P = 0.013) were significantly different between survivors and nonsurvivors. A delta lactate > 4.5 mmol/L was 100% (95% CI: 95 to 100%) specific for nonsurvival in patients with hyperlactatemia measured within 1 hour of admission to the ER. The most common cause of hyperlactatemia was shock in dogs (24%) and urinary tract diseases in cats (22%). Shock was associated with the highest mortality rate in both dogs (61%) and cats (77%). Hyperlactatemia was significantly associated with increased mortality for dogs with shock (P = 0.001), respiratory diseases (P = 0.022), diabetes mellitus (P = 0.018), and liver dysfunction (P = 0.006).
Conclusions: Hyperlactatemia was associated with mortality in both dogs and cats when measured at any time point in the 4 hours following admission to the ER. Serial lactate measurement may also be a valuable tool to guide clinical management decisions.

EXOTICS

Rabbits

Clinical, surgical, and pathological findings in client-owned rabbits with histologically confirmed appendicitis: 19 cases (2015–2019)

Di Girolamo N et al
JAVMA 259: 82-91, 2021; https://doi.org/10.2460/javma.20.08.0446

Objective: To report clinical, surgical, and pathological findings in client-owned rabbits with histologically confirmed appendicitis.

Animals: 19 rabbits.

Procedures: Medical records for client-owned rabbits that had a histologic diagnosis of appendicitis were reviewed.

Results: Median age of the rabbits at presentation was 24.0 months (range, 4 to 84 months). Seventeen cases occurred during the summer and fall seasons. Decreased appetite (17/19 rabbits), abnormal rectal temperature (hyperthermia, 9/16 rabbits; hypothermia, 4/16 rabbits), hypocalcemia (8/11 rabbits), and hypoglycemia (7/15 rabbits) were common signs. Abdominal ultrasonography and CT findings were suggestive of appendicitis in 6 of 8 rabbits and in 1 of 2 rabbits, respectively. Of the 6 rabbits that received medical treatment, 3 died at 48 hours, 1 died at 24 hours after hospitalization, and 1 died at 10 days after presentation; 1 rabbit was alive at 1,030 days after presentation. Of the 8 rabbits that underwent appendectomy, 3 died before discharge from the hospital and 1 died 113 days after surgery; 4 rabbits were alive at 315, 334, 1,433, and 1,473 days after presentation. The remaining 5 rabbits either died or were euthanized before treatment could be instituted. In each of the 19 rabbits, the appendix had evidence of severe inflammation with mucosal ulceration, heterophilic inflammation, and necrotic debris.

Clinical relevance: For rabbits with decreased appetite and an apparently painful abdomen, hyperthermia, hypocalcemia, or hypoglycemia, appendicitis should be considered as a differential diagnosis. Further comparisons of medical and surgical treatments are required to establish treatment recommendations for rabbits with appendicitis.

Guinea Pigs

Diagnosis and management of nasopharyngeal stenosis in four guinea pigs (Cavia porcellus)

Knutson KA et al

Respiratory disease is common in guinea pigs (Cavia porcellus). As obligate nasal breathers, disease of the upper airway can result in significant dyspnea. Nasopharyngeal stenosis is defined as a luminal narrowing of the nasopharynx, which extends from the choana to the caudal margin of the soft palate. This condition can be acquired or congenital and has been diagnosed in other species. However, nasopharyngeal stenosis has not been previously described in guinea pigs. Four guinea pigs were presented with chronic, recurrent upper respiratory signs including stertor, oculonasal discharge, tachypnea, and dyspnea. All four animals had signs suggestive of upper respiratory tract disease on examination. Nasopharyngeal stenosis was identified at the rostral aspect of the nasopharynx at the level of the choana.
via computed tomography (CT) in all cases. Otitis media was also present in three of the four cases. Antibiotic therapy was instituted for all animals. Two of the four guinea pigs were treated with prednisolone and two were treated with meloxicam to control associated inflammation. One animal died 2 months after diagnosis due to complications from severe otitis media. One individual was euthanized due to progressive disease after a year and a half of treatment. One guinea pig was lost to follow up after 6 months. The remaining guinea pig was alive at the time this case series was written (11 months after initial diagnosis) but continues to have signs of upper airway disease. Nasopharyngeal stenosis is an important differential diagnosis for persistent upper respiratory signs in guinea pigs. CT was diagnostic in all cases, identifying nasopharyngeal stenosis at the level of the choana, and allowed identification of comorbidities (otitis media and rhinitis). Medical management resulted in survival times from 2 months to a year and a half following diagnosis. Further investigation into minimally invasive interventions such as balloon dilation and stent placement are warranted for future cases.

Ferrets

The biological variation, index of individuality, and reference change value for haematological and blood chemical analytes in ferrets (Mustela putorius furo)

Sitompul YY et al

Background: Understanding biological variation is important when establishing or using currently published reference intervals (RIs) to evaluate hematological and blood chemical analysis results. Population based RIs may not be sensitive enough to identify clinically significant changes in individuals when the intraindividual variation is lower than the interindividual variation. This is the first study with the aim to investigate the biological variation of hematological and biochemical analytes and then to calculate the reference change values (RCVs) in ferrets.

Methods: This retrospective study analyzed blood test results of 13 ferrets that have been tested every year for 7 years. Intraindividual and interindividual coefficients of variation for each analyte were calculated using restricted maximum likelihood that is suitable for unbalanced design since five ferrets died earlier, before determining the index of individuality (IoI) and RCV.

Results: No analytes had IoI lower than 0.6. The IoI of mean corpuscular hemoglobin (MCH), calcium, blood urea nitrogen (BUN), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total protein, albumin, and globulin were between 0.6 and 1.4. The IoI of red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, MCH concentration (MCHC), white blood cell count, lymphocytes, monocytes, neutrophils, eosinophils, basophils, sodium, potassium, phosphate, glucose, creatinine and amylase were higher than 1.4. In this study, the RCVs varied from 6.87% (sodium) to 391.46% (basophils).

Conclusions and clinical relevance: The results of this study indicate that population based RIs are appropriate to evaluate most analytes in this study. Population based RIs should be used with caution to evaluate MCH, calcium, BUN, ALT, ALP, total protein, albumin, and globulin. The hematological and blood chemical RCVs calculated in this study can assist in diagnosing diseases, and monitoring and evaluating the performance of long-term treatments.
Guidelines for Authors: Writing a case report (review, or scientific paper)

So, you have just been involved with an interesting case. Would you like to tell your colleagues about it? Consider writing a case report for the Australian Veterinary Practitioner! It is not as difficult as you might believe and is a very good way to consolidate your learning. It is also great to see your name in print!

A case report (or series of cases, or a review or scientific study) should be structured along the following lines.

Title
- The title should be succinct and descriptive of the condition you are reporting

Name(s) of the author(s)
- Surname(s) and initials, e.g. Jones AB, Smith XZ,* Young DD
- Corresponding author is identified by *
  The person’s email address given as a footnote, e.g.
  * Corresponding author: smithxz120@zmail.com.au

Addresses/affiliations of the author(s)
- If all authors are from the same practice address, it is included immediately under the names, e.g.
  Jones AB, Smith XZ,* Young DD
  Felix’s Veterinary Practice, 123 Kitty Rd, Catswood 3999, VIC, Australia
- If authors are at different addresses, these need to be listed separately under the names and identified by superscript letters, e.g.
  Jones AB, a Smith XZ, b* Young DD a
  a Felix’s Veterinary Practice, 123 Kitty Rd, Catswood 3999, VIC, Australia
  b Diagnostica, Imogen Place, Brisbane 4004, QLD, Australia

The addresses should be the one(s) at which the authors were working at the time the case was seen. If an author has subsequently moved, this can be indicated by an additional superscript letter, e.g.
- Jones AB, a Smith XZ, b* Young DD a,c
  a Felix’s Veterinary Practice, 123 Kitty Rd, Catswood 3999, VIC, Australia
  b Diagnostica, Imogen Place, Brisbane 4004, QLD, Australia
  c Current address: Pete’s Practice, Glenorchy, TAS, 7999
The paper is then separated into the following headings

ABSTRACT

The Abstract should detail the key facts about the report. It is often useful to use the sub-headings, such as Case Report and Conclusions.

- Case Report: Summarise the salient features of the case, viz signalment, key clinical signs, results of important diagnostic tests/procedures, treatment and outcome (both short- and long-term if known).
- Conclusion(s): Summarise the ‘take-home message’ from the case report.

KEYWORDS

List a few important words or phrases that would be useful to a person who might be searching for a case such as yours on the internet.

ABBREVIATIONS

If you use any abbreviations in your report, list and define them. Avoid the temptation to abbreviate a word (or group of words) that are only used 2-3 times in the paper. Also note that an abbreviation is taken to mean both singular and plural, so there is no need to add an ‘s’ if you defined it as the former and then use it as the latter at some point in the paper.

INTRODUCTION

This is essentially a literature review of pertinent material that sets the scene for the report. Such information needs to be referenced. It helps to summarise why the reporting of this case is important.

The first time that a reference is cited in the text of the paper, it is given a number. Numbers are allocated sequentially, commencing with 1. Thereafter, every time that reference is cited its number is used to identify it. References are listed at the end of the report (see later).

References are usually noted at the end of the sentence to which they refer, as superscript numbers, and after the punctuation mark, e.g. .......... has also been reported.

However, they can also be used within sentence, e.g.

There are six canine\textsuperscript{1-6} and four feline\textsuperscript{7-10} cases that have previously been reported.

CLINICAL FEATURES

Essentially, this section is similar to the SOAP- or HEAP-type approach in the case record. It should be presented in chronological order and, if appropriate, can be presented under the following self-explanatory sub-headings:

- Case history
- Clinical findings
- Diagnostic procedures
- Differential diagnoses
- Treatment
- Outcome, including how it was assessed, and possibly including prognosis.
Tables
• Data may be presented in a Table(s), with reference to it/them in the appropriate part(s) of the text as Table 1, Table 2, etc.
• All Tables are located after the list of references.
• All measurements (in the text of the paper and the Tables) must be in SI units.

Figures
• Relevant, high-resolution images/figures may be included. They must be identified in the appropriate part of the text as Figure 1, Figure 2, etc.
• All Figures are listed after any Tables (after the list of references)
• Each Figure must have a short title, followed by and legend (brief description).

DISCUSSION
The Discussion might include:
• Comparison of the reported case to any similar reports/studies in the literature.
• Strength and/or weaknesses of the present case report (especially its diagnostic procedures, treatment, etc.)
• Conclusion(s): A summary of the most important message(s) from the case report.

ACKNOWLEDGEMENTS
This is the area where you can thank people who have made an important contribution to the paper, but are not listed as an author, e.g. referring veterinarian, radiologist, pathologist.

CONFLICTS OF INTEREST AND SOURCES OF FUNDING
State any of the latter. If none, write “The authors declare no conflicts of interest or sources of funding for the work presented herein.”

REFERENCES
References must conform to the following style:
• For papers:
  Authors. Title of paper. Journal (abbreviated and italics) Year;Issue:pages.
  For example
• For chapters in books:
  For example
TABLES

• Tables must have a succinct title and concise column headings.
• Any abbreviations must be defined in a footnote to the Table.

FIGURES

• Figures must have a succinct title, followed by a short summary of the salient features of the figure/image.
• Photographs should be submitted as high resolution jpeg or tiff files, preferably 300 dpi. The image should be titled Figure 1, etc. to correspond with the text.

SUBMISSION

Submitting a paper to the Australian Veterinary Practitioner is simple.

Write an email to the editor indicating that you are submitting an original piece of work, that is not under consideration, or has not been published, elsewhere. (An exception to the latter may be work that has been presented at a conference, with an Abstract that has been published. If this is the case, let the editor know the details.)

Confirm that all authors have contributed to the paper and agree with its contents.

Attach the paper, plus figures as individual images, and hit send.

Well, that’s about it. Your paper is then sent for peer-review.

If you have any questions as you structure your case report or other article, send the Editor an email at editor.avp@ava.com.au

Which reminds me, the journal also publishes “What is your diagnosis?” papers.

If you have a case that fits such a format, please contact the editor.

Bruce Parry, Editor
March 2022
Ever get asked why veterinary services cost what they do?

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