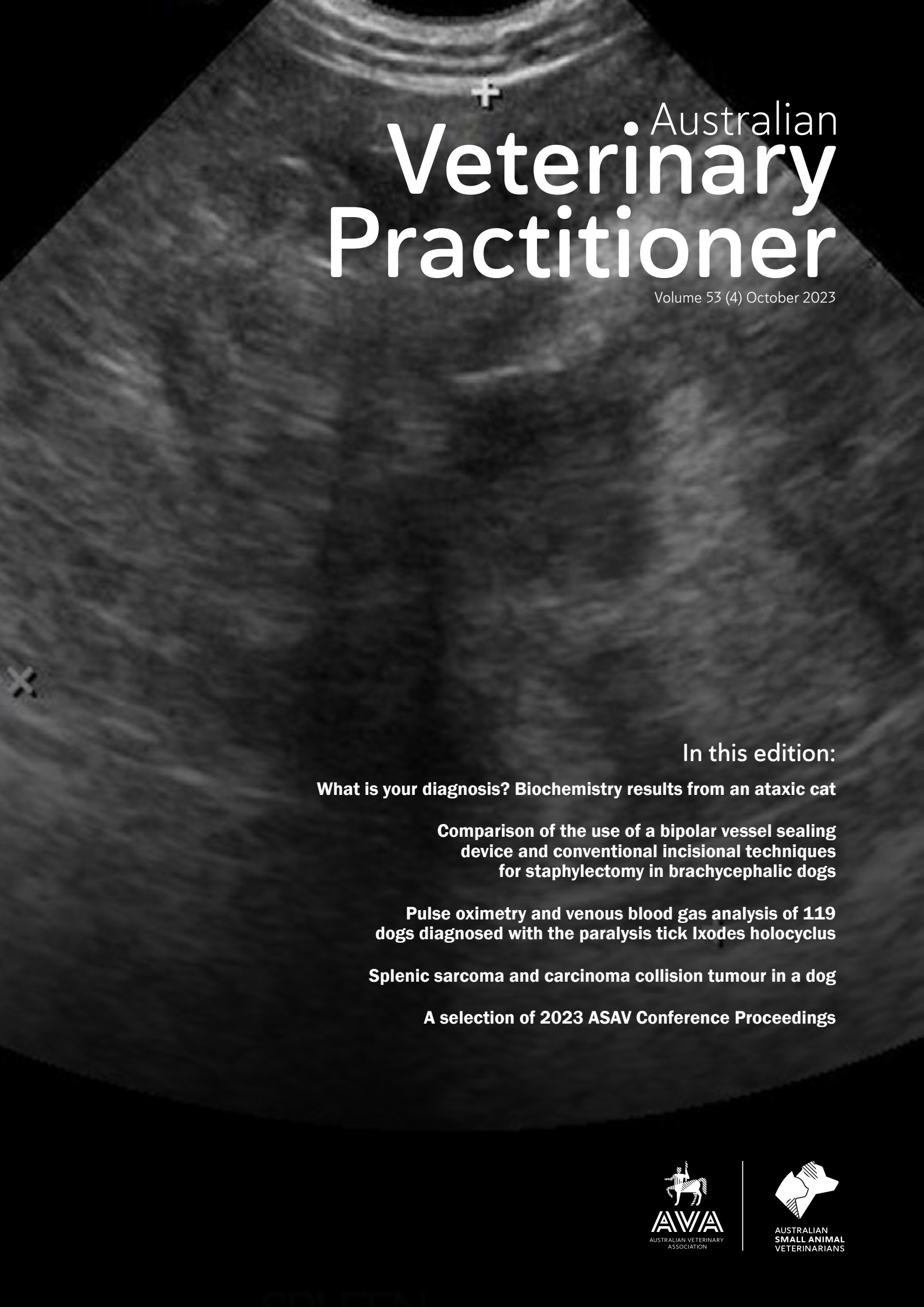

Australian Veterinary Practitioner

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In this edition:

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AUSTRALIAN SMALL ANIMAL VETERINARIANS

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AUSTRALIAN SMALL ANIMAL VETERINARIANS

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/siteassets/library/journal/australian-veterinary-journal/australian-veterinary-practitioner---guide-to-authors-12.9.22.pdf

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Message from the Editor

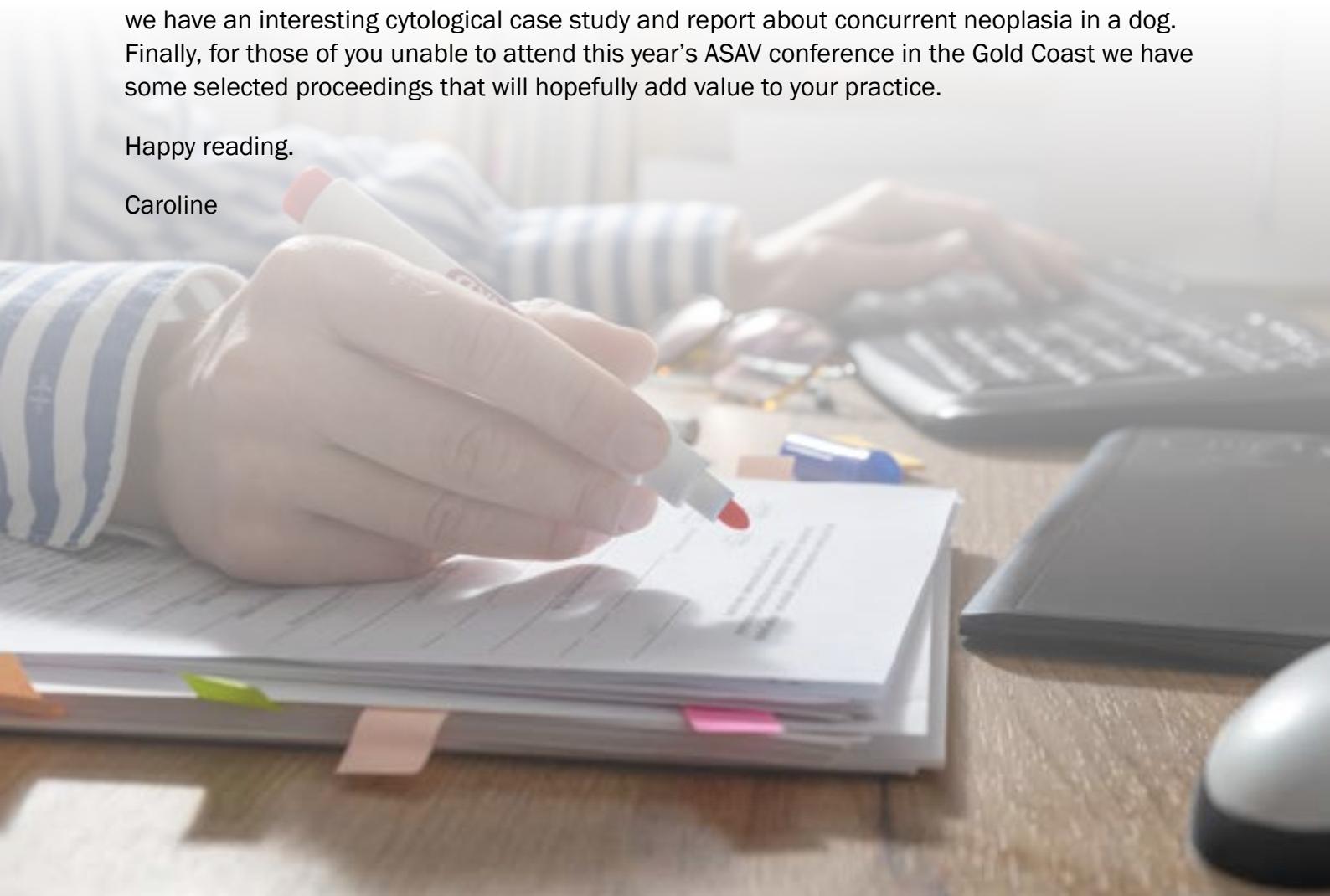
Thank you for reading this volume of the AVP, the penultimate issue for 2023. We are happy to have recently received a large number of submissions to the journal. Many of these are from residents waiting to credential for their upcoming ANZCVSc examinations. This highlights several points. Firstly, there is an important role the AVP plays in providing a forum for Australian residents to submit papers to in the increasingly competitive market. Secondly, that the need for reviewers to be available and able to complete reviews in a timely fashion is equally important for the AVP to achieve this role. Finally, it raises concerns that the timeline many residents set is unrealistic to achieve their goals. Optimally, submission should be completed months prior to the required acceptance date, but likely due to pressures of the residency this is not handled until the last minute for many. Over the coming months, I hope to produce some guidelines for residents (including timelines), assistance for those that may not have academic support in how to appropriately write journal articles and a more streamlined process for submission.

The benefit of the AVP extends beyond resident credentialing completion though, as ideally it should serve as a forum for education and dissemination of new information for all ASAV members. Again, a mix of publication types (original articles) with 1-2 problem-based issues a year is what is currently planned. If you have ideas or suggestions that you think would help increase AVP value, please let us know at editor.avp@ava.com.au.

In this volume, we have two case series that look at relatively common problems in small animal practice: surgical techniques for brachycephalic dogs and tick paralysis. Additionally, we have an interesting cytological case study and report about concurrent neoplasia in a dog. Finally, for those of you unable to attend this year's ASAV conference in the Gold Coast we have some selected proceedings that will hopefully add value to your practice.

Happy reading.

Caroline



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With the theme ‘Living Well’, the program will focus on improving the quality of life for animals with chronic conditions and enhancing veterinary practice to help veterinary professionals achieve longevity and satisfaction in their careers and life.

What is your diagnosis? Biochemistry results from an ataxic cat

Brown JE BVSc (Hons) MVS MVSc MANZCVS (Pathology)

Abbreviations: EDTA, ethylenediaminetetraacetic acid; IgG, immunoglobulin G.

CASE HISTORY

An 8-year-old female desexed domestic shorthair cat presented for sudden onset disorientation, abnormal gait and ataxia. She was up to date with core vaccinations and prophylaxis for gastrointestinal parasites and ectoparasites. On physical examination, the patient was pyrexic (40.0°C), icteric, and was moderately obtunded with a hypermetric hindlimb gait. A healthy 1-year-old cat had been introduced to the household in the previous 1-2 weeks.

Blood was submitted in plain and fluoride oxalate tubes for serum biochemistry (Beckman Coulter AU680 Chemistry Analyzer, Olympus), and a sodium citrate tube for coagulation testing (STA Compact Max 2, Diagnostica Stago). EDTA blood had been submitted the previous day for a CBC, revealing a mild neutrophilia with a left shift on blood film evaluation. Biochemistry results are provided. Briefly, urine collected by cystocentesis was dark yellow and cloudy with 3+ blood (900 red cells x10^6/L), specific gravity 1.058, 3+ bilirubin and 3+ amorphous phosphate crystals.

Analyte	Unit	Result	Ref Interval
Total protein	g/L	53	61 – 83
Albumin	g/L	21	28 – 40
Globulin	g/L	32	29 – 50
Bicarbonate	mmol/L	40	15 – 24
Glucose	mmol/L	8.2	3.8 – 7.4
Na	mmol/L	135	148 – 157
K	mmol/L	6.7	3.7 – 5.5
Cl	mmol/L	104	112 – 122
Total Ca	mmol/L	0.98	2.15 – 2.64
Phos	mmol/L	1.02	1.00 – 2.05
Urea	mmol/L	9.1	5.8 – 11.5
Creatinine	µmol/L	61	69 – 160
Total Bilirubin	µmol/L	69	0 – 4
ALT	IU/L	494	19 – 97
AST	IU/L	5720	19 – 57
ALP	IU/L	< 10	11 – 46
GGT	IU/L	< 5	0 – 5
Cholesterol	mmol/L	2.41	2.6 – 7.5
Triglycerides	mmol/L	0.81	0.1 – 1.4
CK	IU/L	607435	66 – 444
Anion gap	mmol/L	-2.3	13 - 27
Sample appearance	Icterus +		

INTERPRETATION

1. Spurious hyperbicarbonataemia associated with severe rhabdomyolysis
2. Suspected spurious hyperkalaemia and hypocalcaemia associated with EDTA or sodium citrate interference
3. Marked skeletal muscle necrosis
4. Cholestatic hepatopathy

DISCUSSION

The patient had neurologic abnormalities consistent with forebrain disease, as well as a severe myopathy and a cholestatic hepatopathy. A snake venom detection kit was negative, and coagulation times were within normal limits (PT 13.6 seconds, RI: 9 – 15s; aPTT 21.4 seconds, RI: 15 – 25s). An infectious cause was considered most likely, and toxoplasmosis was the primary differential. Both initial serology at the time of acute presentation, and PCR for *Toxoplasma spp.* on bile fluid and jejunal lymph node aspirates were negative. Other differentials that were considered included immune-mediated polymyositis, feline infectious peritonitis, multiple thromboembolisms, and trauma. The patient was an indoor cat with no history of trauma, snake or toxin exposure, or previous significant illnesses, and there was no seizure activity noted in hospital or by the owner. ELISA FIV/FeLV testing was negative.

Biochemistry findings

A marked hyperbicarbonataemia typically reflects a metabolic alkalosis, however in this case the combination of a marked elevation in bicarbonate with a markedly reduced (negative) anion gap suggested an interference or artifact. An anion gap at this level is not compatible with life, given the necessary increase in unmeasured cations (such as Mg^{2+} or Ca^{2+}) would be fatal; in this case, the total calcium was markedly decreased, and magnesium was not measured.

In general, differentials for a decreased anion gap include decreased anionic proteins (e.g. albumin), increased cationic proteins (e.g. IgG associated with multiple myeloma or polyclonal inflammatory disorders),[1] increased cations (e.g. Ca^{2+}, Mg^{2+}, K^{+}, lithium),[1] and specific toxicities (e.g. bromide, iodine, polymyxin B).[2] These causes were considered, however none explained the magnitude of the decrease.

An artefact or interference was therefore suspected. A similar anomaly has been reported in calves, horses,[3] amazon parrots,[4] and humans,[5] occurring when bicarbonate is measured using the enzymatic method. The enzymatic reaction converts bicarbonate to oxaloacetate, which is then reduced alongside oxidation of nicotinamide adenine dinucleotide (NADH). The oxidation of NADH results in decreased spectrophotometric absorbance, which is proportional to the bicarbonate content of the sample. The hypothesised mechanism for the interference is excess lactate dehydrogenase (LDH) causing consumption of NADH, and therefore a falsely elevated spectrophotometric reading. Pyruvate and LDH are found in large quantities in muscle and so are increased with rhabdomyolysis and may overwhelm the LDH inhibitor present in the enzymatic assay. This has been reproduced by the addition of LDH and pyruvate to normal bovine serum samples, demonstrating a linear dose-response relationship proportional to the amount of LDH activity in the sample, with pyruvate augmenting the increase.[3]

In these reports, bicarbonate results were accurate using bench top blood gas analyzers, as bicarbonate is measured indirectly via calculation from pH and pCO_2. Unfortunately, in-house blood gas analyser measurement of bicarbonate was not performed in this case but was recommended.

The combination of a moderate hypocalcaemia and mild hyperkalaemia is typical of EDTA contamination, a common laboratory artefact that may occur when EDTA is introduced

into a plain blood tube (e.g. via needle contamination). Both EDTA and sodium citrate are calcium chelators, causing spurious hypocalcaemia. EDTA is also a monovalent cation (1+) like potassium, and so reacts in a similar way to potassium, causing a spurious hyperkalaemia, while sodium citrate will cause a hypernatraemia. EDTA contamination could not be confirmed with the clinicians in this case; plain, sodium citrate and fluoride oxalate tubes had been submitted to the laboratory on this day, and it is unclear whether EDTA blood had also been collected at the same time (e.g. for in-house CBC). Contamination with sodium citrate may have caused hypocalcaemia, however the concurrent hyponatraemia makes this less likely.

Other potential causes for the marked decrease in total calcium include renal loss, decreased gastrointestinal absorption, or potentially movement of calcium into damaged muscle (tissue mineralisation). The hypoalbuminaemia was likely contributing to the marked hypocalcaemia, and measurement of ionised calcium was recommended but not performed. Potential considerations for the hyperkalaemia included transcellular shifting associated with acidosis, reduced renal excretion (e.g. associated with a myoglobinuric nephropathy), and haemolysis (a mild anaemia was present however this was persistently non-regenerative).

The anion gap is calculated from measured anions and cations. In this case, two components of the calculation were artifactually altered (both potassium and bicarbonate), causing a spuriously negative result.

Case Outcome

A definitive diagnosis was never obtained. With supportive care and clindamycin treatment for presumptive toxoplasmosis, there was overall improvement in presenting signs, and the cat was eventually discharged. At subsequent rechecks, all biochemical abnormalities returned to within the reference intervals, except for ALT and total bilirubin which remained persistently mildly elevated (ALT 198, RI: 19 - 98 IU/L; total bilirubin 0.29, RI: 0 - 0.23mmol/L). Given the clinical improvement, the owner declined repeat serology.

CONCLUSIONS

This case reinforces the importance of identifying laboratory error when results are extreme and not consistent with the clinical picture. A decreased anion gap is often not clinically significant but should alert the diagnostician to the possibility of a laboratory error.

ACKNOWLEDGEMENTS

Bradley Galgut, Natalie Courtman, and laboratory staff at Australia Specialised Animal Pathology Laboratory, Mulgrave, VIC, Australia.

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Comparison of the use of a bipolar vessel sealing device and conventional incisional techniques for staphylectomy in brachycephalic dogs

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ABSTRACT

Objectives: To compare the use of a bipolar vessel sealing device (BSD) and the conventional incisional (CI) technique for staphylectomy in brachycephalic dogs.

Materials and methods: Medical and anaesthetic records from brachycephalic dogs who were treated by staphylectomy in a small animal referral hospital by a single specialist surgeon between April 2017 and April 2020 were retrospectively collated. Data included signalment, clinical severity at presentation, airway exam findings, radiographic or CT imaging findings, perioperative protocol, procedures performed, staphylectomy method, time under general anaesthetic, surgical time and complications encountered.

Results: Seventy-eight dogs were included in the study. There were 35 dogs in the CI group and 43 dogs in the BSD group. A significant difference in complication rates between techniques was not detected.

Clinical significance: Complication rates do not appear to differ between the CI technique or use of the BSD for staphylectomy and both techniques were viable options for staphylectomy in this cohort of brachycephalic dogs.

Keywords Staphylectomy, bipolar vessel sealing device

Abbreviations

BSD – bipolar vessel sealing device CI – conventional incisional

BOAS – Brachycephalic obstructive airway syndrome

INTRODUCTION

Brachycephalic dog breeds continue to be popular despite welfare concerns over the high prevalence of conformation-associated deleterious conditions, including upper airway obstructive respiratory difficulties and developmental vertebral abnormalities.[1] Surgical therapy for upper airway obstruction has been shown to improve these dogs' quality of life[2], but complication rates of 7-23% have been reported.[3-5] Surgical treatment of brachycephalic obstructive airway syndrome (BOAS) frequently consists of alarplasty, staphylectomy and laryngeal sacculectomy.[6] Additional or modified procedures performed can include tonsillectomy, folded flap palatoplasty, arytenoidectomy, and laser-assisted turbinectomy.[7-9]

Surgery for elongated soft palate has historically been performed via the conventional incisional (CI) technique. This involves sharp resection, following which the mucosal layers are apposed by suturing, either in a simple interrupted or continuous pattern.[6] Alternative options for staphylectomy include the use of a bipolar vessel sealing device (BSD)[10], mono- or bi-polar electrocautery[11], a CO2 laser[11], a diode laser[11], air and saline plasma devices[12, 13], or a harmonic scalpel.[14-16] Although many of these alternative techniques appear to have subjectively shorter surgical time and good outcomes, many veterinary surgeons have concerns regarding the issue of thermal damage to remnant palatal and pharyngeal tissues associated with these techniques.[17]

Post-operative complications are frequent following brachycephalic airway surgery.[4, 18, 19] Complications include post-operative regurgitation, post-operative bleeding, dyspnoea, aspiration pneumonia, the requirement of a temporary or permanent tracheostomy, respiratory or cardiac arrest, and death.[4, 13, 18-20] Good clinical outcomes have been reported with the BSD for staphylectomy[9, 10], but it is unclear from the literature whether the associated complication rates differ from the CI technique as a direct comparison has not been performed to date.

The aim of this retrospective cohort study was to compare risk factors and outcomes when performing a staphylectomy using either a BSD or the CI technique.

MATERIALS AND METHODS

Study design and data extraction

Medical records from all dogs who had staphylectomies performed to treat BOAS between April 2017 and April 2020 were reviewed. All dogs included were treated by a single specialist surgeon (PM). Dogs were excluded from the study if they had concurrent disease other than BOAS, other concurrent procedures performed, or had undergone previous upper airway surgery. Data collected included signalment, clinical severity at presentation, airway examination findings (including grade of laryngeal collapse), radiographic or CT imaging findings, anaesthesia and perioperative protocol, surgical procedures performed including staphylectomy method, total anaesthesia and surgical times, post-operative care and any encountered complications during the procedure, and subsequent hospital stay. Complications included regurgitation post-operatively, clinical and radiographic signs indicative of aspiration pneumonia, the need for reintubation, temporary tracheostomy, revision surgery related to the palate, and euthanasia or death.

Clinical severity at presentation and airway assessment

Clinical severity of BOAS symptoms at presentation were graded using the scoring system proposed by Poncet *et al*[21], according to the following criteria: grade 1 - negligible symptoms of airway disease, minimal snoring and no exercise intolerance; grade 2 - moderate clinical symptoms of airway disease including intermittent snoring, increase in respiratory effort and exercise intolerance;

grade 3 - severe clinical symptoms of airway disease with constant snoring and increased inspiratory efforts, frequent exercise intolerance, and/or syncopal episodes.

Laryngeal collapse was graded from 0-3, where no evidence of collapse is graded as 0, eversion of the laryngeal saccules as 1, medially displaced cuneiform process as 2, and collapse of the corniculate processes as 3.[22]

Imaging

Pre-operative computed tomography (CT) of the head, thorax and spine or three-view thoracic radiographs was performed prior to surgery in selected dogs. Imaging was assessed for pulmonary interstitial or alveolar patterns consistent with aspiration pneumonia and hypoplastic trachea, caudal aberrant turbinates[23], and soft palate length and thickness. If CT imaging was not performed, endoscopy was used to assess for caudal aberrant turbinates by retroflexion of the bronchoscope into the choanae. Tracheal diameter:thoracic inlet ratio (TD:TI) was measured as previously reported.[24, 25] Hypoplastic trachea were diagnosed using a cut-off TD:TI of 0.127 as described by Coyne.[24] Imaging was performed under general anaesthesia, immediately after induction, prior to surgery.

Anaesthesia and perioperative protocol

The standard premedication protocol was 3-5mcg/kg medetomidine (Troy Animal Health, NSW, Australia) and 0.3mg/kg of methadone (Jurox Animal Health, NSW, Australia) intramuscularly. All dogs received 1mg/kg maropitant (Zoetis, NSW, Australia) subcutaneously 60-120 minutes prior to surgery and 1mg/kg esomeprazole (AstraZeneca, NSW, Australia) intravenously prior to induction. Dogs were pre-oxygenated for 5-10 minutes prior to induction of their anaesthetic. Induction was performed with alfaxalone (Jurox Animal Health, NSW, Australia) to effect (0.5-1.5mg/kg) and the upper airways were examined prior to intubation. Anaesthesia was maintained with isoflurane in 100% oxygen via a cuffed endotracheal tube. A bupivacaine (Pfizer, WA, Australia) splash block (1mg/kg) of the palate was performed prior to surgery. Following this a mannitol 20% w/v (Baxter, VIC, Australia) soaked surgical gauze (4x4cm) was placed orally, so that it lay in contact with the soft palate, until surgery was commenced. This was replaced in a similar position following soft palate resection until just before the dog was ready for extubation.

Dogs were moved to a recovery cage where they remained intubated with flow-by oxygen until a strong swallow reflex was observed, or they would no longer tolerate the endotracheal tube. They were continuously monitored for at least 24 hours post-operatively.

Oxygen was supplemented with flow-by oxygen or via nasal prongs if mild dyspnoea or hypoxia was noted in recovery. If severe dyspnoea or hypoxia defined as $Sp0_2$ <90% on breathing room air was observed, the dog was reintubated and manually ventilated. The upper airways were reassessed at time of reintubation for swelling and obstruction. A second attempt was made to recover the dog - if this failed again and upper airway swelling and obstruction was a contributing factor, a temporary tracheostomy tube was placed.

Dogs with clinical examination and thoracic radiograph findings consistent with aspiration pneumonia (tachypnoea, dyspnoea, hypoxia, cyanosis, lethargy, crackles or wheezes on thoracic auscultation, pyrexia, and/or an interstitial or alveolar pattern on thoracic radiographs) were treated with antibiotics. Empirical antibiotic selection for each dog suffering from aspiration pneumonia was veterinarian dependent. Whilst the International Society of Companion Animal Infectious Diseases' guidelines[26] recommend antibiotic use based on lower airway sampling, for example transtracheal, endotracheal or bronchoalveolar specimen collection, this was deemed unsafe by the clinician in some

cases. In our cases, lower airway sampling consisted of initially sterile endotracheal tube tip culture and transtracheal wash, both of which have potential risks and limitations. Given the potential risks associated with not treating aspiration pneumonia in this cohort, antibiotics were initiated immediately versus waiting for the results of microbial culture.

If a dog was agitated or stressed in hospital resulting in increased respiratory rate, low-dose medetomidine IV was administered as a bolus (0.5-1mcg/kg) or as an IV continuous rate infusion (0.5-1mcg/kg/hr), repeated or ongoing as necessary.

Food and water were withheld overnight for all dogs following surgery. Dogs were fed soft food 18-24 hours post-operatively with oral omeprazole (AstraZeneca, NSW, Australia) 1mg/kg every 12h and tramadol 2-4mg/kg (Seqirus, VIC, Australia) every 8-12h, providing they had no complications at this time point.

Surgical technique

Dogs were positioned in sternal recumbency with tape placed immediately caudal to the upper canines to allow suspension and elevation of the maxilla. An assistant placed gentle traction on the distal end of the tongue in a cranio-ventral direction to allow adequate exposure to the oro-pharynx. Staphylectomy was performed first, transecting the soft palate at the level of the cranial third of the tonsils. The CI group had a moistened surgical gauze placed at the back of the pharynx prior to staphylectomy to absorb any haemorrhage. Metzenbaum Durotip curved 230mm blunt/blunt scissors (B. Braun, NSW, Australia) were used to sharply excise the palate, prior to apposition of the oropharyngeal and nasopharyngeal mucosal cut surfaces with 4-0 or 5-0 monofilament glyconate suture (Monosyn Quik, B. Braun, NSW, Australia) in a simple continuous pattern.[27]

The BSD group had the staphylectomy performed as previously described, utilising a BSD (Ligasure Small Jaw Instrument and Valleylab™ LS10 energy generation platform, Covidien Inc., Boulder, CO, USA)[9, 10] with the same surgical landmarks as the CI group. The BSD was applied across the palate and coagulation performed with closure of the BSD on the desired tissue. Energy transmission was automatically ceased when the feedback-controlled set endpoint was met, then incision was performed with the integrated blade. This was progressively applied approximately 2-3 times to complete the staphylectomy. Tonsillectomy was subsequently performed using the BSD in both groups.[9] Resection of everted laryngeal saccules, if present, was performed with Metzenbaum scissors.[28] Dogs were extubated for laryngeal sacculectomy, then re-intubated prior to performing the vertical wedge alarplasty.[29]

Statistical analysis

Continuous data were assessed for normality or non-normality using graphical methods. For non-normally distributed data, groups were compared using the Wilcoxon Rank Sum test and summary statistics reported as median (range). Categorical data were compared using a chi-square test, or Fisher's exact test if the expected cell frequency was <5. Statistical significance was set at $p \leq 0.05$. R statistical software (R Foundation for Statistical Computing; Vienna, Austria) was used for all data analyses. A post hoc priori sample size estimation was performed using our results and an online sample size calculator (www.stat.ubc.ca), with a power of 80% and type I error of 0.05.

RESULTS

Signalment

Seventy-eight dogs meeting the inclusion criteria underwent staphylectomy between April 2017 and April 2020. Group allocation was based on staphylectomy procedure performed; 35 were in the CI group and 43 in the BSD group. Breeds included French bulldogs, pugs, English or Australian bulldogs, and Cavalier King Charles spaniels as the most frequent breeds.

French bulldogs were the predominant breed in the CI group, followed by pugs (40% and 28.6% of the sample, respectively). Pugs were the predominant breed in the BSD group, followed by French bulldogs (48.8 and 27.9% of the sample, respectively).

The median (range) weight (CI:11.0 (1.9 – 47.4) kg, BSD: 10.1 (6.1 – 31.5) kg) and sex distribution were not different between groups, with neutered males the most frequent in both groups (Table 1).

Table 1. Signalment and clinical examination findings for 78 dogs.

Continuous variables are compared using Wilcoxon's Rank Sum test and categorical variables using Fisher's Exact test.
†Wilcoxon Rank Sum test
^Fisher's exact test

*Statistically significant, $p \leq 0.05$

	CI, n=35	BSD, n=43	p-value
Age in years, median (range)	3.0 (0.2 – 8.0)	2.0 (1.0 – 10.0)	0.71†
Weight in kg, median (range)	11.0 (1.9 – 47.4)	10.1 (6.1 – 31.5) (n=40)	0.19†
Sex Neutered male Neutered female Entire male Entire female	 15 (42.9%) 9 (25.7%) 10 (28.6%) 1 (2.9%)	 19 (44.2%) 18 (41.9%) 5 (11.6%) 1 (2.3%)	0.17^
Clinical severity at presentation Grade 1 Grade 2 Grade 3	 2 (5.7%) 9 (25.7%) 24 (68.6%)	 0 (0%) 24 (55.8%) 19 (44.2%)	 **0.01^***
Hypoplastic trachea Cutoff ratio 0.127	N=30 1/30 (3.3%)	N=34 6/34 (17.6%)	0.11^
Laryngeal collapse None Grade 1	N = 35 1/35 (2.9%) 34/35 (97.1%)	N=43 7/43 (16.3%) 36/43 (83.7%)	0.07^
Stenotic nares	32/35 (91.4%)	38/43 (88.4%)	0.72^
Aberrant caudal turbinates	N=33 20/33 (60.6%	N=31 12/31 (38.7%)	0.08 (Chi-square test)

Clinical severity at presentation and airway assessment

The distribution of the Poncet (clinical severity) score differed between groups ($p = 0.01$). The CI group had a higher proportion of dogs with grade 3 disease, whereas the BSD group had a higher proportion with grade 2 disease (Grade 2: CI 9/35 (25.7%); BSD 24/43 (55.8%), Grade 3: CI 24/35 (68.6%); BSD 19/43 (44.2%)) (Table 1). Grade 1 laryngeal collapse was present in the majority of dogs in both groups (CI 34/35 (97.1%); BSD 36/43 (83.7%)). The prevalence of stenotic nares, caudal aberrant turbinates and everted or hyperplastic tonsils was not different between groups (Table 1).

Imaging

Most dogs in the CI group had CT imaging rather than radiographs (33/35 (94.3%)), whereas 17/43 (39.5%) dogs in the BSD group had CT imaging and 25/43 (58.1%) had radiographs performed. One dog in the BSD group did not have any imaging performed prior to surgery. None of the 77 dogs imaged had evidence of pre-operative aspiration

pneumonia. The BSD group had more dogs with evidence of a hypoplastic trachea (BSD 6/34 (17.6%); CI 1/30 (3.3%)).

Surgery performed

Thirty-two of 35 dogs (91.4%) in the CI group and 38/43 (88.4%) of those in the BSD group had an alarplasty (Table 1). Thirty-four of 35 dogs (97.1%) in the CI group and 36/43 (83.7%) of those in the BSD group had sacculectomy undertaken. Tonsillectomy was performed in all dogs.

BSD was performed on all dogs between April 2017 and June 2019, except for one dog that had their surgery performed with the CI technique as the very small size of the dog made use of the available BSD handpiece challenging. CI was performed on all dogs from June 2019 and April 2020.

Anaesthesia/Surgery time

Only two dogs deviated from the standard anaesthetic protocol, receiving a premedication with 0.02mg/kg acepromazine (Ceva Animal Health, NSW, Australia) and 0.3mg/kg methadone IM. Total anaesthetic time was available for 75 dogs and was shorter for the BSD group (median 30, range 15 - 75 mins, n = 40) than the CI group (median 50, range 30 - 95 mins, n = 35), p<0.001. When only dogs who had CT imaging were compared, anaesthetic times were still shorter for the BSD group (median 42.5, range 15 – 75 mins, n = 16) than the CI group (median 50, range 30 – 95, n = 33), but failed to attain a statistical significance, p=0.08. Total surgery time was available for 39 dogs, and was shorter for the BSD group (median 20, range 10 – 35 mins, n = 14) than the CI group (median 30, range 20 – 70 mins, n = 25), p=0.001 (Table 2).

Table 2. Outcomes of soft palate surgery for 78 dogs. Anaesthesia time was assessed in a subset of 75 dogs and surgical time for a subset of 39 dogs, where data was available.

Continuous variables are compared using Wilcoxon's Rank Sum test and categorical variables using Fisher's Exact test.

*Statistically significant, $p \leq 0.05$

Outcome	CI	BSD	p-value
Anaesthetic time in minutes, median (range) N = number of dogs assessed	50 (30 – 95) N=35	30 (15 – 75) N=40	**<0.001***
Surgical time in minutes median (range) N = number of dogs assessed	30 (20 – 70) N=25	20 (10 – 35) N=14	**0.001***
Complications			
Post-operative regurgitation	16/35 (45.7%)	13/43 (30.2%)	0.24
Re-intubation	3/35 (8.6%)	4/43 (9.3%)	1.0
Aspiration pneumonia	3/35 (8.6%)	4/43 (9.3%)	1.0
Temporary tracheostomy	2/35 (5.7%)	4/43 (9.3%)	0.69
Repeat palate surgery	1/35 (2.9%)	2/43 (4.7%)	1.0
Time in hospital in days, median (range)	2.0 (2.0 – 9.0)	2.0 (2.0 – 11.0)	0.11
Euthanasia or death	1/35 (2.9%)	3/43 (7.0%)	0.62

Complications

Twenty-nine of 78 (37.2%) dogs had regurgitation post-operatively, with a higher percentage of dogs in the CI group being affected, although this did not reach statistical significance (CI 16/35 (45.7%); BSD 13/43 (30.2%), p = 0.24). Seven of the 78 dogs (9.0%) developed aspiration pneumonia and required re-intubation, with similar proportions in each group (CI 3/35 (8.6%); BSD 4/43 (9.3%), p = 1.0).

One dog from the CI group was euthanised following the diagnosis of aspiration pneumonia; due to severity of clinical symptoms and the owners declining additional treatment. Six of the remaining dogs who had aspiration pneumonia had a temporary tracheostomy placed due to upper airway swelling and obstruction contributing to dyspnoea; and failed attempts at extubation (CI 2; BSD 4).

Of these 6 dogs remaining dogs with aspiration pneumonia; 3 did not survive to discharge, all of which were in the BSD group. One of these dogs suffered cardiac arrest while the other 2 were euthanised due to lack of improvement or deterioration of symptoms. The overall mortality rate was 5.1% (CI 1/35 (2.9%); BSD 3/43 (7%), p = 0.62) (Figure 1). No difference in hospitalisation duration between groups was detected.

Three of the 78 dogs (3.8%) required revision surgery for scar tissue formation, with similar proportions in each group (CI 1/35 (2.9%); BSD 2/43 (4.7%), p = 1.0) (Table 2). These dogs had not previously had a complication. A statistical difference was not noted for any of the observed complications in this study between the CI and BSD treatment groups.

DISCUSSION

In this retrospective cohort study, we did not detect any difference in complication rates or mortality when we compared staphylectomy performed on brachycephalic dogs using the BSD, to the CI technique.

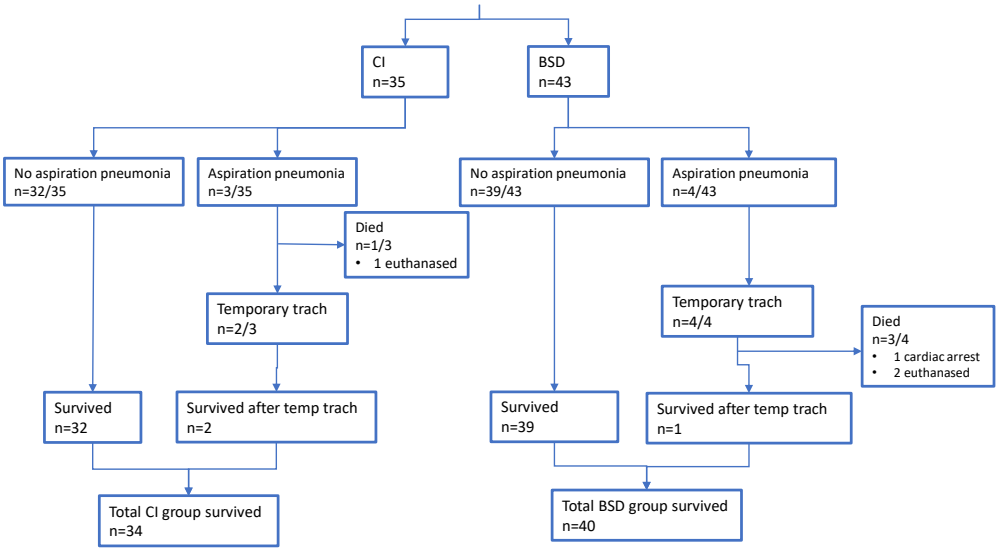
Thermal injury and resulting swelling of the airways leading to complications appear to be the main concern with the use of the BSD for soft palate resection. Despite this concern, in both human medicine and veterinary medicine, the BSD has been used for multiple procedures with positive results.[30 31] Our findings are consistent with studies that showed low levels of complications with use of the BSD for staphylectomy.[9, 10]

The BSD has previously been reported to lead to shortened surgical times.[17] In our study the BSD also led to shorter surgical times in the subset of dogs where surgical times were available. It was faster than the CI technique,

Figure 1

Flowchart of the major complications for dogs undergoing staphylectomy by either the conventional incisional technique or using a bipolar vessel sealing device.

Legend - BOAS = brachycephalic obstructive airway syndrome, CI = conventional incisional, BSD = bipolar vessel sealing device.



where suturing the palate in an often-narrow oropharynx can be challenging.

We detected no difference in the frequency of post-operative aspiration pneumonia and the need for reintubation between groups. Interestingly, the only dog who died in the CI group was euthanised due to a poor prognosis at time of aspiration diagnosis. The remaining two dogs were successfully managed using a temporary tracheostomy and medical management. In the BSD group, despite a temporary tracheostomy and medical management three of the four dogs with aspiration died or were euthanised. It is difficult to determine the sequence of events between dogs developing aspiration pneumonia and upper airway obstruction. Whether there is primary upper airway swelling and obstruction leading to an increased respiratory effort and then an aspiration event, or a primary aspiration event causing an increased respiratory effort and then further upper airway swelling. In our population of dogs both were often diagnosed at time of reintubation when both upper airway examination and thoracic radiographs were performed.

The overall mortality rate of 5.1% was slightly higher than previous reports, where Lindsay et al recorded a perioperative mortality of 2.4% of 248 dogs, Poncet et al a postoperative mortality of 3.3% of 61 dogs, and Jones and Kennedy a perioperative mortality of 4%.[4, 32, 33] Our observation may be consistent with sampling variation in mortality rate in a heterogeneous population, but comparisons may also be complicated by differing definitions of 'perioperative' and 'postoperative', as well as other factors such as clinician propensity to undertake intensive postoperative management in the event of complications.

While the difference in mortality between BSD and CI groups did not reach significance, the BSD group did have a higher proportion of dogs not surviving, compared to the CI group. This is a similar finding to Jones and Kennedy who reported the BSD was associated with a higher mortality rate compared to the CI technique and CO2 laser.[33] It is possible that the failure to reach a statistically significant difference, even if there was a true difference, constitutes a type 2 error. Further investigation of this difference in mortality is warranted. Based on the current data of 2.9% in the CI group and 7.0% in the BSD group, with 80% power and type I error of 0.05, a priori sample size estimation indicates such a study would require 439 dogs in each group to be sufficiently powered. Such large cohorts are challenging to acquire in veterinary medicine and may require multi-institutional collaboration to achieve.

The limitations of this study include those related to retrospective data collection and bias associated with observational studies. These limitations include incomplete data collection, inevitable with retrospective chart review, and inability to account for unmeasured confounding factors. The relatively small number of cases in each group is also a limitation, although the data obtained from this study provides a basis for sample size calculations in a prospective randomised trial. The time period in which each group of dogs were treated is also a limitation, as the BSD group comprised a historical control, which may have had subtly different pre-operative, intra-operative and post-operative care compared with the CI group.

Overall, our study suggested that the incidence of post-operative complications does not differ between the CI and BSD techniques, irrespective of disease severity (Poncet grade) at the time of surgery, and that the BSD technique may have shorter surgical times in this cohort of brachycephalic dogs. However, an appropriately powered randomised controlled trial for further investigation of the differences in outcome is required.

Conflict of interest and sources of funding

The authors declare no conflicts of interest or sources of funding for the work presented herein.

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Pulse oximetry and venous blood gas analysis of 119 dogs diagnosed with the paralysis tick Ixodes holocyclus

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ABSTRACT

Tick paralysis effects many domestic species along the East Coast of Australia each year. Despite its clinical prominence, an evaluation of pulse oximetry and venous blood gas analysis, including specific tick distribution on presentation has not been previously investigated. Data was collected retrospectively from 119 dogs with an engorged paralysis tick showing clinical signs of tick paralysis on presentation. The location of a tick(s) was recorded, including their incidence once clipped in hospital. The hypothesis was there would be a significant difference between low and high tick scored groups for pulse oximetry and PvCO2 only. A significant difference was seen for pulse oximetry between respiratory score B (median 98%) and C (median 95.5%), and between a gait score 1 (median 98%) and 3 (median 96%). No difference was seen between groups for PvCO2. Of the dogs hospitalised presenting with a respiratory score of 3 or C, 20% required mechanical ventilation despite having an SpO2 >97% on presentation. Given the exclusion criteria for the study, only a single case was seen with a respiratory score D and gait score 4. Tick distribution on presentation identified 46.5% of ticks were found on the head with 17.5% found second most common on the neck, and 9.6% having two ticks.

Keywords tick paralysis, blood gas, pulse oximetry, hypoxaemia

Abbreviations and Acronyms

SpO_2 – percentage of oxyhaemoglobin saturation via pulse oximetry

PaO_2 – partial pressure of oxygen in arterial blood

$PaCO_2$ – partial pressure of carbon dioxide in arterial blood

$PvCO_2$ – partial pressure of carbon dioxide in venous blood

IQR – Interquartile range

HCO_3 – bicarbonate

Na – Sodium

K – Potassium

Ca – Calcium

Cl – Chloride

BE – Base excess

INTRODUCTION

Tick paralysis affects domesticated and wild animal species along the Australian eastern seaboard each year, mainly through winter, spring and into early summer.[1–3] Clinical signs are caused by the holocyclotoxin of the Australian Paralysis Tick, *Ixodes holocyclus*. Holocyclotoxin prevents the release of acetylcholine from nerve terminals of motor neurons at the neuromuscular junction via its inhibitory effects on voltage-gated calcium channels on the pre-synaptic terminal.[4,5] In the early stages of the disease, clinical signs in dogs can typically include vomiting/regurgitation, dysphonia, and hindlimb weakness. Clinical signs in mid to late stages progress with bulbar weakness, quadriparesis and dysuria, eventually deteriorating into respiratory fatigue and failure.[1,6–9] As a result, animals with end stage clinical signs eventually succumb to severe hypoventilation, hypercapnia and hypoxaemia.[3,6,9,10] Respiratory failure is accelerated with development of alveolar oedema, bronchopneumonia, or pulmonary aspiration.[6,9] Respiratory dysfunction is best measured by an arterial blood gas and PaO_2 and $PaCO_2$ levels, though collection of an arterial blood gas sample can be distressing in an already respiratory compromised animal. Thus, pulse oximetry is subsequently used as a substitute for measuring hypoxaemia. Despite its poor correlation with PaO_2 in dogs, pulse oximetry remains the only readily available non-invasive method for measuring hypoxaemia.[11] Measuring venous PCO_2 ($PvCO_2$) still requires access to a venous blood gas analyser, though remains a valuable resource in direct monitoring of ventilation due to small variations in comparison to $PaCO_2$ (5.8 +/- 5.5 mmHg).[12] Early identification of an animal's requirement for oxygen supplementation and/or mechanical ventilation from respiratory failure could assist decision making, improve clinical outcomes, and manage owner expectations. The primary objective of this paper was to identify pulse oximetry and venous blood gas abnormalities amongst tick scored groups presenting to an emergency hospital with tick paralysis. The hypothesis is there will be a significant difference between low and high tick scored groups for pulse oximetry and $PvCO_2$ only. The second objective was to report on the specific anatomical distribution of paralysis ticks in dogs at presentation.

MATERIALS AND METHODS

Data collection and selection criteria

A retrospective analysis of electronic medical records was performed on a population of dogs presenting for tick paralysis to four veterinary emergency hospitals in south-east Queensland within a 12-month period from July 2019 to June 2020. Clinical records from the practice database (Rx works; Henry Shein Veterinary Solutions) were searched using the terms 'tick' and 'tick paralysis' generating 547 clinical records. Dogs were included in the study if removal of an engorged paralysis tick was performed at the hospital, clinical signs consistent with tick paralysis were recorded and a tick score provided, and the diagnosis of 'tick paralysis' was stated in the clinical record. The tick score previously described in Table 1 is used routinely amongst all hospitals in the study.[13]

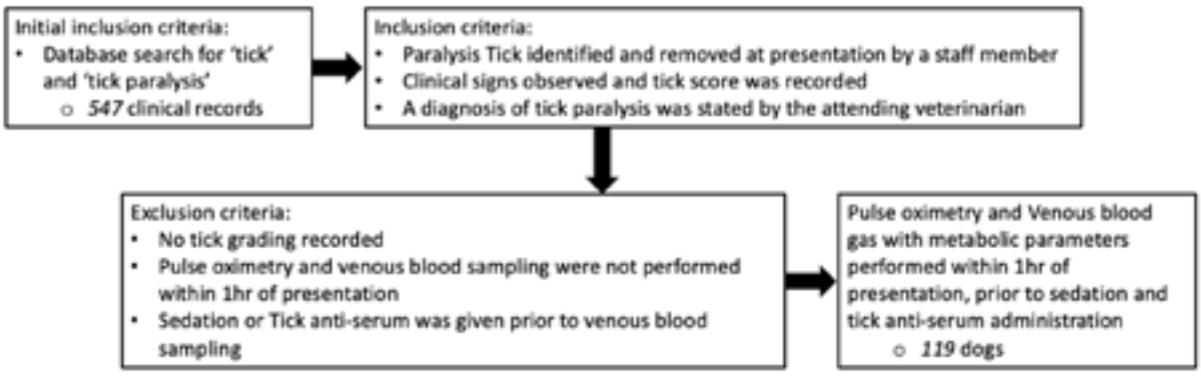
Table 1 – Adapted Gait and Respiratory scoring system used.[13]

Gait Score	Clinical signs
1	Mild ataxia or and weakness
2	Can stand or sit, but not ambulatory
3	Can right and maintain sternal recumbency, non-ambulatory
4	Unable to right and laterally recumbent, no withdrawal reflexes

Respiratory Score	Clinical signs
A	Normal respiratory rate (<30 bpm)
B	Mild tachypnoea (>30bpm), mild increase in respiratory effort
C	Moderate increase in respiratory effort with dyspnoea possibly requiring oxygen, gagging and retching
D	Severe hypoventilation and dyspnoea, reduction in respiratory rate, cyanosis. Requiring mechanical ventilation

Dogs were excluded from the study if no grading of clinical signs were recorded, if pulse oximetry, venous blood gas and metabolic parameters were not obtained within 1 hour of presentation, or the administration of sedative drugs or tick anti-serum had been provided. Following the exclusion criteria, 119 dogs met the criteria to be included in the study. The location of paralysis ticks on presentation was classified anatomically; cranial to shoulders (head, neck, shoulder); thorax; abdomen; front leg, hind leg; genitals and tail. When multiple ticks were located on a patient their locations were recorded separately. Of the dogs hospitalised, the requirement for mechanical ventilation within 24 hours was also recorded.

Figure 1 – Consort diagram demonstrating initial inclusion criteria and specific exclusion criteria



Statistical analysis

Data were analysed for normality using a Shapiro-Wilk test (GraphPad Prism 9.0 La Jolla, CA). For consistency, normal and abnormally distributed data is presented as median (range: minimum to maximum, interquartile range [(IQR): 25%-75%]. Individual measurements were evaluated for differences by both Respiratory Score and Gait Score with a Kruskal-Wallis ANOVA test and when a difference was found a post-hoc Dunn's test for multiple comparisons was used. A P-value < 0.05 was considered significant. Observational statistics were used for the location of paralysis ticks found on presentation and where dogs were clipped to search for further ticks.

RESULTS

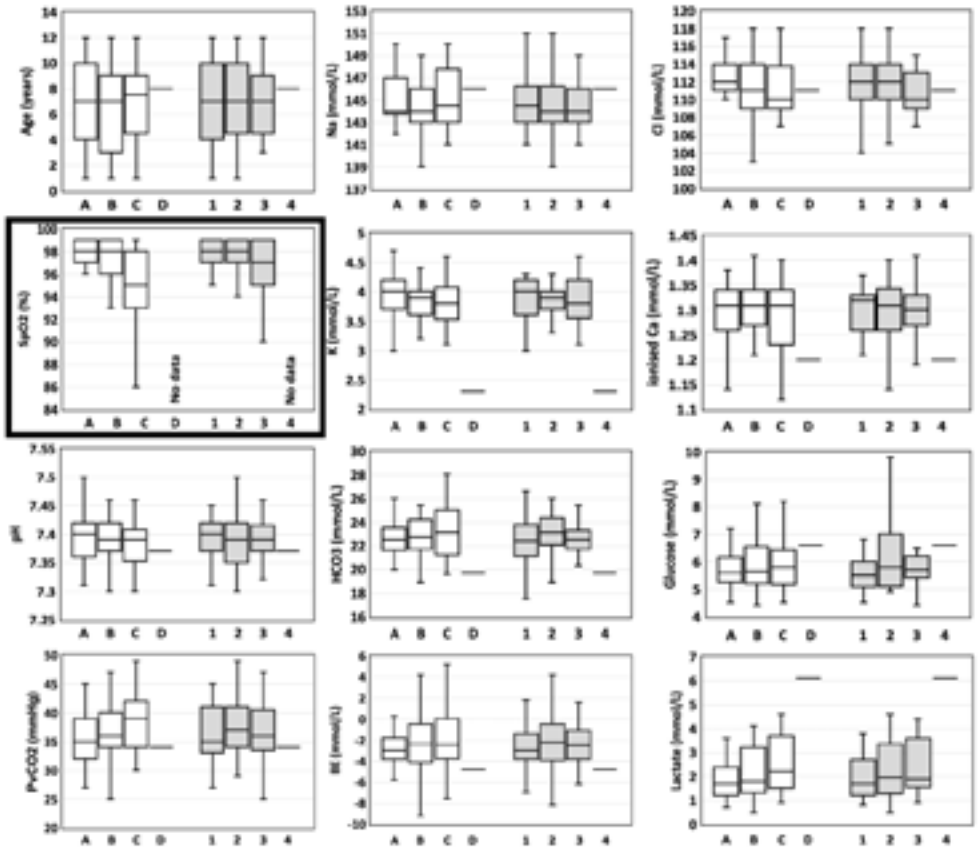
Signalment

The median age of dogs in the study was seven years (Range 1-12 y, IQR 4-9 y). Fifty-four percent were male (89% neutered, 11% entire) and 46% female (93% neutered, 7% entire). The median body weight was 13.9kg (range 2.7 to 51kg) with a median body condition score of 5 out of 9 (range 3 to 8). There were 51 different pure-breeds and crossbreeds identified. Maltese and Maltese X breeds made up a combined 17% of the study group. Other breeds noted to make up between 4-7% of the study group were Australian cattle dog, Kelpie, English Staffordshire terrier, Labrador retriever, Bichon frise and Jack russell terrier. Only one brachycephalic breed was seen amongst 119 dogs.

Data distribution for pulse oximetry, venous blood gas and metabolic measurements

The median SpO_2 was significantly lower for respiratory group C ($P<0.046$) and gait group 3 ($P<0.031$) compared to less severe groups (Figure 2 – highlighted with black box). All other variables have medians within normal reference interval. Notably, there was an increase in $PvCO_2$ and lactate median and IQR ranges with increasing respiratory score severity, though no significant difference was seen amongst the groups.

Figure 2 – Median and IQR ranges for age, pulse oximetry (SpO_2), venous blood gas parameters (pH, $PvCO_2$, HCO_3) and metabolic parameters (Na, K, Cl, Glucose, Lactate, BE). A single data point is shown for respiratory score D and gait score 4 (N=1 for these groups). The black box highlights significance seen for SpO_2 between individual respiratory and gait groups. X-axis label is for respiratory A-D (white) and gait 1-4 (grey) groups.



Analysis of Variance and post-hoc testing between Respiratory and Gait groups

A statistically significant difference is seen for SpO_2 across both respiratory and gait groups, and for [K] across respiratory groups. When comparing data between individual scored groups, there is a significant difference between SpO_2 for respiratory scores B and C, and gait scores 1 and 3 (Table 2). The one-way ANOVA analysis showed statistical difference for serum potassium [K] concentration across all respiratory groups, however no difference was seen on post-hoc analysis between individual groups.

Table 2 – Post-hoc Dunn's test comparison for pulse oximetry demonstrating significance between individual respiratory and gait groups.

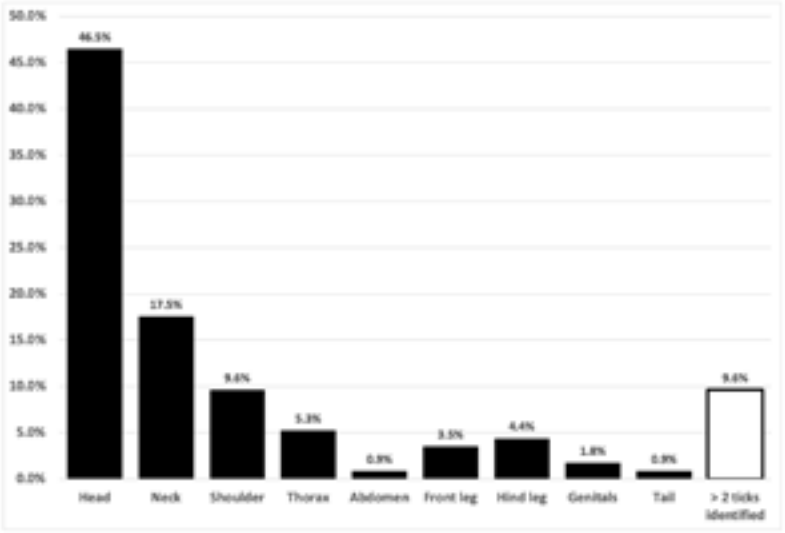
	Dunn's multiple comparisons - Respiratory	**P-value**
SpO_2	**A vs B**	>0.9999
	A vs C	0.1024
	A vs D	>0.9999
	B vs C	***0.0457***
	B vs D	>0.9999
	C vs D	0.4461
	Dunn's multiple comparisons - Gait	**P-value**
	1 vs 2	>0.9999
	1 vs 3	***0.0307***
	1 vs 4	>0.9999
	2 vs 3	0.0941
	2 vs 4	>0.9999
	3 vs 4	0.6021

Of the dogs that were hospitalised, mechanical ventilation was required within 24hrs for 20% of presenting with a respiratory score of C, and 19% presenting with a gait score of 3. This is compared to <3% of dogs for each respiratory scores A and B, and gait scores 1 and 2. Review of the pulse oximetry for dogs requiring mechanical ventilation showed all had an SpO_2 >97% on presentation.

Tick distribution on presentation

From the 119 dogs eligible for inclusion in the study, the location of a paralysis tick found on initial presentation was 46.5% on the head and 17.5% on the neck. The majority (73.6%) of ticks were found forward of the shoulders, with 9.6% found with 2 paralysis ticks (Figure 2). One of the ten cases with two or more paralysis ticks had two ticks found cranial to the shoulders only. Of the 119 dogs, 78 had their hair clipped, of which 10.3% had a second paralysis tick. When including the sets of dogs identified with two paralysis ticks on presentation and those clipped, 20% of dogs had a second paralysis tick overall.

Figure 3 - Tick distribution on dogs at initial presentation. Black bars show cases with a single tick found. The white bar shows cases with >2 ticks found on presentation prior to being clipped.



DISCUSSION

The hypothesis that there will be a significant difference between low and high tick scored groups for pulse oximetry and $PvCO_2$ was partially correct. An abnormal distribution of pulse oximetry findings was identified, though no difference between the groups for $PvCO_2$. This is not surprising given post-mortem histopathology has shown dogs with tick paralysis develop lung pathology across a spectrum of paralysis tick scores.[6,14] Consequently, in this species, sudden respiratory deterioration is more likely to occur at any grade due to pulmonary parenchymal disease rather than ventilatory failure. The sigmoidal relationship between the partial pressure of oxygen and the oxygen saturation of hemoglobin in comparison to the carbon dioxide dissociation curve would exacerbate an earlier onset of hypoxaemia versus a hypercapnoea.[15] Pulse oximetry also varied between neuromuscular gradings 1 and 3 where the lowest pulse oximetry reading was 95% for a dog with gait score of 1, and 90% for a dog with a gait score 3. The lowest pulse oximetry reading was 93% for a patient with respiratory score of B, and 86% for a patient with a respiratory score C. This has not been observed in previous studies of dogs with tick paralysis.

Measuring pulse oximetry is often used as a surrogate marker for PaO_2 in animals presenting with respiratory distress due to its less invasive method for recording blood oxygen levels, particularly if already respiratory compromised.[16] Pulse oximetry has been previously associated with PaO_2 as a diagnostic tool for detecting hypoxaemia in dogs breathing room air.[17] Hypoxaemia is defined as a PaO_2 less than 80mmHg or arterial blood haemoglobin saturation less than 95%. However, recent clinical research has questioned the applicability of pulse oximetry for detecting hypoxaemia as SpO_2 values <95% may falsely identify hypoxaemia.[11] Other factors can also lead to inaccuracy of readings including movement, mucous membrane pigment, peripheral perfusion and haematocrit.[18,19] When an objective measurement of pulmonary function is required, arterial blood gas analysis remains the gold standard as PaO_2 is the driver for oxygen diffusion down to the mitochondria.[20,21] These limitations highlight the importance of making considered decisions involving invasive interventions for these patients considered hypoxemic based on a single measurement. Regardless, mechanical ventilation was required for 20% of dogs presenting with a respiratory score of C and 19% with a gait score 3 within a 24hr period. Less than 3% of dogs with respiratory scores A or B required mechanical ventilation. Consequently, the more severe clinical presentation grade '3C' may support the validity of the clinical grading and lower pulse oximetry findings.

Neuromuscular paralysis with more advanced respiratory and gait scores was expected to cause hypoventilation and consequently increased $PvCO_2$. Given the exclusion criteria, only a single case with an advanced grade '4D' was observed, with the $PvCO_2$ (34mmHg) seen within reference interval. A previous controlled experimental study of tick paralysis in a small group of five dogs found elevated $PaCO_2$ levels were only a feature of advanced clinical cases (Stage 4 and 5), and no significant difference between any other groups.[22] The lack of significance found between groups was likely from an absence of this severely affected population of dogs from the data analysis, or being underpowered due to low sample size. A previous observational study identified 12% of 227 dogs with tick paralysis presented with a respiratory score of D, though all presenting dogs (sedated and non-sedated) were included.[3] The dogs excluded from this study that presented with a '4D' grade received immediate treatment and intervention involving sedation and intubation. Other reasons to consider could include greater awareness of tick paralysis among pet owners, and more available access to effective acaracides. It has been postulated that with greater awareness of the disease and availability of prophylaxis, a predominance of milder presentations is now more likely.[23]

Statistical significance was found for potassium concentration amongst the respiratory groups, though no difference on a post-hoc Dunn's comparison between groups. A previous prospective study had found a significant decrease in potassium concentration between stages 2 (unable to walk) to 5 (moribund) and the control group, which was suspected to be related to sympathetic stimulation and excess release of catecholamines and corticosteroids.[22] A previous prospective study had identified elevations in noradrenaline and cortisol in dogs affected by tick paralysis at admission; however, only an association between noradrenaline concentration and respiratory score B and D was found.[19] The significance of this remains unclear as median potassium concentrations were all within normal intervals for all respiratory and gait scores (3.8-4mmol/L) and is possibly related to a type 1 statistical error.

The specific distribution of paralysis ticks on presentation in dogs has not been previously published. In this study, 73.5% of dogs had a paralysis tick located forward of the shoulder. Of these, 46.5% were found on the head (muzzle, ear, eyelid, chin all in similar frequencies) compared to 17.5% found on the neck. These anatomical locations are similar to other reported sites for locating paralysis ticks in dogs.[13,24–26] A comparative report in cats showed 90% had a paralysis tick found forward of the shoulders with 26% on the head and 48% on the neck, opposite to the main anatomical locations in this study.[26] Interestingly, 10.3% of dogs with a single tick on presentation that were clipped had a second tick, similar to findings for clipped cats.[26] When combined with the number of dogs identified with 2 paralysis ticks on presentation, 20% of dogs in our study had a 2nd paralysis tick. With the presence of lower motor neuron signs identified on physical examination, a search for a paralysis tick should be initially conducted from the shoulders forward, focusing on the head and neck then moving caudally to the shoulders, chest, limbs, and hips.

CONCLUSIONS

The significantly lower SpO_2 associated with a worsening gait and respiratory score suggests this parameter may be valuable in staging dogs at presentation with tick paralysis. The lack of change in $PvCO_2$ in the same grades suggests pulmonary parenchymal disease is likely important in the clinical progression of dogs with tick paralysis and precedes ventilatory failure. Though there is a significant difference between the incidence of respiratory failure requiring mechanical ventilation for grade 3 and C hospitalised patients (20%) to lower grades of tick paralysis (3%), it was not possible to predict the overall requirement for mechanical ventilation based on this dataset as not all owners consented to hospitalisation. The distribution of paralysis ticks in dogs was predominantly cranially located with almost half found regionally on the head. Importantly, a second tick was discovered after clipping the coat in approximately 10% of dogs, compared to 20% overall when including dogs with two paralysis ticks found at presentation. This highlights the requirement for diligent tick searching and consideration of a full body clip. Prospective trials tracking outcomes from hospitalised and treated tick paralysis cases with an arterial blood gas analysis collected at admission may help estimate the likelihood of requirement for mechanical ventilation during the course of treatment from data collected at presentation.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUSTRALIAN SMALL ANIMAL VETERINARIANS

Splenic sarcoma and carcinoma collision tumour in a dog

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ABSTRACT

Collision tumours are rare in dogs. There is currently minimal information regarding treatment recommendations and prognosis.

An 11.5-year-old neutered male Greyhound was presented for routine screening following a right pelvic limb amputation for a tibial osteosarcoma and adjuvant carboplatin chemotherapy four years previously. An abdominal ultrasound identified a splenic and left adrenal gland mass. The dog underwent an exploratory laparotomy with splenectomy and left adrenalectomy. Histopathology of the adrenal mass was consistent with a phaeochromocytoma. Splenic mass histopathology was consistent with a collision tumour involving a high grade visceral soft tissue sarcoma and metastatic carcinoma. The dog remained clinically stable until four months postoperatively when the dog deteriorated clinically and was euthanased.

To the authors' knowledge, this is the first case report of a splenic collision tumour involving a soft tissue sarcoma and carcinoma. Collision tumours should be considered in the differential diagnosis of a splenic mass in dogs.

Keywords: collision tumour; spleen; canine; visceral soft tissue sarcoma; carcinoma

Abbreviations: STS, soft tissue sarcoma

INTRODUCTION

Collision tumours are defined as one macroscopic neoplasm composed of two histologically distinct neoplastic cell populations that are adjacent within the one neoplasm. Collision tumours are rare in human and veterinary medicine and there is minimal information regarding treatment recommendations and prognosis for animals with collision tumours. Collision tumours can be a combination of two benign, one benign and one malignant, or two malignant tumours.[1-3]

There have been few published case reports of histologically diagnosed collision tumours in dogs in the veterinary literature, and most are examples of collision tumours in the testes[2] or skin of dogs.[1,2] There was one published case report of a splenic mast cell and plasma cell collision tumour however this was diagnosed cytologically.[4] In humans, most reported collision tumours are cutaneous.[3] To the authors' knowledge, there have not been any published reports of a histologically diagnosed splenic collision tumour to date, nor of one composed of a visceral soft tissue sarcoma (STS) and carcinoma.

CLINICAL FEATURES

A 30 kg, 11.5-year-old, neutered male Greyhound was presented in June 2022 for routine six-monthly screening. The dog had previously had a right pelvic limb amputation for a distal right tibial osteosarcoma and completed four doses of adjuvant carboplatin chemotherapy postoperatively four years prior. At presentation, the owners reported the dog had been exhibiting progressive hindlimb weakness and intermittent hyporexia in the previous six months. Physical examination revealed weakness in the left pelvic limb and generalised sarcopenia.

Haematology and biochemistry including electrolytes documented a stress leucogram with a lymphopenia (0.71 x 109/L; reference interval [RI] 1.05-5.1 x 109/L) and eosinopenia (0.02 x 109/L; RI 0.06-1.23 x 109/L), and a mild elevation in serum symmetric dimethylarginine (21 ug/dL; RI 0-14 ug/dL). Three view thoracic radiographs were unremarkable, with no visible evidence of thoracic metastatic neoplasia. An abdominal ultrasound identified a heterogenous splenic mass measuring 70 mm by 90 mm arising from the tail of the spleen (Figure 1), and a left adrenal gland mass at the caudal pole measuring 18 mm. The contralateral adrenal gland measured 8 mm at the caudal pole which is within normal limits for a dog this size.[5]

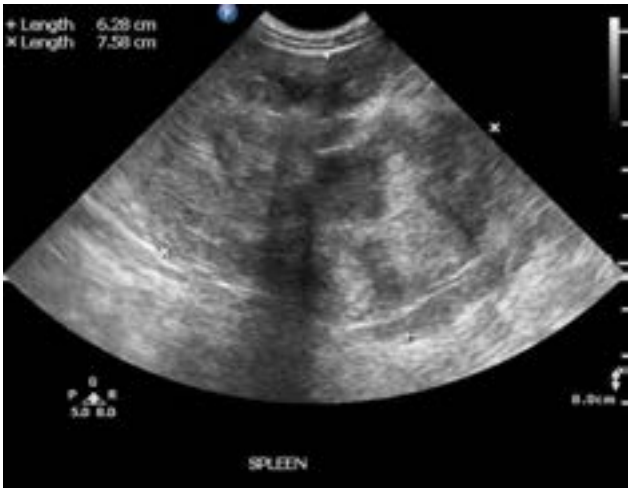

Figure 1: Ultrasound image of the splenic mass
The splenic mass was heterogenous and measured 70 mm by 90 mm arising from the tail of the spleen

Ultrasound-guided fine needle aspirates of the splenic mass were performed under sedation and submitted externally to the laboratory for cytology by a board-certified pathologist. An EDTA blood sample was submitted externally to the laboratory for plasma free metanephrine and normetanephrine assays.

Splenic fine needle aspirate cytology was inconclusive due to low cellularity. There was however a small number of mildly atypical mesenchymal cells with possible differentials being reactive fibroplasia or sarcoma. Due to poor exfoliation of cells in the sample submitted, histopathology was recommended. Plasma free metanephrine (1,693.7 pmol/L; laboratory phaeochromocytoma RI 100 – 102,000 pmol/L) and normetanephrine (10,607.3 pmol/L; laboratory phaeochromocytoma RI 3,300 – 211,000 pmol/L) were within the reference intervals. Although there is considerable overlap in the reference intervals for serum free metanephrine and normetanephrine in healthy dogs, dogs with a phaeochromocytoma, nonadrenal illness or hypercortisolism[6,7], this dog's measurements were consistent with a phaeochromocytoma.

The dog underwent an exploratory laparotomy, splenectomy, and left adrenalectomy. The left adrenal gland mass measured 33 mm by 13 mm by 10 mm. At the time of surgery an enlarged abdominal lymph node was identified in the right caudal abdominal cavity adjacent to the caudal vena cava measuring approximately 20 mm. Due to its proximity to the caudal vena cava, lymph node extirpation or biopsy were not attempted, and it was left *in situ*. The splenic and left adrenal gland masses were submitted externally for histopathology by a board-certified pathologist.

Histopathology of the adrenal gland mass was most consistent with a phaeochromocytoma with multifocal nodular cortical hyperplasia and accessory cortical nodules with no evidence of malignancy in the sections examined. Although there was no clear

indication of malignancy in the adrenal sections examined, a metastatic carcinoma of adrenal origin could not be excluded. Histopathology of the splenic mass identified malignant neoplasia involving two distinct adjacent tumour cells most consistent with a collision tumour of the spleen (Figure 2). Most of the splenic neoplasm was composed of spindle shaped tumour cells with marked anisocytosis and a mitotic index of 12. There were also extensive areas of necrosis and neoplastic cells were infiltrating into a large vessel lumen. These findings were consistent with a high-grade visceral STS.

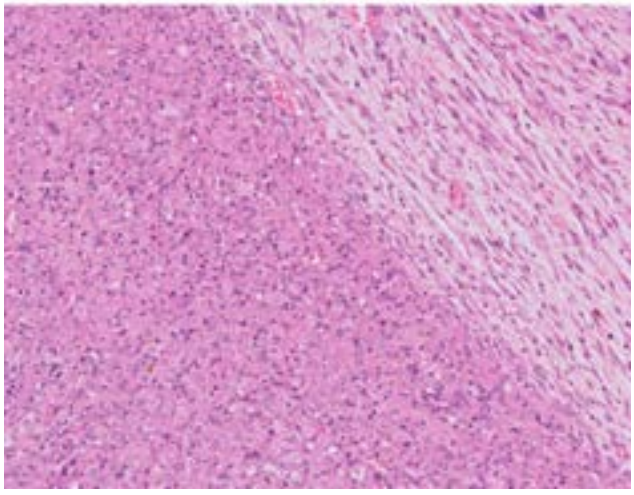

Figure 2: Histopathology of the splenic mass 20x magnification

Two distinct cell populations can be seen in this image.

In addition, there was an adjacent tumour population consisting of round to polygonal cells that appeared to be forming packets. These cells were demonstrating moderate anisocytosis with no significant mitotic activity noted. This second tumour population was most consistent with a metastatic carcinoma. Metastasis from adrenal or hepatocellular origin was considered a possibility based on cell morphology. Even though the adrenal sections examined by the pathologist did not indicate malignancy, there can be poor correlation between the histological features and biological behaviour for neuroendocrine neoplasms. There was no clear indication of osteoid production in the collision tumour to suggest an osteosarcoma. Following these results, it was presumed the enlarged abdominal lymph node found at surgery was metastatic. Immunohistochemistry of the splenic collision tumour sample may have provided further information however the pathologist advised results may have been equivocal or difficult to interpret. Immunohistochemistry was offered to the dog's owners who declined further testing.

Adjuvant chemotherapy to treat both neoplastic cell populations using multi-agent chemotherapy was offered, however effectiveness was unknown due to the minimal literature available on collision tumours. Chemotherapy was declined by the dog's owners.

An abdominal ultrasound performed one month postoperatively did not identify any new metastatic lesions and the previously enlarged caudal abdominal lymph node appeared static in size. An abdominal ultrasound performed three months postoperatively identified progression of suspected metastatic disease with further enlargement of the caudal abdominal lymph node now measuring approximately 20 mm by 30 mm. There were also multiple hepatic masses measuring up to 60 mm by 70 mm involving all hepatic lobes. These were suspected to be metastatic lesions, however other differentials could not be excluded without biopsy and cytology, and/or histopathology, which were declined by the owners.

The dog remained clinically stable until four months postoperatively when it deteriorated rapidly with progressive lethargy and inappetence over one week and was subsequently euthanased at a different practice. A post-mortem examination was not performed.

DISCUSSION

Collision tumours are a subset of mixed tumours. They are defined as two different neoplasms which originate in different foci and fuse at the time of detection, appearing as one macroscopic tumour but are

histologically and immunohistochemically different. Cell populations are not intermingled as is the case in other subsets of mixed tumours including combination, composition, and biphenotypic mixed tumours.[1-3,8] Combination mixed tumours arise from the same germ layer, composition mixed tumours from two different germ layers, and biphenotypic mixed tumours from a common stem cell precursor that undergoes divergent differentiation and have overlapping immunohistochemical and molecular properties.[2,8] The differentiation is important as treatment and prognosis may differ.[4]

To the authors' knowledge this is the first published report of a histologically diagnosed splenic collision tumour. It is also the first report of a collision tumour composed of a high-grade visceral STS and metastatic carcinoma. There is one published case report of a dog with a splenic collision tumour diagnosed cytologically, this was a mast cell and plasma cell collision tumour.[4] Splenic cytopathological and histopathological interpretation has been reported to have a diagnostic correlation of 51-60% in dogs and cats.[9] Cytology has other limitations including that the tissue sampled is usually small which may not be fully representative of the lesion, and cytology does not allow for evaluation of cell architecture.[10] These limitations may not allow distinction between a collision tumour and other subtypes of mixed tumours including, composite, combination or biphenotypic where different neoplastic cell populations are intermingled. In this case cytology was inconclusive, and a diagnosis was achieved with histopathology.

Further confirmation of the dog's splenic collision tumour type may have been obtained with immunohistochemistry however results may also have been equivocal or difficult to interpret. Immunohistochemistry stains that may have been considered include vimentin to investigate mesenchymal origin, cytokeratin for epithelial origin, and synaptophysin and melan-A to investigate adrenal origin. Confirmation of our suspicion that the enlarged abdominal lymph node and hepatic lesions were metastatic may have been obtained with additional biopsies and cytology, and/or histopathology. Post-mortem examination and additional histopathology would also have been of value in this case. Unfortunately, the dog had been euthanased at a different practice and cremated before this information was available to the authors.

A whole-body CT was not considered in this case as the dog underwent thoracic radiographs and an abdominal ultrasound for screening, and this was deemed sufficient at the time. A whole-body CT, however, could have provided additional information regarding extent of disease, especially in this dog which developed multiple malignancies in its life. It is unknown why this dog experienced multiple malignancies, however it is not uncommon for the authors to see geriatric dogs developing multiple malignancies at this practice.

Collision tumours are rare compared with other types of mixed tumours. There are few case reports published, describing mainly collision tumours of the skin or testes. There is minimal information on treatment recommendations and prognosis for collision tumours.[2]

Prognosis in this dog was poor, as would be expected for the two tumour types involved, a high grade visceral STS[11] and metastatic carcinoma. It is unknown whether the prognosis of collision tumours would be similar or different to the prognoses of the two individual tumours. In humans, collision tumours can be less biologically aggressive than or as aggressive as their individual component tumour types.[2,3] Prognosis is usually determined by the prognosis of the more aggressive tumour of the two lesions.[3]

In humans with collision tumours, treatment guidelines recommend treating the more aggressive tumour.[3] These guidelines could

potentially be applied to dogs with collision tumours, or alternatively treatment of both types of tumours could be attempted whether this involves surgical excision followed by multi-agent chemotherapy addressing both tumours. This may or may not differ from the standard treatment for a single tumour with or without metastatic spread. It is currently unknown which approach may yield a more favourable outcome.

This case provides additional awareness and information on the topic of collision tumours for which the veterinary literature is scarce. It also provides information on a novel type of collision tumour involving the spleen.

CONCLUSION

To the authors' knowledge this is the first report of a histologically diagnosed splenic collision tumour and the first report of a collision tumour involving a high-grade visceral STS and metastatic carcinoma. As prognosis was poor in this dog, adjuvant treatment was not pursued, and euthanasia occurred four months following diagnosis due to progressive disease and clinical deterioration. Collision tumours should be considered in the differential diagnosis of a splenic mass in dogs.

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Dietary management for gastrointestinal surgery

Cave NJ

To feed or not to feed?

Perhaps no other organ system is so directly and immediately affected by nutrition than the gastrointestinal tract. Timing and frequency of feeding, route of feeding, macronutrient and micronutrient compositions of the diet have profound influences on oral and intestinal health. In addition to the direct effect of diet on the body, there is a considerable indirect effect through dietary influences on the intestinal microflora. However, there are few controlled clinical trials that have evaluated specific dietary manipulation in either prevention or management of canine and feline gastroenteric diseases.

Malnutrition is a significant risk factor for poor surgical outcomes in human patients.[1-3] Several outcome measures have been shown to be affected including

- Higher surgical complication rates
- Delayed wound healing, fistula, dehiscence
- Decreased immunity
- Systemic sepsis
- Longer hospital stays
- Resources
- Increased hospital readmission rate
- Greater risk of mortality

There are no studies in the veterinary literature where nutritional status has been properly assessed and linked to surgical outcome, and several have used surrogate measures such as serum albumin. However, there is little reason to believe that we cannot infer from human studies to dogs and cats, and in the absence of evidence to the contrary, we should continue to do so.

Dehiscence of anastomoses and biopsy sites is still common enough to be concerning, and can be a catastrophic event in even relatively healthy animals. The incidence of dehiscence in patients managed in primary practice is uncertain, and may be different from reports in referral or teaching hospitals. However, whatever the rate, it is essential that all steps be taken to minimise the risks where those steps are relatively easy to take. Adequate nutrition is one such step.

Benefits of luminal nutrition post-operatively

Even in the absence of enteritis, fasting for even as short a period as one day in rats causes a significant decrease in villous height and/or crypt depth in jejunum, ileum, and, to a lesser extent, colon.[4,5] In addition, fasting is associated with gut mucosal cell impairment marked by decreased levels of reduced glutathione (GSH), the major intracellular antioxidant, enhanced permeability to macromolecules, increased bacterial translocation from the lumen, and increased rates of enterocyte apoptosis.[6] Even with total parenteral nutrition, after 14 days of oral fasting in cats, small intestinal villous atrophy, fusion, and infiltration of the lamina propria with lymphocytes, plasma cells, and neutrophils occurs.[7] Thus oral fasting alone, and in the absence of nutritional deficiency, induces an intestinal insult.

Fasting also significantly reduces the specific activity and expression of certain digestive enzymes in the small bowel mucosa such as disaccharidases, which can lead to impaired digestion following the re-introduction of food.[8] Transient lactase deficiency is common, particularly after rotavirus gastroenteritis.[9] Occasionally it persists, and lactose intolerance may be a cause of

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post-gastroenteritis diarrhoea. Gastric and pancreatic secretions are markedly reduced following a period of under-nutrition.[10] Generalized malnutrition, protein depletion, or deficiencies of specific nutrients, including essential fatty acids, folate, zinc, vitamin A, and vitamin B12 inhibit the growth and turnover of the intestinal mucosa. It has long been recognized that small intestinal enterocytes utilize luminally-derived glutamine as their main oxidative fuel (see above). In addition, glutamine provides the carbon skeleton and amino nitrogen required for purine synthesis and hence is critical for normal DNA synthesis involved in enterocyte turnover. Oral supplementation with zinc improves histological recovery, normalizes absorption, decreases permeability, and decreases NF-κB nuclear binding in experimental models of diarrhoea.[11,12] Additional mechanisms for the effect of zinc treatment on the duration of diarrhoea include improved absorption of water and electrolytes, increased levels of brush border enzymes, and faster regeneration of the intestinal epithelium.

Multiple factors, including luminal nutrients, pancreaticobiliary secretions, and humoral agents have been implicated in controlling the intestinal adaptive response after an intestinal insult. Despite the multifactorial regulation of intestinal adaptation, luminal nutrients are fundamental to the adaptive response such that recovery is minimized or prevented in the absence of luminal nutrients. This conclusion is largely based on studies that show significant adaptive intestinal re-growth in rats and dogs fed orally compared with those fed parenterally following an intestinal resection. Indeed even in the absence of an intestinal insult, total parenteral nutrition (TPN) causes dramatic intestinal atrophy in dogs, cats, rats and humans.[7,13,14] This fasting-induced atrophy is accompanied by inflammatory cell infiltrates in the lamina propria, increased intestinal permeability, and increased bacterial translocation.

It has long been known that the immunological derangements that accompany malnutrition cannot all be prevented when nutrients are delivered parenterally.[15] A lack of luminal nutrients results in an increased expression of proinflammatory adhesion molecules, especially ICAM-1.[16] This results in an increased number of primed neutrophils adhered to the microvasculature throughout the intestinal tract where they are able to contribute to oxidative and enzymatic tissue damage following activation. Fasting or TPN results in decreases in IL-4 and IL-10 that correlate with decreases in IgA and increases in ICAM-1.[17] Lack of enteral feeding impairs the coordinated system of sensitization, distribution, and interaction of T and B cells important in the production of IgA, in the maintenance of normal gut cytokines, and in the regulation of endothelial inflammation.[5,13,18,19] Thus the lack of luminal nutrients has been described as a “first hit”, and increases the inflammatory response to a secondary insult in the GIT, but also the lungs, liver, and potentially other organs as well.

The amino acid glutamine reverses many of these defects and favourably influences the proinflammatory effects of gut starvation.[20] The source of supplemental glutamine can influence gut mucosal glutamine concentrations, suggesting differences in its availability or utilization. Glutamine-rich intact proteins appear to be more effective in increasing mucosal glutamine content than glutamine-enriched solutions.[21] Arginine is an essential amino acid for cats because of their inability to synthesize sufficient quantities in the fasting state. However, beyond its role as an essential intermediate in the ornithine cycle, dietary arginine has long been known to enhance certain aspects of immunity.

Even short periods of enteral fasting result in an increase in intestinal permeability in humans.[22] Early refeeding of dogs and cats with acute gastroenteritis has been shown to reduce the increase in intestinal permeability that occurs in response to the inflammation

and apoptosis.[21,23] Some of the effect of luminal feeding may come from the luminal provision of glutamine alone, which can restore enterocyte glutathione concentrations, proteins synthesis, and normalise intestinal permeability. Even in single layer cell cultures of enterocytes, the application of glutamine to the apical (luminal) membrane normalises permeability to a large molecular weight molecule, whereas applying glutamine to the basal membrane (simulating parenteral nutrition) does not.[24]

There appears to be a linear association between the size of the caloric deficit and the subsequent atrophy that occurs in the intestine, which is notable within 48 hours.[25]

Any effect of hypocaloric feeding will be magnified when a diet is fed that is deficient. In those cases, protein synthesis – including collagen- can be profoundly impaired.[26]

Pre-operative feeding

For some cases we see, there is no alternative to immediate surgical intervention. Those cases would include surgical emergencies such as gastric dilation-volvulus, intestinal foreign bodies, and intestinal perforation. However, for other cases, such as chronic diarrhoea or intestinal mass excision, procurement of biopsy specimens or resection of a mass, are not urgent procedures. A proportion of those cases are malnourished at the time of presentation, and may be in a state of catabolism. Added to that, poor intake post-operatively may well further hinder recovery. These concerns have led to increased interest in whether improved nutrition prior to surgery might significantly affect outcome.

Human patients with intestinal cancer who have a poor nutritional status have a higher risk of an adverse outcome including higher mortality rate.[27] It is often unsure if such observations are indicative of the effect of nutrition on surgical outcome, or simply that sicker patients are more likely to have a poorer nutritional status. The best evidence for the former, comes from studies that show that increasing intake – especially of protein – during the immediate pre-operative period, significantly improves outcome in cancer patients undergoing intestinal resection.[28] Thus, consideration should always be given to whether a delay in surgery is warranted, during which time attention can be given to improving the nutritional status. However, there is little veterinary experience, and no evidence to guide decisions as to what to feed, how long to delay, or even which patients would benefit the most.

Post-operative feeding

The key surgical determinants of anastomosis healing are:

- Excessive resection
- Excessive tension on the anastomotic site
- Disrupted blood supply
- Peritonitis

Those factors are almost solely within the domain of the surgeon. Outside of those, pre- and post-operative feeding are paramount.

The effect of early enteral nutrition has been evaluated in dogs with severe parvoviral enteritis and in cats with severe mucosal damage from methotrexate toxicity. Early enteral nutrition in canine parvovirus reduced the time for normalization of demeanour, appetite, vomiting, and diarrhoea, increased bodyweight, and may have improved mucosal permeability compared with the traditional approach of fasting until resolution of vomiting.[23] In methotrexate-induced enteritis, feeding a complex diet abrogated the proximal small intestinal atrophy and bacterial translocation associated with feeding an amino acid-based purified diet, and was associated with a marked attenuation of the clinical signs associated with the toxicity.[21,29] In contrast, when dogs that presented with severe haemorrhagic gastroenteritis were fed a commercial dry hydrolyzed protein diet

soon after presentation, there was an initial increase in the frequency of vomiting, despite being fed at below maintenance rates.[30] Thus early reintroduction of feeding does not seem to exacerbate disease even in severely affected animals, and complex diets appear to be superior to purified diets in some models. Clinicians must make individual decisions about the risks and benefits of feeding in patients with persistent vomiting.

Immediate post-operative feeding significantly increases the strength of anastomosis sites.[31] Although the presence of luminal nutrients is clearly important, the simple presence of intestinal contents, and the effect of peristalsis is sufficient to increase healing, fibroplasia, and surgical site strength. Mechanical loading stimulates fibroplasia, even without luminal nutrients, as there is a difference between healing rates in animals fasted, and those force fed water.[32]

It can be seen then that not only can the traditional concerns of feeding immediately post-operatively be allayed, but there are considerable arguments for not delaying feeding at all. However, it is unlikely that attempting to feed the daily maintenance energy requirements (MER) is a sensible approach in the short-term management of dogs and cats immediately post-operatively, especially if they are severely ill. Therefore, if only 25% of the animals resting energy requirements (RER) is fed as a highly digestible, low fat diet, mucosal recovery may be optimized, and exacerbation of any diarrhoea or vomiting minimized. This has led to the concept of "minimal luminal nutrition". At the current point of understanding, the ideal dietary characteristics would be:

- High digestibility. This is easier to recommend than it is to specifically practice. Most commercial premium dry diets would qualify, as would many home-prepared ingredients. For protein sources, cooked fresh chicken or fish, cottage cheese, or egg would qualify. Cooked white rice or potato are suitable carbohydrate sources, although rice may be superior (see below). Commercially canned diets generally have a lower digestibility than dry diets, often have a high fat or viscous fibre content, and thus cannot be recommended over a similar dry product. However, there is no evidence that the difference in digestibility has any clinically measurable consequences.
- Low fat. No fat-titration studies have been performed to guide firm recommendations. However, a pragmatic recommendation would be to choose the lowest fat content available. An almost arbitrary cut off of 20% of ME could be made.

Novel antigen content. For cases with existing enteritis, strict adherence to protein novelty is not prioritized over other considerations, and simple avoidance of the staple dietary protein sources of the particular patient is prudent, without being excessive. Some hydrolyzed protein diets are also excellent choices.[33] However, extensively hydrolysed formulae may not produce the mucosal stimulation required, have lower protein contents, and may be less effective than intact protein diets.[34]

- Dietary fibre content. Some fermentable fibre is almost always beneficial, especially following colonic surgery, whilst excessive contents can exacerbate delayed gastric emptying, diarrhoea, flatulence, and abdominal pain. An empirical recommendation is to select diets that contain less than 8% dietary fibre, or less than 5% crude fibre.
- Initial feeding should not exceed 25% of the calculated RER, divided into 3 feeds per day. This amount can be rapidly increased with clinical improvement.

Few commercial diets are currently available that could be considered ideal in all respects, and commercial formulations change such that firm recommendations cannot be made. Most commercial diets both provide significantly more fat (> 25% of ME) but

are complete and balanced. In addition, when feeding as little as 25% of RER, it is unlikely that the fat content will be sufficient to exacerbate post-operative vomiting or diarrhoea, if less than 30% of ME is composed of fat.

The evaluation of diets formulated around protein hydrolysates such as Hill's z/d, Nestle-Purina HA, and Royal Canin Anallergenic, warrants further study. Despite the greater than ideal fat content, the combination of high digestibility and reduced antigenicity make them attractive options for the management of acute gastroenteritis. It may be that the degree of hydrolysis is influential, and not all hydrolysed diets may be equally effective. None-the-less, it is likely that the difference in efficacy between individual diets is considerably less than the difference between early feeding, and the traditional approach of fasting.

Concerns and problems with early enteral feeding

Vomiting: The most commonly voiced objection is with patients with vomiting.[30] As mentioned above, vomiting in dogs with CPV is reduced when they are force fed, even when fed rather aggressively.[23] The sensation of nausea is greatest on an empty stomach, as is evidenced by intractable nausea and vomiting in early pregnancy, which can be effectively managed by nasogastric tube feeding.[35] Vomiting can be exacerbated by over-feeding, especially early in the disease, or by using a poorly digestible or perhaps - high fat formula. However, with judicious introduction (e.g. 25% RER day one), and the use of highly digestible diets, vomiting will not be increased. If vomiting results in little retention of food then outflow obstruction or complete gastric ileus should be suspected.

Pancreatitis: Oral feeding is often withheld when acute pancreatitis is a differential diagnosis. In a recent small study of canine acute pancreatits, early enteral nutrition was compared with parenteral nutrition.[36] Placement of an oesophagostomy tube and instigation of feeding on the day of admission was not associated with signs of abdominal pain or clinical complications, and vomiting and regurgitation was significantly less in the enterally fed group. Although a much larger study is required to determine the magnitude of the benefit, it is clear that early enteral is not associated with a poorer outcome than parenteral, and it is superior to fasting.

Diarrhoea: Diarrhoea is the most common complication of tube feeding in patients in the MUVTH. Diarrhoea is a common complication of tube feeding, and there are several potential mechanisms that should be considered in any patient. Firstly, quantity and rate of feeding should be evaluated. If diarrhoea develops, reduce feeding back to 25% of RER, and if the faeces do not improve in 24 hours, consider another mechanism. If the diarrhoea improves, gradually increase the feeding again until 75% of the previous volume is fed. The presence of fermentable fibre is very important for optimal intestinal function, and some patients may require an increased fibre content than is being fed. In long term patients, a soluble, fermentable fibre source (e.g. hydrolysed guar gum, Benefibre®) can be added. This should be titrated to effect. It is unlikely that a higher fibre content than 10% dry matter will be helpful, so if this is reached without effect, the fibre should be discontinued. If a high fat diet (>30% ME) is being fed, transition to a lower fat diet.

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ASAV Proceedings

Grain free diets for dogs: What every veterinarian should know

Cave NJ

In New Zealand, where we remain blissfully free of heartworm, and throughout most of Australia, dilated cardiomyopathy (DCM) is probably the second most common cardiac disease affecting dogs, after myxomatous valvular degeneration. DCM should strictly be defined as a primary myocardial disorder characterized by reduced contractility, and ventricular dilation involving the left or both ventricles, and is idiopathic or genetic in cause.[1] Most cardiologists insist that when a cause other than genetics is known, the disease is not called DCM, but rather as "cardiomyopathy" of that cause. The example du jour, is "taurine deficiency cardiomyopathy", though that has not been widely accepted. For simplicity, and in keeping with the literature on the subject at the moment, I will adopt the plebeian approach, and refer to taurine as a cause of DCM.

Taurine and DCM

Taurine is an amino acid that is not incorporated into proteins, but has a very high intracellular concentration, notably in neurons, myocytes, and some leucocytes, and has the highest intracellular-to-plasma concentration gradient of all the normal amino acids. The functions of taurine are many, but osmoregulation and calcium regulation are perhaps the two most important. As an osmoregulator, it is very important in neurons, which accumulate high concentrations during sustained dehydration to preserve cellular integrity without disturbing the membrane potential. In muscle, taurine facilitates the binding of Ca^{2+} to actin, although when asked to explain what that means, the cognoscenti usually engage in a lot of hand waving, and resort to terms such as "not completely elucidated". Nonetheless, in deficient states, there is a reduction in actively contracting elements, and a reduction of the shortening fraction of the ventricle. The reduced cardiac output results in activation of the renin-angiotensin system, and initiation of remodelling pathways to cause eccentric hypertrophy. The resulting increase in wall stress exacerbates the contractile failure, leading to more remodelling, and subsequently, clinical DCM.

Taurine deficiency was identified as a cause of DCM in cats in 1987.[2] Not long after, the same phenomenon was identified in the US in farmed foxes that were fed diets that contained only a small amount of taurine.[3] At that time, it was apparent that domestic dogs differed from foxes, because it had been shown that dogs can synthesise taurine from the dietary sulphur amino acids, methionine and cysteine. However, cats have a very high rate of amino acid oxidation, and have lost any appreciable synthetic capacity, meaning they have a dietary requirement. Similarly, foxes probably have a very low synthetic capacity, meaning that they may have an absolute dietary requirement. Taurine deficiency can also cause DCM in humans, rats, and giant anteaters, and probably many other species.

Dogs and cats differ from mice and men in, amongst other things, the bile salts they synthesise. Bile salts are synthesised from metabolites of cholesterol, of which there are many, but the most common are cholic acid, and chenodeoxycholic acid. To make these functional bile salts, they are conjugated to a water soluble compound. Humans and rodents conjugate most bile acids to glycine, and a small amount to taurine. In contrast, dogs and cats both exclusively use taurine as the conjugate, and cannot switch to glycine conjugation in taurine deficiency.

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Once secreted into the intestine, a proportion of bile salts are hydrolysed by the bacterial enzyme bile salt hydrolase (BSH), yielding a bile acid, and its free conjugate. The conjugate is then available for fermentation by bacteria and is lost to the host. To date, more than 100 different genera of bacteria are known to express BSH, although the amount expressed by the whole intestinal bacteriome varies massively between individuals.[4] Thus, different individuals can have very different taurine turnover, or in the case of dogs and cats different requirements, simply because of the bacteria present in their intestines.

Initial studies into taurine requirements in cats revealed that a cat requires more dietary taurine if it is being fed a canned diet, than when being fed a kibbled diet.[5] The difference can be completely abolished if the cats consuming the canned diet are treated with oral antibiotics, which highlights the role of the intestinal bacteria in causing taurine depletion.[6] The difference in diets was related to the creation of maillard compounds (browning products) during the heating process.[6] These compounds decrease the digestibility of the protein, and provide substrate that promotes the proliferation of BSH-expressing bacteria. Surprisingly, at least to me, was that we did not detect a significant expression of that, or similar enzymes, in the fecal bacteriome of cats fed canned or dry diets in our colony.[7] That remains an inconvenient and mysterious side note for the time being. Nonetheless, modification of the intestinal bacteriome can lead to increased loss of intestinal taurine, and over time, depletion of body stores, and clinical deficiency.

As noted above, dogs are capable of synthesising taurine, and it is not considered an essential nutrient. However, in the early part of the century, dogs with DCM and taurine deficiency were being seen.[8] The mechanism in those cases turned out to be identical to that defined in cats. Certain diets modified the bacteriome and led to bile salt degradation and depletion of taurine. If those diets had a low content of methionine and cysteine, and no taurine, then the dogs were unable to synthesise enough, and deficiency developed. Features that were common to the diets originally incriminated were: no added taurine, low protein content, low methionine/cysteine content, low protein digestibility, and the presence of rice bran. A cruel twist of fate occurred when Nutro, who produced of one of the incriminated diets, sponsored and provided food for the Newfoundland breeders association in the US.[9] A perfect storm. Rice bran appeared to be particularly potent at bacterial modification, and was shown to be capable of accelerating taurine deficiency in cats fed a diet not supplemented with taurine.[10] Manufacturers had several options for dietary correction: increase the protein content, add supplemental methionine/cysteine, change the fibre content, or simply add taurine. Problem solved. Or at least, that is what was thought.

Grain-free diets and DCM

In July 2018, the US Food and Drug Administration (FDA) announced it was investigating a possible link between cases of canine DCM and certain diets.[11] At time of writing, they have produced data on 515 cases reported to the FDA from January 1st 2014, to April 30th 2019.[11] They have released the list of brands “incriminated”, but it would be very hard to conclude a causal relationship, since there is uncertainty of the temporal association, most dogs were exposed to multiple foods, and there is a growing potential for recall bias amongst owners and veterinarians. Nonetheless, more than 90% of products were marketed under the moniker “grain-free”, and 93% of reported products included peas and/or lentils as significant ingredients.

Of the diets most strongly associated, there are some familiar common themes. Small or new manufacturers are prominent. A complete absence of testing via feeding trials. The use

of unconventional ingredients with unknown digestibilities. The use of protein sources with low contents of sulphur amino acids (legumes). And probably all are rich in plant fibres that have similar or identical effects to the rice bran. And of course none have adequate taurine to offset those features.

The list of breeds is almost completely concordant with the relative risk of DCM in those breeds, coupled with the breed popularity. In fact, of the breeds identified, only Shi Tzu and Pitbulls are not reported breeds of predisposition - if you count arrhythmogenic right ventricular cardiomyopathy as a cause of DCM. And even for those two outlier breeds, severe mitral valvular disease can lead eventually to myocardial failure that can be difficult to distinguish from primary DCM. Given that the cases were not necessarily diagnosed by a cardiologist with exclusion of other causes, we cannot be confident. Yet had the list been dominated by atypical breeds, it would have been greater cause for concern as to a novel mechanism. Nonetheless, of those cases specifically investigated, taurine deficiency is prominent. In a case series of 24 Labrador Retrievers investigated between 2016 and 2018 at UC Davis (not all included in the FDA series), 23 were taurine deficient.[12] Several different diets had been fed, but none of the diets had been tested using Association of American Feed Control Officials (AAFCO) procedures.

With the exception of the study by Kaplan et al (2018), the quality of information available at present is low.[12] The FDA data set does not have any case controls, and only a subset were tested for taurine deficiency. In addition, the almost complete concordance between affected breeds and breeds of predisposition, and the inconsistency of diagnosis, means that many of the cases were almost certainly breed-associated DCM that were not caused by any dietary effect. Perhaps the most pressing need is to determine if there are cases of DCM in atypical breeds that are not taurine deficient. To emphasise the point, only 1 of the 5 Shi Tzu's in the FDA case series was tested for taurine deficiency, and it was not deficient. However, it had an antibiotic-responsive cough, and there was no information on an echocardiographic diagnosis beyond "heart enlargement on radiographs".

Some studies have taken a broad, "metabolomics" approach, to identify different serum metabolites in dogs eating grain-free, and grain-inclusive diets.[13] Although such studies can form the basis for hypotheses, they are unlikely to elucidate any mechanistic basis for an association, if it exists. Other studies have followed the echocardiographic parameters of dogs consuming diets that have been categorised as "non-traditional", and compared them with dogs eating "traditional" diets. Although two studies have demonstrated changes, interpreted as "improvements" in echocardiographic parameters, they are not known to be clinically relevant, and the studies were not controlled enough to identify what dietary factors might be involved.[14]

More recently, attempts have been made to identify if there is a direct effect of ingredients typically included in grain-free products, most notably legumes. A generous interpretation of the data available so far would be that it is inconclusive. One group identified a biologically irrelevant reduction in the red cell mass in dogs fed one grain-free diet, and an increase in phosphate, compared with dogs fed a grain-inclusive diet.[15] It is not possible to conclude what the significance is, what the relevance to any cardiac disease is, let alone which of the myriad of differences between the diets might have been responsible. Other authors have fed dogs diets with very high concentrations of legumes, and not found any effect on echocardiographic parameters, or cardiac biomarkers, after 20 weeks of feeding.[16] Thus, it remains uncertain if there is any effect, what might cause that effect, and certainly if there is any effect other than taurine depletion, when dogs are fed diets that are "grain-free".

Since 2010, there has been a startling increase in the number and sales of "grain-free" pet foods globally. Their popularity in the US forced even conventional heavyweights such as Hill's Pet Care to hop on the bandwagon ("Ideal Balance Grain Free" range). Sales of "grain-free" diets increased in the US from US$900 million, to US$3 billion between 2011 and 2016, and was the market segment responsible for growth during that period.[17] In short, if you are a new manufacturer, you will want to enter the market with a "grain-free" product.

New and small pet food manufacturers very rarely test products with feeding trials, few have veterinary nutritionists even consulting for them, and many have no animal nutritionist at all. Quality control, consistency of ingredients, careful monitoring of animals fed their diets, and a clear understanding of the problems, are frequently lacking in small and new companies. In contrast, better manufacturers use established ingredients, perform appropriate testing, prove dietary adequacy through feeding trials, have excellent quality control procedures, batch test their products, and have a deep understanding of the complexities that actually lie behind the deceptively simple appearing task of manufacturing dog food.

Conclusion and recommendations

So what should our approach to this subject be? Clearly the "absence of grains" is irrelevant to whether a diet is good or bad, though that hasn't stopped many commentators from suggesting that dogs "should be fed diets that contain grains". Since dogs don't have a requirement for "grain", the absence of "grain" cannot be causal, after all, the diets are also free of rhino horn, tuatara, and the penises of capybara, and they aren't suggested as causes. In addition, diets that are free of grains have been fed for eons in various forms, notably in this country, where the basic ingredients are not as readily available.

Lastly, several excellent companies manufacture diets marketed as "grain free" that clearly do not cause DCM.

So, perhaps I can suggest a few precepts to help the daily grind, and fend off the difficult conversations:

1. Only encourage owners to feed diets that have been formulated to meet the requirements established by AAFCO or FEDIAF.
2. If asked for a specific recommendation, I think we should recommend diets that have been proven in AAFCO / FEDIAF feeding trials.
3. Make sure you understand the added value that manufacturers give when they produce diets using high quality ingredients that they understand, have rigorous quality control regimes, test diets appropriately both in the laboratory and in the animal, and truly know what they are doing. We are not hiding behind corporate muscle like scared sycophants in so doing, we are standing behind our recommendations because of the confidence in the products. I want to have confidence that the diets I feed my animals are complete, balanced, and appropriately tested.
4. Recognise that "grains" are no more responsible for adverse food reactions than any other major conventional ingredients, and whilst they are neither essentially good nor bad, they can be a source of highly digestible and essential nutrients, and there is no nutritional value to avoiding them in the diet of dogs.
5. The success of "grain free" diets is a triumph of marketing over evidence, and the label is neither a mark of quality, nor deficiency. I would happily feed a diet from Hill's Ideal Balance Grain Free range, not because it is grain free, but because it is good. I would unhappily feed my dog a diet from a small manufacturer that has

not demonstrated they have formulated the diet properly, has not tested the diet in a feeding trial, and about which I know nothing, irrespective of whether it is grain free or not.

6. At this point in time, a dog presenting with DCM that is on a diet about which you are not confident, should be treated with taurine until you have reason not to, and the owner offered the option of a taurine assay. Taurine is cheap, readily available, non-toxic, and taurine deficiency cardiomyopathy is reversible.
7. Dog breeds of predisposition for DCM eating “grain free” diets, can develop DCM independent of the diet.
8. If you have a suspicion of any adverse reaction to any diet, please report it.
9. If you wish to directly quiz a manufacturer, consider asking the following:How do they ensure their diets are complete and balanced?

- Have they tested whole blood taurine in dogs fed their diets for long periods?
- What is the taurine content of the diets?
- What is the protein and sulphur amino acid content?
- What is the protein digestibility?

10. It remains to be seen if there is any mechanism other than taurine deficiency by which the current diets are causing DCM in dogs.

Taurine supplementation

Give 500 mg per 10kg, up to a maximum of 2000mg orally per day. It does not have to be given twice daily, and can be given with, or without food.

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Raw food diets: Facts, philosophy, and fallacy

Cave NJ

It would be historically inaccurate to suggest, as some have done, that raw-food diets are a recent phenomenon. Raw animal products and cooked scraps have probably been the dominant diet of domesticated cats and dogs throughout the millennia that we have cohabitated, and although commercial pet foods were probably first developed in the 1880's, they have only been widely available for a few decades. Nonetheless, the popularity of feeding raw food diets has increased considerably recently.

10 to 20 years ago, >98% of pet owners in Australia and New Zealand consistently fed predominantly conventional commercial diets, and almost no owners exclusively fed raw food diets (RFDs).[1-4] However, in the 10 years between 2008 and 2018, the popularity of feeding raw food diets has increased dramatically across the world, and it may be that more than 50% of owners choose raw food to be at least a component of their pet's diet.[5] Although not specifically studied, when prescribed by veterinarians, it is likely that the most common reasons are for the short term management of non-specific gastroenteritis, or for the diagnosis or therapy of food hypersensitivity. Indeed, in cases of food hypersensitivity in the USA, HPDs were more commonly prescribed than commercial diets (prior to the availability of commercial selected protein or hydrolysed protein diets).[6] However, there has been a groundswell of interest specifically in raw food feeding over the past 20 years, which has been fuelled by negative opinions of commercial pet foods and manufacturers.

Australia holds special prominence in this area, largely as the result of the evangelical approaches of Ian Billinghurst and Tom Lonsdale, and the success of popular literature on the subject. The unappealing acronym "BARF" was originally coined to define a "bones and raw food diet", but, for whatever reason, has morphed into the more apparently palatable "biologically appropriate raw food diet". Although for some time, raw food feeding was the domain of the home enthusiast, several companies around the world have followed the call to battle and produce varieties of raw food diets (RFDs). These commercial varieties range from raw meat only, where no attempt is made to formulate a complete and balanced diet, to diets that are formulated to meet the nutrient requirements established by the NRC.[7]

There has perhaps been no topic in veterinary nutrition that has been more emotionally charged over the ensuing 20 years or so. Typical of human dilemmas, interested individuals are characterised as being on one of two sides: you are either a BARF fanatic, fuelled with all the zealous and irrational passions of a religious fundamentalist, or you are a corporate lap dog, having surrendered your willingness to question, and to the detriment of your patients you are slavish soulless sycophants. Caricatures these may be, but unheard they are not. If we are true to our profession and to the "Sc" on the end of our degree letters, we will remain aloof of hysterics, and play the role of the objective and rational philosopher. Truth will out.

Definitions

One of the features of the topic is the confusion of terms. "Raw food" simply means "uncooked", yet the term is rarely limited to that definition. Definitions of RFDs include:

- Uncooked ingredients that are included to emulates whole prey.

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- Uncooked meat, with or without some plant ingredients
- Uncooked meat, with various ingredients and a vitamin and mineral supplement

Owners motives for feeding raw foods are as varied as the diets.[5,8-10] However, by far the most common reasons can be placed into two categories: 1) the perception that RFDs are healthier, or offer some benefit in specific diseases, or 2) the belief that conventional diets are specifically unhealthy. Unsurprisingly, veterinarians are not the major source of these perceptions and beliefs.

The characteristics of the ideal diet have been determined

It is sobering to realise that even the basic nutrient requirements are not completely defined, and we are a very long way from determining what is "ideal", for any life-stage. When we do not know what is ideal for any member of a species, we cannot suggest that one diet is ideal for all. There is no better indicator of the daunting scope of our ignorance than the money that large pet food manufacturers are prepared to spend on nutritional research. So any claim that a dietary composition is ideal, even one regarding a single nutrient concentration, should be treated with a pinch of salt. And then a good dollop of mustard as well. It is simply not true that anyone has identified the ideal diet.

Potential benefits

Dental disease is the most common disease affecting dogs and cats throughout their lives, and it is in this regard that diets containing bones have their greatest measurable benefit. Periodontitis will develop in almost all animals fed commercial diets if they do not have other regular measures to prevent the disease. Even more so, softer diets appear convincingly to be worse. Cats fed dry food develop less calculus and gingivitis than cats fed exclusively canned food.[11] In a large survey of domestic cats in Japan, calculus was more common in cats fed canned or home-cooked (boneless) meals than cats fed dry foods (41% vs. 25%).[12] Similarly, it was shown many years ago that soaking dry food prior to feeding is a reliable method of inducing the rapid formation of plaque, calculus, gingivitis, and eventually periodontitis in dogs.[13] In a study of dogs in Brazil, those that were fed diets of home-prepared foods and scraps (presumably without bones) had significantly more dental disease than those fed commercial dry diets.[14]

Additionally, when commercial diets are supplemented with more abrasive, "natural" ingredients, the development of periodontitis is retarded, or even prevented. Feeding raw oxtails as a supplement to a dry food has been shown to be effective in minimising the development of gingivitis and periodontitis in long term (> 6 years) studies in beagles.[15] Once weekly feeding of oxtails was shown to remove existing calculus to 5% of previous amounts within 2 weeks and to maintain them at that level for years. Further, a diet consisting of raw bovine trachea and attached tissues was much more effective in reducing plaque, calculus and gingivitis than the same diet when fed minced.[16]

Thus, commercial diets are associated with periodontal disease, and softer diets are worse than dry diets, though perhaps there is less difference between the two types of commercial diet than one might expect. In addition, the supplementation of commercial diets with "natural" chews, such as oxtails, dramatically improves oral health.

It should be noted however, that periodontitis still occurs, and is surprisingly common in wild felids and canids. It was present in 41% of African Wild Dogs surveyed, 61% of feral cats on a seabird diet, and in a study in Australia, there was no difference in the prevalence of periodontitis between feral trapped cats and age matched owned cats.[17-19] Thus the "wild diet" does not prevent periodontitis, even though appropriate chewing behaviour significantly helps.

The palatability of RFDs is often claimed to be higher. Much of this claim stems from the neophilic feeding behaviours of dogs, and to a lesser degree cats. Moist diets are almost universally more palatable than dry diets. However, in our nutrition colony, cats reared and fed for years on high moisture canned diets prefer dry premium diets when they are offered. In addition, both dogs and cats generally (though not always) select for the flavour of cooked meat, rather than raw meat.[20-23] Thus the observations of RFD enthusiasts that the palatability is higher, are correct, but only in the respect of novelty and moisture.

The protein digestibility of raw meat can be higher or lower than cooked meat depending on the amount of collagen and the type of cooking. As a general rule however, cooked meat has a lower digestibility than raw meat for both dogs and cats, and especially when compared with meat by-products commonly used in commercial pet foods.[24,25] However, even between types of meat (e.g. horse and beef) there can be significant differences in digestibility and faecal quality when fed raw.[26] In a study that compared home-kill mutton with Tux biscuits, it was found that the protein digestibility of Tux was 83%, whilst that of the raw mutton was 95%.[27] It may be that some animals with severe intestinal dysfunction and maldigestion will show clinical improvement if fed a cooked HPD rather than a commercial diet, but whether feeding the same diet raw will yield any further benefit remains untested. For all other animals, the digestibility of premium commercial diets is still very high, and there is no experimental nor logical reason to abandon commercial diets in favour of RFDs based on digestibility.

Food processing, especially cooking, induces changes in all of the macronutrients, especially proteins. Proteins denature, and can become glycosylated to form Maillard compounds (browning reaction). The effect of heating during the canning process on the immunogenicity of dietary proteins has been evaluated in cats.[28] Using soy and casein proteins, the canning process resulted in the creation of new antigens not present in the uncooked product. In addition, a product of heated casein induced a salivary IgA response that was not induced by the raw product. Thus, commercial food processing can qualitatively and quantitatively alter the immunogenicity of food proteins. Although the significance of this finding is uncertain at present, it emphasises that food processing can have effects that are not always benign.

Other claims regarding health benefits, faecal consistency, and increased activity have not been tested, are unable to be critiqued, and are probably unfounded.

Risks to pet

Microbial contamination of meat varies according to the source. Meat products not intended or suitable for human consumption are commonly used as pet foods. The nature of these tissues and the less stringent handling requirements compared with products approved for human consumption, increases the risk of bacterial contamination.

There are numerous reports in the literature that describe the prevalence of contamination of fresh meat with Salmonella spp, Campylobacter spp, Yersinia spp, and enterotoxigenic E.coli.[29-33] Equally numerous are the reports of high rates of intestinal carriage in dogs and cats fed such diets.[31,34-37] Studies originating in Canada and the USA dominate the literature, and poultry based diets are the most frequently incriminated. Regional differences in farming, slaughtering, and meat storage and handling procedures could lead to very different results elsewhere in the world, and such data may not apply to Australia and New Zealand where raw poultry is much less commonly fed than beef, lamb, and other red meats. However, in a recent survey of 50 different commercial RFDs in New Zealand, most of which were red-meat based, Campylobacter jejuni or coli were isolated from 22%.[38]

One study that clearly demonstrated the potential for disease was conducted at a greyhound breeding unit in which there had been several cases of acute enteritis and death associated with Salmonella spp infection in puppies.[36] Salmonella was isolated from many locations and insect vectors. Salmonella spp were isolated from 57 of 61 (93%) faecal samples and the majority were genetically identical, and that organism was recovered from raw meat fed at the facility.

It can be concluded then that feeding RFDs to dogs and cats commonly results in intestinal colonisation with important human pathogens. Intestinal and even systemic disease can occur as the result of this colonisation. However, intestinal disease is not commonly reported in dogs or cats fed RFDs, and intestinal carriage of these organisms is not normally associated with clinical signs, and only sporadic reports of intestinal disease associated with RFD feeding exist.[39,40] Thus, although the risk to the pet of colonisation is great, the risk of disease has not been established, will be difficult to quantify, and is likely to be small.

In contrast to bacterial contamination, parasitic contamination leading to infection and disease of dogs and cats is well established. Toxoplasma, Neospora spp, and Sarcocystis have all been reported as causes of disease in pets fed RFDs in North America, and Australia.[32,41-43] The high rates of meat contamination and successful infection of pets consuming the diets makes protozoal disease of greater concern than bacterial when considering the risk of RFD feeding.[32,44]

The ingestion of bone fragments is associated with tooth fracture, intestinal irritation, obstruction and perforation, diarrhoea, and constipation.[45] An interesting suggestion is that puppies and kittens that are introduced to bones early in life may be less likely to experience adverse effects because they learn through observation of their mothers, and presumably through experience. In contrast, adult dogs that are fed bones for the first time may be more likely to swallow large fragments or whole bones. This theory is intriguing, but untested.

Nutritional adequacy

RFDs can, and should, be formulated to be the equal of commercial diets. However, a combination of inadequate recipes, owner (and veterinarian) ignorance, and the natural tendency for “recipe drift” combine to produce a large proportion of inadequate diets.

In Europe, a survey of HPDs (mostly cooked diets) found that energy, fat and protein were above AAFCO recommendations, whereas calcium, Ca:P ratio and vitamins A and E, and potassium, copper and zinc concentrations were below recommendations.[46] Relative fatty acid contents of serum phospholipid fractions of HPD-fed dogs were significantly lower in 18:2(n-6) and 20:4(n-6) than those from a population of 37 normal dogs consuming commercial dry, US-manufactured diets. In the USA, previous studies have found that the great majority (>90%) of HPD recipes are nutritionally inadequate.6 I have evaluated 43 HPD recipes, mostly RFDs, fed to dogs (predominantly) and cats in New Zealand, and not one recipe was complete and balanced. The most common nutritional inadequacy would be a deficiency of calcium and too low Ca:P ratio, which is an inevitable consequence of an unsupplemented meat-based diet. Other common deficiencies include vitamins B_{12}, E, D, and A; copper, manganese, and iodine. Common excesses include total fat, 18:2(n-6), and B-vitamins (>1000x NRC maximum for B_{12} in racing greyhounds is common).

Most properly formulated HPDs contain a minimum of 6, and up to 9 separate ingredients. Although not studied, client compliance probably decreases, the larger the ingredient list is. Formulating complete diets without using “supplements” is perfectly possible, but requires many more ingredients.

An unpublished phone-survey of clients of the Nutrition Consulting Service of the University of California, Davis, found that within weeks of starting a prescribed HPD, the great majority of clients either modify, add commercial food, or abandon the diet completely.

That dogs and cats do not apparently become ill with short-term feeding of such diets, or that owners that feed RFDs on an ongoing basis with no apparent ill effects, is credit to several factors including:

1. Our inability to measure the effects of short-term nutritional inadequacy
2. The uncertainty of the absolute physiology requirements
3. The difference between long term requirements averaged out as a daily requirement, vs a true short-term requirement
4. Non-compliance, and the pragmatic tendency for a varied diet to be more likely to be complete than a restricted one
5. The robust nature of our patients!

Risks to owner and society

Although carriage of the "classic" enteric pathogens by dogs and cats rarely seems to cause overt disease, there is growing realisation of the potential for dogs and cats to infect household members. Campylobacteriosis is the most frequently reported notifiable human enteric infection in the USA, and household contact with dogs is a significant risk factor for development of campylobacteriosis in humans.[47] Transmission of Yersinia enterocolitica from a pet dog to a family resulting in clinical disease has also been reported.[48] Surveys of public understanding suggest that most owners are unaware of the potential for transmission of enteropathogens between their pets and themselves, and we are obliged to fill that knowledge gap since it is unlikely to be discussed by other health care professionals.[49]

As stated above, dogs routinely fed RFDs are commonly infected with Sarcocystis spp, and may contaminate the environment by shedding sporocysts in their faeces, posing a risk for livestock grazing in the same environment.[50] Taenia ovis and hydatigena shedding by dogs and subsequent infection of livestock results in condemnation of tissues at slaughter and related economic losses. Not surprisingly, working farm dogs remain the overwhelming source of infection for livestock, although it has been observed that properties bordering highways are at an increased risk, suggesting roadside contamination from passing dogs, enjoying some rural roadside relief. We should remember that the feeding of uncooked offal to dogs in New Zealand remains illegal, under the Biosecurity act. Although the risk of infection from tripe is probably small, it is still illegal and uncooked tripe should not be fed.

For countries with significant agricultural industries, veterinarians should be in the vanguard of holistic public and livestock health, and reducing needless parasitic infections is one avenue for intervention.

Arguments against feeding commercial diets

Much of the rhetoric directed against commercial diet feeding is fuelled by an intrinsic dislike of large corporations, xenophobia, and a feeling that companies that profit from selling food, are unlikely to work with the animals' best interests at heart. Although we should disregard such sentiments as unfounded, we should continue to question the ethics of our feeding practices. Many veterinarians object to the conditions that intensively reared pigs and poultry are kept in, and reasonably choose to eat only free range, or even vegetarian diets. We should apply the same moral reasoning to pet food manufacturing, since the suffering of the production animal is the same regardless of its end use. Products manufactured from farming practices that we find more acceptable - perhaps those of pasture reared beef and sheep - could be argued to be more

ethical than those made from intensively reared chickens or pigs. Likewise, for those that are concerned with the energy cost, and carbon output from shipping food across the globe may wish to favour pet foods of equal quality that are manufactured on our own shores. And the recent recognition of the imbalance in polyunsaturated fatty acids (PUFA) that has resulted from the most commonly used ingredients, has lead to the increased incorporation of fish by-products to increase the content of n-3 PUFA. The section of humanity that truly believes our modern fishing practices are sustainable is dwindling.

Perhaps the future of ethically produced pet foods will depend on the production of diets that are even less "natural", than the currently available ones. Complete and balanced nutrition can be provided using vegetable ingredients, when careful formulation and supplementation is applied. If we can do it, perhaps we should.

Conclusion

There are arguments for and against the feeding of RFDs, but there is an unfortunate dearth of any research that documents the objective benefits of such feeding practices. Several concerns about the diets could be allayed simply by cooking, with little, if any, loss of the presumed benefits. Arguments for RFDs based on the premise of what is "natural" are flawed, and should not be promoted. In nature, the life expectancy African Wild Dogs is about 5 years, and very few feral cats live longer than 4 years. The life expectancy of domestic dogs and cats, including animals kept in colonies and maintained on commercial diets, is 2-4 times that "naturally" seen. That difference between wild and domestic life expectancy is sobering. The establishment of nutritional requirements of dogs and cats through the research efforts of many individuals over the past 50 years has lead to the development of diets that, although imperfect, have transformed pet ownership. Modern commercial diets are not perfect, and there is no feeding practice that has zero risk. Many reasonable people may object to some commercial diets, and we have a long way to go before they are ideal, let alone ideally made. None-the-less, those companies with rigorous quality control measures, that subject their diets to properly conducted feeding trials, produce diets of extremely high quality on which we can rely.

Our role

Owners that feed RFDs are not stupid, and they have the same concerns for the health of their pets that any owner does, and that we should. We should start from a position of commonality – we want what is best for their pets. If an owner wishes to feed a raw diet, I suggest that our approach should be as follows:

- Be supportive of the intention to feed a healthy diet
- Ask how they ensure that the diet is complete and balanced. Feeding a pet a deficient diet is no more acceptable than any other form of mistreatment.
- Explain that it is possible, but difficult to do so without the use of vitamin or mineral supplements.
- Suggest the means to feed a complete and balanced diet

a) Feed a commercially prepared diet that has been formulated to meet the requirements established by AAFCO

b) Create a recipe that is supplemented with a balanced vitamin and mineral product. E.g. www.balanceit.com

c) Feed a recipe that has been formulated by a veterinary nutritionist

- Ensure that the owner is aware of the small bacterial and parasitic risks, and that freeze-thawing of ingredients would reduce, and cooking would resolve the risks.

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How to approach a cat with a gastrointestinal mass

Chan, C

Introduction

As a veterinarian, you will be presented with a cat with a gastrointestinal mass. These notes will discuss the cancer biology, prognosis, diagnostics, and treatment options for the three most common gastrointestinal cancers in cats (lymphoma, adenocarcinoma and mast cell tumours). Other diseases (such as adenomatous polyps), and less common gastrointestinal cancers (such as carcinoids, sarcomas and plasma cell tumours), can also occur in cats. It is important to recognise these types of cancers. However, discussion of these diseases and less common gastrointestinal cancers is beyond the scope of these notes.

Lymphoma

Lymphoma is the most common haematopoietic cancer in cats. Lymphoma usually arises in lymphoid tissues such as the lymph nodes, spleen, and bone marrow. However, lymphoma may arise in any tissue of the body.

Lymphoma is the most common primary gastrointestinal cancer in cats. Gastrointestinal lymphoma can be confined to the intestinal or gastric location, or a combination of intestinal, mesenteric lymph node, and hepatosplenic involvement. These tumours may be solitary, but more commonly are diffuse throughout the intestines.

Cats with gastrointestinal lymphoma typically present with a palpable abdominal mass and non-specific clinical signs of vomiting, diarrhoea, inappetence or weight loss.

The median age of affected cats is approximately 10 to 13 years of age. However, lymphoma may occur in cats of any age. Oriental breeds (such as Siamese breed) are predisposed. However, most cases occur in domestic shorthair (DSH) cats. Males appear slightly more frequently affected than females (1.1-1.5:1 male-to-female ratio).

The prognosis for lymphoma in cats is highly variable and depends on several factors. Unfavourable prognostic factors include not achieving complete remission with therapy,[1-3] high histologic grade, large-cell morphology,4 positive FeLV status,[1] clinical substage b[1,5,6] (particularly weight loss and anaemia at presentation), transmural gastrointestinal lymphoma,[4] not receiving doxorubicin in a treatment protocol,[1,7] possibly pre-treatment steroids,[2] and probably T-cell immunophenotype for cats with high-grade or large-cell lymphoma.

Overall there are many prognostic factors associated with lymphoma in cats. However, the single most important independent prognostic factor is achieving complete remission with therapy. The response to therapy will not be known until therapy is trialled.

Diagnosis is usually confirmed by cytology or histopathology of the gastrointestinal mass. B- and T-cell immunophenotyping, flow cytometry, and PARR (PCR for Antigen Receptor Rearrangement) are special tests sometimes required to confirm lymphoma. Three-view thoracic radiographs and abdominal ultrasonogram are recommended to determine if there are other sites of lymphoma and to help monitor responses to therapy. Haematology (including blood film review), serum biochemistry and routine urinalysis are a minimum database, recommended in all cats with lymphoma, particularly before starting chemotherapy, to assess the cat's general health and determine if there are any co-morbidities. Renal and hepatic function is crucial to assess before chemotherapy because if there are any abnormalities, chemotherapy may be contraindicated. The results of these tests will allow veterinarians to develop individualised treatment recommendations for each cat. Feline leukaemia virus (FeLV) and feline immunodeficiency virus (FIV) retroviral testing are also recommended. FeLV-positive cats are associated with a worse prognosis and are more

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likely to have systemic involvement. FIV-positive cats anecdotally have been associated with a higher risk of myelosuppression (particularly neutropenia) with chemotherapy.
The prognosis for untreated high-grade lymphoma in cats is guarded, with a median survival time of approximately two months or less. Most cats are humanely euthanised due to poor quality of life.

The treatment of choice is multiple-agent chemotherapy. The reported complete remission rate and median survival times with multiple-agent chemotherapy are approximately 50-70%, for approximately 4 to 12 months, respectively. Some cats are cured, living up to 2.5 years or longer. However, this is less likely (although not impossible) with gastrointestinal lymphoma. Also, cats that achieve a complete remission with chemotherapy have reported median survival times between 8 months and 1.5 years, compared to 2 to 3 months in cats that do not achieve a complete remission (i.e. cats that achieved partial remission, stable disease or progressive disease). Single-agent lomustine (CCNU) is also a reasonable option. A recent retrospective study evaluated 32 cats with treatment naïve intermediate to large-cell gastrointestinal lymphoma treated with single-agent CCNU.8 Some cats received a single dose of l-asparaginase with the first CCNU treatment. The response rate (i.e. complete and partial remission) to CCNU was approximately 50%. Most cats had a clinical benefit from treatment. However, 30% of cats did not respond to therapy. The median survival time for all cats in this study was 3.5 months. However, if cats achieved complete remission with CCNU, the median survival time increased to 10 months.

What if the gastrointestinal mass is solitary? In these cases, surgery followed by chemotherapy or chemotherapy alone is recommended. Surgery alone is not recommended. Which cats do I take to surgery? I recommend surgery in cats with discrete/solitary gastrointestinal mass, when gastrointestinal perforation is suspected/confirmed, or there is a high risk of gastrointestinal perforation. However, before considering surgery, I strongly recommend thorough staging to ensure there is no evidence of lymphoma present elsewhere.

Is there a survival advantage with surgery and chemotherapy, over chemotherapy alone? This is a challenging question. In one study of 20 cats with high-grade discrete gastrointestinal lymphoma undergoing surgery followed by CHOP chemotherapy, the median survival time was 14 months.[9] In another study evaluating 40 cats with discrete intermediate- or large-cell gastrointestinal lymphoma undergoing surgery ± chemotherapy, the overall median survival time was three months.[10] The median survival time of cats with small intestinal lymphoma was two months. Whilst the latter study showed no survival benefit with the addition of chemotherapy after surgery, only 25% of cats that underwent surgery received chemotherapy. The median survival time in cats with complete histologic margins was seven months, compared to 2.5 months in cats with incomplete histologic margins. Based on these two studies, the median survival times with surgery followed by chemotherapy was three months and 14 months. Chemotherapy alone is associated with a median survival time of between 4 and 12 months. Therefore, at this stage, it is uncertain whether the addition of surgery provides cats with a survival advantage over chemotherapy alone.

In one study of 23 cats with discrete intermediate- or large-cell gastrointestinal lymphoma, the risk of gastrointestinal perforation appears to be low at 17%, between 23 and 87 days after the induction of chemotherapy.[11] The magnitude of weight loss within 2 to 4 weeks of chemotherapy was greater in cats with perforation.

For cats with small-cell or low-grade alimentary lymphoma (LGAL), the gold standard treatment involves oral administration of chlorambucil and prednisolone indefinitely, which cat owners can administer from home. The prognosis is excellent, with an overall response rate of 85-95% and reported median survival times of around 1.5-3 years. Occasionally, cats will not respond to therapy or transform into large-cell or high-grade lymphoma or develop a second malignancy. These cats have a worse prognosis.[12-14]

It can be challenging to distinguish LGAL from inflammatory bowel disease (IBD). Cats with both LGAL and IBD can both present with diffusely thickened small intestines, a segmental/focal gastrointestinal mass, with or without lymphadenopathy. The most common sonographic feature of LGAL is diffuse thickening of the

muscularis propria of the small intestines. In general, LGAL has more pronounced thickening of the muscularis propria, when compared to the submucosa.[15,16] Full thickness intestinal biopsies are recommended. PARR can sometimes be helpful in distinguishing between LGAL and IBD. However, PARR only has an accuracy of 77% in determining if cats have LGAL.[17]

Gastrointestinal adenocarcinoma

Carcinoma is the second most common gastrointestinal tumour in cats. The small intestines (particularly ileum) are the most common site. Older cats (mean age of 10 to 12 years) are primarily affected. Males appear slightly more frequently affected than females. Siamese cats and domestic short-haired cats may be overrepresented.

Cats usually present with a palpable abdominal mass and non-specific clinical signs such as anorexia, vomiting, weight loss, lethargy, diarrhoea, melaena, and abdominal pain. Generally, the clinical signs are not distinguishable from other benign or malignant conditions, and consequently, the disease is often insidious in onset. Most cats present with clinical signs for one to three months before a diagnosis of small intestinal carcinoma is made. Some cats present with partial or complete obstruction.

Intestinal carcinomas are locally invasive and highly metastatic, with around 76% having distant metastasis at the time of presentation. Around half of cats have metastasis to regional lymph nodes, 30-81% to the peritoneal cavity (carcinomatosis), and 9-20% to the lungs. Intestinal carcinomas are often advanced at the time of diagnosis.

The prognosis for untreated cats is poor, with most cats humanely euthanised within two weeks from poor quality of life. Positive prognostic factors include cats that present with a solitary mass and surgery to achieve complete histologic margins. Negative prognostic factors include the presence of metastasis or carcinomatosis and unresectable tumours. Cats with evidence of nodal or distant metastasis usually have a survival time of less than a few months, compared to more than one year in cats without evidence of metastasis.[18]

However, long-term survival can be seen in cats with the presence of metastasis or carcinomatosis after surgical excision of the primary tumour. Diagnosis is similar to all cats with a gastrointestinal mass, with sampling of the primary tumour and staging to check for evidence of metastasis. Of particular importance is histopathology to remove the locoregional lymph nodes at the time of surgery. The presence of nodal metastasis is associated with a worse prognosis.

In one study of 18 cats with small intestinal carcinoma, the median survival time after intestinal resection anastomosis was one year. The median survival time in cats without metastasis was 2.3 years, compared to one year in cats with gross nodal or distant metastasis.[18] In the most recent study of 58 cats with intestinal carcinoma that were treated with surgical resection and chemotherapy in half of the cats, the median survival time was just over nine months.[19] In that study, approximately half of cats had nodal metastasis, and 81% had carcinomatosis. Therefore, surgery is still recommended in cats with evidence of metastasis. In one study of 32 cats with small intestinal carcinoma, carcinomatosis was associated with a median survival time of 4.5 months. However, if surgery was performed, the median survival time was improved to 2.3 years.

Surgery with intestinal resection and anastomosis with wide surgical margins of 5.0-cm on either side of the tumour is recommended to achieve adequate resection of small intestinal tumours. If this is not possible, then at least 3.0-cm surgical margins are recommended. Removal of a mesenteric lymph node and biopsies of any abnormal structures is recommended for prognostic purposes.

Currently, there is no standard of chemotherapy treatment for cats with small intestinal carcinoma. In the adjuvant setting, I recommend carboplatin and/or doxorubicin.

Mast cell tumour

Feline intestinal mast cell tumour (MCT) is the third most common gastrointestinal cancer in cats. There are three distinct syndromes in cats

with MCTs that may overlap, including cutaneous, splenic/visceral, and intestinal MCT. Older cats are primarily affected (mean age of 13 years). Most cats present with non-specific signs of illness, such as vomiting, diarrhoea, hyperoxia and a solitary palpable abdominal mass. Signs are often chronic and progressive over weeks to months. Clinical signs associated with the release of mast cell mediators, such as gastrointestinal ulceration, haemorrhage and hypotensive shock, may be seen. Occasionally, cats present with no clinical signs of illness.

The most common site is the small intestines, and lesions may be solitary or multiple. Most cats (>65%) present with metastasis to the regional lymph nodes, liver and spleen.

There is also a unique histologic variant of sclerosing intestinal MCTs. However, the biologic behaviour is similar to cats with intestinal MCTs.

Diagnosis is similar to all cats that present with a gastrointestinal mass with sampling of the primary tumour and staging to check for evidence of metastasis. However, it is important to check for involvement of MCT in the locoregional lymph nodes, skin, spleen and liver. It is also important to sample any peritoneal effusions, and perform a buffy coat smear to look for peripheral mastocytosis. The most common sonographic feature of feline intestinal MCTs is focal, hypoechoic jejunal wall thickening, noncircumferential and eccentric location.[20] However, they can look like anything!

The prognosis for feline intestinal MCT is usually poor because most cats are diagnosed with metastasis and usually die or are humanely euthanised due to poor quality of life within two months of diagnosis. For cats with solitary intestinal MCTs, I usually recommend surgery followed by adjuvant chemotherapy. Surgery alone is unlikely to be successful, with most cats still dying within three months of surgery. Because most cats present with metastasis (or will go on to develop metastasis within a short period following surgery), I recommend adjuvant chemotherapy or Palladia®, alongside prednisolone following surgery.

However, in two recent studies on 48 cats with intestinal MCT, treatment with surgery and/or medical management (e.g. Palladia®, lomustine, chlorambucil, and/or prednisolone) is associated with a more favourable prognosis, with a median survival time of 1.5 years.[21] Surgery is recommended for palliation of clinical signs (e.g. gastrointestinal obstruction) or in cats that have gastrointestinal perforation (e.g. septic peritonitis).

For owners with financial constraints or do not wish for chemotherapy treatment, prednisolone concurrently with antihistamines, gastroprotectants, and serotonin antagonists is recommended. In one study of feline intestinal MCTs, six cats treated with prednisolone had a median survival time of 1.5 years.[21] However, these numbers were small. I still think surgery or Palladia® (concurrently with prednisolone) has a higher chance of working.

Vets, I hope this information helps you understand a bit more about how to approach a cat with a gastrointestinal mass. If you have a question about this topic, please do not hesitate to get in touch. Email: info@thepetoncologist.com.

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Remote tocodynamometry monitoring using WiFi to support veterinarians in home-based obstetrical management

Copley K

Parturition management has been the gold standard for achieving optimal maternal and foetal outcomes in the human world for over 100 years. Technology to support management of canine and feline patients was first introduced in the mid 1990's by Karen Copley RNC BSN, whose monitoring service "WhelpWise" demonstrated significantly better outcomes for canine and feline patients by placing a tocodynamometer and hand-held ultrasound doppler in breeders' homes. This equipment is capable of transferring data through a WiFi connection to a 24 hour staffed monitoring centre. This ability for remote parturition management allows expert veterinary guidance while facilitating a comfortable whelping experience for the bitch and her care-giver, allowing them to whelp in a familiar location and only sending animals in for a veterinary evaluation that have demonstrated abnormalities in the veterinarians prescribed plan of care.

WhelpWise is only offered in conjunction with the clients' veterinarian. How we approach care of the animal on service is guided by specific veterinary orders provided to us by the veterinarian[1]. The WhelpWise service monitors both uterine contractions, and foetal heart rates using obstetrical equipment specifically designed for remote data collection. This data is transferred to the monitoring centre for evaluation and discussion with the client or veterinarian about what the current data shows and what the next step in whelping management should be. Prior to having the ability to objectively monitor uterine contractions and foetal heart rates parturition management was based on a "best guess" plan of care; using interventions from subjective symptoms or unreliable parameters such as temperature change. By using objective data as the base for interventions, assessments and interventions can now be made with a higher degree of safety and reliability for both the dam and foetuses. Clients that have utilized our services are interested in improving maternal and foetal outcomes by being proactive in the detection and management of whelping issues. A significant benefit offered by the service is to be able to safely manage inertia through labour augmentation protocols developed specifically for canines, and designed for safe use in the home setting.

Currently we have monitored over 45,000 whelpings; maintaining a data base that has included parity, prior dystocias, diet history, progesterone/LH timing for breeding, X-ray counts, and specific parturition events. The most scrutinized part of our data analysis is maternal/foetal outcomes (live vs. deceased births) and parturition management; evaluating medication doses and their tocometric response.

What have we learned in our 45,000 litters?

The balance of my paper will explain what we see with our uterine monitoring and foetal doppler equipment and how we use this information to manage whelpings through our monitoring service. I also will address some of the more common perceptions of how the whelping process takes place by using what we see with our monitoring equipment both to educate but also to dispel many common myths about canine parturition.

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Temperature drop prior to parturition

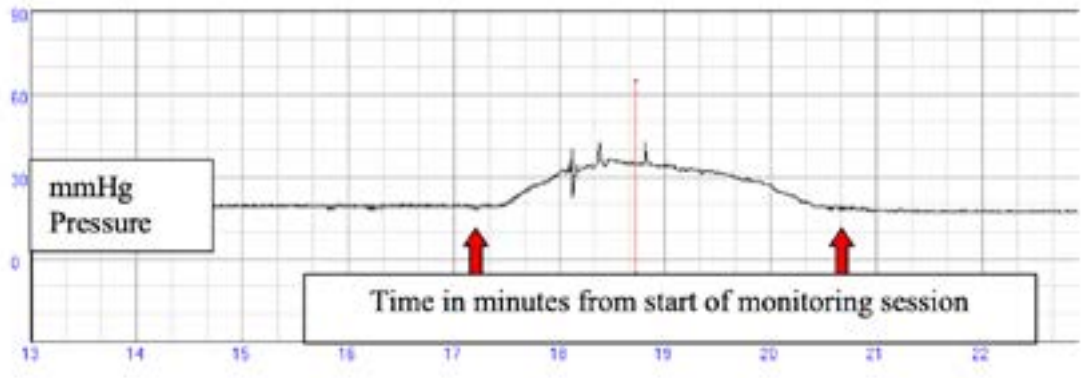
As described in a prior WhelpWise study, maternal core temperature change occurs in only 33% of bitches in a predictable manner, contrary to what is described in a multitude of veterinary resources. [2,3] These time-honoured veterinary studies, conducted in a controlled kennel situation, describe a change in basilar temperature, with parturition occurring 8 hours after the nadir of the decline. A more recent study of one hundred multiple breed bitches on the WhelpWise service, utilised data that was collected in the home setting. This data was compared to data from the uterine monitor, documenting the onset of labour. When comparing temperature changes to uterine activity it showed that 35% of the time there was no temperature change of more than 1 degree Fahrenheit. If a detectable temperature change of more than one degree was noted, delivery of the foetuses averaged 37-48 hours after the change rather than 12-24 hours as veterinary resources describe.[4] Additionally, multiple fluctuations in temperature were common and overall temperature changes had no impact on maternal/foetal outcomes.

Length of labour

Labour, as defined for this document, is the presence of an organised pattern of uterine contractions that is detected by our external monitoring equipment. Our definition of labour is not related to behavioural symptoms of parturition, temperature changes or the presence of vaginal discharge. A detectable uterine contraction pattern, i.e. “labour” is sustained until the completed delivery of the foetuses, and throughout early uterine involution. We have found that labour patterns will vary with breed, litter size, and abdominal mass of the bitch, and that every bitch tends to have her own variety of a labour pattern.

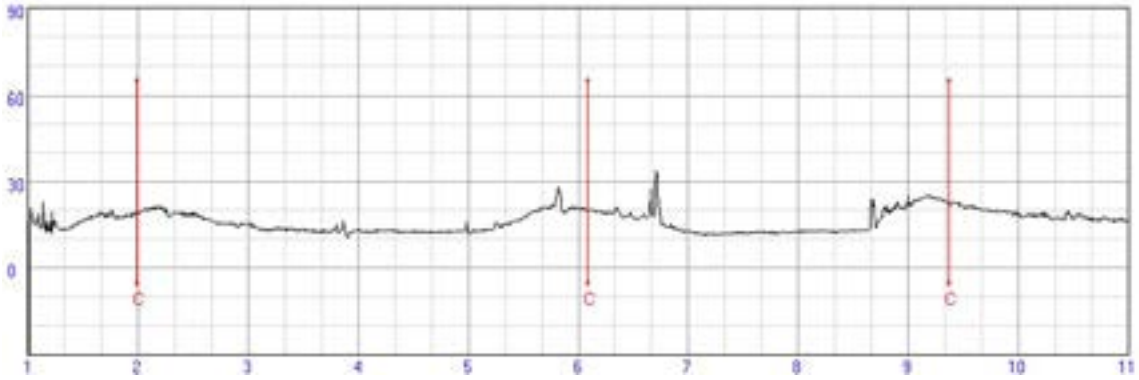
Uterine contractions are detected by applying an external uterine pressure sensor. This sensor detects changes in intrauterine pressure using a tocodynamometer specifically designed for use in animals. “Contractions” are traced on a linear axis, graphing changes in intrauterine pressure. As the myometrium contracts, the pressure inside the uterus will increase, as the contraction relaxes, the pressure decreases. Uterine activity graphs are documented as time in minutes on the X-axis, and strength of the contraction shown as an increase in pressure in millimetres of mercury on the Y-axis (figure 1). To obtain optimal data it is important that the bitches are monitored in a lateral recumbent position. This position will eliminate uterine contractions caused by physical activity.

Uterine contraction (figure 1)



During normal gestation it is expected that uterine contractions are present in a frequency of 1-3 per hour beginning about 56 days post LH surge.

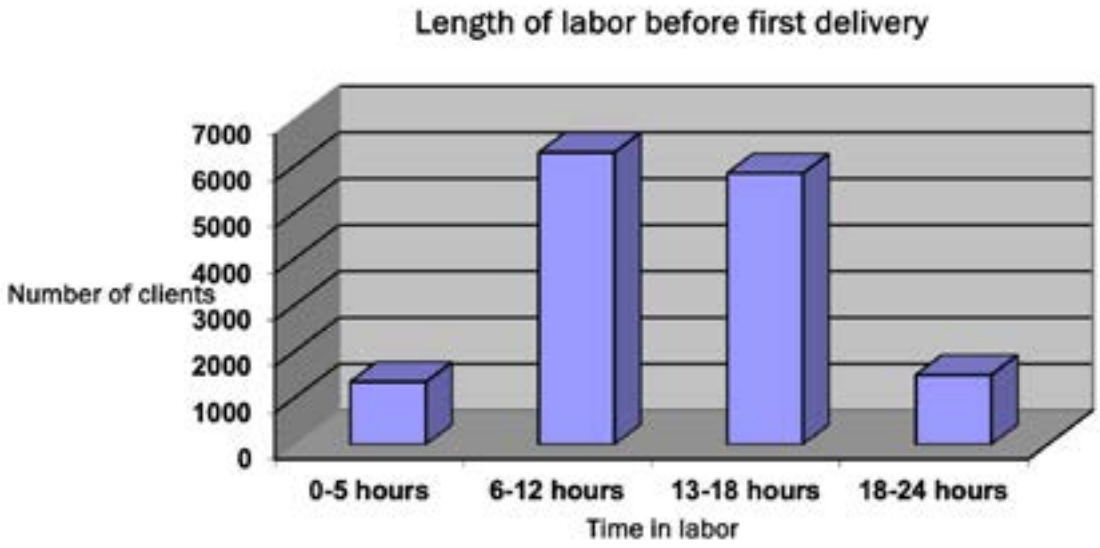
Labour (figure 2)



Presence of an organised pattern of uterine contractions. (figure 2)
Contractions are marked with a “C” and red line.
Note the consistency in spacing and strength.

Once first stage labour is established, our data strongly supports that deliveries will begin on an average of 9 hours from the presence of an organised pattern of labour. The range for delivery times averaged 9 to 14 hours, with a significant increase in foetal mortality and cesarean section rates when labour is extended beyond 14-16 hours of an organised labour pattern. During our early research the difference in foetal outcomes related to prolonged labour were so clear that labour augmentation protocols were established early in the development of the service. These protocols were based on the human model of parturition management.[5]

Human labour management strongly documents that parturition should follow a specific progression once active labour has been established.[6, 7] This predictable passing through parturition in human medicine has been called “Friedman’s curve” after the physician who documented that poor foetal outcomes were the result of an ineffective labour; pioneering the concept of human labour management to improve foetal outcomes.[8]



Inertia

Inertia describes the failure to maintain an adequate contraction pattern during active labour. Inertia may be the inability to move from first to second stage labour, or once second stage has occurred, the lack of contractility to continue to deliver pups.

The incidence of primary uterine inertia has been an extremely rare occurrence (less than .1%). In almost every client with acceptable timing, we have noted an attempt by the bitch to establish first stage labour. This attempt is frequently asymptomatic and will not be associated with a change in temperature change. It is not uncommon for maiden bitches to establish a short episode (3-5 hours) of mild contractions that are in a disorganised pattern that will subside and return within 12-24 hours; moving into an organised active labour pattern. If this attempt to establish labour re-occurs more than twice without progression to active labour, we have found that there is a strong correlation with dystocias. These dystocias are frequently from an over distended uterus from polyhydramnios, foetal malposition, or exceptionally large pups.

Medical management of labour

Using the human model for medical management of labour, foetal outcome data consistently shows that lack of progression of labour per Friedmans Curve with an active labour pattern requires medical intervention, as low Apgar scores are strongly associated with prolonged labour.[6,7,8]

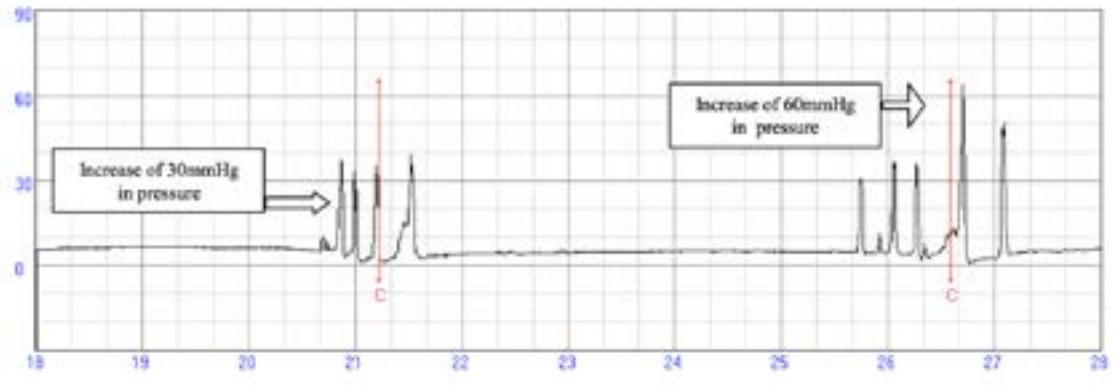
Early studies for our service evaluated whelping outcomes associated with prolonged labour. These studies also documented a strong increase in foetal loss correlating with lengthy labour, and early intervention with medical management when inertia is identified drastically reduced foetal demises from 33% to around 6%. In the whelping study a prolonged first stage also was associated with increased foetal deaths.

Also noted was an increased incidence of fading puppy syndrome; 19% compared to the labour managed group 1%.[5]

Secondary inertia, or the inability to progress from either stage one labour to stage two, or stage two to stage three appears to be the primary cause for foetal mortality and morbidity in our client population. Early detection and proactive medical management of inertia is a priority for our clients. Whelping management protocols have been modified over the last 26 years of data collection, fine-tuning the “art” of whelping management. This fine-tuning has further decreased our foetal mortality rate to around 4% for home breeder management, and less than 1.5% for educated whelping kennels such as the service dog organisations. Our average C-section rate is 16%, broken down; 6% for abnormal uterine contraction patterns, 10% for foetal distress. When inertia is detected early we expect that 80% of our clients will respond favourably to medical management protocols, titrating small doses of either oxytocin, injectable calcium, or both, with our only goal being to return the bitch to her “normal” labour pattern without causing uterine hyper-stimulation, uterine tetany or foetal distress.

Evaluating a bitch to determine if she has inertia (subjectively) is very difficult. As demonstrated with the uterine monitor session below, there is no inherent contraction strength in the labour pattern, but the veterinarian evaluating the case felt that the “observed contractions were strong”. What the veterinarian was evaluating was the abdominal expulsive efforts of the bitch, as she was indeed pushing very hard. However, if the contraction strength was improved by labour augmentation the bitch would require less physical effort to deliver the pups.

Pushing with severe inertia (figure 3). Spikes are caused by increased abdominal pressure as bitch bears down.



(Figure 3)

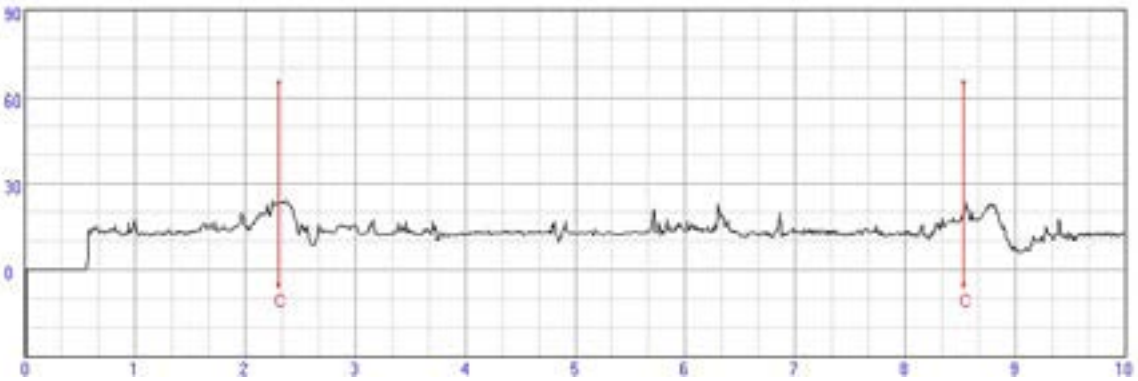
Injectable calcium

The use of injectable calcium to assist parturition has been documented as an uterotonic since 1947[9] Uterine myometrium is dependent on adequate calcium levels to contract effectively and creates its own calcium consumptive state.[3,10] It is this author's opinion that frequently calcium levels can be within an acceptable range based on traditional laboratory values, but the bitch may be experiencing a calcium-based inertia, as her calcium levels may have decreased but are still within a normal range. This decrease has impacted the contractility of the uterus. We believe this to be the case, as we have administered injectable calcium (sub-cutaneous) and seen a marked improvement in the contraction pattern even though calcium levels were "normal".

Inadequate calcium levels are also suspect in bitches that will establish a pattern of labour and then stop contracting. I question the ability of the parathyroid gland to rapidly respond to a declining calcium level because of foetal consumption or active labour. We have seen that calcium supplementation both oral and injectable have frequently supplied the needed base for an effective contraction pattern. We have objectively noted that administration of calcium will increase the strength of the contraction rather than the frequency of the contractions. A study of serum calcium levels conducted at the Guiding Eyes, also has documented that low ionized calcium had direct impact on stillbirths.[11]

Miniature Schnauzer, labour pattern X 10 hours, beginning of inertia (figure 4)

Figure 4



Session beginning 20 minutes after administration of Calcium Gluconate 10% SQ (figure 5)

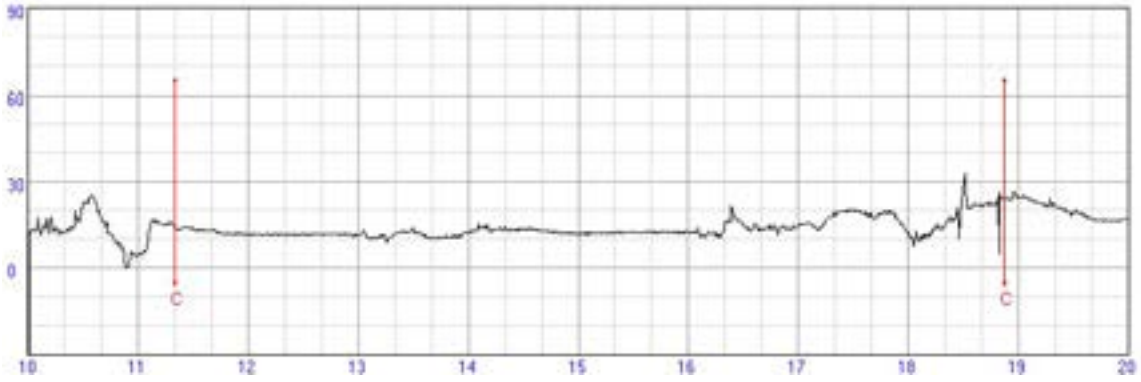


Figure 5

Note not only the increase in strength, but also the improvement of overall shape and duration of the contraction.

Dosage range for injectable calcium has been successful at ½ to 1 ml of 10% calcium gluconate, per 4.5kg current gravid maternal body weight, administered subcutaneously. Adverse effects have not been noted unless a stronger concentration of calcium has been used (23%). Injection sites using 23% calcium have been very painful for the animal and a corresponding tissue slough have been reported, but rarely. No cardiac problems have been experienced with the subcutaneous administration of the 10% solution because of the gradual absorption of the medication. We have had no reported incidence of accidental IV infusion when administering the medication subcutaneously.

In our client population, oral calcium supplements have been successful for proactive prevention of calcium-based inertias especially for bitches that are inappetent or for exceptionally large litters, which appear to be somewhat predisposed to calcium imbalances. Beginning oral supplementation based on meeting minimal dietary needs 2-3 days prior to parturition or as early first stage labour is established does seem to be beneficial, without noted complications of antepartum eclampsia. The presence of adequate Vitamin D levels in the diet has also been significant to the prevention of calcium-based inertia. Vitamin D is frequently markedly decreased to completely absent for owners feeding the raw diet, and whelping complications related to this imbalance are frequently not medically manageable, and surgical intervention is required for deliveries. We have not seen a corresponding improvement in contraction patterns from the oral calcium gel products and have had several dogs using these products experience G.I. bleeding after their use.

Oxytocin

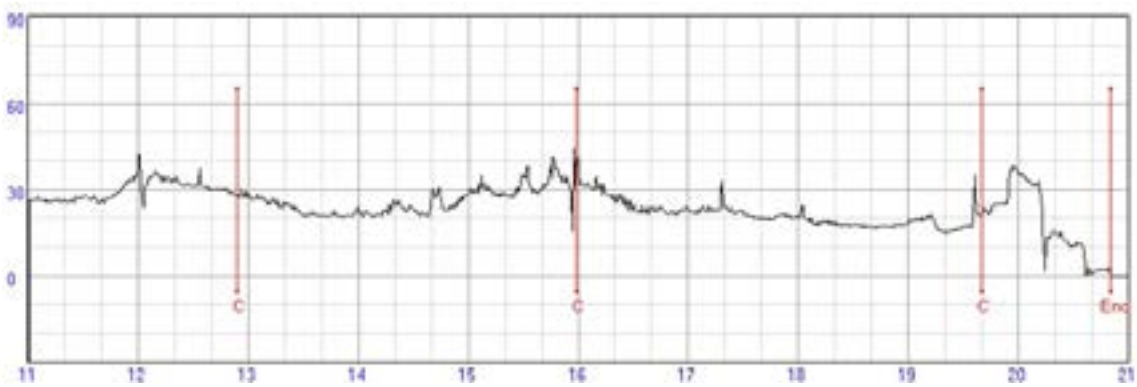
Oxytocin historically has been the most frequently used drug for labour augmentation. Dosing prior to the use of the uterine monitor was arbitrary, usually based on animal weight, not uterine contraction patterns.[13] Administering oxytocin in excessive amounts can be a detriment to both labour progression and foetal well-being, as a hyper stimulated uterus does not contract effectively, and the constriction of the myometrium will impede blood flow to the foetus. The relaxation phase between each contraction is important to allow blood to circulate to the foetus. Excessive doses of oxytocin can cause uterine rupture. According to our database, effectiveness of oxytocin is related to length of labour, with best response noted after first

stage labour has been present for at least 8 hours, but not over 16 hours. Administering oxytocin before 8 hours of active labour or after 16 hours of labour frequently has minimal effect on the contraction pattern.

From our perspective oxytocin dosing should always be titrated to the existing uterine contraction pattern, without regard for body weight of the bitch. Our general protocol begins with ½ unit of oxytocin; administered either subcutaneous or intramuscular, depending on the desired rate of response and duration of action. Our protocol describes that Oxytocin is only administered after 8 hours of first stage labour and documented inertia. Expected results with oxytocin would be an increased frequency of the uterine contractions. Because of the short half-life of oxytocin, dosing is usually every 45-60 minutes. If the desired response of increased uterine contractility is not achieved with the first dose, doses are increased in ½ to 1 unit increments until an adequate pattern of contractions is achieved. After administering 3 subsequent doses of oxytocin, incrementally increasing each dose, critical evaluation is made of the success of the augmentation. Failure to improve the inertia after 3 doses of oxytocin and one dose of calcium generally shows that medical management of the dystocia will not be successful and surgical intervention is a frequent necessity.

When medical management is contraindicated

A marked change in the contraction pattern is usually noted as the foetus enters the uterine body that presents on our monitoring sessions as fairly strong, close coupled contractions. With the presence of close-coupled contractions a delivery should occur within 1 hour. Frequently when this type of contraction pattern is noted the presenting foetal part may be palpated on vaginal exam. Note of interest, the bitch was sleeping during this session, showing once again that subjective symptoms are not adequate markers of labour progression. Medication would be contraindicated with this uterine contraction pattern, as there is no inertia. The first pup was delivered 15 minutes after the end of the session.



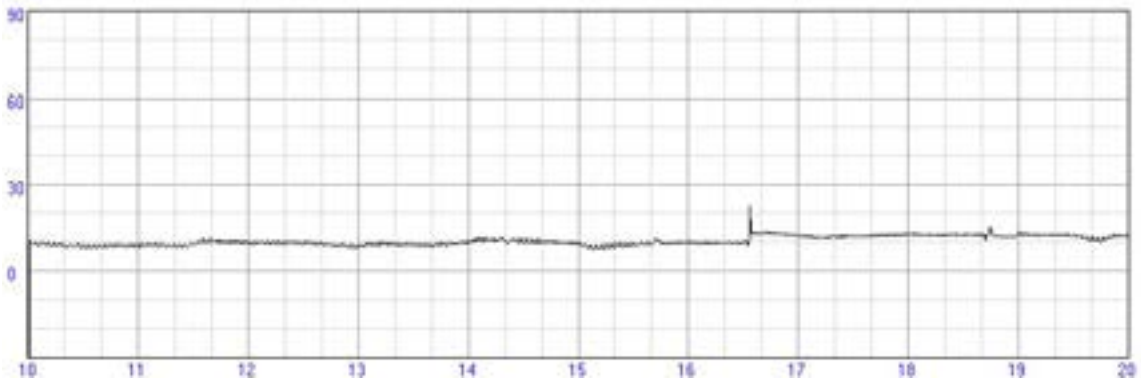
Contraction pattern with foetal/pelvic engagement (figure 6)

High risk pregnancy management

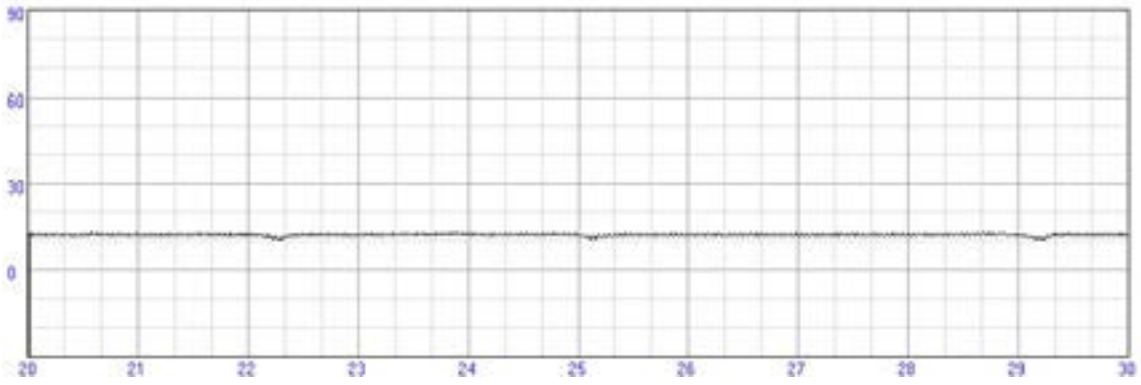
Premature labour

The presence of uterine contractions in an organised fashion in the canine was first documented in 1989 by G.C van der Weyden et al, by surgically implanting electrodes in the canine myometrium.[9] van der Weyden's observation of the presence of 1-3 contractions an hour 7 days before the onset of an active labour pattern has been strongly duplicated in our client population. We consider the occurrence of 1-3 contractions an hour a normal "baseline" uterine contraction pattern after 53 days post LH surge. Uterine contractions occurring BEFORE day 53, especially with the presence of irritability (contractions that are less than a minute in length) have a high incidence of premature delivery and/or premature placental separation.

Our overall client base consists of about 15% "high-risk" premature labour clients, either being monitored because of a problematic history or acute premature labour. Documented conditions associated with the increased premature contractions from our client population have included uterine infections; both acute pyometra and low-grade metritis, hypolutealism, and uterine contractions associated with no known cause. Regardless of the cause, premature labour has been controllable in 99% of our clients. Keys to successful management have been the early documentation of uterine contraction patterns, early intervention, and medication titration to maintain uterine quiescence.



Uterine irritability at 27 days post LH surge, prior history of losing litter around 40-45 days of gestation. Irritability is defined as uterine contractions that are less than 1 minute in duration.



Uterine irritability 20 days post LH surge. History of complete litter loss at ultrasound in two litters

Of particular concern for premature labour management is the presence of a pattern within the uterine contractions or irritability. Once a pattern of contractility is established the pattern frequently will escalate into active labour within 48 hours if not treated. Clients using the WhelpWise service have a high motivation for success; in most cases they have already lost litters. Our "failure" rate, or "what happens if you don't treat the contractions" has occurred from clients that are non-compliant with treatment protocols. Clients that have not been treated aggressively have gone on to lose a significant amount of pups in the litter, or lose the entire litter. Foetuses that have been compromised by preterm labour but have managed to make it to the end of gestation frequently are intrauterine growth retarded and have severely compromised placentas. It is also very important to note that rarely are there symptoms associated with premature labour, nor is premature labour associated with a decline in maternal temperature. Frequently the presence of uteroverdin is the first symptom of a problem with the pregnancy.

In the era of dog "over population", one must ask the question of, why do you want to breed this bitch with all her whelping problems? The answer in many cases is because this is the last animal from a specific lineage, or frequently bred as an older bitch because of obtaining multiple working titles. Also, painstakingly selective breeding has eliminated many adult health issues in a line but has not been selective for good whelpers.

Medications for premature labour management

Antibiotics

As documented in both human and veterinary medicine infection plays a significant role in preterm labour because of the prostaglandin F2 alpha release with resulting leutolysis.[12] The presence of infection can be difficult to ascertain and frequently high-risk bitches, especially those with a prior history of infective loss, are prophylactically placed on antibiotic therapy.

Tocolyitcs

Terbutaline, (Brethine) was one of the most frequently used drugs in the treatment of human preterm labour. Unfortunately, thanks to a spate of corporate espionage, Terbutaline has received a "black-box" warning from the United States FDA. Removing this medication from preterm labour management in humans has resulted in a static level of preterm birth rates from the 1990's to 2021.[18] Currently, in human medicine, patients are managed with long-term maternal hospitalization and intravenous Magnesium Sulfate to control the preterm contractions. This therapy continues until the foetus reaches a date where the administration of cortical steroids will promote enough surfactant that the foetus can be allowed to deliver and will usually survive in the NICU. Unfortunately, these babies are left with life-long health issues that could have been prevented if the preterm labour was managed more effectively. For the canine population we have found Terbutaline Sulfate (Brethine) to be the most effective medication to manage preterm labour in dogs. We have managed around 6,750 clients using Terbutaline with no untoward effects.

Terbutaline is in the class of drugs called beta-mimetics. These Beta 2-adrenergic receptor agonists are sympathomimetic, causing smooth muscle relaxation by decreasing free intracellular calcium ions.[14] Controversy exists in human medicine about the long-term effectiveness of Terbutaline; some of this controversy is related to the b-site saturation causing the drug to become ineffective. Titrating doses: beginning with the smallest effective dose to control the uterine activity, proactively monitoring uterine activity, and increasing the doses in very small amounts to maintain control has proven effective in human medicine.[15, 16] We use this model for preterm labour management, and I believe that a primary reason for our success with Terbutaline is that we do not begin with an arbitrary dose, but rather titrate dosing to control concerning uterine contraction

patterns, increasing doses as needed. I do see an increased C-section rate for high-risk clients primarily because most high-risk clients do not want to take the chance of any foetal loss. Of those that do choose to free whelp, the incidence of foetal distress or severe inertia is high, (70%) so clients are informed before the parturition date of the potential risks of a free-whelp so they may plan with their veterinarian the best choice for the whelp.

Hypolutealism

Progesterone decline during gestation leading to active labour has been well accepted in veterinary research.[3, 11, 17] What is unclear in the current general management of hypolutealism is the correlation of an "acceptable" level of progesterone for a specific point in gestation, without factoring in the litter size, prior history of litter loss and breed pre-disposition for hypolutealism. Data from our high-risk clients strongly suggests that the perception of a progesterone level that is "greater than 2ng/ml will maintain a pregnancy" appears valid only in the last 2-3 days of gestation. One can only know if the progesterone level is adequate by assessing uterine activity. Documented progesterone levels within our client population range greatly and are strongly influenced by the breed of dog and the number of whelps in the litter.

In our high-risk client population proactive uterine and progesterone monitoring have given early evidence that the existing progesterone level, regardless of laboratory value, is or is not adequate to promote a healthy uterine environment. For clients experiencing preterm labour that is hypoluteal based, using information from the uterine monitor can document the need to obtain further progesterone levels or modifying current supplemental progesterone. This need to modify treatment plan is alerted by changes in the uterine activity rather than lab values alone. Extremely difficult preterm labour cases have occasionally been managed by adding in progesterone even with a "normal" progesterone level. Cooperative management with the clients' veterinarian; evaluating uterine contractility, actual progesterone levels and foetal well-being have provided an effective team approach.

In clients experiencing hypolutealism, we have seen the best response and long-term stability when using injectable progesterone (50mg/ml) in an oil-based carrier, usually sesame, apricot, or cottonseed oil. The oil-based medication is absorbed slower and maintains a more constant progesterone level. Additionally, the efficacy of oil-based therapy can also be documented through laboratory testing. Injectable progesterone doses have ranged from 1-3mg/kg, given QD to every 4th day, with dosing schedules determined by both laboratory values and uterine monitor results. While the uterine monitor provides early notification for an unstable uterus monitoring can also be helpful in weaning progesterone at term gestation. If concerning uterine activity presents while weaning the progesterone, other short acting medications such as Terbutaline can be added or adjusted to promote uterine quiescence while the progesterone is allowed to dissipate from the system. Weaning the progesterone also allows for a normal transition into lactation and maternal skills.

Oral progesterone (Regumate/Prometrium) has not shown a significant impact in the control of uterine contractions in our client population. While it appears somewhat effective in some clients, the majority have not demonstrated a stable uterine environment. These medications may prohibit actual delivery of the foetuses, but rarely does it promote a healthy placenta and good foetal weights.

In extremely difficult cases of premature labour the use of combinations of progesterone, terbutaline and antibiotics have been employed. Management of these

exceptionally high-risk clients is a day-to-day, monitor session-monitor session plan of care. Unfortunately, because of the multiple dynamics and the multifaceted nature of high-risk pregnancy management, no specific "cook-book" technique exists.

How can the WhelpWise service help you take care of your clients?

How often is your day interrupted by a phone call from one of your breeding clients who is concerned about their bitch? They are concerned but can't really articulate exactly what they are concerned about. "She was panting all night", "she doesn't want to eat", "I think she was in labour and stopped".

Wouldn't it be helpful to have objective information about what is occurring with the whelp? Instead of "she is panting", we can say she is panting, has a very nice labour pattern established and we would expect to see puppies start to deliver in three to four hours, or she is having symptoms, but she is not having contractions. All the heart rates on the puppies are doing well so nothing to worry about!

Would it help you to receive communication from us that lets you know that "we believe that we are beginning to see an issue with the whelping". She could be beginning to demonstrate a contraction pattern that would be consistent with an obstructive dystocia. Having the information that her labour pattern is abnormal and the concern is an obstruction would help prevent uterotonics from being administered incorrectly.

Consider the owner that has a bitch that is an amazing example of excellent standards and health for their breed, except for a prior history of pyometra not associated with pregnancy. The owner would really like to get a litter of puppies but on her first breeding she experienced a litter failure for no known reason. Bitches with a history of a prior uterine or vaginal infection tend to have an issue with preterm contractions or actual preterm delivery. Uterine monitoring can be initiated at pregnancy confirmation and proactive management of preterm labour can be initiated and she can have a successful pregnancy outcome!

Whelping success

Successful management of all aspects of medicine is dependent upon objective information on which to base decisions. Management of diabetic patients requires the measurement of objective blood glucose parameters to determine how to dose insulin, Orthopedic problems require x-rays or MRI to assist the veterinarian with their diagnosis and treatment. Maternal and foetal management is no different.

The best whelping outcomes will be achieved when decisions are based on objective data; detecting whelping issues early and interventions based on objective rather than subjective data.

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Desexing: Making sense of the literature and conversations with clients

Tipler AE

The decision whether to desex a dog and the ethics surrounding the decision are complex. There is a lack of evidence that desexing reduces the population of shelter dogs, and in some countries where desexing is not performed, there are lower rates of shelter surrender. This likely means that vets and owners need to make decisions based on the individual dog and the owner circumstances (e.g. do they have a fenced yard etc), versus a simple calculation of 'desexing is the responsible pet ownership decision'.

In one owner survey, 61% of male dog owners and 47% of female dog owners reported that they would not make the same decision, if given the choice again to desex. This highlights the importance of giving pet owners all the available information to make the decision. This may also provide a huge opportunity to build a more loyal client base with pet owners.

This pros and cons list should be interpreted in light of the disease prevalence, which can vary based on breed and region. For example, although desexing females reduces the risk of ovarian tumours, these tumours are uncommon. Some breeds are more prone to orthopaedic disease or various cancers, and it may be more important to delay desexing or find an alternative, in these breeds.

Therefore, although this information gives an overview, more detailed information may be required. The information should also be combined with the recommendation from a dog's own veterinarian, who will have knowledge of the region and pet owner base.

A **printable handout**, that may help assist to give some of the information to pet owners, can be found at this link. Warn owners that this information may change over time.
https://www.vss.net.au/desexing-your-dog.html

In regards to desexing, there are some generally accepted trends based on the literature. The literature is a constantly changing entity, however there are some useful summary papers that have been published in the last two years and these references can be found within these notes. Three useful references are;

"Assisting Decision-Making on Age of Neutering for 35 Breeds of Dogs: Associated Joint Disorders, Cancers, and Urinary Incontinence"
https://www.frontiersin.org/articles/10.3389/fvets.2020.00388/full

"Assisting Decision-Making on Age of Neutering for Mixed Breed Dogs of Five Weight Categories: Associated Joint Disorders and Cancers"
https://www.frontiersin.org/articles/10.3389/fvets.2020.00472/full

"An Ancient Practice but a New Paradigm: Personal Choice for the Age to Spay or Neuter a Dog"
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8017224/

The generally accepted trends are as follows;

1. Desexing at greater than 12-18 months will result in less influence on developmental diseases e.g. orthopaedic disease
2. Desexing at a later age, can still have effects on degenerative disease. Preserving the hormones for longer, may reduce these diseases – e.g. neoplasia

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Veterinary Specialist Services

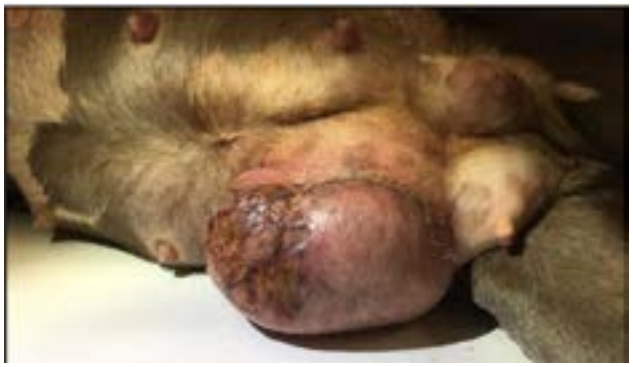
3. Hormones have an effect on growth plate closure, ligament and muscle formation, relaxin and Luteinizing Hormone (LH).
4. There is literature bias. Literature bias is often the result of studies being retrospective in nature. When interpreting the literature, we need to look at why a patient is desexed or kept entire. For example, desexing in many countries is often coupled with better general husbandry and more compliant owners. Therefore any paper that shows a lifespan advantage with desexing is likely to be affected by bias. Some dogs are screened for orthopaedic disease because they are breeding dogs. These dogs will be intact. In some regions where a study is performed, there are greater numbers of various breeds, which can effect results. These are just three sources of bias, but there are many.

One other factor involved in decision making, is you have your pros and cons list - but also consider relative risk. An example, is that there is an increased risk of prostate cancer, however this is a low cause of overall dog mortality.

Below, is an overall summary of the Pros and Cons of desexing, with a few comments.

PROS OF DESEXING IN FEMALES

Mammary Cancer potential reduction



There is likely a reduction in risk of mammary neoplasia. The evidence is conflicting and a meta-analysis found overall the evidence showed only a weak association. Prevalence of mammary cancer varies by breed, so taking a look at the breed related studies is advised.

You can monitor a dog for mammary neoplasia via palpation, so mammary cancer can be diagnosed early by dedicated owners (versus for example hemangiosarcoma).

Age, hormonal control and breed are the main influencing factors when it comes to mammary cancer.

A recent 2021 summary paper by Hart, expressed that the dangers of not desexing, in regards to mammary neoplasia, may be overrated. Mammary cancer in dog is generally treatable. (note - mammary cancer in cats is generally much more malignant).

“An Ancient Practice but a New Paradigm: Personal Choice for the Age to Spay or Neuter a Dog”

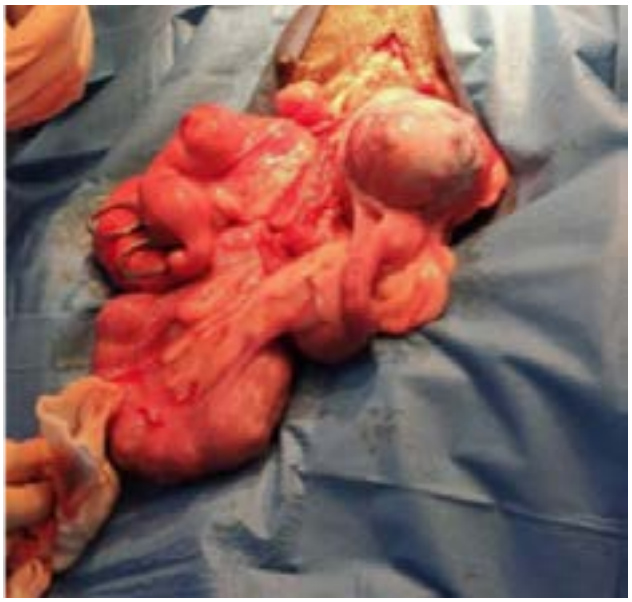
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8017224/

“Epidemiology of canine mammary tumours on the Canary Archipelago in Spain”

https://bmcvetres.biomedcentral.com/articles/10.1186/s12917-022-03363-9 supports the trend towards neutering being protective, and identified at risk breeds. These breeds seem to be consistent across multiple papers.

The breeds most at risk – Samoyed, Schnauzer, Poodle, German Pinscher, Cocker Spaniel, Dobermann, West Highland White Terrier, Dalmatian, Dachshund, Yorkshire Terrier and Boxer.
Lower risk – Chihuahua, English Pointer, Labrador Retriever.

Ovarian tumours, uterine neoplasia, vaginal and vulval tumours.



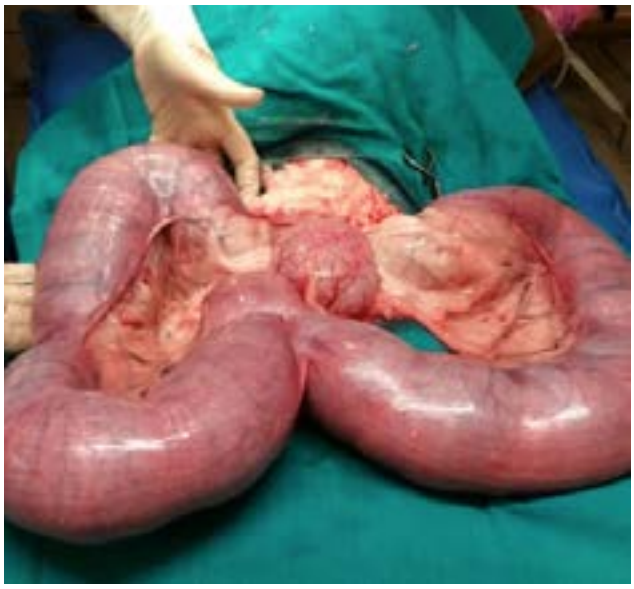
These tumours are rare with a low mortality.

Uterine neoplasia is often benign so ovariohysterectomy is curative.

Ovarian tumours are rare and ovariectomy and ovariohysterectomy are protective. Mortality rate for these is low.

Desexing may be protective against vaginal and vulval tumours, which are commonly leiomyomas. In dogs with confirmed leiomyoma, desexing is often part of the treatment.

Pyometra, metritis and ovarian cysts



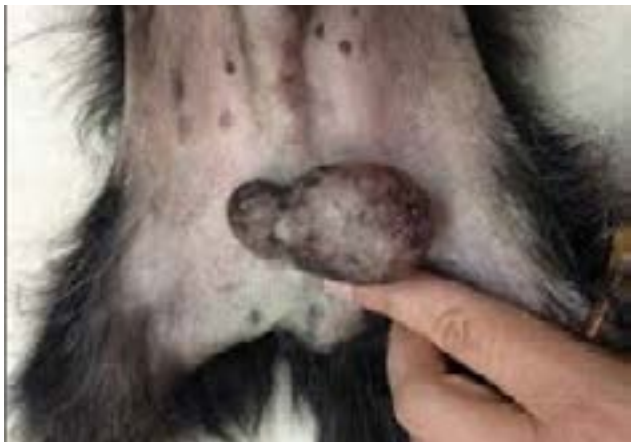
Ovariohysterectomy, ovariectomy and ovary-sparing hysterectomy prevent and treat pyometra and metritis. Ovariohysterectomy and ovariectomy prevent ovarian cysts. They all prevent problems associated with pregnancy and parturition.

Incidence in intact dogs has been reported to be between 2 and 25% by 10 years. The incidence also seems to vary based on breed, so referral to breed related studies as above is recommended. Pyometra can result in septic shock and renal failure and mortality rates between 4 and 17% have been reported.

It is important to note, that in regards to ovary sparing hysterectomy, it is important to remove the entire uterus.

PROS OF DESEXING IN MALES

Testicular tumour reduction



Testicular tumours are common, but they have a low rate of metastasis. Castration is preventative and generally curative. Cryptorchid testicles may be more prone to testicular tumours. This condition is also heritable so it is recommended that cryptorchid dogs are castrated for both these reasons.

Reduction in benign prostatic hyperplasia, chronic prostatitis, perianal adenomas and perianal hernias

Benign prostatic hyperplasia (BPH) affects around 50% of intact dogs by 5 years of age and 95-100% by 9 years. Dogs with BPH are prone to prostatic cysts, prostatitis and prostatic abscesses.

PROS OF DESEXING IN MALES AND FEMALES

Reduction in transmissible venereal tumours

Transmissible venereal tumours are fairly common in regions where there are lots of intact dogs. Maybe if we start advocating against desexing we may see a greater prevalence of these. They are sexually transmitted and metastasis occurs in 5-17%.

Overall lifespan advantage?

One study found that lifespan was increased in dogs that were desexed. They found that although the risk of death by neoplasia increased, the risk of death by trauma and infectious disease increased. There are biases in this type of research, in that in some regions desexing is often associated with better husbandry and compliant owners. It does highlight however, that it is important for dogs that are kept entire, to be kept in a secure yard to avoid escape episodes that can result in vehicular trauma.

Lifespan studies also do not take age at desex into account, so some dogs may have been exposed to hormones for longer than others. Also, the finding of increased lifespan seems more consistent in desexed females and the association is less for desexed males.

Lifespan studies also do not take into account quality of life. Is it better to live for a shorter period of time in less pain? This is an ethical dilemma.

CONS FEMALES

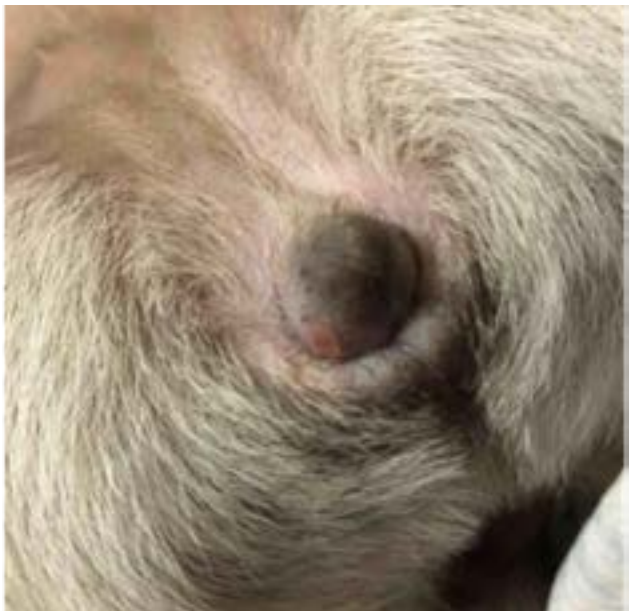
Urinary incontinence

This problem affects around 6-9% of neutered females and larger breeds are more prone to this. There is some evidence to suggest that those dogs spey prior to 3 months of age have the highest risk. Desexed females in general, have a much higher prevalence compared to intact females. Prevalence also varies by breed, so checking breed specific studies is recommended (see examples above). Dogs greater than 10kg, as especially dogs greater than 30kg, are at the greatest risk.

It can be medically managed, however this can be an expense to owners.

Female vulval development

Development of the female vulvar is dependent on sex steroids. There is an increased risk of recessed vulva when females are desexed before development.



CONS OF DESEXING IN THE MALE

Increased risk of prostatic carcinoma

Prostatic carcinoma is potentially more prevalent in desexed dogs. Prostatic carcinoma is an aggressive neoplasia with a high metastatic rate.
There is a low prevalence of this disease. Risk varies by breed.

CONS OF DESEXING IN MALES AND FEMALES

Cancer

The prevalence of various cancers, and whether or not the risk is increased or not with desexing, varies by breed. It may also vary depending on the age the patient is desexed i.e. period of time they were exposed to hormones.

Briefly, these are the cancers that evidence suggests are increased with desexing. All of these cancers have multiple factors affecting their development, prevalence and prognosis and cancer is a complex disease. For further information on these neoplasias an excellent resource is vsso.org, specifically the webpage, https://vsso.org/home/#homecancercatsdogs

I also highly recommend The Pet Oncologist. https://www.thepetoncologist.com/

This below reference looks at 35 common dog breeds and the prevalence of joint disorders, cancers and urinary incontinence. https://www.frontiersin.org/articles/10.3389/fvets.2020.00388/full

It is important to note, that this article does not take into consideration the potential decreased risk of trauma and infectious disease in the desexed population.

In a similar article examining mixed breed dogs, no increased risk of cancer was found in any weight group with desexing. They examined lymphoma, mast cell tumour, hemangiosarcoma and osteosarcoma.

Transitional cell carcinomas

Transitional cell carcinomas account for around 2% of cancer. Desexing increases the risk. It is also an aggressive cancer with a high metastatic rate. Risk also varies by breed.

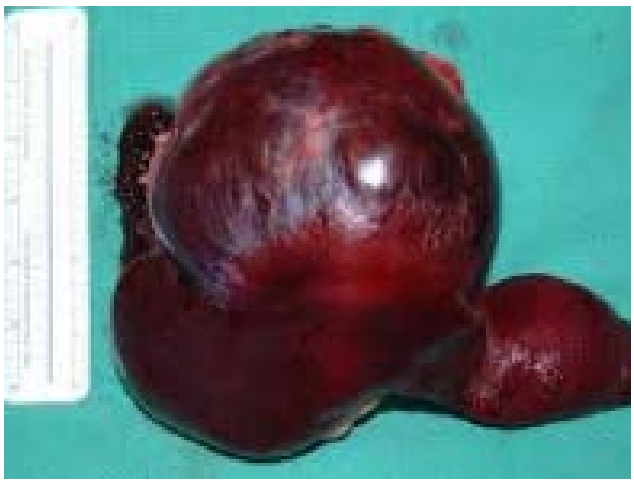
Lymphoma

Lymphoma is a fairly common tumour. There is an increased prevalence in desexed dogs. It has fairly high remission rates with chemotherapy (60-90%). Risk varies by breed.

Mast cell tumours

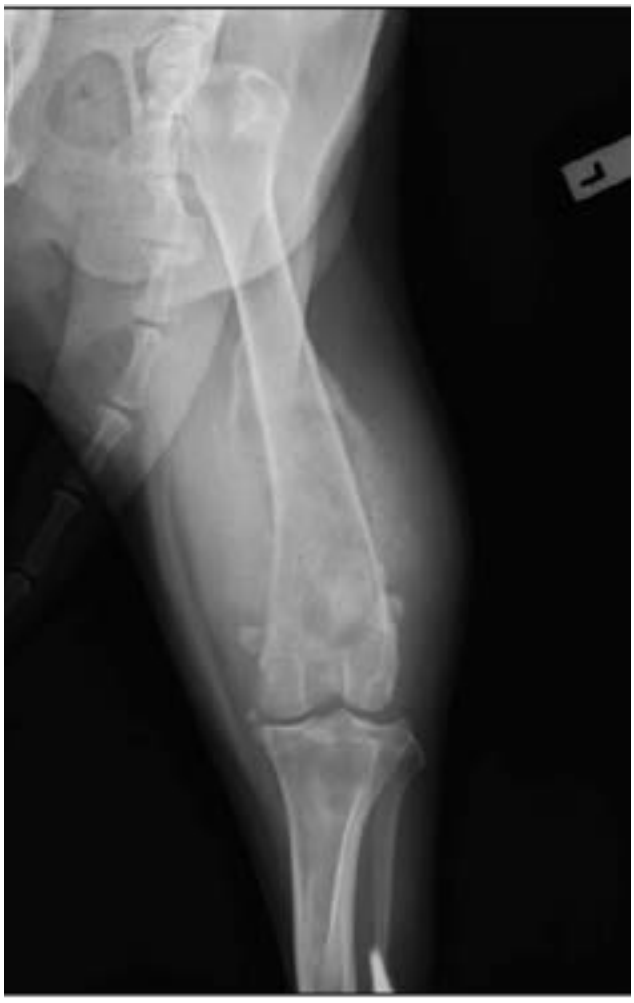
These are common tumours and account for around 20% of cutaneous tumours. The prognosis is variable depending on the grade and stage of mast cell tumour. Risk varies with breed.

Hemangiosarcoma



Hemangiosarcoma accounts for around 5-7% of non-cutaneous neoplasia. It has a poor prognosis and only 10% of dogs survive greater than 12 months even with surgery and chemotherapy. Risk of splenic and cardiac hemangiosarcoma is increased in desexed dogs. Risk varies by breed.

Osteosarcoma



Osteosarcoma is a malignant bone tumour. It is malignant in nature with local aggressiveness and a high rate of metastasis often to the lungs. Around 90% of patients die of metastatic disease within a year if amputation is the only treatment. There is an increased risk in desexed dogs. Risk varies by breed, and larger breeds are more prone. Of important note, is the Rottweiler, 25% of which will develop an osteosarcoma. The earlier the Rottweiler is desexed, the higher the risk of osteosarcoma. This trend is seen in some other breeds, and desexing after a year of age may reduce the risk, some studies have shown.

Orthopaedic disease

There have been a number of breed specific studies and the finding is generally that some breeds, when desexed prior to skeletal maturity, have an increased risk of joint diseases. The finding is not always consistent among males and females.

A few examples of breeds at increased risk of orthopaedic disease are Golden Retrievers, Labrador Retrievers, German Shepherds, Rottweilers, male Beagles and female Australian cattle dogs. This is evidence that for these patients, we should consider desexing at skeletal maturity.

This below reference looks at 35 common dog breeds and the prevalence of joint disorders, cancers and urinary incontinence.
https://www.frontiersin.org/articles/10.3389/fvets.2020.00388/full

A similar article examined mixed breeds of various weight ranges.

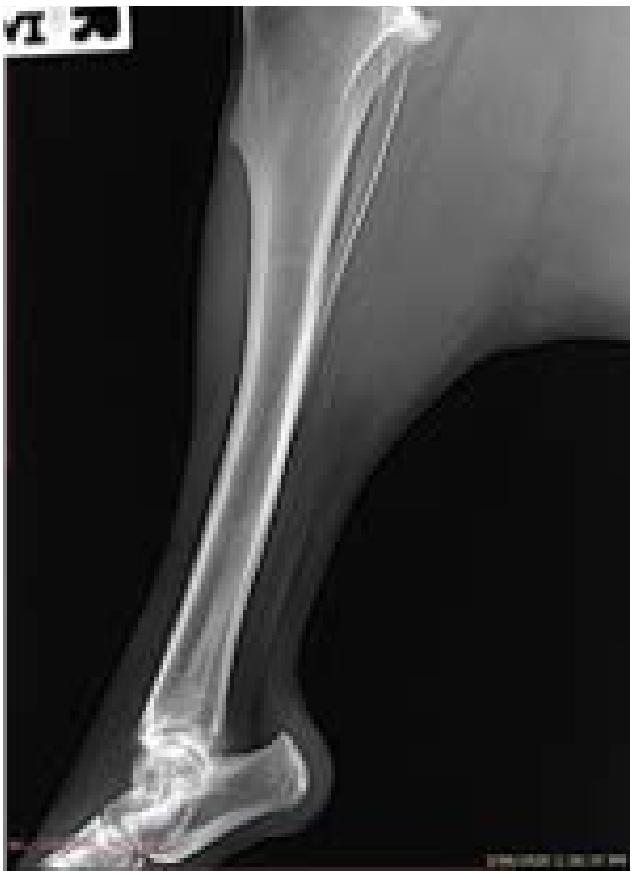
“Assisting Decision-Making on Age of Neutering for Mixed Breed Dogs of Five Weight Categories: Associated Joint Disorders and Cancers”
https://www.frontiersin.org/articles/10.3389/fvets.2020.00472/full

It is important to note, that these articles do not take into consideration the potential decreased risk of trauma and infectious disease in the desexed population.

Orthopaedic disease is also complex, with many different proposed etiological contributors. Further information beyond the scope of this post, should be obtained as there are other factors that can reduce the incidence of orthopaedic disease (namely, weight control and core strengthening activities).

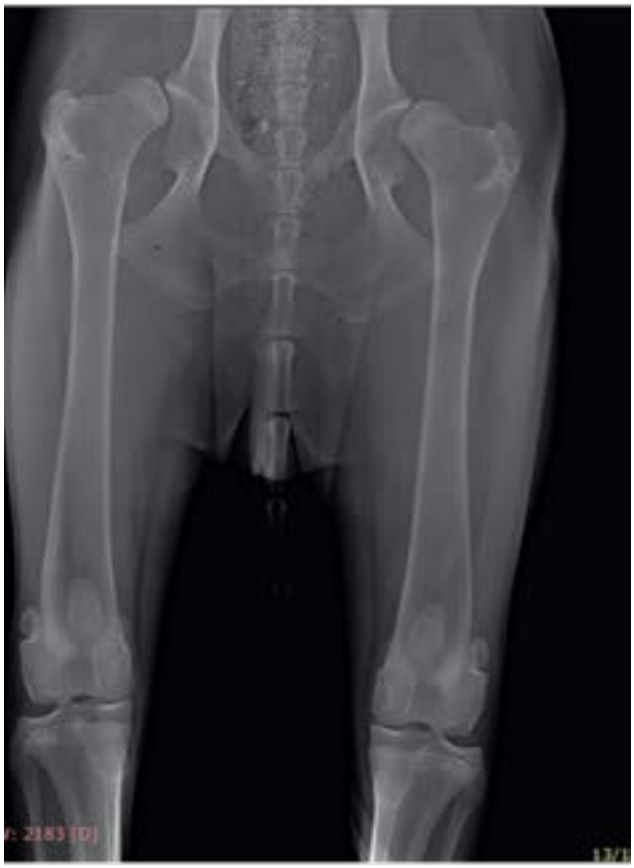
Briefly, specific orthopaedic diseases, that may have an increased prevalence in the desexed population are;

- *Cruciate ligament disease*



2-4% of dogs get cruciate disease
Desexing is a risk factor for some breeds and larger mixed breeds.
One study found dogs desexed prior to skeletal maturity had a 3 fold increase in tibial plateau angle

- *Hip dysplasia*



Some breeds and mixed breeds >20kg desexed prior to skeletal maturity, have an increased risk of hip dysplasia.
Golden Retrievers have an increased risk in males desexed prior to 1 year of age.
Boxers de-sexed at least 6 months prior to diagnosis were 1.5x more likely to develop hip dysplasia.

- *Elbow dysplasia*

The link between elbow dysplasia and desexing is less well defined. Desexed mixed breed dogs over 20kg had a higher risk of elbow dysplasia if desexed <12 months.

OTHER CONS OF DESEXING (NOT RELATED TO CANCER OR ORTHOPAEDIC DISEASE)

Obesity

Desexing results in increased appetite and slowed metabolism. It results in a 30% less energy requirement.

Diabetes

There is an increased risk in the desexed population

Autoimmune disease

There is a possible increase in risk of immune-mediated disease, addisons, hypothyroidism, IBD, cushings and epilepsy – the effect tends to be stronger in females.

Intervertebral disc disease

There is an increased risk in desexed females and an increased risk in males and females desexed prior to 12 months of age. Consider desexing dachshunds >12 months of age.

Other

There is a possibly an increased risk of GDV and cardiomyopathy but the literature is inconclusive and one study doesn't always reproduce another.

Surgery and anaesthetic risk

The anaesthetic mortality rate in cats is around 0.11% cats and in dogs around 0.05%.

Other anaesthetic complications include hypotension, hypoventilation, bradycardia, arrhythmias and hypothermia.

Surgical complications occur in roughly 10% of patients. These include haemorrhage, wound infection, stump pyometra, ovarian remnant syndrome, seroma, iatrogenic ureteral ligation, pain, splenic laceration, iatrogenic urethral trauma.

Older, larger dogs may have an increased risk and this may need to be considered if we are recommending a delay in desexing.

Behaviour - Mixed results - Pros and cons

The effects on behaviour are less straightforward than it was once believed. This is especially true for aggressive and nuisance behaviours, where there are multiple factors involved.

A summary of the pros of desexing are;

- It decreases urine marking, mounting and roaming in some studies of dogs (one study reported around a 40% reduction in these behaviours). One study revealed that the effect of reducing urine marking was lost as the age of desexing increased. This seemed specific to males. A recent paper (link below) found an increase in problem behaviours however in the desexed population.
- It can reduce hormonally based inter-dog aggression (one study reported around a 20% reduction only however)
- The most serious human bite injuries involve intact dogs. This could be related to the desexed population being tied to better husbandry and owner compliance however. There are many factors involved in dog bite behaviour. Overall, a recent human systematic review was in favour of desexing to reduce dog bites. It did however note many limitations to the observational studies included in the review.
- Intact dogs were significantly more likely to be referred for aggression and reactivity in one study (the same bias as above may apply)

A summary of the cons of desexing are;

- Intact German shepherds were found to be more trainable in one study - it is unknown if this applies to other breeds
- In one recent paper, there was an increased number of dogs that were fearful of unfamiliar dogs/humans and had increased sound phobia in the desexed population
- Potential negative effect on aggressive behaviours - see below.
- A recent 2023 paper, found that the longer the dog was exposed to hormones, the less nuisance and problematic behaviours were exhibited. This paper defined problematic behaviour as aggression, anxiety-based behaviours, and extreme fears, and nuisance behaviours as urine marking and mounting behaviour.

Aggression

The effect on aggression is conflicting. Aggressive behaviours in ENTIRE dogs may decrease as dogs age.

There is potentially an increased dominance aggression towards family members. Females and puppies that had already shown signs of aggression had the highest risk. The risk reduced the older they were de-sexed. This finding of increased aggression towards family members is not replicated in all studies and one study found a 30% reduced risk.

Age to desex, in regards to behaviour

In terms of the age to desex. In one study they compared groups desexed prior to around 6 months versus post 6 months of age. Those desexed early were more likely to display noise phobias and sexual behaviours and males were more likely to show aggression towards family members and bark at visitors, but the post 6 month group were more likely to develop separation anxiety, urination due to fear and escape behaviour.

In a further study however, there was no difference before and after the 6 month mark in these behaviours.

A 2022 paper, based on owner questionnaire, found that desexing reduced aggressive behaviours towards other dogs, roaming, mounting, urine marking and decreased dogs overall activity.

In 2023, a paper found a decrease in nuisance and problematic behaviours, in dogs with longer exposure to hormones. https://avmajournals.avma.org/view/journals/javma/261/3/javma.22.08.0382.xml

Summary - there are very conflicting results on the evidence of desexing on behaviour.

Procedure options

Females:

Ovariohysterectomy – traditional approach.

Ovariectomy – spares the uterus. This is the traditional method for laparoscopic spey. Because you remove the hormonal effect on the uterus this procedure will not result in pyometra etc. It is essentially the same procedure as above in most respects.

Ovary-sparing hysterectomy – this procedure renders a dog sterile, however the hormones are maintained. You can leave one or both ovaries and it should be outlined in the records which ovary is left. The dog has a heat cycle and there may be a small amount of bloody discharge and they will be attractive to male dogs. They may have the behavioural side effects of being on heat such as yowling etc. Theoretically they cannot get a pyometra, however if you leave any uterine stump then this can result in a stump pyometra. You need to aim to remove the uterus beyond the cervix.

There is a new paper reporting on the outcomes and complications of this procedure, that was published in 2023. https://avmajournals.avma.org/view/journals/javma/261/3/javma.22.08.0382.xml

Salpingectomy - Tubal ligation – in every way this dog is intact, but just can't become pregnant. There are no major advantages to this procedure, the exact technique has not been reported in the literature, it can be technically challenging and one complication is iatrogenic uterine ligation instead, which leads to fluid building up in the uterus and problems. It is not my preferred technique for hormone-sparing sterilisation for these reasons.

Males:

Traditional castration - removes the hormones

Vasectomy - preserves the hormones.

The outcomes of vasectomy were also looked at in the 2023 paper https://avmajournals.avma.org/view/journals/javma/261/3/javma.22.08.0382.xml

In summary, the new paradigm, is for the vet and pet owner to use the available data-based information to decide on the best age and procedure for the dog dependent on owner situation and dog breed. If there is no data available on a certain breed, extrapolation from similar breeds may be possible.

Description of vasectomy and OSS can be found by following the link to this paper https://www.frontiersin.org/articles/10.3389/fvets.2020.00342/full

AVA statement
https://www.ava.com.au/policy-advocacy/policies/companion-animals-health/desexing-surgical-sterilisation-of-companion-animals

American College of Theriogenology Statement
https://cdn.ymaws.com/www.theriogenology.org/resource/resmgr/Docs/spay-neuter_basis.pdf

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Neptra, a great first-line choice

Neptra™ is a revolutionary canine otitis externa (OE) medication offering convenience and compliance in just one dose. It contains 3 key ingredients within an effective, single-dose formulation for acute canine otitis externa cases involving gram-positive bacteria Staphylococcus pseudintermedius and Streptococcus canis and yeast, Malassezia pachydermatis. These are the most common pathogens seen in acute canine otitis externa, accounting for 70-90% of cases[1]. Neptra's unique ingredients include the anti-fungal terbinafine hydrochloride, a potent but softer glucocorticoid mometasone fuorate and the antibacterial, florfenicol in a long-acting treatment combination. It's been used by vets globally for over 6 years.

Florfenicol is an antibiotic in the amphenicol class and is registered exclusively for veterinary use, as a first-line[2] antibiotic, recommended by the BSAVA[3] for the treatment of gram-positive bacterial otitis externa in dogs. This means that the day-to-day use of Neptra for common canine OE cases constitutes good antibiotic stewardship by selecting a niche antibiotic to treat cocci, according to cytological findings from infected ear-samples.

Neptra's liquid consistency allows rapid and even distribution within the dog's external ear canal providing fast relief from inflammation and pruritis and clinical improvement in 58%[4] of cases by day 7, with 87% of cases demonstrating treatment success by day 28. Also, by providing a single dose and no ear cleaning for 30 days, using Neptra allows the pet owner avoid the stress of administering potentially painful ear drops daily – leaving them free to maintain their bond with their pet.

According to a recent market survey[5] conducted by Elanco in Canada, France and the UK, veterinarians reported a 98% satisfaction rate with Neptra, with 96% of them saying they would recommend it to other vets! The obvious benefit and convenience that the single-dose, vet-administered treatment offers, puts the power of managing acute canine OE cases in the veterinarian's hands.

Neptra also allows you to arrange follow-up checks arranged to suit you and your client's schedules, and its long shelf life and means there's no need for refrigeration.

With its high degree of efficacy and the convenience and compliance it offers, it's easy to see why there's been such a rapid uptake of Neptra locally and in other countries, which has solidified its position as a first-choice treatment of acute canine otitis externa. Have you tried it?

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Link: https://www.bsavalibrary.com/content/book/10.22233/9781910443644
4. Treatment success is defined by a reduction in total clinical score of ≥3 on monitored criteria. Mensinger, S. An easier way to manage otitis externa (OE): Efficacy and safety of a new combination of florfenicol, terbinafine and mometasone furoate (Neptra®) in a randomised positive-controlled trial. BSAVA congress proceedings 2020
5. Industry survey of 225 companion animal vets. Elanco market research, March 2022

Neptra is not recommended in cases with rod-shaped bacteria present on cytology sample, as these may represent Pseudomonas aeruginosa. C & S testing should be performed when appropriate to determine the identity and susceptibility of the causative organism(s). Read and follow label instructions. For further information contact: 1800 995 709 from anywhere in Australia Monday to Friday or email productsupportau@elancoah.com.

THRIVE
An industry-led wellness initiative for the veterinary profession.

Download the THRIVE Mental Health and Suicide Prevention Framework

Is a thriving veterinary community important to you?

THRIVE Mental Health and Suicide Prevention Framework Snapshot

PREVENT

Preventing harm from psychosocial hazards in the industry

We are well prepared to fulfill our roles in the veterinary industry.

We work in a safe and supportive team environment.

Regulatory frameworks support our psychological health and safety.

PROMOTE

Promoting strengths, capabilities and the rewards of work

We are recognised and rewarded for the work we do and the value that it brings.

We work in an industry where belonging and diversity are embraced.

We are supported to grow and to be well.

PROTECT

Protecting us when we experience stress and are unwell

We are able to speak openly about stress and mental ill-health.

We check in and support each other to get the help we need.

Our work-places make reasonable adjustments to allow us to contribute.

This industry specific framework has been informed and led by stakeholders of the veterinary profession and is for all members of the veterinary community.

Download the THRIVE Mental Health and Suicide Prevention Framework and take the first steps to implement an integrated approach to wellness in your workplace.